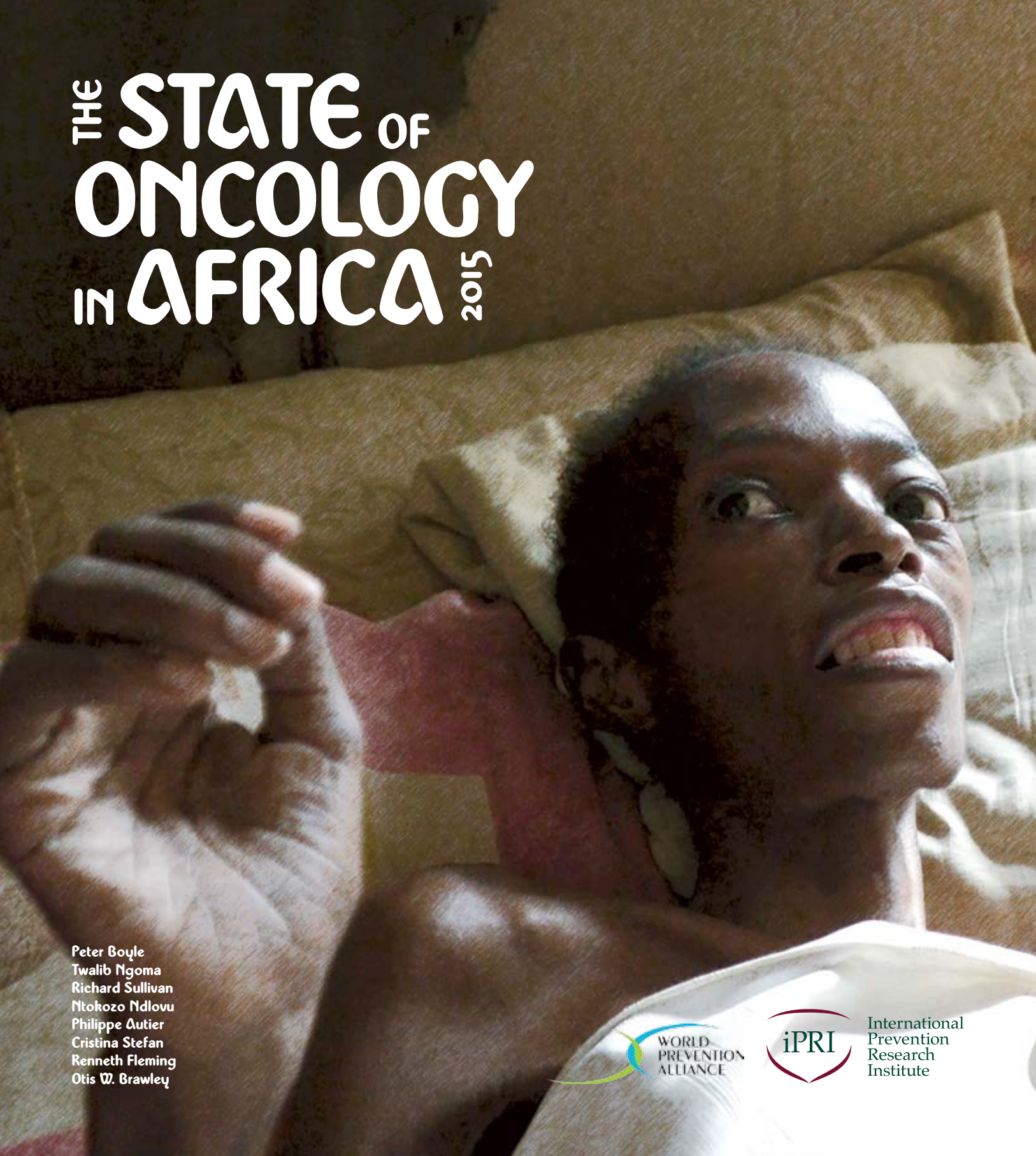
THE STATE OF ONCOLOGY IN AFRICA 2015



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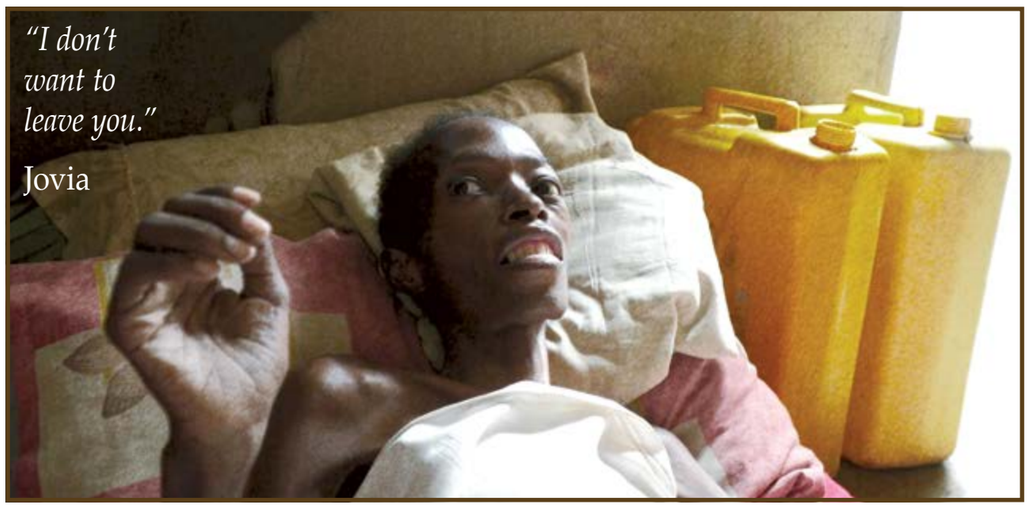
WORLD PREVENTION ALLIANCE
iPRI International Prevention Research Institute

We dedicate this book and its companion film to Jovia and all those African children, women and men who needlessly and prematurely suffer and die from cancer.



The State of Oncology in Africa 2015

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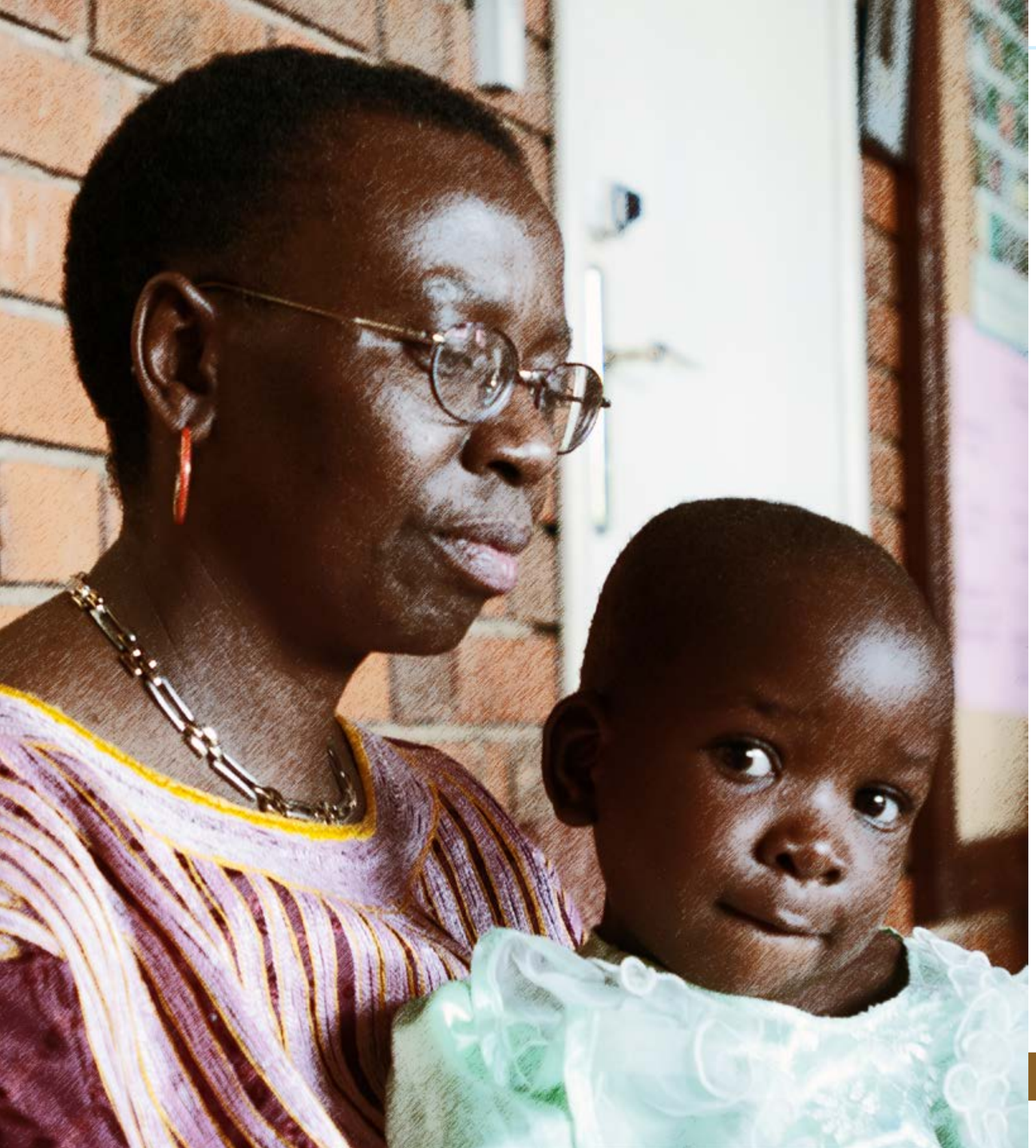
“The situation with
cancer in Africa is critical.
Global Society cannot,
once again, react too slowly
to an African health crisis.”
Prof. Peter Boyle



Contents


"I am angry;
we should all be angry."
Dr. Mamadou Diop

Executive Summary

Written about cancer in Africa by health professionals working in Africa or international colleagues working closely with Africa, identifies 'The State of Oncology in Africa, 2015' as a unique report. Overall, it paints a depressing and deplorable picture of the current situation regarding cancer in Africa. Many patients do not seek traditional medical advice. Those who do, do so when the cancer is at an advanced stage when cure is no longer possible. There is a lack of oncologists from all disciplines, nurses and the necessary health professionals and technicians to support their work. There is a lack of treatment centres. There is a lack of treatments. Most countries do not have any Radiotherapy equipment. Most countries do not have access to opioid drugs for palliative care and pain control. The situation is bound to get worse as the population grows and ages and cancer risk factors imported from high-resource countries begin to have their effect. The evidence is clear. Over the next decades, cancer will cause Africans to suffer and die in greater numbers; much greater numbers.

Throughout the individual chapters there are monotonous statements about patients not being able to afford the cost of the most basic chemotherapy protocols. The introduction of Universal Health Coverage would be a great advantage to cancer patients in Africa.

Yet there is hope. There are oncologists, nurses and other healthcare professionals and technicians doing a magnificent job in frequently desperate circumstances, without adequate resources or infrastructure, who deserve our full admiration. There is hope from the success of high-quality, sustainable projects such as the AMPATH model in Eldoret (Kenya) and in the activities of Hospice Africa Uganda (Kampala, Uganda). Unfortunately, it is not enough. Significantly, both these extraordinary examples rely on international charitable donations rather than local or international government funding.

There is a wide variety of statistics available regarding cancer in Africa, many just estimates of the situation. However, statistics are patients with the tears wiped away. It is bad to have cancer and worse to have cancer if you are poor. The gap between rich and poor, highly educated and less educated and the North-South divide is substantial and continuing to grow. Radical solutions to improve the situation in the poor countries are urgently needed: the status quo is not an appropriate response to the current situation. Recognising that no single Government or source of philanthropy has the means to solve this problem, new models are needed to cope with and improve this situation.

It is impossible to avoid the conclusion that there is a need for a major Private-Public partnership, involving a number of sources from different areas, to make the necessary progress with the briefest delay. The partnership needs the commitment of the wide span of industries involved in the technology for diagnosis and treatment. It needs the commitment of Governments and Non-Governmental Organisations to be effective. Effective will be measured against the Right of every patient with cancer to have the most appropriate treatment and care for their disease.

Working to improve health must cease to be viewed as a competition. Public and Private organisations have an underlying suspicion of each other that must be overcome in the interests of improving cancer care and outcome worldwide. The situation as portrayed in this Report is dramatic and urgent and it behoves all parties to put this frequently deep-rooted suspicion behind them and develop an effective collaboration to improve this key aspect of Public Health throughout the world.

It is essential to move from a passive position to an active one. We can turn our heads and walk away from this situation and betray all those wonderful clinicians, nurses and other personnel grasping with the overwhelming problem of cancer on the Continent. Or, we can do something. As with cancers everywhere, African cancers deserve to be prevented, to be treated, to be cured and to be palliated. If we don't do it now, starting immediately, it will be too late and Africa's cancer crisis will continue to grow out of control.

We make this call to action to African governments, foreign governments and international organizations to address the challenge posed by Cancer in Africa with specific, coordinated actions as laid out on the facing page.

The situation with cancer in Africa is critical. Global Society cannot, once again, react too slowly to an African health crisis.

Peter Boyle, Twalib Ngoma, Richard Sullivan, Ntokozo Ndlovu, Philippe Autier, Cristina Stefan, Kenneth Fleming and Otis W. Brawley

Cancer in Africa: Call to Action

This is a call to African governments, foreign governments and international organizations to address the challenge posed by Cancer in Africa with specific, coordinated actions:

1. There is a need to **train** more oncologists and health professionals in cancer care and provide the **necessary infrastructure** which is urgently needed to identify and treat patients. More general and specialist surgical capacity is critical as are concomitant enhancements in imaging and pathology.
2. The **drugs and equipment** necessary to treat patients with cancer must be made available. As a minimum, each country should ensure the supply of all cancer drugs on the WHO Essential Medicines List. We need to deliver, install and maintain adequate numbers of resource appropriate **Radiotherapy** machines. It should be the right of cancer patients, no matter where they are to have access to the appropriate treatment of their disease.
3. **Opioids** must be available for controlling the pain of patients with terminal cancers (and other diseases). International Agencies should make this a priority activity and come to agreements with Governments of countries where these are not available.
4. Since half of cancer in Africa is currently caused by chronic infection, relevant infection control and **vaccination programmes** must be funded and implemented continent-wide.
5. **Information and education campaigns** to wipe out stigma and misinformation must be conceived and disseminated.
6. Making **Universal Health Coverage** globally available and **strengthening health systems** is critical for improving cancer care. This is also a critical area for the corporate and social responsibility agendas for the private industries including all trans-African corporations.
7. High quality cancer institutions, all over the world, should establish **collaboration ventures** with cancer centres and institutes in every African country, as well as with public health services.
8. **International philanthropy** is vital to help fund these efforts.
9. The United Nations International Covenant on Economic Social and Cultural Rights (ICESCR) should be invoked as the basis for action. This multilateral treaty provides that State Parties to the Covenant recognize **the right of everyone to the enjoyment of the highest attainable standards of physical and mental health**. Article 12.2 contains important determinants of **the right to health** such as prevention and treatment of diseases essential for the enjoyment of the right.

Documentary

Film: *Cancer is... Attacking Africa*

Cemil Alyanak, Peter Boyle, Twalib Ngoma

When this book, *The State of Oncology in Africa 2015*, was envisioned, the editors felt strongly that there was a part of Africa's cancer battle which could not be done justice in print. The human side of efforts made by medical professionals, the agony of those without access to care or palliation needed to be told and shown on film. The idea of a full-length documentary companion film was born.

Cancer is... Attacking Africa, was filmed in 2016 in various African countries, Europe and the United States. The film's goal was to discover the human side of cancer, the pains and the joys, the efforts and the defeats, the ideas and the obstacles.

Cancer is... Attacking Africa features interviews with Africa's leading cancer advocates, with doctors making their rounds in over-filled wards, or with Jovia, a cancer patient in her last days of life. It also features the opinions of academics and policy makers both in Africa and worldwide, who see a way forward, so long as the effort and resources are made available, sustainably.

This 90-minute television documentary was made possible by an unrestricted grant from Pfizer Inc. who had no influence on the film's content or any contact with the film's director prior to or during filming.

The film was directed by Cemil Alyanak. It was co-produced by Cemil Alyanak and Peter Boyle. Twalib Ngoma provided guidance and support, especially while the team was in Africa. The International Prevention Research Institute provided logistics and financial support as did the World Prevention Alliance. The production company was Excess Noise and the film's narrator was Kim Lombard of Toronto, Canada.

The film is free for all to watch. Its goal is to spread knowledge and provide advocacy and fundraising support to all those who aim to combat cancer's attack on Africa. The best place to view it is directly on the iPRI website at www.i-pri.org.

This film is the fifth in the Cancer is... series, the first two of which were introduced by President George H. W. Bush. At the time of writing, there are two further films planned focussing on cancer in India and neighbouring countries and Latin America and the Caribbean.

Chapter 1

Introduction

Peter Boyle,* President, International Prevention Research Institute

* This chapter should be referenced as: Boyle P. Introduction. In: Boyle P, Ngoma T, Sullivan R, Ndlovu N, Autier P, Stefan S, Fleming K and Brawley OW. The State of Oncology in Africa 2015. iPRI Scientific Publication 4, iPRI, Lyon, France (2016).

Another volume to gather dust on a bookcase? Or a report which will generate action? I truly hope that this report contributes to the latter.

I have organised an annual meeting of leaders in Oncology since 2003. Initially, the attendees were directors of National Cancer Institutes and it became known as the National Cancer Institute Directors (NCID) meeting. Each year, more National Cancer Institute Directors came and the audience extended to national leaders in Oncology from countries where there was no National Cancer Institute. As time progressed, the participation from lower-resource countries increased. There are now over 100 participants each year with a majority from lower-resource countries.

The presentations revealed the day-to-day challenges faced in lower-resource countries and the huge difficulties in providing adequate care for so many patients with cancer. I wrote that cancer was increasingly a global issue (Boyle, 2006) and became increasingly aware of the enormous disparities which existed between countries and groups at different levels of deprivation, even within the same country (Boyle et al, 2008).

While preparing 'The State of Oncology 2013' (Boyle et al, 2013) and in the aftermath, I became increasingly aware that too few people were aware of these disparities and the critical situation in poor countries. Among international policy makers the attitude was that nothing could be done about chronic disease disparities since these low-resource countries were being ravaged by infectious disease. Even if it was possible to take action, how could something be done about cancer while diabetes and cardiovascular disease were also health threats? Hand wringing of the diplomatic sort.

In recent times, there have been various publications many of which focused on cancer statistics. Statistics tell us a lot about our world. Statistics tell us that the total number of cancers is increasing every year as the population grows and ages. This increase is compounded in Africa by the impact of the importation of cancer risk factors associated with western lifestyle. However, cancer is not a statistical disease: statistics are patients with the tears wiped away.

'The State of Oncology in Africa 2015' provides a unique assessment from the African perspective. It paints a depressing and shocking picture of the current situation: however, it reflects the reality in Africa. It demonstrates how too many patients do not seek, or cannot access, professional medical services. Those who do, do so when their cancer is at an advanced stage when cure is no longer possible. Africa suffers from a lack of oncologists in all disciplines, oncology nurses and the other necessary health professionals and technicians to conduct their work. There is a lack of treatment centres. There is a lack of treatments. Most countries do not have any radiotherapy equipment at all. Most countries do not have access to opioid drugs for palliative care and pain control. Most countries do not have the cancer drugs on the WHO Essential Medicines List.

The gap in cancer outcomes between high- and lower-resource countries continues to increase. Action is needed urgently to close this gap. Private public partnerships are to my mind the best way forward. Private investment has to lead, and then public action will follow. I am extremely impressed by the work the Gates Foundation has done in Africa and the PEPFAR programme. Concentrating on a single domain over a longer period appears essential to make a real impact.

Too many reports and volumes on global health end up unread and gathering dust on bookshelves. I hope and pray that this report has a different fate: lack of action now will impact on the fate of many thousands of cancer patients in Africa. The report will be made available without cost and can be downloaded from the website of the International Prevention Research Institute (www.i-pri.org).

The fight against cancer begins with knowledge and I encourage everyone to use these materials to build their personal understanding of the health of the world today. Do whatever you can to bring about change. Global Society cannot once again react too slowly to an African health crisis.

Boyle P. The Globalisation of Cancer. Lancet 2006; 368: 629-30.

Boyle P and Levin B (Eds). World Cancer Report 2008. IARC, Lyon (2008)

Boyle P, Sullivan R, Zielinski C and Brawley OW. State of Oncology 2013. International Prevention Research Institute Scientific Publication No 3, iPRI, Lyon (2013)

Chapter 2

Africa: Cancer Statistics

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*This chapter should be referenced as: Brawley OW, Torre LA, Jemal A. Africa: Cancer Statistics. In: Boyle P, Ngoma T, Sullivan R, Ndlovu N, Autier P, Stefan S, Fleming K and Brawley OW. The State of Oncology in Africa 2015. iPRI Scientific Publication 4, iPRI, Lyon, France (2016).

Africa is a vast and diverse continent comprised of 54 countries with an estimated 1.1 billion inhabitants. It is the second most populous continent with 13 percent of the world's population (Fitzmaurice et al, 2015). The populations of Africa have diverse habits, customs, languages and religions. North Africa is predominantly Arab and Berber with Muslim influences. Sub-Saharan Africa has fifteen ethno-linguistic super groups with a number of religions. There are also pockets of people of European ancestry. Africa is commonly divided into five regions (Northern Africa and Eastern, Central, Southern, and Western Africa; the latter four form sub-Saharan Africa).

African Regions

Northern Africa: Algeria, Egypt, Libya, Morocco, Sudan, Tunisia, and Western Sahara
Eastern Africa: Burundi, Comoros, Djibouti, Eritrea, Ethiopia, Kenya, La Reunion (France), Madagascar, Malawi, Mauritius, Mozambique, Rwanda, Somalia, Tanzania, Uganda, Zambia, and Zimbabwe
Central Africa: Angola, Cameroon, Central African Republic, Chad, Democratic Republic of Congo, Republic of Congo, Equatorial Guinea, and Gabon
Southern Africa: Botswana Lesotho, Namibia, Republic of South Africa, and Swaziland
Western Africa: Benin, Burkina Faso, Cape Verde, Cote d'Ivoire, Gambia, Ghana, Guinea-Bissau, Guinea, Liberia, Mali, Mauritania, Niger, Nigeria, Senegal, Sierra Leone, and Togo
Sub-Saharan Africa: refers to the combined Eastern, Central, Southern, and Western regions

Synopsis

The African population is growing faster than that of any other continent. It is set to double by 2050, when it is estimated to comprise 24% of the world's population. By the end of the century, it will nearly quadruple and it is estimated that 40 percent of the world's population will be from Africa (Parkin et al, 2014). The African population is also aging as it grows in size. The median age was 19.7 years in 2012 and is projected to increase to 25.4 years by 2050. Life expectancy for all Africans is currently 52 years, but varies considerably. It is estimated that African life

expectancy will reach 65 years within the next two decades. (Torre et al, 2015). Figure 1 lists current life expectancy in each of the fifty-four countries compared to life expectancy in the Americas and Europe.

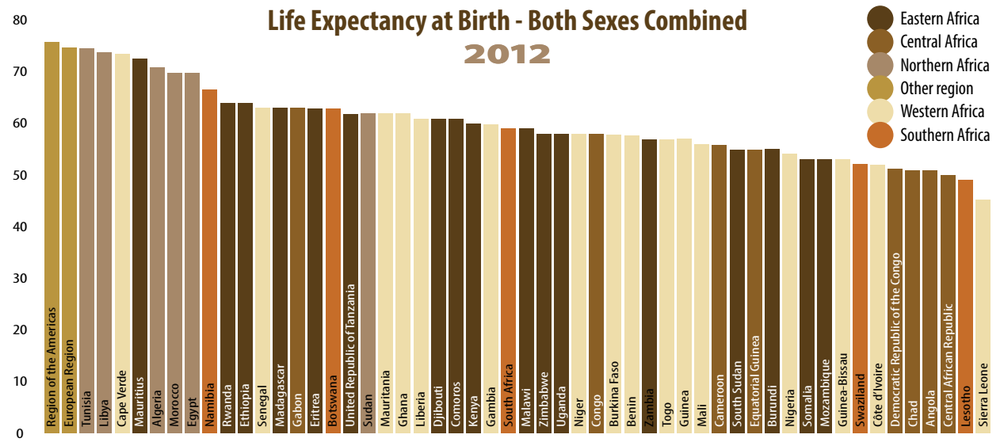

Figure 1: Life expectancy at birth, both sexes combined, 2012

Source: World Health Organization Global Health Observatory Data Repository, Mortality and Global Health Estimates 2012. http://apps.who.int/gho/data/?theme=main. Accessed October 5, 2015

Most areas of Africa are undergoing westernization, including dietary changes, increasing obesity, increased dependence on automobiles, and decreased physical activity (Bray et al, 2012). Smoking rates are fairly low in most African countries, but there is a trend toward an increase in tobacco use, especially among men (Thun et al, 2014). Indeed, many tobacco companies view Africa as a place for growth in sales and much effort has been expended to promote tobacco use (van Walbeek, 2015).

There is much poverty in Africa and much of the population boom is occurring in the poorest and most fragile countries of western Africa such as Niger and Nigeria. GDP per capita varies 70 fold in Africa and is listed in Table 1 (Bray et al, 2012). In keeping with the widespread socioeconomic deprivation, medical resources are limited in much of Africa for all but a small upper class. Often quoted is the shortage of physicians qualified to treat cancer, but there is also a shortage of radiologists and pathologists needed to diagnose cancer as well as a shortage of diagnostic and radiation therapy equipment.(Abdel-Wahab et al, 2013; Gopal et al, 2013; Kingham et al, 2013).

Table 1: 2014 Gross domestic product per capita

Source: International Monetary Fund World Economic Outlook (October 2014)

	GDP per capita (USD)	Rank in Africa	Rank in World
Equatorial Guinea	32,266	1	36
Seychelles	25,607	2	46
Gabon	22,924	3	55
Mauritius	18,553	4	64
Botswana	16,036	5	76
Libya	15,706	6	77
Algeria	14,259	7	83
South Africa	13,046	8	88
Tunisia	11,300	9	97
Egypt	10,877	10	99
Namibia	10,765	11	102
Swaziland	7,797	12	112
Morocco	7,606	13	115
Angola	7,203	14	118
Republic of Congo	6,559	15	121
Cabo Verde	6,324	16	122
Nigeria	6,031	17	124
Mauritania	4,288	18	137
Sudan	4,267	19	138
Ghana	4,129	20	139
Zambia	4,064	21	140
São Tomé and Príncipe	3,153	22	147
Côte d'Ivoire	3,131	23	148
Kenya	3,084	24	149
Djibouti	3,051	25	150
Cameroon	2,981	26	152
Lesotho	2,764	27	153
Tanzania	2,667	28	155
Chad	2,617	29	156
Senegal	2,311	30	160
South Sudan	2,280	31	161
Zimbabwe	2,046	32	162
Sierra Leone	2,027	33	163
Uganda	2,023	34	164
Benin	1,870	35	167
Mali	1,729	36	169

	GDP per capita (USD)	Rank in Africa	Rank in World
Rwanda	1,698	37	171
Burkina Faso	1,682	38	172
The Gambia	1,599	39	173
Ethiopia	1,589	40	174
Comoros	1,548	41	175
Togo	1,450	42	176
Madagascar	1,437	43	177
Guinea-Bissau	1,436	44	178
Guinea	1,313	45	179
Eritrea	1,195	46	180
Mozambique	1,174	47	181
Niger	1,048	48	182
Burundi	911	49	183
Liberia	882	50	184
Malawi	780	51	185
Republic of the Congo	704	52	186
Central African Republic	607	53	187

There are very few cancer registries and fewer countries keep vital statistics, which makes cancer burden assessment and resource allocation difficult (Parkin et al, 2014). There are now approximately thirty cancer registries covering a total of less than 4 percent of the population on the continent (Gakunga et al, 2015). Several have incidence data that is judged of high quality and are included in the International Agency for Research on Cancer publication Cancer in Five Continents, Volume X (Bray et al, 2015). The African registries also have limitations beyond existing in a medically scarce environment. Most are located in urban areas, while the majority of Africans live in rural environments. Several registries are also located in areas of significant social upheaval. Quality vital registration data in Africa is even scarcer than cancer registration. Of the 54 countries of Africa, 33 had no vital registration as of 2010-2012, while 18 had vital registration with very low performance (Mikkelsen et al, 2015).

The International Agency for Research on Cancer of the World Health Organization periodically publishes estimates of the worldwide cancer burden in GLOBOCAN. These include estimates of cancer incidence and mortality for the world regions and 184 countries or territories. The data sources and methods are described elsewhere (Jemal et al, 2012). However, the limited number of African registries means cancer incidence statistics for many areas of Africa are estimates derived from the registry data in neighbouring countries. In addition, most published African mortality data is estimated from estimated incidence data using the proportion of those diagnosed with cancer that die of their disease in areas with mortality data. Of the 54 African countries, estimates were based on data from neighbouring countries or regions for 20 countries for incidence and for 49 countries for mortality (Ferlay et al, 2012; Ferlay et al, 2015).

One should be cautious since much cancer incidence and mortality data are estimates derived from estimates. However, even with the limitations, the data produced provide a reasonable picture of the magnitude of the cancer problem and are useful for planning purposes (Ferlay et al, 2015). A separate estimate of global breast and cervical cancer rates using a different methodology suggested that Globocan under estimated incidence and mortality for these cancers (Forouzanfar et al, 2011).

The Number Diagnosed and Dying of Cancer

It is estimated that 847,000 Africans were diagnosed with cancer and 591,000 died of cancer in 2012. Eastern Africa had the largest number of cancer cases and deaths (Table 2). Overall, prostate cancer was the most commonly diagnosed cancer among African men, followed by liver and Kaposi's Sarcoma (Table 3). The leading cause of cancer death among men was prostate, followed by liver and lung. Among women, the most commonly diagnosed cancer and the leading cause of cancer death was breast, followed by cervix and liver. Kaposi's Sarcoma, prostate, and liver cancers were the most commonly diagnosed cancers among men by region, while breast and cervical cancers were the most commonly diagnosed among women (Table 4).

Table 2: Estimated total number of cancer cases by region

	Diagnosed			Deaths		
	Men	Women	Overall	Men	Women	Overall
Eastern Africa	116,800	170,500	287,300	92,400	116,100	208,500
Central Africa	30,300	43,800	74,100	25,600	31,200	56,900
Northern Africa	105,800	114,800	220,600	77,000	66,500	143,400
Southern Africa	39,900	43,000	82,900	25,100	25,900	51,000
Western Africa	69,200	112,900	182,100	57,800	73,600	131,400

Table 3: Estimated number of cancers by type

Source: Ferlay J, Soerjomataram I, Ervik M, et al. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Available from: http://globocan.iarc.fr, accessed July 7, 2014.

African men			
Cases		Deaths	
Prostate	59,500	Prostate	42,800
Liver	38,700	Liver	37,000
Kaposi's Sarcoma	23,800	Lung	19,400
Lung	21,800	Kaposi's Sarcoma	16,300
Colorectum	21,200	Colorectum	15,100
Non-Hodgkin lymphoma	21,100	Non-Hodgkin lymphoma	15,000
Bladder	17,700	Oesophagus	14,700
Oesophagus	16,100	Stomach	12,000
Leukaemia	13,300	Leukaemia	11,600
Stomach	13,200	Bladder	9,400
All sites but skin	362,000	All sites but skin	277,800

African women			
Cases		Deaths	
Breast	133,900	Breast	63,200
Cervix uteri	99,000	Cervix uteri	60,100
Liver	20,000	Liver	19,000
Colorectum	19,900	Colorectum	14,300
Ovary	17,800	Ovary	13,100
Non-Hodgkin lymphoma	15,700	Non-Hodgkin lymphoma	11,400
Kaposi's Sarcoma	13,700	Oesophagus	10,500
Oesophagus	11,500	Stomach	9,800
Corpus uteri	11,400	Leukaemia	9,500
Leukaemia	10,700	Kaposi's Sarcoma	9,200
All sites but skin	484,900	All sites but skin	313,300

Table 4: Most Common Cancers by Region

Most common cancers diagnosed								
	Men				Women			
	First		Second		First		Second	
Eastern Africa	Kaposi's Sarcoma	17%	Prostate	15%	Cervix Uteri	27%	Breast	20%
Central Africa	Prostate	23%	Liver	12%	Cervix Uteri	26%	Breast	25%
Northern Africa	Liver	12%	Lung	11%	Breast	34%	Colorectum	5%
Southern Africa	Prostate	26%	Lung	12%	Breast	24%	Cervix Uteri	20%
Western Africa	Prostate	25%	Liver	22%	Breast	35%	Cervix Uteri	24%

Most common cause of cancer death								
	Men				Women			
	First		Second		First		Second	
Eastern Africa	Kaposi's Sarcoma	15%	Prostate	15%	Cervix Uteri	24%	Breast	15%
Central Africa	Prostate	23%	Livers	12%	Cervix Uteri	25%	Breast	19%
Northern Africa	Liver	17%	Lung	14%	Breast	23%	Liver	8%
Southern Africa	Lung	17%	Prostate	15%	Cervix Uteri	18%	Breast	16%
Western Africa	Liver	26%	Prostate	25%	Breast	28%	Cervix Uteri	22%

Due to projected increases in the size of the population and the aging of that population alone, the number of cancer cases is projected to increase to 1.43 million total diagnoses and 1 million deaths by 2030 (Armitage et al, 1954; Sylla et al, 2012). This will put even greater burden on a continent that is already stressed by HIV, malaria, and tuberculosis. At the same time, Africa will also experience an increasing burden of other

chronic diseases associated with tobacco smoking and westernization of diet and aging of the population, such as diabetes mellitus, cardiovascular disease, and orthopaedic injury.

Estimates of lifetime risk of certain cancer diagnosis and lifetime risk of death for North Africa and Sub-Saharan Africa are shown in Figure 2. The ratio of diagnosis to death is 0.72 and 0.65 in each region, respectively (Parkin et al, 2014).

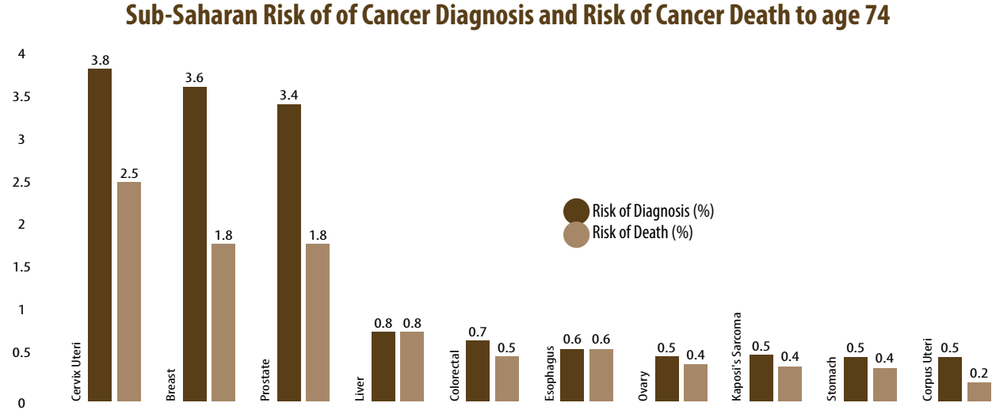

Figure 2a: Sub-Saharan risk of of cancer diagnosis and risk of cancer death to age 74

Diagnosis to Death Ratio = 0.72

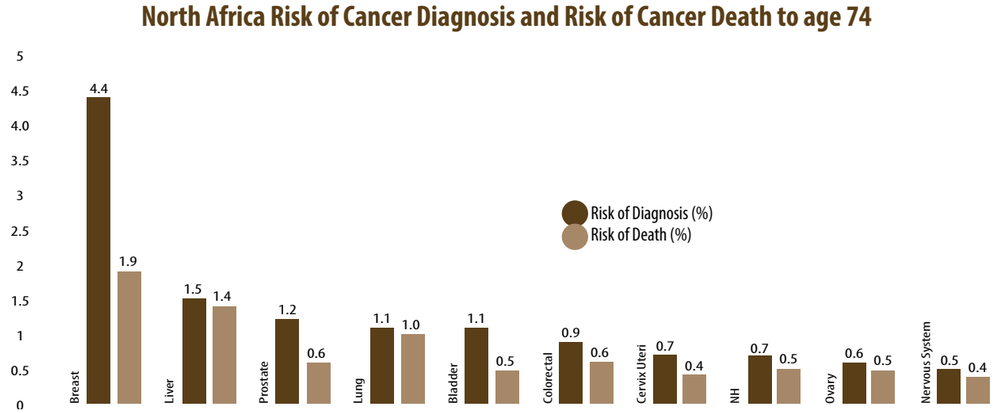

Figure 2b: North Africa Risk of Cancer Diagnosis and Risk of Cancer Death to age 74

Diagnosis to Death Ratio = 0.65

Cancer Rates by Region

Age-adjusted cancer rates are relatively low in Africa compared to other continents (Figure 3). Cancer is the second leading cause of death world-wide accounting for 14.7% of all deaths. It is the second leading cause of death in North Africa, accounting for 12.4% of all deaths. It is currently sixth in sub-Saharan Africa, causing 4.4% of all deaths (Table 5).

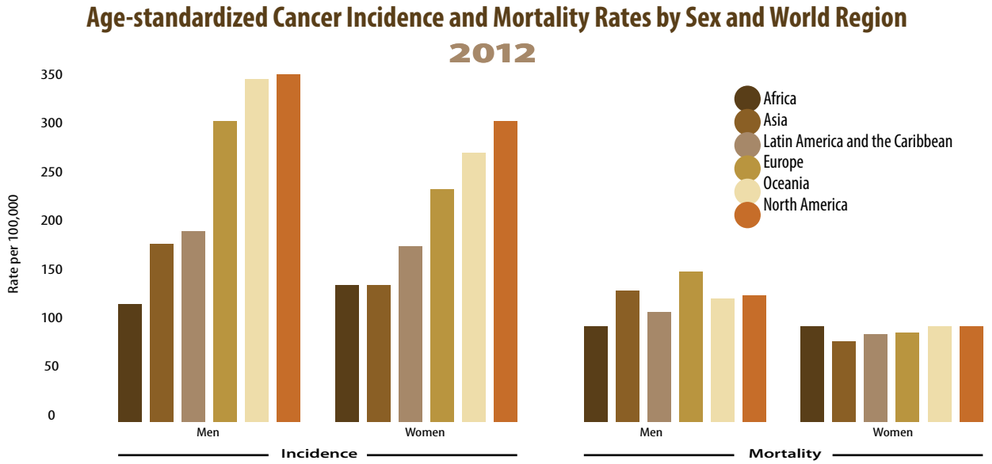

Figure 3: Age-standardized cancer incidence and mortality rates by gender and world region, 2012

Source: Ferlay J, Soerjomataram I, Ervik M, et al. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Available from: http://globocan.iarc.fr, accessed July 7, 2014.

Table 5: Leading causes of death worldwide and in Africa, sub-Saharan Africa, and Northern Africa, 2012 (thousands)

Source: World Health Organization Global Health Observatory Data Repository, Mortality and Global Health Estimates 2012. http://apps.who.int/gho/data/?theme=main. Accessed October 5, 2015

	Africa			Sub-Saharan Africa*			Northern Africa*			World		
	Rank	Deaths	%	Rank	Deaths	%	Rank	Deaths	%	Rank	Deaths	%
Infectious and parasitic diseases**	1	2,257	21.2	1	2,215	23.0	6	43	4.1	3	4,897	8.8
Cardiovascular diseases	2	1,400	13.1	4	959	10.0	1	441	42.7	1	17,513	31.4
Respiratory infections	3	1,143	10.7	3	1,106	11.5	8	37	3.6	6	3,060	5.5
HIV/AIDS	4	1,113	10.4	2	1,110	11.5	14	3	0.3	8	1,534	2.7
Unintentional injuries	5	780	7.3	5	726	7.5	4	53	5.2	5	3,716	6.7
Malignant neoplasms	6	591	5.2	6	426	4.4	2	128	12.4	2	8,204	14.7
Digestive diseases	7	424	4.0	8	351	3.6	3	73	7.1	7	2,263	4.1
Nutritional deficiencies	8	368	3.4	7	360	3.7	12	7	0.7	12	559	1.0

	Africa			Sub-Saharan Africa*			Northern Africa*			World		
	Rank	Deaths	%	Rank	Deaths	%	Rank	Deaths	%	Rank	Deaths	%
Respiratory diseases	9	229	2.1	10	187	1.9	7	42	4.0	4	4,040	7.2
Diabetes mellitus	10	227	2.1	12	176	1.8	5	51	5.0	9	1,497	2.7
Intentional injuries	11	224	2.1	9	214	2.2	11	10	1.0	10	1,428	2.6
Maternal conditions	12	185	1.7	11	182	1.9	15	3	0.3	14	296	0.5
Congenital anomalies	13	176	1.7	13	155	1.6	10	21	2.0	13	556	1.0
Genitourinary diseases	14	166	1.6	14	132	1.4	9	34	3.3	11	1,195	2.1
Skin diseases	15	36	0.3	15	34	0.4	17	1	0.1	17	111	0.2
Musculoskeletal diseases	16	34	0.3	16	33	0.3	16	2	0.2	15	216	0.4
Other neoplasms	17	23	0.2	17	17	0.2	13	6	0.6	16	193	0.3
Oral conditions	18	0	0.0	18	0	0.0	18	0	0.0	18	2	0.0
Sense organ diseases	19	0	0.0	19	0	0.0	19	0	0.0	19	1	0.0
All Causes		10,661			9,627			1,034			55,843	

* Countries are grouped according to the regional groupings used by the United Nations for reporting progress toward the Millennium Development Goals (http://mdgs.un.org/unsd/mdg/Host.aspx?Content=Data/REgionalGroupings.htm)

**Excluding HIV/AIDS

Cancer rates vary substantially by region. Among men, the highest incidence rates are for prostate cancer in Southern, Central, and Western Africa; Kaposi's Sarcoma in Eastern Africa; and liver cancer in Northern Africa (Table 6). Among women, the highest incidence rates are for breast cancer in Southern, Northern, and Western Africa; and cervical cancer in Eastern and Central Africa. The highest mortality rates for men were for prostate cancer in Central Africa, liver cancer in Northern and Western Africa, Kaposi's Sarcoma in Eastern Africa, and lung cancer in Southern Africa. (Table 7). Among women, the highest mortality rates were for cervical cancer in Southern, Eastern, and Central Africa and breast cancer in Northern and Western Africa.

Table 6: Age-adjusted incidence rates* for the most common cancers in Africa, by gender, 2012

Source: Ferlay J, Soerjomataram I, Ervik M, et al. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Available from: http://globocan.iarc.fr, accessed July 7, 2014

Men														
	Africa		Sub-Saharan Africa		Southern Africa		Eastern Africa		Central Africa		Northern Africa		Western Africa	
	Rank	Rate	Rank	Rate	Rank	Rate	Rank	Rate	Rank	Rate	Rank	Rate	Rank	Rate
All sites but skin		115.6		108.9		210.3		120.7		91.8		133.5		78.7
Prostate	1	23.2	1	27.9	1	61.7	2	23.3	1	27	4	10.6	1	25.1
Liver	2	12.4	2	10.1	6	6.7	7	4.9	2	10.5	1	18	2	16.4
Kaposi's Sarcoma	3	5.5	3	7.2	5	7.6	1	15.1	12	1.2	23	0.3	11	0.9

Men														
	Africa		Sub-Saharan Africa		Southern Africa		Eastern Africa		Central Africa		Northern Africa		Western Africa	
	Rank	Rate	Rank	Rate	Rank	Rate	Rank	Rate	Rank	Rate	Rank	Rate	Rank	Rate
Lung	4	7.7	7	4.8	2	26.1	10	3.8	11	2	2	15.6	10	1.7
Colorectum	5	7	5	6.4	3	14.2	5	7.1	4	4.7	5	8.5	4	4.5
Non-Hodgkin lymphoma	6	5.5	4	4.7	8	5.2	4	5.6	3	4.4	6	7.6	3	3.7
Bladder	7	6.3	11	3	9	7.5	11	3.3	9	2.2	3	15.1	6	2.1
Oesophagus	8	5.6	6	6.8	4	13.7	3	11.9	6	4.2	15	2.4	16	0.8
Leukaemia	9	3.3	9	2.7	15	3.6	6	3.8	8	2.6	7	5.6	9	1.4
Stomach	10	4.5	8	4.5	7	7.2	8	5.2	5	4.1	9	4.3	5	3.3

Women														
	Africa		Sub-Saharan Africa		Southern Africa		Eastern Africa		Central Africa		Northern Africa		Western Africa	
	Rank	Rate	Rank	Rate	Rank	Rate	Rank	Rate	Rank	Rate	Rank	Rate	Rank	Rate
All sites but skin		132.4		133.9		161.1		154.7		110.7		127.7		112.4
Breast	1	36.2	1	33.8	1	38.9	2	30.4	2	26.8	1	43.2	1	38.6
Cervix uteri	2	27.6	2	34.8	2	31.5	1	42.7	1	30.6	4	6.6	2	29.3
Liver	3	5.8	3	5.4	12	3.3	10	3.3	3	5.7	3	7	3	8.1
Colorectum	4	5.8	4	5.4	4	8.7	5	6.1	5	4.8	2	6.9	5	3.8
Ovary	5	4.8	6	4.5	8	5.2	6	5.5	6	4.1	5	5.6	4	3.6
Non-Hodgkin lymphoma	6	3.8	7	3.2	9	4.1	7	3.5	4	3.2	6	5.4	6	2.4
Kaposi's Sarcoma	7	2.9	5	3.7	7	4.7	3	7.6	22	0.4	25	0.1	16	0.6
Oesophagus	8	3.5	8	4.2	5	6.7	4	7.8	10	2	19	1.5	21	0.4
Corpus uteri	9	3.5	9	3.7	6	6.5	11	3.4	8	3.4	12	3.1	7	3.3
Leukaemia	10	2.6	11	2.3	14	2.6	8	3.4	9	1.8	9	3.9	10	1.2

*Rates are per 100,000 and age-standardized to the world standard population

Table 7: Age-adjusted mortality rates* for the most common cancers in Africa, by gender, 2012

Source: Ferlay J, Soerjomataram I, Ervik M, et al. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Available from: http://globocan.iarc.fr, accessed July 7, 2014

Men														
	Africa		Sub-Saharan Africa		Southern Africa		Eastern Africa		Central Africa		Northern Africa		Western Africa	
	Rank	Rate	Rank	Rate	Rank	Rate	Rank	Rate	Rank	Rate	Rank	Rate	Rank	Rate
All cancers excl. non-melanoma skin cancer		92.9		90.4		136.5		103.8		82.3		99.9		68.5
Prostate	1	17	1	20.9	2	24.4	2	18.7	1	24.2	4	7	2	21.2
Liver	2	11.8	2	9.6	5	6.7	7	4.6	2	9.9	1	17.4	1	15.6
Kaposi's Sarcoma	3	7	3	6.5	6	4.3	1	14.2	14	1	22	0.2	12	0.9
Lung	4	4.9	8	4.4	1	23.8	9	3.5	9	1.8	2	14	8	1.5
Colorectum	5	5.1	5	4.9	4	10	5	5.5	5	3.8	5	5.6	3	3.5
Non-Hodgkin lymphoma	6	4.3	6	3.8	9	4	4	4.6	3	3.8	6	5.4	4	3
Bladder	7	5.3	12	1.9	12	3	11	2.2	11	1.6	3	7.6	9	1.5
Oesophagus	8	4.1	4	6.4	3	12.8	3	11.2	6	4	11	2.3	15	0.8
Leukaemia	9	3.1	9	2.6	10	3.4	6	3.7	7	2.5	7	4.9	7	1.3
Stomach	10	3.5	7	4.2	7	5.2	8	5	4	4	9	3.9	5	3.2

Women														
	Africa		Sub-Saharan Africa		Southern Africa		Eastern Africa		Central Africa		Northern Africa		Western Africa	
	Rank	Rate	Rank	Rate	Rank	Rate	Rank	Rate	Rank	Rate	Rank	Rate	Rank	Rate
All cancers excl. non-melanoma skin cancer		88.7		93		98.7		110.5		82.3		75.7		75.7
Breast	1	17.3	2	17.2	2	15.5	2	15.6	2	14.8	1	17.4	1	20.1
Cervix uteri	2	17.5	1	22.5	1	17.9	1	27.6	1	22.2	8	3.2	2	18.5
Liver	3	5.6	3	5.1	9	3.2	10	3.1	3	5.4	2	6.7	3	7.7
Colorectum	4	4.2	4	4.1	5	5.8	5	4.6	4	3.9	3	4.5	5	3
Ovary	5	3.8	5	3.7	6	3.8	6	4.4	7	3.3	4	4.1	4	3
Non-Hodgkin lymphoma	6	2.9	8	2.6	10	2.9	8	2.9	5	2.7	5	3.7	6	2
Kaposi's Sarcoma	7	3.3	7	2.9	8	2.8	3	6.2	22	0.4	25	0.1	15	0.5
Oesophagus	8	3	6	3.9	4	6.2	4	7.3	9	1.8	15	1.4	21	0.4
Corpus uteri	9	2.4	14	1.4	13	1.8	17	1.3	10	1.5	17	0.9	9	1.4
Leukaemia	10	2.2	10	2.2	12	2.3	7	3.3	8	1.7	6	3.4	8	1.1

*Rates are per 100,000 and age-standardized to the world standard population

A Note About Age Adjustment

Age is a key determinant of risk of developing every type of cancer (Armitage et al, 1954). Age distribution varies widely from country to country. Crude incidence or mortality rates do not take into account the varying age structures in the underlying populations. Comparisons of incidence rates must be made independent of the effects of age in order to be meaningful. Age adjustment, referring to a common standard population, allows for comparisons of incidence across populations and within the same population over time

The age adjusted rates presented in this chapter use the World Standard Population first introduced by Segi in 1960 and drawn from a pooled population of 46 countries and modified by Doll in 1966. This is commonly referred to as the Segi–Doll world standard (Bray et al, 2002).

Age specific analysis may provide insight into the biology and aetiology of cancer in the specific population or populations under study.

Cancer Rates by Country

Among women, the most common cancers by country include breast (26 countries) and cervix (28) (Figure 4, Table 8). Among men, however, there is considerable variation, with the most common cancer by country including prostate (23 countries), liver (13), Kaposi's Sarcoma (6), lung (5), colorectal (2), non-Hodgkin lymphoma (2), oesophagus (1), leukaemia (1), and stomach (1). Table 8 also details estimates of the years of life lost due to cancer, risk of a cancer diagnosis by age 75, and the prevalence of adult cancer survivors per 100,000.

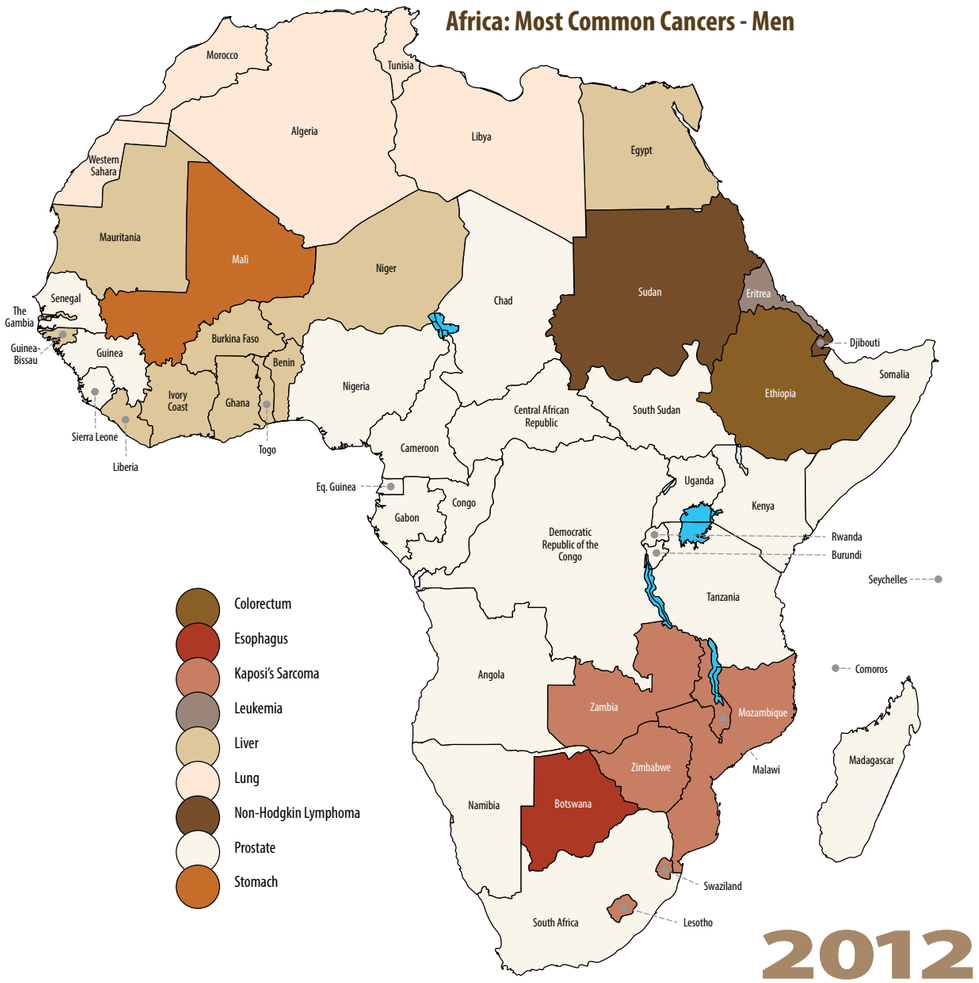

Figure 4a: Most common cancer sites in Africa, Men, 2012

Source: Ferlay J, Soerjomataram I, Ervik M, et al. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Available from: http://globocan.iarc.fr, accessed July 7, 2014

Figure 4b: Most common cancer sites in Africa, Women, 2012

Source: Ferlay J, Soerjomataram I, Ervik M, et al. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Available from: http://globocan.iarc.fr, accessed July 7, 2014

Table 8: Cancer statistics in African Countries

Country	Most commonly diagnosed cancer, men (estimated 2012)	Most commonly diagnosed cancer, women	Years of life lost to cancer	Risk of cancer by age 75	Prevalence of cancer survivors
	Estimated 2012	Estimated 2012	Estimated age-standardized total years lost per 100,000 people, 2008	Cumulative risk (%), 2012	Survivors diagnosed with cancer within the past five years per 100,000 adults (15 years and older), 2012
Algeria	Lung	Breast	2,103	12.8	322.7
Angola	Prostate	Cervix uteri	1,980	10.8	206
Benin	Liver	Breast	2,131	9.6	207.1
Botswana	Oesophagus	Cervix uteri	1,786	10.6	232.5
Burkina Faso	Liver	Cervix uteri	2,247	9.1	164.4
Burundi	Prostate	Cervix uteri	2,612	14.3	267.7
Cameroon	Prostate	Breast	2,097	9.6	248.6
Cape Verde	Liver	Cervix uteri	2,130	7.5	199.1
Central African Republic	Prostate	Breast	2,008	9.9	216
Chad	Prostate	Breast	2,010	9.1	203.3
Comoros	Prostate	Cervix uteri	2,203	10.7	219.8
Congo	Prostate	Breast	2,067	10.2	194.8
Congo (Democratic Republic of)	Prostate	Cervix uteri	2,258	12	205.7
Côte d'Ivoire	Liver	Breast	1,522	9	194
Djibouti	Non-Hodgkin lymphoma	Breast	2,171	9.8	208.5
Egypt	Liver	Breast	2,042	15.4	372.2
Equatorial Guinea	Prostate	Breast	2,145	8.9	224.4
Eritrea	Leukaemia	Breast	2,049	10.5	201.7
Ethiopia	Colorectum	Breast	2,242	11.1	250.9
Gabon	Prostate	Cervix uteri	2,018	9.7	207.3
Gambia	Liver	Cervix uteri	2,338	4.6	82.8
Ghana	Liver	Cervix uteri	2,244	9.3	211.7
Guinea	Prostate	Cervix uteri	2,303	9.7	178
Guinea-Bissau	Liver	Cervix uteri	2,251	8.2	183.6
Kenya	Prostate	Cervix uteri	2,860	19	335.1
Lesotho	Kaposi's Sarcoma	Cervix uteri	2,424	10	197.2
Liberia	Liver	Cervix uteri	1,939	9.4	172.2
Libya	Lung	Breast	2,035	13.2	282.4
Madagascar	Prostate	Cervix uteri	2,528	14.6	288.5
Malawi	Kaposi's Sarcoma	Cervix uteri	4,028	14.6	341.7
Mali	Stomach	Cervix uteri	2,624	11.6	231.2
Mauritania	Liver	Cervix uteri	2,209	8.5	178.2
Mauritius	Colorectum	Breast	1,558	18	530.2
Morocco	Lung	Breast	1,926	12.6	336.1
Mozambique	Kaposi's Sarcoma	Cervix uteri	2,722	13.5	308.3
Namibia	Prostate	Breast	1,341	8.8	197.4
Niger	Liver	Breast	1,924	6.7	151.2
Nigeria	Prostate	Breast	2,283	10.4	243.6
Reunion	Prostate	Breast	2,243	20.1	589
Rwanda	Prostate	Cervix uteri	2,743	14.4	255.1
Senegal	Prostate	Cervix uteri	2,173	10.6	194.1
Sierra Leone	Liver	Cervix uteri	1,999	9.5	166.8
Somalia	Prostate	Breast	2,393	14.7	299.1
South Africa	Prostate	Breast	3,127	19	464.3
South Sudan	Prostate	Breast	na	14	297.2
Sudan	Non-Hodgkin lymphoma	Breast	1,592	9.5	198.8
Swaziland	Kaposi's Sarcoma	Cervix uteri	2,218	10.9	238.3
Tanzania	Prostate	Cervix uteri	1,784	12.8	269.4
Togo	Liver	Breast	1,944	9.3	195.8
Tunisia	Lung	Breast	2,040	11.8	310.1
Uganda	Prostate	Cervix uteri	3,703	17.6	307.6
Western Sahara	Lung	Breast	2,415	10.3	244.3
Zambia	Kaposi's Sarcoma	Cervix uteri	3,073	13.5	286.8
Zimbabwe	Kaposi's Sarcoma	Cervix uteri	3,392	18.9	373.7
Source information:	Ferlay J, Soerjomataram I, Ervik M, et al. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Available from: http://globocan.iarc.fr, accessed July 7, 2014.	Ferlay J, Soerjomataram I, Ervik M, et al. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Available from: http://globocan.iarc.fr, accessed July 7, 2014.	Soerjomataram I, Lortet-Tieulent J, Parkin DM, et al. Global burden of cancer in 2008: a systematic analysis of disability-adjusted life-years in 12 world regions. Lancet. 2012;380(9856):1840-50.	Ferlay J, Soerjomataram I, Ervik M, et al. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Available from: http://globocan.iarc.fr, accessed July 7, 2014.	Ferlay J, Soerjomataram I, Ervik M, et al. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Available from: http://globocan.iarc.fr, accessed July 7, 2014.

All-sites cancer incidence rates (per 100,000 population) among men range from 56.7 in Niger to 242.5 in La Reunion (Table 9). All-sites cancer mortality rates among men range from 50.0 in Cape Verde to 152.7 in Uganda. Among women, incidence rates range from 69.6 in the Gambia to 209.1 in Zimbabwe, while mortality rates range from 45.5 in Namibia to 146.5 in Zimbabwe.

Table 9: Cancer incidence and mortality by country of Africa

Country	All cancers incidence (excluding non-melanoma skin cancers), men	All cancers mortality (excluding non-melanoma skin cancers), men	All cancers incidence (excluding non-melanoma skin cancers), women	All cancers mortality (excluding non-melanoma skin cancers), women
	Estimated age-standardized rate per 100,000 men, 2012		Estimated age-standardized rate per 100,000 women, 2012	
Algeria	116.2	79.8	132.7	70.9
Angola	89.9	77	112.2	76
Benin	87.2	78.1	102.7	71.5
Botswana	113.9	85.6	104.7	60.4
Burkina Faso	75.9	72.1	99.8	80.3
Burundi	132.2	125.3	143	115.2
Cameroon	81.2	66.9	114.1	73
Cape Verde	60.9	50	88.4	51.5
Central African Republic	86.9	76.8	99.7	73.5
Chad	77.4	71.9	99.2	74.8
Comoros	81.9	75.1	121.8	89.4
Congo	83.7	65	94.1	56.6
Congo (Democratic Republic of)	102.5	96.1	115.2	93.4
Côte d'Ivoire	78.2	69.6	101	72.1
Djibouti	73.7	66.7	111.3	79.6
Egypt	158.4	120.5	147.8	88.7
Equatorial Guinea	76.1	67.6	98.5	65
Eritrea	82.8	76.3	118.6	90.7
Ethiopia	73.2	64.9	140.9	103.1
Gabon	79.9	54.9	101.5	55.4
Gambia	67.3	62.6	69.6	54.2
Ghana	79.2	63.8	104.8	64
Guinea	88.9	79.9	94	71
Guinea-Bissau	70	64.4	96	71.4
Kenya	167.2	139.1	196.6	133.3
Lesotho	114	95	96.7	67.1
Liberia	82.9	78.1	97	76
Libya	135.9	88.9	113.1	62.2
Madagascar	142.4	117.2	134.3	92
Malawi	123.5	110.7	186.4	137.8
Mali	83.8	77.3	135.6	101.4
Mauritania	74.4	68.3	97.7	68.2
Mauritius	171.1	127.2	193.9	84.3
Morocco	122.7	92.3	114.4	66.8
Mozambique	118.3	108.6	153	121.4

Country	All cancers incidence (excluding non-melanoma skin cancers), men	All cancers mortality (excluding non-melanoma skin cancers), men	All cancers incidence (excluding non-melanoma skin cancers), women	All cancers mortality (excluding non-melanoma skin cancers), women
Namibia	86.3	61.2	81.5	45.5
Niger	56.7	53.7	71	55.2
Nigeria	79	67.4	121.7	78
Reunion	242.5	116.8	142.1	52.7
Rwanda	130.2	114	142.3	104.6
Senegal	85.5	76	115	80.8
Sierra Leone	83.8	82.2	97.7	78.4
Somalia	111.9	96	165.2	116.7
South Africa	224.3	144.1	168.9	103.3
South Sudan	123.1	108.4	143	106
Sudan	92	80.1	91	67
Swaziland	122.1	101.9	111.9	73
Tanzania	115.8	96.9	132.7	89.3
Togo	77.2	68.3	104.8	74.8
Tunisia	127	84.1	95.7	49.3
Uganda	175.7	152.7	167.4	120.3
Western Sahara	89	71.7	107.8	60.7
Zambia	115.1	100.5	157.8	110.8
Zimbabwe	167	138.2	209.1	146.5
Source information:	Ferlay J, Soerjomataram I, Ervik M, et al. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Available from: http://globocan.iarc.fr, accessed July 7, 2014.	Ferlay J, Soerjomataram I, Ervik M, et al. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Available from: http://globocan.iarc.fr, accessed July 7, 2014.	Ferlay J, Soerjomataram I, Ervik M, et al. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Available from: http://globocan.iarc.fr, accessed July 7, 2014.	Ferlay J, Soerjomataram I, Ervik M, et al. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Available from: http://globocan.iarc.fr, accessed July 7, 2014.

Breast cancer is the most commonly diagnosed cancer and the leading cause of cancer death among women in Africa as a whole. It is the leading cancer diagnosed in North Africa and the leading cancer diagnosed in many Sub-Saharan countries. Breast cancer incidence rates (per 100,000 women) in Africa range from 9.0 in Lesotho to 64.2 in Mauritius, while mortality rates range from 4.4 in Lesotho to 25.9 in Nigeria (Table 10). Rates of breast cancer appear to be increasing due to increases in the prevalence of risk factors such as early menarche, late child bearing, having fewer children, and obesity, in addition to the effects of increased awareness and detection (Parkin et al, 2014).

Table 10: Breast cancer incidence and mortality and cervical cancer incidence

Country	Breast cancer incidence, women	Breast cancer mortality, women	Cervical cancer incidence
	Estimated age-standardized rate per 100,000 women, 2012		
Algeria	48.5	17.5	8.5
Angola	23.5	11.7	35.5
Benin	30.2	16	27.6
Botswana	19.9	7.9	30.3
Burkina Faso	22.7	14	23.3
Burundi	23.5	13.9	49.3
Cameroon	35.3	17.6	30
Cape Verde	25.1	10.1	29
Central African Republic	31.4	17.8	21
Chad	34.1	19.9	18.8
Comoros	17.4	9.8	61.3
Congo	31.7	14.5	25.2
Congo (Democratic Republic of)	23.5	14.2	33.1
Côte d'Ivoire	33.7	18.5	21.7
Djibouti	35.9	19	17.3
Egypt	49.5	19.3	2.3
Equatorial Guinea	25.2	12.8	25.1
Eritrea	35.9	20.5	17.4
Ethiopia	41.8	23	26.4
Gabon	16.1	5.8	19.9
Gambia	9.8	5	26.1
Ghana	25.6	11.7	35.4
Guinea	14.5	7.9	38.4
Guinea-Bissau	26	14.3	29.8
Kenya	38.3	17.3	40.1
Lesotho	9	4.4	38.4
Liberia	24.1	14.2	30.1
Libya	24.1	8.4	9.7
Madagascar	26.6	13.4	44.6
Malawi	16.8	8.8	75.9
Mali	29.8	16.5	44.2
Mauritania	25.8	13.5	29.4
Mauritius	64.2	18.8	15
Morocco	40.8	18	14.3
Mozambique	14.5	7.9	65
Namibia	24.4	9.6	14.7
Niger	23.8	14.5	8.6
Nigeria	50.5	25.9	29
Reunion	46.6	9.5	15.3
Rwanda	15.9	8.1	41.8
Senegal	22.4	11.7	41.4
Sierra Leone	24.4	14.7	30.2
Somalia	40.6	20.6	33.4
South Africa	41.5	16.5	31.7
South Sudan	27.8	15.2	30.4
Sudan	27.8	15.2	7.9
Swaziland	10.5	5	53.1
Tanzania	19.4	9.7	54
Togo	27.2	14.3	21.5
Tunisia	31.8	10.9	4.8
Uganda	27.5	13.6	44.4
Western Sahara	36.2	15.1	31.1
Zambia	22.4	11.1	58
Zimbabwe	28.5	14	56.4
Source information:	Ferlay J, Soerjomataram I, Ervik M, et al. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Available from: http://globocan.iarc.fr, accessed July 7, 2014.	Ferlay J, Soerjomataram I, Ervik M, et al. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Available from: http://globocan.iarc.fr, accessed July 7, 2014.	Ferlay J, Soerjomataram I, Ervik M, et al. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Available from: http://globocan.iarc.fr, accessed July 7, 2014.

Cervical cancer is the second most commonly diagnosed cancer and the second leading cause of cancer death in African women as a whole, but rates vary across the continent. Cervical cancer rates are lower in North Africa compared with sub-Saharan Africa (Tables 6 and 7). Cervical cancer incidence and mortality rates (per 100,000 population) range from 2.3 and 1.0, respectively, in Egypt to 75.9 and 49.8 in Malawi (Table 10). Variation in cervical cancer incidence is primarily due to both underlying prevalence of oncogenic HPV infection as well as availability of screening (Forman et al, 2012).

Prostate cancer is the most frequently diagnosed cancer in African men and the leading cause of cancer death (Table 3), and it is among the top two most frequently diagnosed cancers and leading causes of cancer death in all sub-Saharan African regions (Table 4). Prostate cancer is the most frequently diagnosed cancer in men in 23 of 54 African countries. Prostate cancer incidence rates (per 100,000 men) range from 6.4 in Ethiopia to 67.9 in South Africa, while mortality rates range from 4.9 in Algeria to 40.2 in Burundi (Table 11). Prostate cancer in Africa is poorly understood, but it is known that men of African descent worldwide suffer from a disproportionate burden (Rebbeck et al, 2013).

Table 11: Prostate cancer incidence and mortality

Country	Prostate cancer incidence	Prostate cancer mortality
	Estimated age-standardized rate per 100,000 men, 2012	
Algeria	8.8	4.9
Angola	25	21.9

Country	Prostate cancer incidence	Prostate cancer mortality
Benin	25.7	22.8
Botswana	12	8.3
Burkina Faso	19.1	18.8
Burundi	41.4	40.2
Cameroon	23	18.6
Cape Verde	19	11
Central African Republic	23.6	20.2
Chad	18.3	17.5
Comoros	23.2	20.8
Congo	37.4	26.9
Congo (Democratic Republic of)	31.1	29.4
Côte d'Ivoire	19.6	16.8
Djibouti	8.5	8
Egypt	7.8	5.1
Equatorial Guinea	19.4	17.9
Eritrea	8.5	7.6
Ethiopia	6.4	5.6
Gabon	15.8	9.4
Gambia	6.7	6.4
Ghana	13	9.6
Guinea	34.7	30.2
Guinea-Bissau	19	17.5
Kenya	31.6	24.7
Lesotho	12.1	8.9
Liberia	27.2	25.4
Libya	15.5	7.4
Madagascar	32.9	25.1
Malawi	10.8	9
Mali	12.8	12.1
Mauritania	19	17.9
Mauritius	22.9	16.6
Morocco	18.5	12.9
Mozambique	9.6	8.3
Namibia	22.2	15.4
Niger	9	8.8
Nigeria	30.7	25.3
Reunion	54.4	11.3
Rwanda	25.6	21.7
Senegal	23.6	20.8
Sierra Leone	27.2	28.5
Somalia	19	15.4

Country	Prostate cancer incidence	Prostate cancer mortality
South Africa	67.9	26.4
South Sudan	25.5	21.5
Sudan	10.3	8.7
Swaziland	17.4	13.5
Tanzania	34.6	27.9
Togo	14.6	12.2
Tunisia	11.3	5.9
Uganda	48.2	38.8
Western Sahara	16.2	13.5
Zambia	21.9	18.2
Zimbabwe	37.3	25.9
Source information:	Ferlay J, Soerjomataram I, Ervik M, et al. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Available from: http://globocan.iarc.fr, accessed July 7, 2014.	Ferlay J, Soerjomataram I, Ervik M, et al. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Available from: http://globocan.iarc.fr, accessed July 7, 2014.

Lung cancer is the fourth most commonly diagnosed cancer and the third leading cause of cancer death in African men, but it is not among the top ten cancers for African women (Table 3). Among men, it is among the top two most common cancers only for the regions of Northern and Southern Africa (Table 4). Table 12 is the estimates of incidence for lung cancer in men and in women by country. Lung cancer rates are expected to increase in Africa (Parkin et al, 2014). Tobacco use is a major cause of lung cancer, but exposure to environmental smoke due to cooking and heating is a major factor in lung cancer development, especially among women (Mortimer et al, 2012). In Africa, an estimated 23% of lung cancer deaths among women are attributed to household air pollution from solid fuels (Institute for Health Metrics and Evaluation, 2015).

Table 12. Lung cancer incidence

Source (Lung cancer incidence, men): Ferlay J, Soerjomataram I, Ervik M, et al. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Available from: http://globocan.iarc.fr, accessed July 7, 2014

Source: (Lung cancer incidence, women): Ferlay J, Soerjomataram I, Ervik M, et al. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Available from: http://globocan.iarc.fr, accessed July 7, 2014

Country	Lung cancer incidence, men	Lung cancer incidence, women
	Estimated age-standardized rate per 100,000 men, 2012	Estimated age-standardized rate per 100,000 women, 2012
Algeria	17	3.4
Angola	2.9	1.3
Benin	2.2	0.9
Botswana	8.9	1.5
Burkina Faso	3	2
Burundi	1.8	1.6

Country	Lung cancer incidence, men	Lung cancer incidence, women
Cameroon	2	1
Cape Verde	1.5	0.2
Central African Republic	2.2	0.9
Chad	1.5	0.9
Comoros	2.6	0
Congo	1.8	0.5
Congo (Democratic Republic of)	1.6	0.6
Côte d'Ivoire	2	1.4
Djibouti	2.9	2.5
Egypt	11.2	3.8
Equatorial Guinea	5.9	1.7
Eritrea	3	2.2
Ethiopia	3.3	3.1
Gabon	8.3	4.4
Gambia	3.5	1.2
Ghana	3.8	1
Guinea	2	0.9
Guinea-Bissau	2	1.3
Kenya	3.4	2
Lesotho	5.3	1.1
Liberia	1.9	1.1
Libya	28	3.7
Madagascar	12.5	2.4
Malawi	1.2	0.7
Mali	3.8	1.9
Mauritania	2	0.9
Mauritius	16.3	5.3
Morocco	25.5	2.8
Mozambique	4.2	1.8
Namibia	4.9	2.1
Niger	0.4	0
Nigeria	1.1	1.1
Reunion	32.3	4.9
Rwanda	1.6	0.8
Senegal	2.9	1.4
Sierra Leone	1.9	1.3
Somalia	3.3	2.5
South Africa	28.7	11.2
South Sudan	2.7	1.3
Sudan	2.7	1.3
Swaziland	5.4	1.4

Country	Lung cancer incidence, men	Lung cancer incidence, women
Tanzania	0.9	0.5
Togo	2.2	0.8
Tunisia	31.1	1.7
Uganda	2.7	2.7
Western Sahara	14.8	0.9
Zambia	2.4	1.4
Zimbabwe	7.2	3.2

Colorectal cancer is the fifth most common cancer and leading cause of cancer death among men, and the fourth among women (Table 3). Rates are highest in Southern Africa (Tables 6 and 7), and several Northern countries including Libya, Algeria, and Tunisia also have among the highest rates. Colorectal cancer was once rare in Africa, but rates in many countries have increased with increasing sedentary lifestyles and dietary transitions (Parkin et al, 2014).

Oesophageal cancer is the eighth most commonly diagnosed cancer and the seventh leading cause of cancer death among African men and women (Table 3). It is the most commonly diagnosed cancer among men in Botswana. Incidence rates in Southern and Eastern Africa are among the highest in the world, while those in Northern and Western Africa are among the lowest (Torre et al, 2015). The causes of oesophageal cancer in Africa are poorly understood, but are thought to include alcohol, diet, and fungal contamination of maize (Jemal et al, 2012).

Liver cancer is the second most common cancer and leading cause of cancer death among men, and the third among women (Table 3). Rates in Northern and Western Africa are among the highest in the world (Torre et al, 2015). The high rates in Africa are primarily due to the high prevalence of hepatitis B infection, although foods contaminated with aflatoxin also play a role.

Table 13 is the five-year net survival percentages for selected cancers among adults aged 15 years of age and older in select countries, 2005-2009. This data is drawn from several African registries. There are definite limitations to the reliability of these data.

Table 13: Five-year net survival rates* (%) for selected cancers among adults 15 years of age and older in select countries, 2005-2009

Source: Allemani C, Weir HK, Carreira H, et al. Global surveillance of cancer survival 1995-2009: analysis of individual data for 25,676,887 patients from 279 population-based registries in 67 countries (CONCORD-2). Lancet. 2015;385:977-1010. Available at http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2814%2962038-9/abstract

	Stomach	Colon	Rectum	Liver	Lung	Breast (women)	Cervix	Ovary	Prostate	Leukaemia
Algerian registries	10†	57†	46†	18†	15†	60†	55†	42†	59†	14†
Libya (Benghazi)	3†	31†	51†	0†	2†	77†	39†	22†	41†	6†
Mauritius	41	56	69	53	37	87	87	83	77	57†
Nigeria (Ibadan)	-	0†	46†	-	-	-	96†	-	91†	83†
South Africa (Eastern Cape)	-	-	-	10†	19†	53	55	91†	100†	
United States registries	29	65	64	15	19	89	63	41	97	52

*Survival rates are age-standardized.

†Data are subject to limitations. Please see source.

Childhood Cancers

Compared to Africa, childhood cancer rates are higher in developed countries where it is the second leading cause of death in children. The actual incidence and mortality rates in Africa are not known, but they are certainly not among the ten most common causes of death. There are areas with high rates of Burkitt's lymphoma and Kaposi's Sarcoma in children (Parkin et al, 2014). These are diseases almost unheard of in North America and Europe. There are also anecdotal reports of high incidence of retinoblastoma in some countries of sub-Saharan Africa (Zambia, Zimbabwe and Congo) (Parkin et al, 2014). In a survey of cancer treatment facilities the proportion of cancers occurring in children varied from 1.4% of all cases in a Ghanaian facility to 10.0% in a Rwandan facility (Parkin et al, 2014).

Nephroblastoma appears to be the most common solid tumour in children in all of Africa, exceeding 10% of total paediatric cancers in many countries (Rwanda 21.3%, Senegal 22%, Cote d'Ivoire 14.5%, Mali 17.6%, Congo 15.5%, etc.) (Stefan, 2015). In Mozambique and Uganda, Kaposi's Sarcoma was the most common childhood malignancy (15.8% and 22.0% of all cases respectively) and it was the second most common cancer in children in Zambia (15.6%) and Malawi (12.4%) (Mukiibi et al, 1995).

Non-Hodgkin lymphoma was the most common childhood cancer in West Africa: Ghana (53.6%), Cote d'Ivoire (73.6%) and Mali (32.7%). In Eastern Africa, two Kenyan centres reported Burkitt's lymphoma as the most common tumour (25.1 and 37.1%, respectively). In the Congo, retinoblastoma was the most common childhood cancer with an incidence of 20.1% (Kruger et al, 2014).

The South African Children's Tumour Registry is not population based and likely provides an underestimate of the problem in South Africa. In a ten year period from 1997 to 2007, it produced an overall incidence rate which is a third that of the United States or Europe. The most commonly

diagnosed cancers among children were leukaemia (25.4%), lymphoma (13.5%), brain tumours (13.5%), nephroblastoma (12.3%), soft tissue sarcoma (9.5%), and retinoblastoma (7.1%) (Kruger et al, 2014).

Cancer Risk Factors

Many cancer risk factors common in western countries such as tobacco use, physical inactivity, and excess body weight are increasing in many African countries. At the same time, infection remains an important cause of cancer in Africa. It is estimated that infections cause 33% of cancers in sub-Saharan Africa and 13% of cancers in North Africa (de Martel et al, 2012). In comparison, infection is thought to cause 7% and 4% of cancers in Europe and North America, respectively. It is well known that H. pylori is linked to gastric cancer, Hepatitis B and C viruses cause hepatocellular carcinoma and human papillomavirus causes cervical, anogenital, and certain head and neck cancers. Less appreciated is the fact that Burkitt's lymphoma is thought to be caused by chronic inflammation due to falciform malaria and squamous cell cancer of the bladder common in Egypt is caused by schistosomiasis (Molyneux et al, 2012; Mostafa et al, 1999). Aflatoxin found in dietary grain and produced by the aspergillus species of mould is also a cause of liver cancer. HIV infection is linked to lymphoma, Kaposi's Sarcoma and a number of other cancers (Sasco et al, 2010). While tobacco smoking is generally less common in Africa than elsewhere in the world, it is more common in some countries, especially in Northern Africa and among men, and is said to be increasing (Table 14). The use of solid fuels for heating and cooking, the source of indoor air pollution, is common in many African countries. This is a significant cause of respiratory disease and lung cancer in Africa and especially in women (Table 15) (Mortimer et al, 2012). Excess body weight is also increasing in Africa, although many African countries still have the lowest percentages of overweight people worldwide. In South Africa and several Northern African countries, 50% or more of adults are overweight or obese (Table 16).

Table 14: Smoking prevalence in African Countries

Source: Institute for Health Metrics and Evaluation. United State of America, 2015. Available from: http://www.healthdata.org/data-visualization

Country	Smoking prevalence, adult men	Smoking prevalence, adult women
	(Age-standardized percentage estimate among men aged 15 and older,2013)	(Age-standardized percentage estimate among women aged 15 and older, 2013)
Algeria	21.7	0.9
Angola	16.7	1.6
Benin	13.7	1.9
Botswana	21.5	6.1
Burkina Faso	19.8	3.8
Burundi	24.6	9.8
Cameroon	15.4	0.6
Cape Verde	11.6	3.2
Central African Republic	15.9	1.5
Chad	14.1	2.3
Comoros	18.1	2.5
Congo	16.2	1.4
Congo (Democratic Republic of)	15.3	1.4

Country	Smoking prevalence, adult men	Smoking prevalence, adult women
Côte d'Ivoire	18.7	1.8
Djibouti	38.9	7.4
Egypt	36.1	1.2
Equatorial Guinea	16.4	1.5
Eritrea	11.3	0.6
Ethiopia	7.7	1
Gabon	19.1	2.9
Gambia	24.9	0.8
Ghana	8.3	1.3
Guinea	12	1.6
Guinea-Bissau	12.5	2
Kenya	20.2	1.4
Lesotho	35.6	1
Liberia	13.2	1.3
Libya	29.5	0.9
Madagascar	26.6	1.6
Malawi	21.9	2.7
Mali	18.7	3.9
Mauritania	21.7	3.8
Mauritius	34	2.8
Morocco	26.7	0.8
Mozambique	22.3	4.2
Namibia	24.5	10
Niger	8.9	1.6
Nigeria	7.4	1.4
Reunion		
Rwanda	16.3	2.7
Senegal	14.5	1.2
Sierra Leone	30.7	6.3
Somalia	19.7	2.3
South Africa	22.2	9
South Sudan	8.3	1
Sudan	8.3	1
Swaziland	14.8	2.7
Tanzania	19.9	1.5
Togo	13.8	1.5
Tunisia	45.1	4.4
Uganda	17.4	2
Western Sahara		
Zambia	23.9	3.3
Zimbabwe	24.6	2.7

Table 15: Percentage of population using solid fuels 2010

World Health Organization. Global Health Observatory Data Repository, Population using solid fuels (estimates), 2010, data by country [online database]. Available from: http://apps.who.int/gho/data/view.main.1701?lang=en, accessed July 9, 2014

Solid Fuels	Percentage of population using solid fuels
Algeria	0
Angola	56
Benin	94
Botswana	37
Burkina Faso	95
Burundi	98
Cameroon	78
Cape Verde	31
Central African Republic	97
Chad	93
Comoros	71
Congo	76
Congo (Democratic Republic of)	93
Côte d'Ivoire	79
Djibouti	14
Egypt	0
Equatorial Guinea	78
Eritrea	63
Ethiopia	98
Gabon	21
Gambia	95
Ghana	84
Guinea	96
Guinea-Bissau	98
Kenya	84
Lesotho	62
Liberia	98
Libya	0
Madagascar	98
Malawi	97
Mali	98
Mauritania	56
Mauritius	0
Morocco	3
Mozambique	96

Solid Fuels	Percentage of population using solid fuels
Namibia	55
Niger	94
Nigeria	75
Reunion	
Rwanda	98
Senegal	56
Sierra Leone	98
Somalia	96
South Africa	13
South Sudan	97
Sudan	72
Swaziland	62
Tanzania	96
Togo	95
Tunisia	0
Uganda	97
Western Sahara	
Zambia	83
Zimbabwe	70

Table 16: Proportion of population overweight

Source: World Health Organization. Global Health Observatory Data Repository, Overweight (Body Mass Index > 25) Data by Country, 2008 [online database]. Available from: http://apps.who.int/ghodata/, accessed November 9, 2012

Country	Overweight prevalence, adult men	Overweight prevalence, adult women
	Percentage of overweight and obese men aged 20 and older, 2008	Percentage of overweight and obese women aged 20 and older, 2008
Algeria	41.8	54.5
Angola	20.4	30.7
Benin	20.4	31.7
Botswana	18.3	52.3
Burkina Faso	11.9	14.2
Burundi	16	14.7
Cameroon	32.6	42.3
Cape Verde	30.8	42.6
Central African Republic	12.4	20.9
Chad	14.6	16.9
Comoros	19.4	21.1

Country	Overweight prevalence, adult men	Overweight prevalence, adult women
Congo	16.9	27
Congo (Democratic Republic of)	6.1	14.5
Côte d'Ivoire	21.8	32.3
Djibouti	30.2	37.4
Egypt	62.4	76.9
Equatorial Guinea	33	38.9
Eritrea	9.6	11.4
Ethiopia	7.1	9
Gabon	36.5	51.6
Gambia	14.9	40.9
Ghana	24.2	36.7
Guinea	22.2	20.8
Guinea-Bissau	15.3	26.3
Kenya	15.2	25.5
Lesotho	17.3	58.1
Liberia	17.7	27.5
Libya	60.4	71
Madagascar	12.6	8.8
Malawi	16.7	24.3
Mali	15.3	25.7
Mauritania	22.8	53.9
Mauritius	46.7	51.7
Morocco	43.1	53.6
Mozambique	16.5	28
Namibia	23.3	44.7
Niger	11	16.6
Nigeria	26.2	31.2
Reunion		
Rwanda	24	17.5
Senegal	18	37
Sierra Leone	21.2	33.4
Somalia	18.9	24
South Africa	62	73.6
South Sudan	21.6	28.2
Sudan	21.6	28.2
Swaziland	28.2	68.2
Tanzania	22.1	25.8
Togo	17.4	23.3
Tunisia	47.5	64.2
Uganda	22.2	20.4
Western Sahara		

Country	Overweight prevalence, adult men	Overweight prevalence, adult women
Zambia	9.1	26
Zimbabwe	17.6	40.3

African Cancer Registries

There are eight registries with data included in the recent publication *Cancer Incidence in Five Continents*. These registries have been judged to produce high quality data.

The Sétif Population-based Cancer Registry, Sétif, Algeria

The Sétif Population-based Cancer Registry covers Sétif, a province in the Arab-Islamic North African country of Algeria. It covers approximately 1.5 million people, which is 4.7% of the Algerian population. The population is relatively young (with 63% aged less than 30 years and 6.4% aged 60 years or more). Approximately half live in urban areas. The registry is population based. The registry is based within Sétif University. It uses active case finding from 16 data sources. These consist of public and private hospitals, laboratories, insurance offices, other cancer registries, and death registration offices. Data are cross-checked to assure accuracy (Hamdi Cherif et al, 2014; Zanetti et al, 2010) (Table 17).

Table 17: Age-adjusted incidence rate of cancer (world standard) in selected area in Africa: Setif, Algeria

Setif, Algeria - 10 Major cancers, ASR (world) per 100,000			
Men		Women	
Trachea, bronchus and lung	19.9	Breast	29.8
Bladder	8.6	Cervix uteri	9.0
Larynx	6.3	Gallbladder etc.	7.4
Nasopharynx	5.7	Thyroid	6.1
Stomach	5.7	Colon	5.2
Prostate	5.4	Other and unspecified	3.7
Non-melanoma skin cancer	5.2	Rectum	3.5
Colon	4.9	Stomach	3.4
Non-Hodgkin lymphoma	4.3	Non-Hodgkin lymphoma	2.7
Other and unspecified	3.7	Trachea, bronchus and lung	2.6
All sites	99.6	All sites	98.1

The Gharbiah Population-based Cancer Registry, Gharbiah, Egypt

The Gharbiah Population-based Cancer Registry covers eight districts within the Gharbiah Governorate (Tanta, Elmahalla Elkobra, Kafr Elzayat, Zefta, Kotour, Elsanta, Basyoun, and Samannoud) in the Nile Delta region of Egypt. It covers approximately 4 million, accounting for 5.5% of the

overall population of Egypt. About 30% of residents live in urban areas. The registry is based in the Tanta Cancer Centre in Gharbiah. It utilizes active case finding from 63 data sources (Dey et al, 2011) (Table 18).

Table 18: Age-adjusted incidence rate of cancer (world standard) in selected area in Africa: Gharbiah, Egypt

Gharbiah, Egypt - 10 Major cancers, ASR (world) per 100,000			
Men		Women	
Liver	24.8	Breast	45.4
Bladder	19.0	Non-Hodgkin lymphoma	10.8
Non-Hodgkin lymphoma	13.5	Liver	6.2
Trachea, bronchus and lung	11.9	Ovary	5.3
Prostate	7.6	Bladder	5.0
Other and unspecified	6.1	Other and unspecified	4.1
Pancreas	4.5	Trachea, bronchus and lung	3.7
Non-melanoma skin cancer	4.4	Corpus uteri	3.6
Brain, nervous system	4.3	Colon	3.4
Colon	3.6	Brain, nervous sytem	3.2
All sites	137.1	All sites	125.1

The Benghazi Cancer Registry, Benghazi, Libya

The Benghazi Cancer Registry covers eight districts in the eastern part of Libya (Tobruk, Derna, Bayda, Al Marj, Benghazi, Ajdabiya, Al Wahat, and Al Kufra). The population covered is approximately 1.6 million, which is 28% of the total population of Libya. The registry is located within the Medical School of Benghazi University. The registry uses active case finding from cancer service units, general and regional hospitals, university hospitals, private hospitals and clinics, specialized hospitals and centres outside the region, and pathology laboratories. Death certificates are actively investigated. (El Mistiri et al, 2015) (Table 19)

Table 19: Age-adjusted incidence rate of cancer (world standard) in selected area in Africa: Benghazi, Libya

Benghazi, Libya 10 Major cancers, ASR (world) per 100,000			
Men		Women	
Trachea, bronchus and lung	27.8	Breast	22.9
Bladder	14.9	Colon	9.0
Prostate	14.7	Uterus unspecified	8.3
Colon	8.8	Other and unspecified	4.9
Non-Hodgkin lymphoma	5.8	Ovary	4.7
Larynx	5.5	Cervix uteri	4.5
Pancreas	5.4	Non-Hodgkin lymphoma	4.3

Benghazi, Libya 10 Major cancers, ASR (world) per 100,000			
Men		Women	
Brain, nervous system	5.2	Thyroid	3.8
Rectum	5.0	Liver	3.7
Liver	4.9	Rectum	3.3
All sites	138.5	All sites	110.0

The Malawi Cancer Registry, Blantyre District, Malawi

The population of Blantyre District (urban and rural) was slightly more than 1 million in 2008. The registry is population-based and uses active case finding from 15 hospitals serving the Blantyre catchment population, and three histopathology laboratories (Gopal et al, 2013; Msyamboza et al, 2012) (Table 20).

Table 20: Age-adjusted incidence rate of cancer (world standard) in selected area in Africa: Blantrye, Malawi

Blantrye, Malawi 10 Major cancers, ASR (world) per 100,000			
Men		Women	
Kaposi's Sarcoma	91.8	Cercix uteri	76.3
Oesophagus	37.6	Kaposi's Sarcoma	43.6
Prostate	15.7	Oesophagus	23.0
Bladder	13.3	Breast	14.3
Non-Hodgkin lymphoma	12.6	Other and unspecified	10.7
Other and unspecified	10.6	Eye	9.8
Eye	7.4	Non-Hodgkin lymphoma	9.4
Liver	7.0	Bladder	9.2
Non-melanoma skin cancer	6.8	Liver	4.4
Bone	3.4	Non-melanoma skin cancer	4.3
All sites	226.4	All sites	237.8

The PROMEC Registry, Transkei, South Africa

The PROMEC Cancer Registry operates in the rural Transkei region of the South African province of the Eastern Cape. The registry covers the population of eight magisterial areas: Butterworth, Centane (Kentani), Idutywa, Nqamakwe, Willowvale, Bizana, Flagstaff, and Lusikisiki. The vast majority of residents are Black Africans and speak isiXhosa. The PROMEC Cancer Registry collaborates with 19 hospitals and one state laboratory. Case finding is performed both passively and actively (Somdyala et al, 2003). Data are shown in Table 21.

Table 21: Age-adjusted incidence rate of cancer (world standard) in selected area in Africa: PROMEC, Transkei, South Africa

PROMEC, South Africa 10 Major cancers, ASR (world) per 100,000			
Men		Women	
Oesophagus	32.0	Cervix uteri	23.8
Prostate	6.2	Oesophagus	19.6
Trachea, bronchus and lung	4.8	Breast	7.3
Other and unspecified	3.6	Other and unspecified	1.5
Larynx	3.4	Kaposi's Sarcoma	1.4
Kaposi's Sarcoma	3.1	Liver	1.2
Liver	2.7	Ovary	1.0
Mouth	2.1	Corpus uteri	0.9
Tongue	2.1	Trachea, bronchus and lung	0.9
Eye	1.0	Non-Hodgkin lymphoma	0.6
All sites	73.6	All sites	67.4

The Cancer Registry of North Tunisia, Tunisia

The Cancer Registry of North Tunisia covers 11 provinces in the northern area of the country (28,000 km^2). The covered area includes urban regions such as the cities of Tunis, Bizerte, and Nabeul. Farming and fishing are the main occupations in the rural areas of the region. The region is mainly Arabic and Islamic. The registry collects data actively from 85 healthcare sources both public and private (Missaoui et al, 2012). (Table 22)

Table 22: Age-adjusted incidence rate of cancer (world standard) in selected area in Africa: North Tunisia

North Tunisia 10 Major cancers, ASR (world) per 100,000			
Men		Women	
Trachea, bronchus and lung	30.6	Breast	30.9
Bladder	12.9	Non-melanoma skin cancer	5.7
Prostate	11.4	Colon	5.5
Non-melanoma skin cancer	7.4	Cervix uteri	4.6
Colon	6.3	Ovary	4.0
Larynx	6.0	Other and unspecified	4.0
Stomach	5.8	Non-Hodgkin lymphoma	3.8
Non-Hodgkin Lymphoma	5.7	Rectum	3.7
Other and unspecified	5.5	Corpus uteri	3.4
Rectum	4.2	Thyroid	3.3
All Sites	129.9	All sites	99.7

The Kampala Cancer Registry, Kyadondo County, Uganda

The Kampala Cancer Registry covers the population of Kyadondo County, which includes the city of Kampala and a semi-urban area. The majority of the population is of the Ganda ethnic group. The registry is based in the Department of Pathology at the Makerere University College of Health Sciences. Registration is primarily through active case finding. Registrars visit hospitals, hospices, and histopathology laboratories regularly. Death certificates are incomplete and therefore not used as a source of information by the registry (Wabinga et al, 2014). (Table 23)

Table 23: Age-adjusted incidence rate of cancer (world standard) in selected area in Africa: Kyadondo, Uganda

Kyadondo, Uganda 10 Major cancers, ASR (world) per 100,000			
Men		Women	
Prostate	42.5	Cervix uteri	54.3
Kaposi's Sarcoma	29.5	Breast	32.9
Oesophagus	15.6	Kaposi's Sarcoma	20.2
Liver	11.4	Oesophagus	11.5
Non-Hodgkin lymphoma	9.6	Liver	8.7
Stomach	8.0	Other and unspecified	8.1
Other and unspecified	6.5	Non-Hodgkin lymphoma	7.2
Trachea, bronchus and lung	5.2	Ovary	6.9
Colon	4.1	Stomach	5.9
Rectum	3.8	Corpus uteri	5.6
All sites	180.8	All sites	214.9

The Zimbabwe National Cancer Registry, Harare, Zimbabwe

The Zimbabwe National Cancer Registry became population-based in 1990. It covers approximately 1.4 million residents. Active case finding is carried out through visits to health care facilities. There are routine visits to the central referral hospitals, searching of medical records of discharged and deceased cancer patients, visits to oncology outpatient clinics, and review of histology reports from the public and private sectors (Chokunonga et al, 2015). (Table 24)

Table 24: Age-adjusted incidence rate of cancer (world standard) in selected area in Africa: Harare, Zimbabwe

Harare, Zimbabwe 10 Major cancers, ASR (world) per 100,000			
Men		Women	
Prostate	62.4	Cervix uteri	86.7
Kaposi's Sarcoma	37.3	Breast	33.9
Oesophagus	22.2	Kaposi's Sarcoma	23.5
Liver	16.7	Oesophagus	15.3

Harare, Zimbabwe 10 Major cancers, ASR (world) per 100,000			
Men		Women	
Stomach	11.7	Stomach	14.2
Trachea, bronchus and lung	10.1	Liver	13.9
Bladder	9.4	Ovary	10.9
Non-Hodgkin lymphoma	8.8	Non-Hodgkin lymphoma	10.0
Colon	8.0	Corpus uteri	10.0
Other and unspecified	6.7	Trachea, bronchus and lung	6.4
All sites	244.5	All sites	299.5

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Chapter 3

Africa: Pathology in the Sub-Sahara

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Dr. Matonga looked over the young woman sitting in the examination room and sighed deeply. Her left breast contained a palpable mass of about 2 cm. She had no nipple discharge, no obvious lymph nodes in her left axilla, and no pain. The woman's mother had died several years before with a protuberant mass of the right breast that had spread all over her body. It was assumed to be breast cancer but no one was sure. Dr. Matonga remembered pathology and histology from medical school but there was no one within 100 km to whom he could send a biopsy for diagnosis. Because she was only 38, he didn't want to have the surgeon (who was about 60 km away) simply remove her breast with no further treatment available. But what if it was benign? If he told her to watch the mass, she may return in a few months with tumour in her axilla. He stepped out of the room for a moment to ask his nurse a question and noticed a row of women and a few men all sitting on the bench waiting to be seen, several with obvious lumps and masses for which he would, again, have no answer.

The above scene, played out daily in many nations around the globe, is most dire in less developed countries (including Sub-Saharan Africa; SSA) and new, often late-stage cases are presenting every day. It illustrates the fact that, in the absence of access to good pathology, clinicians are often left treating patients without an accurate diagnosis; this leads to inappropriate therapy in a significant proportion of their patients.

Why is Good Cancer Pathology Needed in Sub-Saharan Africa?

Global health efforts over the past quarter century have improved quality and length of life in many countries. Across SSA highly prevalent infections such as tuberculosis, HIV, malaria and other tropical diseases are being detected and treated, lowering the infectious disease burden. For example, between 2000 and 2015, malaria incidence rates fell by 42% and mortality rates fell by 66% in Africa, thanks to substantial strategic investment by many agencies (World Malaria Report, 2015). As a consequence, the relative burden of non-communicable diseases (NCDs) including diabetes, hypertension and especially cancer is increasing (Ferlay et al, 2012). The latter is also increasing because of increasing longevity, including long-term HIV survivors (Adebamowo et al, .2014,Vaccher et al, 2014). With respect to pathology and laboratory medicine needs, cancer is very different from diseases such as malaria, tuberculosis, or HIV, in which a very limited number of low complexity laboratory tests and

a specific drug regimen alleviates a huge burden of disease. In contrast, cancer is a complex disease that requires a health system to manage adequately.

In this chapter we define pathology as cellular or anatomic pathology (including cytology); i.e., morphological assessment of tissue. Pathology has many sub disciplines; cellular pathology, haematology, microbiology, clinical chemistry, immunology etc., and all are important in the diagnosis and management of all diseases. However diagnosing, staging and grading cancer is essentially only possible through cell or anatomic pathology and this will be the focus of this chapter. Appendix 1, and boxes 1 and 2 outline the staff and infrastructure needed for cell pathology provision.

Pathology as a tool for both primary diagnosis and for subsequent management of cancer is crucial and, to date, has been severely lacking across SSA. While efficient and reliable diagnosis remains one of the most important factors in utilization of resources for all forms of patient care and public health, most importantly, in cancer, patients simply cannot be treated accurately without a pathologically-determined diagnosis. At its most basic, cell pathology, using simple hematoxylin and eosin stains, determines the answers to questions such as: is this lesion a tumour? Is the tumour benign or malignant? If malignant, what type of tumour is it and how far has it invaded? Has it been fully excised and has it metastasized to lymph nodes? Thus the clinician is provided with not just the diagnosis, but information to guide therapy, the likely prognosis and what follow-up is advisable (e.g. further surgery if an excision is inadequate). In the absence of such information, the clinician is treating the patient more or less blindly.

Even where pathology provision exists, another crucial issue compounds the problems outlined above, in many countries in SSA, namely the relative isolation of pathology and pathologists from much of the rest of the health care system, in particular the lack of regular clinical interaction. For optimum patient benefit, pathology and pathologists should be an integral part of the clinical team. This need for interdisciplinary coordination of care is especially important in cancer where complications of disease and therapy need be monitored and treated as necessary (Figure 1).

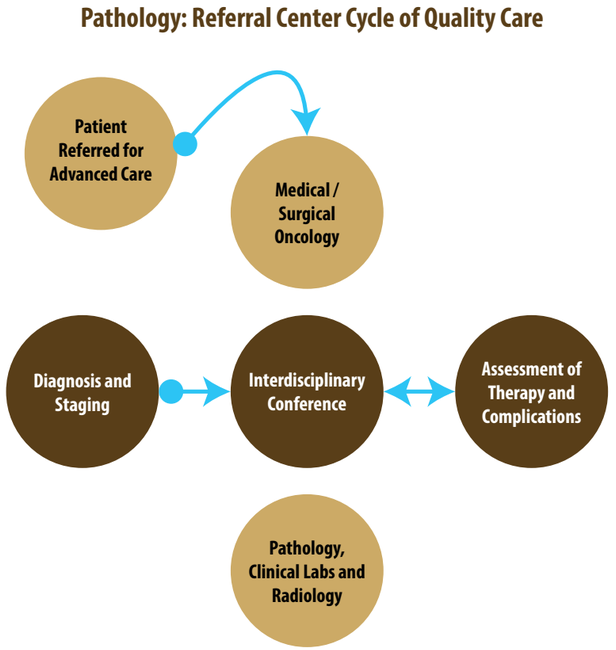

Figure 1: Referral Centre: Efficient cancer care requires both medical and surgical teams with capacity to accept referrals, provide accurate diagnoses, implement therapy and access outcomes. An interdisciplinary care team/conference is essential for appropriate integration of care, follow-up and data collection.

Furthermore a particular challenge for pathology in SSA is that many clinical interactions are single encounters, necessitating rapid (immediate) diagnostics and treatment decisions. The most rapid turnaround time for current modern pathology technology is 24 hours, and considerably more for traditional histology. Thus a single encounter clinical interaction is in immediate conflict with the requirements of pathology assessment of cancer. This is an issue which must be addressed if cancer pathology is to develop appropriately to face the current and future cancer burden in Africa. As a result of the above, although very few accurate data are available, it is clear that many cancer patients in SSA do not receive a tissue diagnosis. One publication from the cancer registry in Makerere in Uganda has shown that at least 32% of cancer cases did not have a histology report (Parkin et al, 2001). Given the rather special nature of this Registry, it is likely that the rate is lower in many other places (see below). This inevitably leads to wrong/delayed diagnosis, unnecessarily prolonged burden of illness, failed opportunities for curative treatment and wasted use of limited resources. Furthermore, at a policy level, the development of cancer policies and of national cancer plans by Ministries of Health needs accurate registration data, based on pathology diagnoses (fig 2). These data can also be used to inform primary care providers on approaches to triage of patients, including which patients to refer to more specialized centres. In addition, tissue-based disease prevalence is

needed to develop treatment protocols and stock appropriate medications. In the absence of accurate data on the epidemiology of cancer in the country, components of national cancer plans and policies are undoubtedly misdirected.

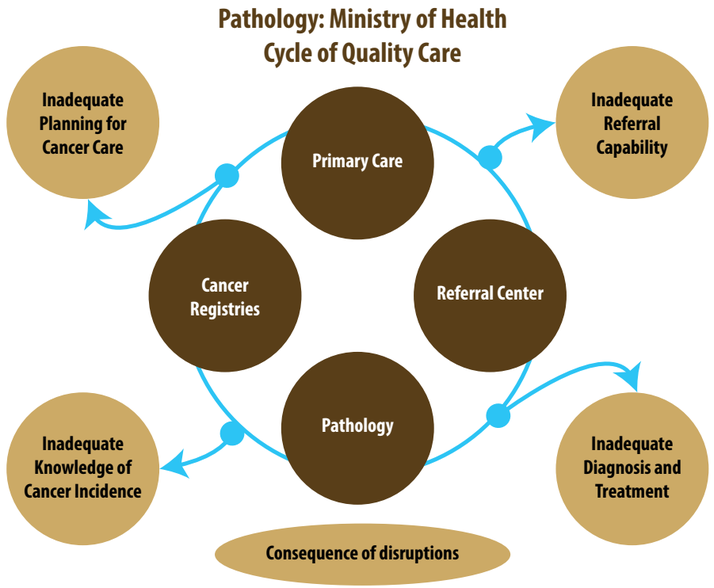

Figure 2: MOH: Cancer care depends on a functional health system. The MOH should have both referral and feedback mechanisms in place to a) inform primary health care facilities using evidence-based disease prevalence b) provide guidelines for accessing the referral centre c) have services (anatomic and clinical pathology, radiology) to diagnose and treat patients and d) maintain cancer registries to be used for national cancer plans.

Current Status of Pathology Practice and Education in Sub-Saharan Africa

In view of all the challenges and issues outlined above, what is the current situation of pathology in SSA? Unfortunately there is a paucity of data on all aspects of pathology provision across SSA, including knowledge of manpower, infrastructure, standards, etc. In some countries, there is not even an accurate count of the number of active pathologists.

In order to determine the current status of pathology practice and training, we conducted a survey of the professional and technical workforce, of training, workload (type, volume and turn-around-time) and facilities/equipment infrastructure - note that this questionnaire addressed public sector laboratories primarily but in several countries the same pathologist works in both public and private sector. The goal was to provide a framework for each country to create a strategic plan for the advancement of pathology services to the highest level. This information will help to 1) identify opportunities to bridge services, 2) match donors with country specific needs for funding, equipment, training or mentoring and 3) encourage regional and international integration and collaboration to achieve maximal output with limited resources.

An online-survey of 65 questions was developed and made available in English, French, and Portuguese. Emails were sent to more than 200 African pathologists and collaborators in Africa, United States and Europe using lists from the four International Academy of Pathology (IAP) divisions in Africa – Francophone Africa, South Africa, Anglophone West Africa and Anglophone East Africa. Responses were received from 60 individuals and included data from 49 institutions in 30 countries. Duplicate entries for the same institution were compared and any discrepancies were resolved by sending a query to the chief of pathology at that institution. Data on 9 of the remaining 12 countries of SSA were obtained from various sources using extensive networking. Information was verified and updated in 2015 (Nelson et al, 2016; African Strategies for Advancing Pathology, 2015).

Pathologist Numbers

Overall, we have identified 724 pathologists in SSA, which is less than 1 pathologist per million population (Fig 3, Table 1). The highest rate is 4 pathologists per million in South Africa, with Botswana and Namibia having around 2 per million. Most of the other countries have gradually decreasing rates from around 1 per million down to around 0.1 per million. Just over 50% percent of this workforce is located in two countries – Nigeria and South Africa.

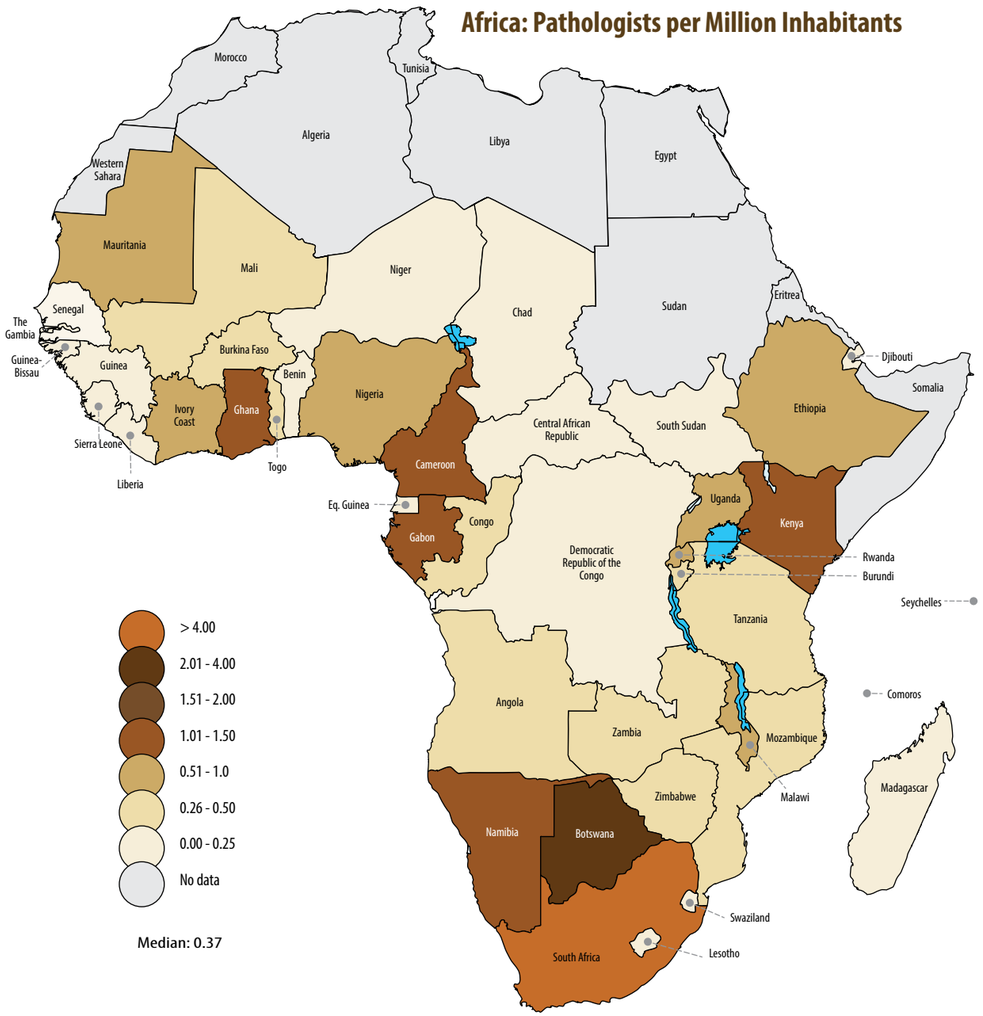

Figure 3: Pathologists per million, by country, in SSA

Table 1: Countries showing population, number of pathologists and pathology trainees

Country	Population	Pathologists	Pathologist Trainees	AP or Both	Number of years
Benin	11 M	2	0	No Data	4
Burkina Faso	18 M	8	8	AP	No Data
Burundi	10 M	3 (1)	1	AP	5
Cameroon	22 M	23	4 (2)	AP	4
Chad	13 M	2	1	AP	4
Cote d'Ivoire	25 M	15 (3)	7	AP	4
Central African Republic	5.5 M	1	2	AP	4
Democratic Republic of Congo	74 M	15	11 (4)	AP	4
Gabon	2.3 M	3	2	No Data	No Data
Guinea	11 M	2	0	No Data	No Data
Guinea-Bissau	1.8 M	0	0	No Data	No Data
Mali	18 M	5	0	No Data	No Data
Mauritania	3.7 M	3	1	AP	4
Niger	19 M	2	0	No Data	No Data
Senegal	14 M	7	2	AP	4
Republic of Congo	4.6 M	2	1	AP (5)	4
Rwanda	11 M	7	13	AP	4
Togo	7 M	3	0	No Data	No Data
Ghana	27 M	30 (6)	5	Both	4
Nigeria	182 M	150	211	AP (7)	5
Gambia	2 M	0	0	No Data	No Data
Liberia	4 M	0	0	No Data	No Data
Sierra Leone	6.4 M	0	0	No Data	No Data
Ethiopia	89 M	55	36	AP	4
Kenya (8)	44 M	60	34	Both	4
Malawi	16 M	9	1	AP	4
South Sudan	12 M	2	0	No Data	No Data
Tanzania	48 M	22	5	Both	4
Uganda	35 M	24	6	AP	3
Zambia	15 M	6	7	AP	4
Angola	25 M	12	4	No Data	No Data
Botswana	2.2 M	6	5	AP (9)	4
Lesotho	2.2 M	0	0	N/A	No Data
Madagascar	23 M	3	0	N/A	No Data
Mozambique	25 M	8 (10)	4	AP	4
Namibia	2.2 M	4	0	N/A	No Data
South Africa	54 M	242	78	AP	5
Swaziland	1.1 M	0	0	No Data	No Data
Zimbabwe	13 M	5	2	AP	4

(1) One resident who has had training in France and Belgium and completed 5th year in Burundi, now working in the public sector.
(2) Anatomic and cytopathology training. 13 pathologists trained in France for all or part of their residency.
(3) One pathologist currently working out of the country (Canada).
(4) Six in Lumbumbashi, only 2 continued due to lack of funds to support themselves.
(5) Anatomic and cytopathology training, started in 2016. The two active pathologists trained in France.
(6) Two Nigerian pathologists in Kumasi.
(7) Data for AP only, 5-year program. 20 training programs. Currently no foreign nationals training in Nigeria.
(8) UON has 8 part 1and 13 part 2 residents in combined AP/CP. Of the 5 who completed last year, 1returned to Rwanda, 3 in public sector in Kenya, 1in private sector in Kenya. Tuition required, 1/2 of participants pay their own tuition. AKU pays salary 4 residents per year.
(9) AP only, 4 years, will spend 6 months in South Africa, get certification with the SA College of Pathology.
(10) All who have completed residency in recent years (8) are still in Mozambique in the public sector (3 also part-time in the private sector).

For comparison, the United Kingdom has rates of around 30 per million (personal communication, Royal College of Pathology). For SSA to achieve the same level of population cover as the United Kingdom would need around an additional 27,000 pathologists!

There are no known public sector pathologists in 6 countries: Gambia, Guinea Bissau, Lesotho, Liberia, Sierra Leone and Swaziland. We were unable to obtain data on pathology in Somalia, Eritrea and Equatorial Guinea. Namibia and Botswana have no indigenous pathologists, while pathologists from Nigeria, Uganda and DRC work in other African countries. Although we have no hard data, we are aware that in smaller institutions, some staff shortages in diagnostic work and teaching are covered by non-African pathologists who come for short or long-term assignments. In contrast a larger, un-quantified number of African and African-trained pathologists are working in the United States, Europe or Canada.

Table 2 shows the change in the population, the number of pathologists and the ratio between them for the years 1990 and 2015 for the 14 countries for which we have data. For example, Ethiopia and Rwanda have shown remarkable progress (albeit from very low numbers) while Kenya and Nigeria have also shown substantial increases. It is likely that there are several reasons for this but vigorous investment in educational programmes (see below) is at least partly responsible. Most of the other countries, while increasing overall numbers of pathologists, have, at best, simply kept pace with the increase in population, while a few have lost both in absolute numbers and in population ratio. Although we did not ask about attrition rates in the survey, personal communication from pathologists in several countries suggests that it is less than 5%/ per year. However, in countries such as South Africa and Kenya with active private sector practices, 10% or more of the of residents migrate full or part time from public to private sector within the first 5 years of completing training (M. Hale personal communication).

Table 2: Changes in pathologist numbers over the past 25 years. Compares data collected in 1990 with current data.

	Population		No. of Pathologists		Pathologists Per Million		
Country	1990	2015	1990	2015	1990	2015	Change
Cote d'Ivoire	11 M	25 M	5	15	0.50	0.60	20.0%
Democratic Republic of Congo	32 M	74 M	5	15	0.20	0.20	0.0%
Ethiopia	42 M	89 M	1	55	0.02	0.60	2900.0%
Kenya	20 M	44 M	7	60	0.40	1.40	250.0%
Lesotho	1.6 M	2.2 M	1	0	0.60	0.00	-100.0%

	Population		No. of Pathologists		Pathologists Per Million		
Country	1990	2015	1990	2015	1990	2015	Change
Liberia	2.5 M	4 M	1	0	0.40	0.00	-100.0%
Malawi	7.5 M	16 M	2	9	0.30	0.60	100.0%
Nigeria	96 M	182 M	22	150	0.20	0.80	300.0%
Rwanda	6.5 M	11 M	1	7	0.20	0.60	200.0%
Republic of Congo	2 M	4.6 M	3	2	1.50	0.70	-53.3%
Tanzania	24 M	48 M	10	22	0.40	0.50	25.0%
Uganda	16 M	35 M	5	24	0.30	0.70	133.3%
Zambia	7 M	15 M	4	6	0.60	0.40	-33.3%
Zimbabwe	9 M	13 M	3	5	0.30	0.40	33.3%

Technician Numbers

All countries with pathologists have histology technicians except South Sudan. Only eighteen of 42 countries (42%) have one or more cytotechnologists. The quality of technical workforce in histology and cytology varies considerably. Some have an academic background with a laboratory science diploma or degree. Most countries have some type of certification process but the criteria are not uniform from country to country. A few institutions and private laboratories with advanced techniques for diagnosis or research such as Kenya, South Africa and Nigeria do have university-trained scientific staff but the information was not available in most responses.

Fourteen countries have technician training programs (range of 2 to 16 trainees per country, not including South Africa which trains significantly more), while others rely on on-the-job training. Only 10 countries have cytotechnology training programs.

Some research grants are now beginning to incorporate technical training, especially for special stains and immunohistochemistry (IHC). External groups provide continuing education technicians on a sporadic basis.

Although the survey did not include questions on quality assurance officers or laboratory managers, informal discussions indicate that these positions are not common in the public sector except in large institutions.

Infrastructure and Service Provision

In Figure 4 we give the number of annual diagnostic procedures performed in each country - we defined diagnostic procedures as small surgical or fine needle aspiration biopsies taken to determine diagnosis prior to therapy. South Africa reported more than 100,000 biopsies and 50,000 FNAC/B per year. Kenya reported more than 50,000 biopsies and between 5 -10,000 FNAC/B per year (combining both public and private sectors). Nigeria reported more than 25,000 biopsies and between 5-10,000 FNAC/B per year, with Uganda, Ghana and Tanzania averaging 5-10,000 biopsies and 1-5000 FNAC/B per year. Most of the other countries reported less than 5000 biopsies per year and less than 5000 FNAC/B per year. Only 5 countries reported processing more than 5000 cervical cytology smears per year with the majority processing less than 1000. As mentioned above, all these data are aggregated for the country. Table 3 shows the workload numbers for individual labs in Kenya.

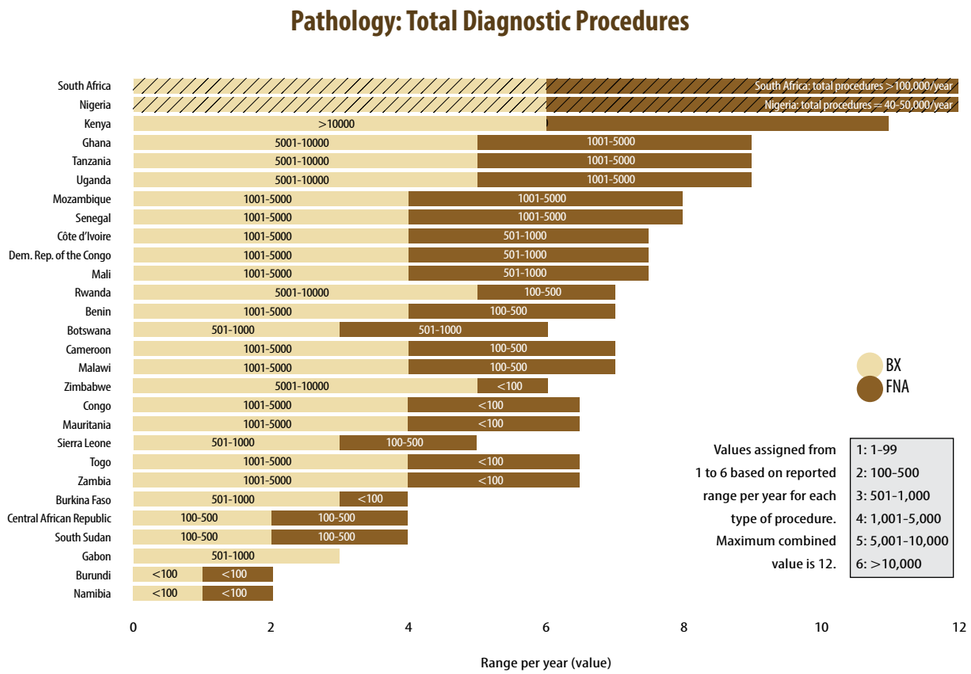

Figure 4: Number of diagnostic procedures (Surgical biopsies and Fine needle aspiration cytology/biopsy) per year, in descending order by country.

Table 3: Distribution of workload between the public and private sectors in Kenya

Name of Facility	Public/Private	Biopsies per year	FNACs
Kenyatta National Hospital	Public	6000	2400
Aga Khan Hospital	Private	18000	1200
All other hospitals	Public and faith based	7000	1000
All other hospitals	Private	10000	1000
All labs	Private	25000	4000

For comparison, the cell pathology laboratory at the Oxford University NHS Trust in the United Kingdom, which serves a population of around 3 million, had around 59,000 resections/biopsies, 39,000 cervical cytology samples and around 4,760 FNAC/B cases in 2015

We asked what proportion of patients who needed a tissue diagnosis, received such a diagnosis, Of the 23 countries responding to this question, 5 (22%) estimated that at least 50% of such patients actually received one; conversely 5 other countries reported that less than 10% of patients received one. The average turn-around-time (TAT) for small biopsies was 5 days (range 1 day to 4 weeks) and for FNAC/B was 3 days. However cases sent from outlying hospitals and clinics often had much longer turn-around-times due to delays in sending specimens and getting reports back which significantly diminish the impact of a correct diagnosis on clinical management.

While special stains for infections (Zeihl Neelson for mycobacteria, Gomori Methenamine Silver for fungi) can be done in most laboratories, immunohistochemistry (IHC), which has become the primary "stain" for cancer in high income countries, is not used for routine care, except in South Africa. Thirty percent of countries surveyed do have some antibodies available but the supply is frequently linked to research projects on lymphoma or breast cancer. Six countries reported not having any special stain capability. Molecular pathology techniques, flow cytometry, and FISH which are particularly needed to provide "precision" diagnosis in cancer are not available in the public sector except in a few tertiary centres in South Africa.

Around half the countries reported providing intra-operative cytology, with twenty-five percent of countries having a cryostat for frozen sections. However, the patient volume for frozen section is low in most hospitals.

The great majority of countries reported having autopsy provision, but most did fewer than 50 medical and 50 forensic autopsies per year. By comparison over 1200 autopsies were performed in Oxford in 2015.

Only 8 countries subscribe to quality assurance programs and over half do not have integrated laboratory information systems.

All the laboratories have at least one functioning embedding station and microtome. However, in many cases, the equipment is often inadequate, dysfunctional, and unserviceable. The lack of adequate equipment is compounded by insufficient supply of consumables such as formalin, paraffin and cassettes and other laboratory chemicals, which for most must be imported with significant delays and high import duties. Furthermore, electric and water supplies needed to operate this equipment are often unreliable so that automated equipment (present in the majority) is used in only a few countries

Private laboratories are few in number outside of South Africa and we have no data on workload, staffing and standards except for some of the Aga Khan hospitals in East Africa.

Finally, there are virtually none of the private-public partnerships, which, in Europe and America, allow manufacturers to lease their equipment.

Education / Training

Training of pathologists for Africa historically happened outside of the continent through collaborations with the United States, Canada, the United Kingdom, Europe, and Australia (Hutt et al, 1982). These programs were either scholarship based or required funding from the foreign trainee. In either case, the programs were "traditional" in that the trainee was expected to complete a full training in anatomic pathology and either pass a local or African-based examination to be licensed to practice.

As their overall medical school and health care capacity has grown, twenty-one countries in Africa have developed training programs which can train not only their own medical school graduates but accept trainees from other countries, usually for fees. The benefit of this on-continent training is that graduates more often return to their home countries (the goal), rather than staying at the site of training. The use of retention contracts as well as robust return packages for these pathologists can help in maintaining and building the workforce locally.

Several countries – Botswana, Chad, Malawi, Rwanda Tanzania, Zambia and Zimbabwe - previously sent trainees for all or partial training in neighbouring countries. Botswana, Rwanda (Mpunga et al, 2014) and Zambia have started residency training programs in the past 5 years. A major problem (which is not confined to SSA) is that less than 1% medical school graduates chose to study pathology.

These training programmes have allowed 6 countries (Ethiopia, Kenya, Malawi, Nigeria, Rwanda, and Uganda) to improve coverage. Kenya now has 1.4 pathologists per million population, but as in South Africa, a significant (see above) percentage of the workforce has migrated to the private sector full or part time.

There are only a few accrediting bodies such as the Nigerian and South African Colleges of Pathology and COPECSA (College of Pathology of East, Central and Southern Africa). External examination of residents prior to certification is often done by senior pathologists from neighbouring countries.

As a result of the above, we estimate that around 80/90 pathologists are trained each year (table 1). However, we do not know the number leaving the public sector each year due to retirement, emigration, move to the private sector, administration or NGOs, or other reasons (although this appears to be decreasing recently). If we assume an attrition rate of around 2.5% per year, then this means that around 20 pathologists (2.5% of 724) are lost each year, resulting in a net increase of around 60/70 pathologists/year. At such a rate, it will take around 400 years to achieve United Kingdom levels of population cover (there is a "shortfall" of around 27,000, but note that this "shortfall" does not take into account the expected 50% increase of the population by 2030).

Continuing Professional Development (CPD)

In the context of very limited resources for travel, of over-burdening workload and of limited access to the literature, access to CPD is one of the most frequent requests from pathologists in SSA. A number of Continuing Professional Development programmes are provided by organisations such as the International Academy of Pathology (IAP) and its divisions and the Association of Pathologists of east, central and southern Africa (APECSA), but details are difficult to collect. For many years, but in particular in the last 10 to 20 years, a number of organisations and individuals external to SSA have provided education and training opportunities in pathology, both within and external to the continent. The majority of such initiatives are the result of concerned individuals providing short term visits, usually through personal connections and undertaken during annual leave. As such, these programmes are almost inevitably unsustainable in the long term, given their personal nature. In contrast, externally-provided, inter-institutional programmes of pathology education and training are more likely to be sustainable and therefore more significant in the long term. To attempt to quantify this latter activity, we contacted 25 senior pathologists based in a broad range of charitable, academic and governmental organisations.

Although we recognize that the information probably considerably under-represents the situation, in summary, 19 external organisations were identified (although these were often highly dependent on single individual). These included 10 professional societies and 9 universities/hospitals. Eighteen African countries were involved – 3 west, 1 central, 4 east, 7 southern and 3 north east Africa, with more than 19 different African centres in these countries. No Francophone or Lusaphone country was identified.

There were around 20 separate programmes. Fifteen of the twenty programmes were research-related, but incorporated education or CPD within them. About half the programmes were confined to one country while the others extended across several countries. Sixteen were in-country programmes (e.g. over 100 attendees at a fine needle biopsy practicals) while 4 were out-of-country. Several different CPD activities and support were being provided, including courses, workshops, conferences and provision of DVDs and journals. Funding to attend international meetings was also being provided.

The Way Forward

Given the severe limitations in pathology services outlined above, it is unrealistic to expect relatively quick solutions. It will take many years to ensure reasonable coverage for the majority of the population. Undoubtedly there are numerous strategies which could and should be adopted. However, overall these strategies probably come under three main headings:

1. Advocacy
2. Collaboration
3. Innovation for improved capacity and standards

Advocacy

Advocacy is absolutely key for the future success of pathology services in SSA. The major reason for the orphan status of pathology is that it's crucial importance in the provision of good quality health care is unrecognized, resulting in a low profile, with accordingly poor resource allocation. The case for pathology must have robust data on the value of pathology clinically - getting the right diagnosis, for the right patient, at the right time, with the right outcome. It should also include analysis of the economics of pathology, not just the costs, but importantly, the socio-economic impact of poor/absent vs. adequate pathology. For instance, a wrong diagnosis results not only in wasted resources treating the wrong condition, but the patient is off work for much longer. Recently it was claimed that globally cancer costs US$2 trillion a year in direct costs and lost output (Cavalli et al, 2015). If having good pathology saved only 1% of this, it would represent a saving of US$20billion, undoubtedly far less than the cost of providing the good pathology services.

Collaboration

Given the size of the challenge, it is vital that cooperation to maximise limited resources is undertaken. Accordingly, gathering interested parties and agreeing plans jointly to address the issues is another key aspect of a long-term solution.

An initial gathering of pathologists (subsequently named African Strategies for Advancing Pathology, ASAP) in June 2014 produced a preliminary 5-year plan for a way forward for pathologists (African Strategies for Advancing Pathology Group Members, 2015). It identified 4 major strategic areas: creation of an advocacy plan; creation and support of education and training networks; definition of what is needed for an acceptable operational laboratory (including definition of standards for such a lab); and leverage of private, public, research and commercial sectors and resources to address the issues.

However ASAP is only one group and there are other parties with similar interests, including the International Academy of Pathology (and affiliated groups such as the United States and Canadian Academy of Pathology, the British Division of the IAP and IAP's African branches), the Association of Pathologists of East, Central, and Southern Africa (APECSA), the Royal College of Pathologists, the African Organization for Research and Training in Cancer (AORTIC), the American Society of Clinical Pathology, the African Society for Laboratory Medicine, Partners in Health,

Patologi oltre Frontiera, WHO, World Bank, United States CDC and United States NCI. All have active roles in either bringing pathologists together, training pathologists, or deploying pathology equipment/services.

The most important feature of success for any of these efforts is buy-in from both the Ministry of Health and the Ministry of Finance of a given country so that the strategy is implemented within the context of an overall health plan and that the financial resources are available in a sustained way to support them.

Innovation for Improved Capacity and Standards

Capacity

By this we mean increasing and optimising the number and geographic distribution of labs, the tests and functions that each lab performs and the staff within them. There are many ways in which this could be done and we highlight some important examples below.

With regard to increasing numbers of pathologists, as highlighted above, at the current rate of increase in pathologists, it will take around 400 years to achieve the same levels of population cover as in the United Kingdom. Certainly more pathologists are needed, but it is evident that simply training more pathologists to try to develop a high-income country laboratory system is totally unrealistic in the foreseeable future. Alternative models of provision are needed (see below), but for those pathologists who are trained, their role should be as much in leadership and advocacy as in service provision. There is also the vital role of liaison with clinicians particularly in deciding what tests are needed and in interpretation of the results. Furthermore their role in education of medical, scientific and technical students and staff will be crucial as this will be the basis of creating the workforce of the future.

Given the limited resources, it would be more sensible to build on the pre-existing educational programmes rather than creating a large number of new ones. Similarly encouraging sharing of resources (especially of teachers) between new and existing programmes and between existing programmes would maximize their impact. Harmonisation of curricula and mutual recognition of training programmes across countries would also increase impact.

There will have to be considerably more skill-shifting, with non-medical scientists and technical staff taking on many of the tasks of pathologists than at present. This is already happening, particularly in the non-cell pathology disciplines where, for instance, many microbiology, clinical chemistry, and virology labs in Africa are run by scientists.

There must be much greater use of cytology (cervical, non-gynaecological and fine-needle aspiration) all of which are rather patchily available in SSA. These techniques require only a slide and a stain (+/- a centrifuge for cell blocks) and can give results in a matter of an hour or so - this can address the challenge of the single encounter mentioned at the beginning of this chapter. They are also much cheaper than conventional histology and importantly, immunohistochemistry can be performed on cytology slides allowing some molecular analysis. It appears that the reason for the relative underuse is lack of training for both those taking the samples and those assessing them, so training programmes (Field et al, 2012) to address this, should be a priority.

There will also need to be much further innovation in point of care tests. These are already providing rapid results with blood and other tissue fluids and an increasing volume of such tests is reaching the market (Wu et al, 2012). However, there are problems with cost and quality control, which will need to be addressed.

In addressing the need for improvement in laboratory infrastructure, the issue is not so much the details of any specific item of equipment, but the crucial concept that all of the parts must be in place to take a piece of tissue and turn it into a diagnostic slide. One-off donations of used equipment without service contracts or accompanying hands-on training are useless across any aspect of the medicine, but especially true in pathology where each piece of equipment has different requirements (e.g., water, electricity, reagents, and tools) and can be quickly destroyed without preventative maintenance.

Beyond this, assessment of a given laboratory prior to donations can quickly identify what is missing in a laboratory to make it function well. Most often the problems are related to reagents, which are difficult to import and/or manufacture locally. However, as pathology laboratories on the continent are created and expand, the demand for these reagents should improve the flow and availability. Advocacy at the level of the Ministries of Health and Finance may help to cut delays and exempt medical supplies from significant import taxes.

Innovation in the model of pathology provision will be necessary. Currently pathology provision is largely confined to the major cities and not the rural districts where significant proportions of the population reside. Given the lack of resources this is entirely understandable. However, as travel difficulties and costs can have significant impact on a patients' willingness to engage with the health system, where possible, cancer diagnoses and treatment options (and thus pathology services) should be provided as close as possible to home.

To achieve this, one development option may involve greater numbers of hub and spoke networks; a number of lower cost, lower level/tier labs linked to a regional or national centre. For instance, a structure of basic labs in district hospitals or clinics for specimen collection, preparation and performance of a few simple tests, linked to provincial hospital labs with greater capacity and capability, which in turn are linked to a centre with a critical mass of sustainable specialist expertise. The benefits and costs of such a model should be explored. Telepathology could be part of such a model. An education network, including regional or national CPD programmes, based on this hub/spoke model would also be key in building sustainable long-term capacity. Linking such centres to other centres of excellence (north/south, south/south) to provide access to further expertise and resources would also be vital in ensuring continuing long-term development.

Standards

Obviously most of the above proposals would not only contribute to increase in capacity but also contribute towards improved standards. However there are also approaches specific to improving standards. Examples of these are given below.

Arguably the most important would be the expansion of the current system of accreditation of labs in two ways; first in the number of labs involved and second in extending the system to involve cell pathology to a much greater extent than currently exists. To date the WHO has created the Stepwise Laboratory Improvement Process Towards Accreditation (SLIPTA) in the African Region (World Health Organization, 2015). This is a check-list process by which labs can measure and subsequently improve their quality in a stepwise fashion up a 5 level scale, the highest level being commensurate with international standards. It provides a network of laboratory inspectors and monitors to provide oversight, quality assurance, and proficiency testing. Several organizations are spearheading this including the African Society of Laboratory Medicine (ASLM). In parallel, there is a similar process for Strengthening Laboratory Management Toward Accreditation (SLMTA), aimed at the lab managers (Strengthening Laboratory Management Toward Accreditation, 2015) the two processes combining to produce sustainable high quality labs. However both are largely designed for non-cell pathology labs – microbiology, clinical chemistry etc. There is a great and urgent need to produce a similar process for cell pathology labs and this should be a priority.

There are several organisations from outside SSA which accredit cell pathology labs there, but these tend to be expensive and while they can be somewhat modified to fit local circumstances, they do not have the advantageous stepwise structure which is a feature of SLIPTA.

A perhaps unexpected area of potential benefit to standards is in the development of robust IT systems. These latter have considerable ability to improve rapid communication with clinicians and patients and with other pathologists using, for instance, smart phones and tablets, thereby reducing turnaround times significantly. IT-based specimen tracking through the lab can reduce handling errors and help manage more rapid processing of cases. Furthermore, IT-based structured reporting in cell pathology (synoptic reports using datasets) can ensure that a report cannot leave the lab until all the relevant information needed for best clinical care is detailed (Ellis et al, 2016). It should also be noted that there are an increasing number of digital image analysis systems which aim to make a diagnosis based on assessment of digital images of a tissue section (He et al, 2012). If these systems achieve the abilities predicted for them, then the need for trained morphologists will become more manageable.

Creation of all of the above (especially any organizational changes) will take time but additional support is needed now. Fortunately components such as opportunities for periods of training abroad, funding/fellowships to attend international meetings and exchange programmes with centres abroad currently exist and efforts to increase these in the short term would be beneficial.

We also recognize that the above can be seen as a counsel of perfection, but it provides a framework within which improvements can be made. Furthermore as different countries are currently at different levels of development, not all of the possible solutions listed above will apply everywhere. Indeed each country and region will presumably choose to adopt those components which best suit their needs, but the key objectives for all will be to increase both capability and capacity to an appropriate level.

Conclusion

Fifty years ago, there were few African pathologists working in SSA. Pathology practice was limited to a few centres with ex-patriot specialists or samples were sent to Europe and the United States. Since that time many of the independent African nations have expanded the number of medical schools and developed medical specialty training. From that very basic starting point, pathology has improved a little.

However, although we are fully aware that the data presented in this chapter are incomplete and probably inaccurate in many ways, it is clear that there is still a massive deficit in pathology provision in the great majority of countries. In a few countries, there are some labs with a full range of services, but in most countries much of the population has almost no access to good quality, timely and appropriate services.

Addressing the issues will be a long-term project and we have suggested a variety of ways in which the problems can be tackled. However the region is a diverse collection of countries operating at a huge range of functional levels and there is no single solution that will work for all. Despite this, if use of internal and external resources is properly strategized, much progress can be made relatively quickly.

Appendix

What does it take to provide pathology services?

To have a functioning anatomic pathology lab providing histology services, a series of adequately stocked and well maintained stations are required which include the following: specimen receiving/logging, grossing, formalin to paraffin processing, embedding, microtomy, staining, and cover slipping. To provide special stains, an additional series of stations after microtomy are required based on the special stains desired. To provide immunohistochemistry, an additional set of reagents (antibodies and secondary antibodies) are required based on the immunoprofile being offered. Each station requires adequate clean fresh water and electricity, which must be uninterrupted for some pieces of equipment. A computerized laboratory management system can be overlain which tracks samples, predicts resource needs, and creates efficiency and quality control. All of these stations can be run by a qualified histotechnologist; however, for effective throughput, 2 to 3 histotechnologists per lab are required. Histotechnologist training requires a technical degree with one year or more of apprenticeship in a specialized histology training program. One pathologist, reading the slides produced by such a lab, can manage perhaps 5000 surgical specimens alone, assuming they have full mastery of all specialties (i.e., a true general expert). But anatomic pathology is a complex specialty where many different types of cancer—often subtle and with different treatments and prognoses—occur in the same organ. Thus, having two or more pathologists per laboratory allows for diversification of specialty. At a minimum, all pathologists should have a network of other pathologists on whom they can rely to share and diagnose difficult cases. Major referral centres in a given country must consider the need for a full cadre of professions.

Components of a Maximally Resource Pathology Department

Professional Staff

- Certified Anatomic and Clinical Pathologists with sub-specialty expertise
  - Surgical Pathology, Autopsy Pathology/Forensic Sciences, Cytopathology, Hematology/Coagulation, Blood Banking, Clinical Chemistry, (Microbiology), (Molecular Biology)
- PhD/MS Level Researchers
  - Clinical Chemistry, (Molecular Biology), Systems Analysts, Epidemiologists, Immunohistochemists
- Certified Lead Technologists
  - Histotechnology, Cytotechnology, Mortuary Science

Academic Teaching and Training Programme

- Medical student curriculum in anatomic and clinical pathology
  - Linked to other disciplines, case-based learning
- MMed Pathology
  - Linked to clinical research programs
- PhD Pathology/Clinical Laboratory Sciences
  - Sandwich programs/clinical research programs
- Special Courses/Continuing Medical Education
- Histotechnology training
  - 1 year certification
  - Short courses in advanced techniques (Special Stains, IHC)
- Cytotechnology training (would require several years)
  - Certification and continuing education
- Molecular Pathology
  - MMed or PhD programs
- Mortuary Sciences
  - Autopsy assistants (local and regional) and research assistants (study based specimen collection)

- Database staff
- Medical photography

Research

- Primary
  - Retrospective reviews of archives (Morphologic, epidemiologic, pathogenesis and molecular)
  - Test development/validation of diagnostic tests for relevant diseases
  - Use of medical and forensic autopsies for disease surveillance (Cause of death statistics, emerging infections, medical audit)
- Collaborative
  - Provide histopathologic or clinical laboratory diagnosis in support of clinical research studies
  - Provide case and control material for research studies from autopsy
  - Assist in development of protocols to improve quality of research

Minimum Cell Pathology Standards for Cancer Care

- Fine needle aspiration cytology and biopsy with availability of imaging facilities for deep seated lesions and sub-centimeter masses
- Specimen collection in agreed format (e.g. margins identified, appropriate fixative, etc.)
- Specimen grossing and sampling according to agreed protocols
- In addition to H&E sections, availability of agreed minimum set of special stains (including immunostains)
- Agreed synoptic/data set reports
- Agreed turn-round times which are clinically relevant
- Regular, frequent case discussion at multi-disciplinary meetings of pathologists and clinicians
- Agreed minimum staff numbers, responsibilities and training (pathologist, scientist and technical)
- Participation in CPD and EQA (both technical and medical) with a mechanism for second opinion
- Archive space for review, research and auditing of cases
- IT which provides Laboratory Information Management system (data retrieval, histo-cyto correlation, etc), links to cancer registries, external communication

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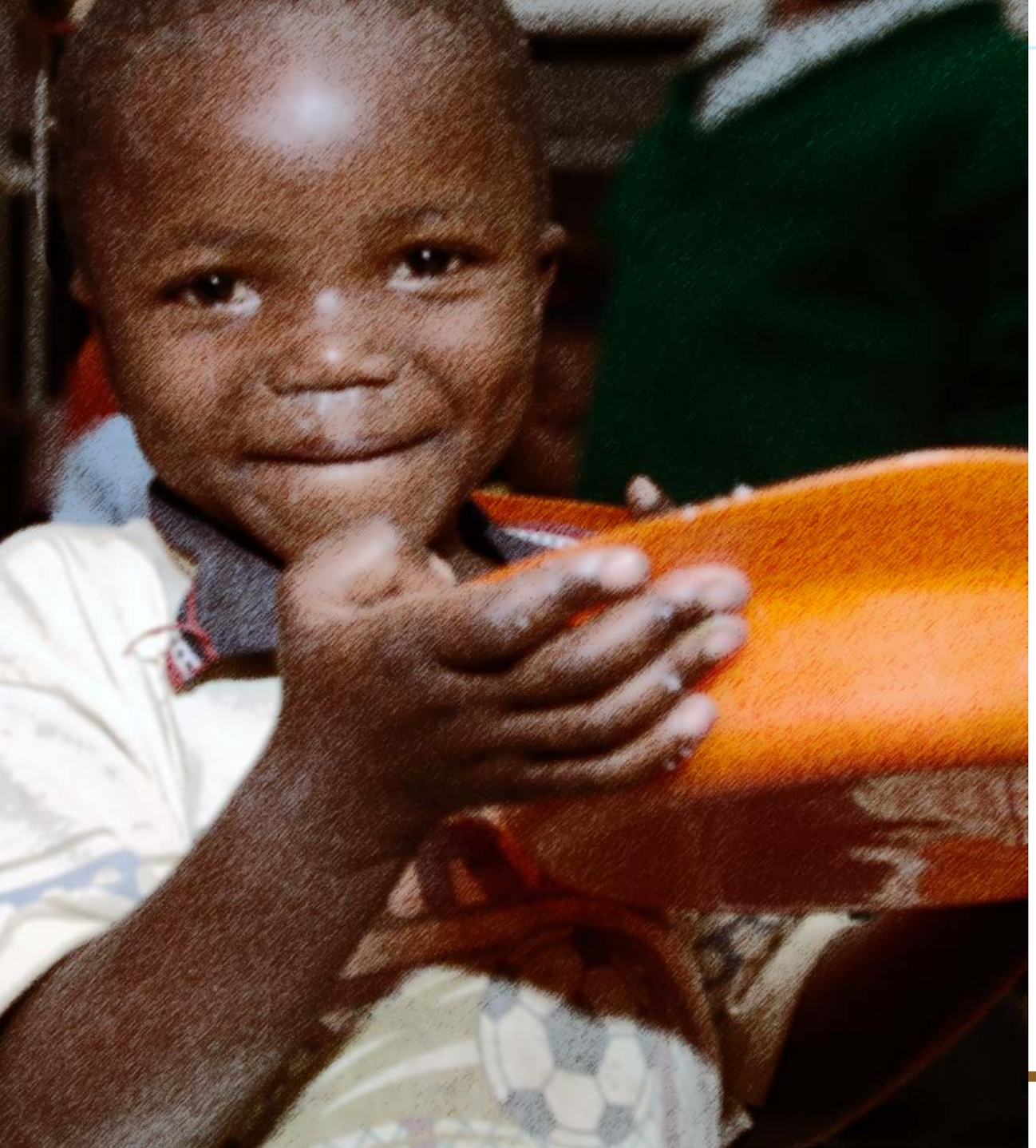

Chapter 4

Africa: Surgical Oncology Platforms

Population-Level Scale-Up of Surgical Oncology Platforms in Africa, with a Particular Focus on Women's Cancer Care

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Expanding Surgical Care for Cancer

Africa is facing an unprecedented rise in annual cancer incidence burden of nearly 70% by 2030, relative to 2010 (Bray et al, 2012). The vast majority of these malignancies will be tumours of the solid type, most of which require surgery as a key management approach across the spectrum of presentations. Women's cancers, including breast, cervical, vulvar, endometrial, and ovarian cancers, represent a substantial fraction of rising cancer rates (Bray et al, 2012). Advanced and high-intensity surgical approaches remain cornerstones of treatment of advanced stage women's cancers, and such interventions are often restricted to facilities with highly specialized workforces and well-resourced infrastructures. On the other hand, interventions for cancer prevention and control rely on the performance of relatively lower-intensity surgical procedures on healthy or minimally symptomatic individuals. Examples of such include loop electrosurgical excision procedure (LEEP) for precancerous cervical lesions, total hysterectomy for atypical endometrial hyperplasia or endometrial intraepithelial neoplasia, breast lumpectomy for ductal carcinoma in situ (DCIS), prophylactic mastectomy and salpingo-oophorectomy in cases of women with BRCA1/2 gene mutations. Quite often, if not always, such interventions are performed in contexts of, and linked to, active screening programs, since a vast majority of these conditions are only discovered through early detection efforts such as population-based screening programs or risk-based screening for well-identified familial/genetically-linked conditions.

The demand for public health cancer surgery platforms is expected to grow as the global focus on cancer prevention increases and the discovery and implementation of more accurate methods of screening results in detection of earlier stage disease. This is particularly true in low-income countries where the need for such services is rapidly increasing and efforts to develop and bring them to scale have been few (Uribe-Leitz et al, 2015). Training cadres of surgeons who can treat advanced stage disease is essential to cancer care. However, they must also be equipped

to perform the equally critical and increasing surgical interventions that prevent cancer (preventive surgery), and to become activist leaders in cancer control. This will require creative disruption of the traditional curative-focused, technologically-heavy, biomedical model of cancer surgery training. A more expanded vision will need to approach malignancies as complex disease entities that have unique social, economic, and cultural determinants, and are partially manifestations of unjust, inequitable, and dysfunctional health care systems (Confortini and Krong, 2015).

Mapping Resources to Garner Political Support and Tailor Interventions to The Local Context

A prerequisite to scaling up cancer surgery service platforms is an assessment of the specific country's cancer burden and state of cancer care. Interviews with appropriate government officials, healthcare providers and members of civil society, including patients and their families, community workers, traditional healers, tribal chiefs, etc. are critical to identifying gaps and local and national priorities. Uncovering the factors that (i) delay the decisions of patients to seek care, (ii) delay their arrival at health facilities, and (iii) delay the provision of adequate care, will provide the basis for targeting scarce resources (Thaddeus and Maine, 1994). The quantity, quality and functionality of equipment and supplies, availability of running water and electricity, access to safe blood transfusion services, chemotherapy and radiation, the presence of postoperative facilities, numbers, types and qualifications of health care personnel, are examples of the questions that should be included in the assessment (Komen Grants). The desired end result is a data-driven map of problems, gaps and needs specific to each country/region, which in turn constitutes the pathway for developing, planning, implementing, evaluating, and further modifying the surgical intervention. The accumulated information can also be used to advocate for resources and generate the political will that is needed for program expansion and sustainability.

Integrating Surgical Care for Cancer Within Existing Health Care Systems

Cancer surgery service platforms across Africa must be tailored to address the specific needs of the particular country, integrated into existing public health infrastructures, and be part of a larger effort to strengthen the public health sector's overall response to non-communicable diseases. However, the challenges of setting up disease control initiatives in low-resource settings are compounded by the fact that funding and interest are often aligned vertically, i.e., with a narrow and singular focus on a disease or aspect of a disease. On the other hand, most health related problems are multifactorial and require a broad response.

Integrating vertical initiatives within existing broad-based primary health systems, and thereby achieving horizontal synergies across several diseases and domains is critical to achieving long term success and sustainability. An example is the use of previous investments in HIV-related related diagnostic, laboratory and blood transfusion services as platforms for cancer care. The diverse subsystems of the cancer care continuum, from prevention to palliation, including access to services, procurement and distribution of medical equipment and supplies, accountability, user fees and indirect payments, must be tightly integrated across the health care system. Weaknesses in any one has cross-cutting effects on the other aspects of service delivery, leading to short term success at best. Anticipating how any new interventions will follow through, interact with, and impinge on each subsystem is thus crucial (Sterman , 2000; World Health Organisation, Mutale et al, 2013).

Essential Components of a Scale-up Effort

Building upon the few examples of surgical care scale-up in low-resource African settings, a few clear themes to inform a conceptual framework emerge (Figure 1).

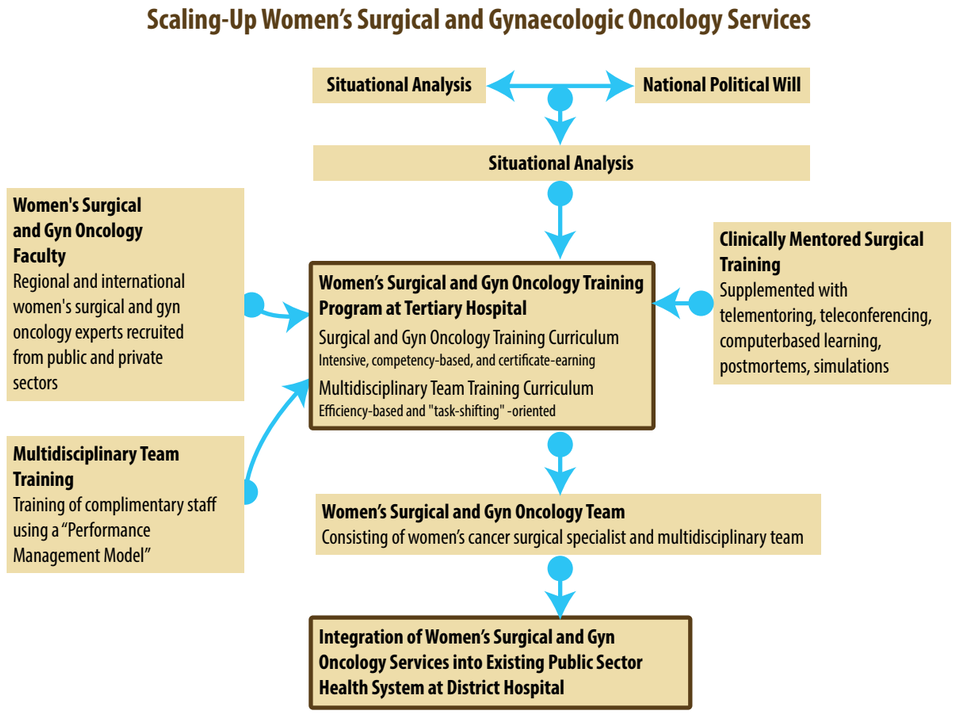


Figure 1: Conceptual Framework for Scaling-Up Women's Surgical and Gynaecologic Oncology Services in Low- and Middle-Income Countries

Start by Doing What's Best, Easiest and Most Impactful

Focusing on cancers that have the greatest burden in the population, and in which surgery has been shown to have significant impact, is a critical initial priority. Simultaneously implementing contextually-appropriate screening and early detection programs for such priority cancers, alongside the scale-up of cancer surgery service platforms, and tightly linking positive screening results to diagnostic and treatment interventions, is a necessity. Examples of such interventions in the women's cancers domain include "screen and treat" using VIA (visual inspection of the cervix using acetic acid) and cryotherapy/cold coagulation/loop electrosurgical excision procedure for cervical cancer prevention; clinical breast examination and ultrasound-guided biopsy of palpable breast masses for breast cancer early detection. Initially choosing only a few sites (and

aiming for those with the best infrastructure, adequate levels of human resources and highest burden of disease) for testing the scale-up model would facilitate success.

Select a Surgical Intervention Model that is Safe, Achievable, Resource-Appropriate and Sustainable in the Environment

It is critical to use resource-stratified guidelines and cost-effectiveness as the basis for treatment algorithms (e.g., Breast Health Guidelines International (BHGI) for breast cancer (Anderson et al, 2011) and National Comprehensive Cancer Network (NCCN) for cervical cancer (Koh et al, 2013)). Centralizing complex surgical procedures that are highly resource and infrastructure-dependent to a central training centre, and initially scaling up only the less complex surgical procedures to district hospitals will lead to a sustainable and cost-efficient approach to expansion (Figure 2). Neoadjuvant chemotherapy could facilitate operability of advanced cases of cervical and breast cancer at the district hospital level as it has the potential to reduce tumour volume and intraoperative blood loss (Osman, 2014; Mauri et al, 2005; Kehoe et al, 2015).

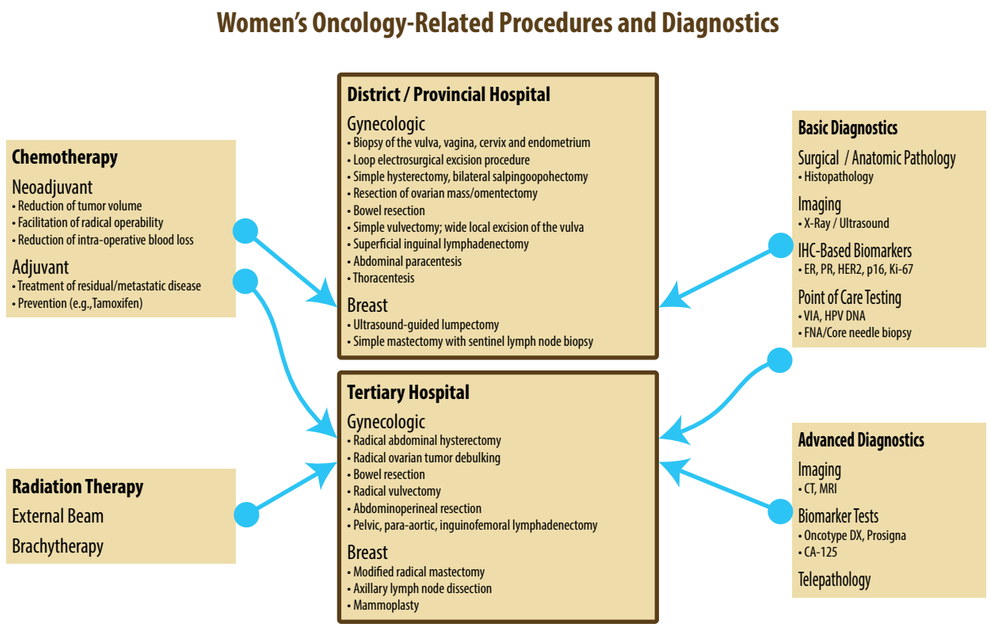


Figure 2: Stratification of women's oncology-related procedures and diagnostics by hospital level

Train Local Cadres of Women's Cancer Surgical Specialists and Multidisciplinary Care Teams

A critical component of the global response to the HIV/AIDS epidemic has been delivery of care by multidisciplinary teams (Rabkin and El-Sadr, 2015). Borrowing from this successful model, local mid/senior-level general surgeons and gynaecologists would undergo intense, competency-based training designed to produce women's cancer surgical specialists, capable of performing surgical procedures for the priority-cancers in their environment, e.g., radical abdominal hysterectomy and pelvic lymphadenectomy for cervical cancer; lumpectomy and modified radical mastectomy with axillary node dissection for breast cancer. Training would take place at a central training centre under the tutelage of surgical and gynaecologic oncology faculty. Classic bedside and intraoperative teaching could be enhanced with computer-based learning, telementoring, low-cost simulations, and post mortem anatomic dissections (if allowable) to optimize the training experience and training time (Autry et al, 2013). For remaining members of the multidisciplinary team training would be aimed at enhancing their capacity to support the delivery of surgical cancer care in district hospital settings, under the leadership of the newly trained cadres of surgeons. Core multidisciplinary team members could include obstetrician/gynaecologists, general surgeons, anaesthesiologists, pathologists, radiologists, licentiates/clinical officers, nurses, social workers, program managers, operations managers (with a specific focus on the supply chain), community educators/patient navigators. Ancillary team members could include operating room technicians, psychosocial counsellors, pharmacists, pharmacy technicians, monitoring and evaluation specialists, radiographers and pathology technicians. Following their training, the women's cancer surgical specialists and their multidisciplinary teams could be dispersed to district hospitals where they will deliver surgical cancer care in a 'hub and spoke' relationship with a central training centre. At all levels of care the importance of strong clinical leadership, professionalism and transparency, as well as an intolerance of corruption and disrespectful attitudes, must be emphasized.

Find Innovative Approaches to the Severe Shortage of Healthcare Workers

One approach to expanding women's cancer surgical care in the face of limited numbers of cancer surgical specialists is task-shifting selected responsibilities to generalist physicians and non-physicians under close guidance and monitoring. Women's cancer surgical specialists at district hospitals would be directly supported by cadres of less specialized physicians (e.g., family physicians or 'general medical officers') or physician assistants (e.g., clinical officers, licentiates) to whom well-defined clinical tasks can be redistributed, according to specific national/regional regulations and local contextual necessities (Autry et al, 2013; Chu, Ford and Trelles, 2011; Federspiel et al, 2015). Although nurses are typically not licensed to undertake surgical procedures in these settings, context specific adaptations may allow them to provide front-line surgical care for relatively low-risk surgery (e.g., biopsy of lower female genital tract lesions including loop electrosurgical excision of the cervix, biopsy of the vulva, endometrial biopsy, ultrasound-guided biopsy of palpable breast masses) after adequate training and under constant supervision. Attention should be paid to health worker satisfaction, career development, and competitive remuneration.

Harness and Incorporate Affordable Technology into the Women's Cancer Surgery Platform

The adoption of point-of-care tests that generate real-time diagnoses without the need for sophisticated laboratory platforms can greatly enhance surgical care accessibility without the need for repeat visits (a factor seen as critical for unhampered access). The use of tele-pathology for both training/mentoring as well accessing expert opinion (Parham et al, 2010), and the use of low-cost mobile-health technologies for supporting patient follow-up and community-wide education, can be vital adjuncts to the success of any surgical cancer care system. Finally, the use of key tumour markers for risk stratification and treatment decision-making (e.g., oestrogen and progesterone receptor and human epidermal growth factor receptor markers for breast cancer (Toss and Cristofanilli, 2015); CA-125 for ovarian cancer) and novel gene expression prognostic tests (e.g., Oncotype DX, Pam50 for breast cancer) to predict response to treatment are vital.

Set Up a Rigorous Process to Collect Data, Monitor and Evaluate Interim Outcomes Metrics, and Make Adaptations for Program Expansion

There is a paucity of data relative to the role of surgery in the treatment of cancer in LMICs, thus establishment of surgical cancer care databases (or an electronic medical record system) should be an integral component of any cancer care program. Several models for peer-review and integrated quality improvement systems exist and need adaptations to the low-resource context. Use of standardized checklists for surgical procedures (Haynes et al, 2009), morbidity and mortality conferences, clinical audits and the use of multidisciplinary conferences to discuss case management have all been used in high income countries to improve internal procedural quality.

Collateral Benefits of Women's Surgical Cancer Care Training

The skills acquired during women's surgical cancer care training can be leveraged to improve the care of women with genitourinary fistulae, complex non-malignant gynaecologic problems (e.g., severe endometriosis, tubo-ovarian abscesses, pelvic floor prolapse etc.) and difficult Caesarian sections, the latter a component of Safe Motherhood.

The scale-up of surgical care systems for women's cancers in low-income countries should be aligned with the overall objectives of the WHO Global Action Plan for the Prevention and Control of Noncommunicable Diseases (WHO, 2013). Implementing and scaling up surgical care services in a public health framework will help ensure they are integrated in a manner that strengthens health systems at all levels – improvement of basic infrastructure (running water, electricity, waste disposal, electronic communication), maintenance (sterilization of equipment, house-keeping), procurement and distribution of supplies (equipment and drugs, shared instruments for all surgery cases), laboratory and diagnostics (hematologic and blood chemistry, basic imaging techniques, pathology services), blood transfusion, etc. Unlike the current model focused on high-tech, expensive and protracted approaches used to train surgical subspecialists in high-income countries, training in LMICs should be resource-contextualized and aimed at the efficient production of cadres of women's cancer surgical specialists who will serve as leaders capable of competently and safely performing specific surgical oncology procedures using intensive, competency-based curricula. While international partnerships should be formed to help ensure the realization of these goals, local leaders must provide conceptual guidance to ensure contextual relevance of training activities is maintained. Multidisciplinary support teams should be trained to function efficiently as a cohesive unit. Types of surgical procedures and diagnostic services offered at tertiary and district hospitals should be resource-stratified. Rigorous monitoring and evaluation of services are mandatory, and their expansion should be facilitated using affordable technology and closely monitored task-shifting, as infrastructure and health policy permit. Scale-up should be gradual and designed to obtain early success and high impact. Advocacy, community education and involvement must be central to the effort to create health-promoting environments and reduce modifiable risk factors and underlying social determinants. Implementation science research, and monitoring and evaluation of outcomes and progress are critical.

Conclusions and Policy-Impact

The Lancet Oncology Commission into Global Cancer Surgery (Sullivan et al, 2015) and Global Surgery 2030 (Meara et al, 2015) provides the respective frameworks for building affordable, equitable, safe and sustainable cancer surgical systems across Africa. The key messages remain:

Over 80% of the 15.2 Million People Diagnosed with Cancer Worldwide in 2015 Will Need a Surgical Procedure at Some Pointin their Treatment.

The demand for cancer-related surgery is growing. By 2030 there will be an estimated to be 21.6 million cancer patients every year, of whom around 17.3 million will need surgery. 10 million of those patients needing surgery in 2030 will live in LMIC and of these about 6 million will be living in Africa. Across Africa three-quarters of the surgical burden will be from cancers of the breast, head and neck, oesophagus, stomach, lung, cervix, stomach and prostate. Overall the global surgical community in 2030 will need to deliver an estimated 45 million procedures for cancer (Africa will need some 18 million of these), and even low income countries will experience a 59% increase in need. Surgery, of which there are nearly 300 procedures needed for cancer care, is essential for prevention, diagnosis, palliation, reconstruction and cure across all age groups; 20% of children with cancer will need a surgical procedure. Surgery has one of the biggest impacts on patient outcomes, with over 50% of survival in breast cancer, for example, attributable to surgery alone. However, estimates from Global Surgery 2030 suggest that today over three-quarters of patients globally do not receive safe, affordable or timely surgery for their cancer.

Countries Are Projected To Lose 0.5 To 1.5% Of Gdp, Annually, Between Now and 2030 if Surgical Systems for Cancer are not Strengthened.

Without urgent and strategic investment in surgical services for cancer care, global economic losses from cancers amenable to surgical treatment are estimated to total US$12,120 billion by 2030. This equates to losses of 1 to 1.5% of GDP, in HIC and 0.5-1% of GDP in LMIC, annually. With 54 countries Africa stands to be one of the biggest losers without scale up. In countries where there is no universal financial risk protection against the costs of cancer surgery, a diagnosis of a surgical cancer can be financially devastating for individual patients and their families. In LMIC about a third of patients experience financial catastrophe and another quarter discontinue treatment because they cannot afford the cost. Scaling up surgical cancer services and ensuring patients are protected from catastrophic health expenditure related to accessing cancer surgery represents a sound health investment with broader implications for poverty alleviation, economic productivity and development. In Africa we estimate one year after diagnosis with cancer nearly three quarters of patients have died or experienced catastrophic expenditures, particularly on surgery. Surgical cancers have a major impact on economic output at a national level and scaling up these systems is both cost effective and affordable.

National Cancer Control Plans Must Include the Strengthening of Surgical Systems Through Investment in Public Sector Infrastructure, Education and Training.

Country studies have found a many universals around barriers to accessing safe, affordable and timely surgery for cancer. There are also many novel solutions being undertaken from which the global cancer surgery community can learn. Effective cancer surgery can only be delivered if the patient presents early enough, which requires addressing socio-cultural barriers, as well as key interdependencies in cancer surgery - imaging and pathology (both of which need very significant improvement). In the context of inequities among and within countries in terms of access to surgery services there is a serious shortage of cancer surgeons in over 82% of countries, are this is a universal feature across all African countries. There is an critical need to up-skill general surgeons to deliver basic cancer surgery and to create more surgical oncology training programmes through high quality, accredited training across a range of site-specific cancers. This is best achieved with country-specific initiatives and by

scaling up successful inter-country institutional partnerships and surgical societies, such as SSO and ESSO, global engagement. High income-African models such as Eldoret in Kenya and Indiana University (AMPATH) and intra-African models such as women's surgical oncology training led by UNC/University of Zambia. It is also essential that NCCP planning must include at its core the cancer surgical system, and this can start with building into IMPACT assessments surgical capacity and capability assessments.

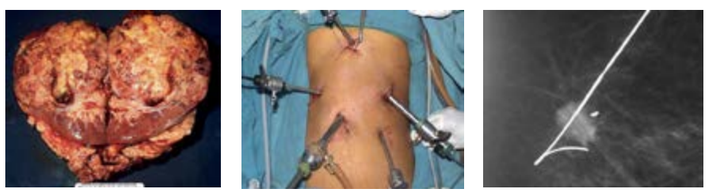
Less than 5% of Global Cancer Research is Devoted to Surgery Despite its Huge Impact on Patient Outcomes and its Importance to Personalized Cancer Medicine.

There is an urgent need to increase research funding for cancer surgery. Despite its central role in improving patient outcomes, only 1.3% of public cancer research funding goes towards cancer surgery research (in Africa this is less than 0.2%). LMIC only account for around 15% of global research in cancer surgery yet these countries urgently need to conduct their own context specific cancer surgical research. Investment in cancer surgical research has significant value for health systems as innovations not only have significant impact on patient outcomes, but they also leverage multiple other areas of cancer research critical for driving research into personalized cancer medicine.

Global Cancer Surgery Needs to be a Political Priority for Policymakers in Countries, Research Funders, International Organisations and Global Alliances.

Policymakers at all levels have low awareness of the central importance of surgery in cancer control. The political and social culture of cancer surgery is shaped by organisational, symbolic, economic, scientific, and politicians' perspectives that need to be better understood by the cancer surgical community. Cancer surgery needs to better articulate its impact and lead changes necessary for delivering safe, affordable and timely surgery to all. Lastly cancer surgery must be represented at all levels of cancer control planning and advocacy, and those institutions delivering research, training and education should be the target of ODA and philanthropic funding from major organisations (Dare et al, 2015).

Pathology Surgery Imaging



Down-staging with neo-adjuvant radio-chemotherapy

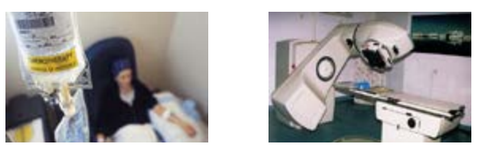


Figure 3: Cancer Surgical Trinity

Table 1: Economic losses to Africa due to lack of surgical capacity

	% loss of potential GDP in 2030	GDP loss in 2030	Cumulative GDP Loss (2015-2030)
GBD Region	Neoplasm		
North Africa and Middle East	0.367%	37,967,965,223	3.60028E+11
Eastern sub-Saharan Africa	0.489%	5,733,885,587	48691489419
Western sub-Saharan Africa	0.495%	3,529,036,620	31609787040
Central sub-Saharan Africa	0.534%	6,887,676,026	6459240952
South Asia	0.571%	74,165,928,581	6.40842E+11
Southern sub-Saharan Africa	0.574%	4,005,025,644	44093861522
Central Latin America	0.671%	32,730,099,701	3.09369E+11
Central Asia	0.673%	3,238,576,472	31557258656
Andean Latin America	0.701%	7,151,553,008	65999355867
Tropical Latin America	0.738%	23,985,817,879	2.42002E+11
Western Europe	0.751%	1.36293E+11	1.51654E+12
Caribbean	0.760%	1,263,504,726	12225499457
Southeast Asia	0.788%	43,841,468,590	3.9527E+11
Eastern Europe	0.941%	36,222,364,701	4.04651E+11
High-income North America	0.960%	2.27384E+11	2.38167E+12
Central Europe	1.006%	23,051,641,333	2.65831E+11
Australasia	1.049%	15,513,996,731	1.6275E+11
Southern Latin America	1.092%	18,104,450,126	1.83757E+11
Oceania	1.112%	63,196,5591.3	5861874801
East Asia	1.284%	4.21458E+11	3.45078E+12
High-income Asia Pacific	1.500%	1.4181E+11	1.56037E+12
Average or Total	0.696%	1.25877E+12	1.21204E+13

Table 2: Surgical rate and volume for countries with observed surgical data from African countries with data available, compared to other LMIC and high income countries

Country (year of reported surgical data)	Population in 2012	Total health expenditure per capita adjusted to 2012 US$	Annual number of operations	Total surgical rate per 100,000 population*	Total cancer surgical rate per 100,000 population
Afghanistan (2008)[1]	29,824,536	37	61,920	229	32 to 46*
Armenia (2012)[2]	2,969,081	150	123,861	4,161	-
Australia (2012)[3]	22,723,900	6,140	2,477,096	10,901	5,444
Austria (2012)[4]	8,429,991	5,407	1,178,284	13,905	
Bahrain (2012)[5]	1,317,827	895	5,1992	3,945	
Bangladesh# (2011)[6]	154,695,368	28	247,178	162	

Country (year of reported surgical data)	Population in 2012	Total health expenditure per capita adjusted to 2012 US$	Annual number of operations	Total surgical rate per 100,000 population*	Total cancer surgical rate per 100,000 population
Belgium (2012)[7]	11,128,246	4,711	1,976,833	17,764	
Bhutan (2012)[8]	741,822	90	19,954	2,690	
Bolivia (2010)[9]	1,0496,285	112	228,622	2,251	
Bulgaria (2005)[10]	7,305,888	322	398,180	5,145	
Burkina Faso (2012)[11]	16,460,141	38	54,379	330	
Canada# (2012)[12-16]	3,4754,312	5,741	2,382,956	6,778	2,561
Chad (2012)[17]	12,448,175	31	6,593	53	
China (2012)[18]	1,350,695,000	322	39,500,000	2,910	
Colombia (2012)[19]	47,704,427	530	5,108,304	10,708	
Costa Rica (2012)[20]	4,805,295	951	202,519	4,214	
Cuba (2012)[21]	11,270,957	558	539,528	4,789	
Cyprus (2011)[22]	1,128,994	2,168	29,663	2,657	
Czech Republic (2012)[23]	10,510,785	1,432	658,811	6,262	
Denmark (2007)[24]	5,591,572	6,321	892,682	16,345	
El Salvador (2009)[25]	6,297,394	244	172,972	2,797	
Estonia (2012)[26]	1,325,016	1,010	126,883	9,576	
Ethiopia# (2011)[27]	91,728,849	14	38,220	43	
Finland (2012)[28]	5,413,971	4,232	428,000	7,905	
France (2012)[7]	65,676,758	4,690	10,709,393	16,306	
Georgia (2012)[29]	4,490,700	333	189,478	4,232	
Germany (2012)[7]	80,425,823	4,683	9,802,610	12,188	
Guatemala (2012)[30]	15,082,831	226	231,288	1,533	
Hungary (2012)[7]	9,920,362	987	319,718	3,223	
Ireland (2012)[7]	4,586,897	3,708	299,335	6,526	
Israel (2012)[31]	7,910,500	2,289	400,808	5,067	
Italy (2012)[7]	59,539,717	3,032	4,118,831	6,918	
Latvia (2011)[32]	2,034,319	843	119,184	5,791	
Liberia# (2010)[33]	4,190,435	45	11,502	331	
Lithuania (2011)[34]	2,987,773	906	262,270	8,140	
Luxembourg (2012)[7]	530,946	7,452	116,452	21,933	
Mali (2009)[35]	14,853,572	48	450,260	3,321	
Malta (2012)[36]	419,455	1,835	55,501	13,232	
Mexico (2012)[37]	120,847,477	618	1,613,405	1,335	489
Myanmar (2011)[38]	52,797,319	16	337,726	650	
Nepal (2011)[39]	27,474,377	42	56,768	209	
Netherlands (2012)[7]	16,754,962	5,737	2,787,778	16,639	
New Zealand (2012)[40]	4,433,000	3,292	280,310	6,270	
Nicaragua (2010)[41]	5,991,733	118	278,874	4,594	
Oman (2012)[42]	3,314,001	690	90,804	2,740	

Country (year of reported surgical data)	Population in 2012	Total health expenditure per capita adjusted to 2012 US$	Annual number of operations	Total surgical rate per 100,000 population*	Total cancer surgical rate per 100,000 population
Peru (2011)[43]	29,987,800	289	894,243	3,020	
Poland (2012)[7]	38,535,873	854	583,957	1,515	
Portugal (2011)[44]	10,514,844	2,350	890,965	8,439	
Qatar (2009)[45]	2,050,514	1,762	29,572	1,891	
Rwanda# (2010)[46]	11,457,801	59	86,041	850	
Saudi Arabia (2012)[47]	28,287,855	795	1,002,474	3,544	
Sierra Leone (2012)[48]	5,978,727	96	24,152	400	35
Slovakia (2012)[49]	5,407,579	1,326	475,111	8,786	
Slovenia (2012)[7]	2,057,159	1,942	116,009	5,639	
South Korea (2012)[50]	50,004,441	1,703	1,709,706	3,419	
Spain (2010)[51]	46,761,264	3,056	4,657,900	10,110	
Sri Lanka (2012)[52]	20,328,000	89	579,820	2,920	
Sweden (2012)[7]	9,519,374	5,319	1,485,940	15,610	
Switzerland(2012)[7]	7,996,861	8,980	2,073,050	25,923	
Syrian Arab Republic (2010)[53]	22,399,254	105	339,825	1,578	544**
Turkey(2012)[7]	73,997,128	665	1,223,059	1,653	-
Uganda# (2011)[27]	36,345,860	42	84,874	241	-
United Kingdom (2012)[54]	63,695,687	3,647	9,732,653	15,280	6,552
United States (2007)[55]	313,873,685	8,895	36,457,210	12,087	7,480
Yemen (2012)[56]	23,852,409	71	65,114	273	-
Zambia (2010)[57]	14,075,099	79	94,145	722	266*

* Surgical rate is calculated using the total population for the year the surgical data was available.

Regional rates extrapolated to entire country.

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Chapter 5

Africa: Radiotherapy

The Role of Radiotherapy in Improving Cancer Care in Africa

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Radiotherapy is one of the main treatment modalities for cancer. This form of treatment has been used for treatment of cancer for more than 100 years (Bernier et al, 2004; Thariat et al, 2013). Shortly after the discovery of x-rays, both low-energy x-rays and radium sources were used for treatment of superficial tumours (Bernier et al, 2004). Regression of tumours was often noted, but so were radiation side effects or toxic effects. With growing experience and knowledge of the effects of radiation on normal tissues and tumours which led to the use of fractionation, careful dose calculation, and better targeting, radiotherapy has secured its place as indispensable for cancer treatment and control (Thariat et al, 2013). The invention of high energy radiotherapy, delivered by 60 Co machines and linear accelerators, the use of computers, simulators, Computer Tomography and other new imaging techniques and better clinical care have led to improved outcomes and significantly fewer side-effects.

It is well known that the benefits of radiotherapy can be optimized if it is deployed to appropriate patients, in early-stage disease, and when indicated in combination with other treatment modalities. Patients must first be identified and then assessed by multidisciplinary teams to determine the best management plan. This process starts with accurate diagnosis made after physical examination, investigation and biopsy followed by histopathological assessment. This might include immuno -histochemistry and molecular and cytogenetic testing, followed by disease staging, before establishing the overall treatment plan. Pathology and medical imaging are the mainstays of cancer diagnosis while surgery, radiotherapy, chemotherapy are the mainstay of cancer treatment. The three treatment modalities that is surgery, radiotherapy and chemotherapy are not interchangeable, but complementary.

The role of radiotherapy within the National Cancer Control Plan is well defined in the management of cancers. It is integral to the management of most cancers, including breast, lung, prostate, head and neck, and cervical cancers, which together account for more than two-fifths of cases worldwide. Radiotherapy can provide excellent local tumour control, which is not always achievable with surgery, and preserves normal form and function. For example, radiotherapy for laryngeal cancer allows larynx and hence voice conservation, an important factor contributing to quality of life and ability to return to work after treatment.

Incorporation of radiotherapy into multimodal management of breast cancer or limb sarcomas makes mastectomy or amputation unnecessary. Radiotherapy can be used alone as in early-stage prostate cancer, in which most patients are cured or in combination with surgery and chemotherapy, as in breast cancer and lung cancer. Radiotherapy can be used preoperatively to shrink tumours in order to improve their resectability, or postoperatively to eradicate residual microscopic cancer deposits in tissues surrounding the resected area. Radiotherapy is also frequently used in combination with chemotherapy.

Neoadjuvant chemotherapy is given before radiotherapy to reduce tumour volume and improve the effectiveness of radiotherapy where indicated. Concurrent chemotherapy is given in a wide range of indications to enhance the effect of radiotherapy. Adjuvant chemotherapy is used to eradicate occult distant cancer spread where radiotherapy is expected to achieve control of the local tumour mass.

Nowadays, in an era of personalized medicine, technological advances in radiotherapy make it possible for beams to be shaped and modulated to conform to the exact shape of tumours, maximizing radiation dose deposition in the cancer while sparing normal tissues from unacceptable high doses i.e. those most likely to evoke normal tissue toxic effects (Bortfeld, 2006; Jaffray et al, 2007). Radiotherapy is also a powerful instrument in palliation of symptoms associated with cancer. Modern approaches to cancer treatment frequently rely on all treatment modalities—surgery, radiotherapy, and chemotherapy, to achieve the best results with least damage. With improvement in control of metastatic disease, local tumour control is more important than ever.

In African countries, although cancer is rapidly becoming a public health crisis, the use of radiotherapy to treat patients with cancer is still limited due to lack of equipment, low cancer awareness, health-care infrastructures which are stretched to the limits due to competing priorities, high cost of cancer care, and the scarcity of radiation oncologists, medical oncologists, pathologists, surgical oncologists, and other health-care workers who are needed for cancer care. The few trained radiation oncologists and technicians who work in Africa are overwhelmed and cannot cope with the increasing demands from cancer patients.

At the moment out of the 52 African countries, only 23 offer radiotherapy (Datta et al, 2014a). South Africa and Egypt, however, account for roughly 60% of all radiation therapy resources in the continent. Ethiopia, which at the time of writing this report has one radiotherapy machine, has been estimated to need 74–85 machines to meet patient requirements (Datta et al, 2014a; Moraes et al, 2015). External beam radiotherapy is the most widely used form of radiation treatment in sub-Saharan Africa, with brachytherapy rarely used. The two types of radiotherapy machines used are cobalt-60 and linear accelerators. Cobalt-60 machines are simpler, easier to use and relatively inexpensive to acquire and maintain compared with linear accelerators, but they are not capable of complex treatment plans and have a fixed energy level and a lower percentage depth of dose. Linear accelerators can do complex and precise treatment plans with lower skin doses than cobalt-60 machines, but are relatively expensive and difficult to maintain, which may result in treatment delays. This perception is however changing rapidly as appropriately priced linear accelerators are becoming available. These Linacs can be small enough to place in old 60Co bunkers as replacement for such technology and yet be functionally of a high standard.

Figure 1: The countries in dark color have national radiotherapy facilities and are included in the summary information provided in this chapter

Brachytherapy machines can be used to treat patients with cancers such as cervical cancer. Radiotherapy is indicated for many cancers in Africa, including breast and cervical cancers (Smigielska et al, 2012). Investigators of one study conducted in Brazil estimated that 83% of patients with breast cancer should receive radiotherapy, but only10.8% actually receive it (Moraes et al, 2015). Availability of radiotherapy compliments surgical options for cancers such as breast and rectal cancers and can improve outcomes of resection.

Because of poor availability of radiotherapy services in many countries in Africa, alternative approaches have been investigated. Intra operative breast radiotherapy, for example, can address the inadequate infrastructure and poor patient compliance associated with long treatment protocols. In a study in South Africa (Shulman et al, 2014; Borras et al, 2015a), women with early breast cancers were treated with 21 Gy intraoperative radiotherapy. After 7 years of follow-up, only one patient (2.6%) had local recurrence, four (10.3%) had regional recurrences, and three (7.7%) had systemic relapses. The cost was $1300 per patient, compared with $9000 for standard external beam radiotherapy. More short-course options such as this need to be developed to optimise the use of the few resources available to most patients and health-care systems in the region.

Consideration of the complications of radiotherapy is important in discussion of its use in African countries. In a report from Nigeria in which records from 331 patients treated with radiotherapy from 2000 to 2002 were examined, 105 patients (31.7%) received a higher dose than planned and 65 patients (19•6%) received a lower dose than planned. In the report, 16 deaths (4.8%) were believed to be potentially related to the treatment. However, there are reports that this situation is improving with support from the International Atomic Energy Agency, whose approach includes support for training and infrastructure and peer review by quality assuranceteams (Samiei, 2013).

A recent addition in brachytherapy is electronic brachytherapy (EBT) which administers of high dose radiotherapy (HDR) brachytherapy without the use of radioactive isotope and with minimal shielding requirements due to the low energies utilized with the system. This means that the machine can be used in controlled settings without a specially shielded vault as required for isotope based brachytherapy machines, such as in the office of an authorized user or in an operating room. EBT uses a disposable miniature low energy (50Kv) X-ray tube into a pre-positioned applicator within body/tumour cavities or skin surfaces to rapidly deliver high doses of radiotherapy. Through the manipulation of radiation intensity and dose distribution, EBT delivers more intense therapy directly to cancer sites with minimal radiation exposure to surrounding healthy tissue. Another potential advantage includes a shorter treatment schedule. Electronic brachytherapy can be used to treat breast cancer, non-melanoma skin cancer, gynaecological and other cancers.

In this chapter we describe the role of radiotherapy within the National Cancer Control Programme in relation to medical and surgical oncology, the status of radiotherapy resources in Africa, socio-cultural aspects and Radiotherapy, the role of Government, Civic Society and Donors and argue that radiotherapy must be included in public health efforts to improve cancer care in the Africa

Introduction

The main treatment modalities for cancer are surgery, radiotherapy and chemotherapy. In developed countries such as Australia it is estimated that about half of cancer patients would benefit from radiotherapy for treatment of localized disease, local control of advanced disease, and palliation (Barton et al, 2014). In Africa this figure can be as high as 75% and above due to advanced stage disease at presentation, yet this crucial form of cancer treatment has been largely absent from the health agenda in African countries. It has over the years also continued to receive very little funding. As a result, there is an unacceptable shortfall of radiotherapy services, with more than 90% of the population in African countries lacking access to radiotherapy (Zubizarreta et al, 2015). Furthermore, the growing burden of cancer places increased demand on the already very limited radiotherapy services in Africa.

A lot has been written about the need for a comprehensive approach to population-based cancer control but very little action has been taken to improve the situation of radiotherapy in Africa. In 2011, the UN General Assembly made a resolution to address the prevention and control of non-communicable diseases(NCDs) (UN, 2011). In 2013, WHO member states agreed at the World Health Assembly to develop comprehensive NCD global monitoring framework targets to reduce by 25% relative to their 2010 levels, premature mortality from cardiovascular and chronic respiratory diseases, cancers, and diabetes by 2025 (WHO, 2012; WHO, 2013). At least 1•5 million deaths from cancer will need to be prevented each year to achieve the so-called 25 by 25 target, but global efforts to control cancer are woefully inadequate so far (Atun, 2014; Wild et al, 2014), especially in low-income and middle-income countries, which have only 5% of the resources but 80% of the global cancer burden(Farmer et al, 2010) The 25 by 25 target can only be achieved by effective preventive measures to reduce future burden of disease, and health-care systems that provide accurate diagnosis and high-quality multimodality treatment. Such multimodality treatment should include radiotherapy, surgery, drugs, and access to palliative and supportive care.

The population of Africa as shown in fig 2 is bound to grow within the next few decades in a predictable manner. With longer life expectancy being achieved from better socioeconomic conditions and control of infectious diseases in the next two decades, the population of persons over 50 years of age will significantly increase. This will, in combination with other factors, result in higher cancer incidence in the continent within that age group and that can lead to the straining of cancer treatment resources and infrastructure if not well planned for.

Since radiotherapy is perceived as a complex treatment there is a misleading assumption that its deployment in Africa is not feasible. As a result, radiotherapy is not frequently considered when planning cancer control systems in Africa. This perception is false and leads to unnecessary cancer deaths and suffering which could be avoided. Several studies have been done (Rosenblatt et al, 2015; Einck et al, 2014; Kigula-Mugambe et al, 1996; Chowdhury et al, 2013) and have shown that radiotherapy services can be effectively standardised and delivered irrespective of socioeconomic, political, and cultural context if the required set of skills, resources, and leadership, that could help develop an inclusive response, is put in place.

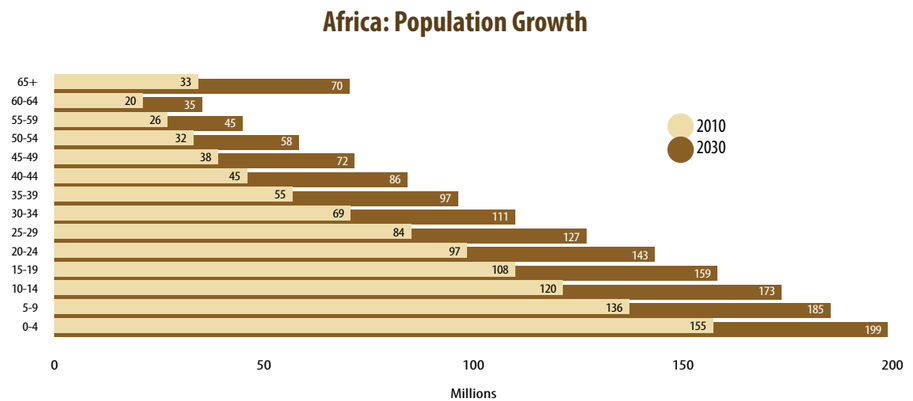

Figure 2: African population for 2010 and projected for 2030 adapted from Briefing Notes for AFDB's Long-Term Strategy

In this chapter, since investment in radiotherapy in Africa is crucial, unavoidable and an imperative, an economic case for investment in radiotherapy will be presented. This will hopefully dispel the misleading perception that deployment of radiotherapy services in Africa is not feasible.

The Role of Radiotherapy in the Management of Cancer

Currently, radiotherapy ranks with surgery as the two most important methods of curing localised cancer. Radical radiotherapy can affect cures in head and neck cancers, cancer of the cervix, prostate and early Hodgkin Disease, and also in a number of unresectable brain tumours of young people. Radiotherapy can be administered pre operatively when surgery is undertaken to preserve function, after surgery where clear excision margins cannot be achieved (adjuvant) and after debulking surgery when gross residual tumour is left behind. Radiotherapy can either facilitate surgery or consolidate surgical gains, as well as reducing local recurrence in cancers such as anal and rectal carcinomas, brain tumours, and where breast-conserving surgery has been employed for breast cancer.

Palliative radiotherapy is of value in life-threatening situations, such as profuse bleeding from a tumour, or the superior vena cava syndrome. Radiation also provides effective palliation in cases of pain secondary to bone metastasis, tumours causing bleeding or compressive syndromes, such as spinal cord compression or cerebral metastatic disease. In these circumstances radiotherapy is given as emergency treatment. A single dose fraction, or a small number of fractions, will often have an appreciable palliative effect and remove the need for protracted therapy schedules.

Although radiotherapy is a capital-intensive specialty, found only in tertiary centres, requiring high technology equipment and skilled technicians, the costs per patient treated are low if the equipment is used optimally. This is due to the fact that most of the costs are initial capital expenditure with relatively low running costs or consumables that can be easily met. For this reason it is important to realize that savings on personnel which reduce machine use, will increase the costs per patient treated to a level far beyond the savings realized.

Where radiotherapy is indicated, the patient may be treated using two broad groups of equipment: teletherapy - treatment from a distance; or brachytherapy - treatment with radioactive sources placed temporarily within body cavities or tissues. For both techniques, quality assurance is essential, with demands on imaging and medical physics services. Teletherapy is commonly administered with cobalt machines or linear accelerators. Both machines serve the same purpose and the clinical outcomes are almost identical, especially in palliative settings. The use of cobalt machines is still predominant in Africa where there is a technological lag. Cobalt machines are however said to be less expensive and more robust which may be perceived as an advantage in less developed countries even though it is not proven. The dose rate is predictable and minimal checks are required. Maintenance of machines is simple. The source should be changed at regular intervals of about 5–6 years to keep the treatment time as short as possible. There are many challenges with source changing in African countries ranging from lack of financial planning for the change to inability to dispose of the old sources. In brachytherapy the use of electronic brachytherapy (EBT) which administers of high dose radiotherapy (HDR) brachytherapy without the use of radioactive isotope and with minimal shielding requirements due to the low energies utilized with the system should be considered in Africa to avoid challenges with source change and the need for shielded rooms. The EBT machine can be used in controlled settings without a specially shielded vault as required for isotope based brachytherapy machines, such as in the office of an authorized user or in an operating room. EBT uses a disposable miniature low energy (50Kv) X-ray tube into a pre-positioned applicator within body/tumour cavities or skin surfaces to rapidly deliver high doses of radiotherapy. Through the manipulation of radiation intensity and dose distribution, EBT delivers more intense therapy directly to cancer sites with minimal radiation exposure to surrounding healthy tissue. Another potential advantage includes a shorter treatment schedule. Electronic brachytherapy can be used to treat breast cancer, non-melanoma skin cancer, gynaecological and other cancers.

Linear accelerators are generally more expensive and require sophisticated maintenance and frequent calibration, unlike the cobalt machines. The requirements for stable electrical power and water supplies are higher but achievable. In the absence of a maintenance contract, the breakdown of major components may incur significant emergency funding. The higher dose rates that linear accelerators can provide will reduce treatment times which is desirable for the patients and enabling for more patients to be treated. This equipment will also permit more exact treatment of the fields, but improved imaging, planning and immobilization are required to realize these advantages. A further advantage is the availability of electrons, which are used in about15% of all radiotherapy patients in advanced radiotherapy departments, especially for the treatment of neck nodes, sparing dose to the spinal cord and skin tumours. To ensure optimal use of teletherapy resources, extended treatment days are advantageous if population coverage is an issue. As an example, two shifts, starting at 06.00hrs extending to 20.00 hrs, have been shown to be feasible and achievable in Tanzania.

Brachytherapy may be delivered by a number of different devices: low dose rate (LDR) using caesium and high dose rate (HDR) using iridium or cobalt. LDR is predominantly confined to the treatment of cervical cancer. HDR can be used in the treatment of cervical cancer plus other cancers (for example, nasopharynx and oesophagus), reduces the need for hospital bed occupancy, but demands more expertise and has higher costs. Medium dose rate (MDR) equipment was once available but did not gain any popularity due to lack of obvious advantage over the two former forms of brachytherapy. Electronic brachytherapy (EBT) is new hence time is required to evaluate its performance and acceptability.

In planning a National Cancer Control Programme, the accessibility of radiotherapy services in the country has to be carefully considered. A single centre may suffice in small countries, or even in large countries with a small population if transport services between centres of population are adequate. In general, however, a network of oncological services will be required, with a radiotherapy centre within each region of a country. Multidisciplinary cancer management is essential for good treatment decision-making and treatment outcomes. Centres for radiotherapy treatment should therefore be ideally planned with that in mind. In all eventualities, a tumour board or multi-disciplinary clinic should define which types of patients should be referred for radiotherapy and what treatments should be instituted. For those patients living at a distance from the radiotherapy centre, funding would have to be set aside for the costs of transport. Accommodation facilities within easy reach of these facilities should ideally be made available as part of radiotherapy service provision, especially in Africa where patients travel far and spend a lot of time away from home to get these services.

The staffing needs of radiotherapy services should also be reviewed as an important part of service delivery. Where possible, training should be undertaken locally to ensure that students are trained with patients and equipment relevant to the needs of the country. Staff welfare that is holistically addressed is important in order to have motivated staff and prevent skills flight.

Radiotherapy Service Provision in Africa – Gaps and Inequities

Infrastructure

Africa is a large and diverse continent with many and diverse infrastructural needs varying from country to country. There is no one size fits all recommendation due to the variations in cancer epidemiology, cultures, socioeconomic structures and allocation/availability of resources for cancer management in the various countries. Overall African countries are burdened by different communicable diseases, nutritional concerns and vector control strategies that have hogged the limelight and reduced the realization of cancer as one of the major priorities. The situation of radiotherapy infrastructure in the continent says it all.

Generally there are no set plans for development of infrastructure, be it setting up of new radiotherapy centres, expansion to achieve adequate facilities for population size nor maintenance and replacement of existing equipment. As a result most radiotherapy infrastructure currently in use is old or poorly maintained with comparatively long machine downtime to what is considered as the norm. Access to these centres is limited by the shear inadequacy of treatment facilities, long distances that patients have to travel, long waiting lists and in some instances the cost of treatment.

It is however worth noting that there is some development in radiotherapy treatment facilities in Africa with most new well-equipped centres being set up in countries that are relatively better resourced. These are mainly in North Africa and South Africa. In countries like Tanzania, Zimbabwe and Ethiopia new radiotherapy machines have been installed or are being installed. Some centres in sub-Saharan Africa have undertaken extensive refurbishment exercises to a high standard and a few new centres have been set up there as well. There is still however a serious shortage of radiotherapy resources, both human and infrastructural. Recently the only radiotherapy machine in Uganda broke down causing untold suffering to cancer patients. On the whole radiotherapy is still not well addressed in national cancer control plans and is little understood at policy-making levels.

External Beam Equipment (Teletherapy Equipment)

Table 1 shows the status of radiotherapy treatment equipment in Africa at the end of 2015.This was obtained from self-reported information by 22 of the countries with radiotherapy facilities in the public sector. Of these 6 were from North Africa and 15 from sub-Saharan Africa with South Africa being the 22nd of these countries shown separately on this table. It is noteworthy that most of this external beam equipment is situated in North African countries and South Africa. Whilst these two sub regions are still relatively under-equipped somewhat, it is in sub-Saharan Africa that radiotherapy facilities still fall far short of expectation.

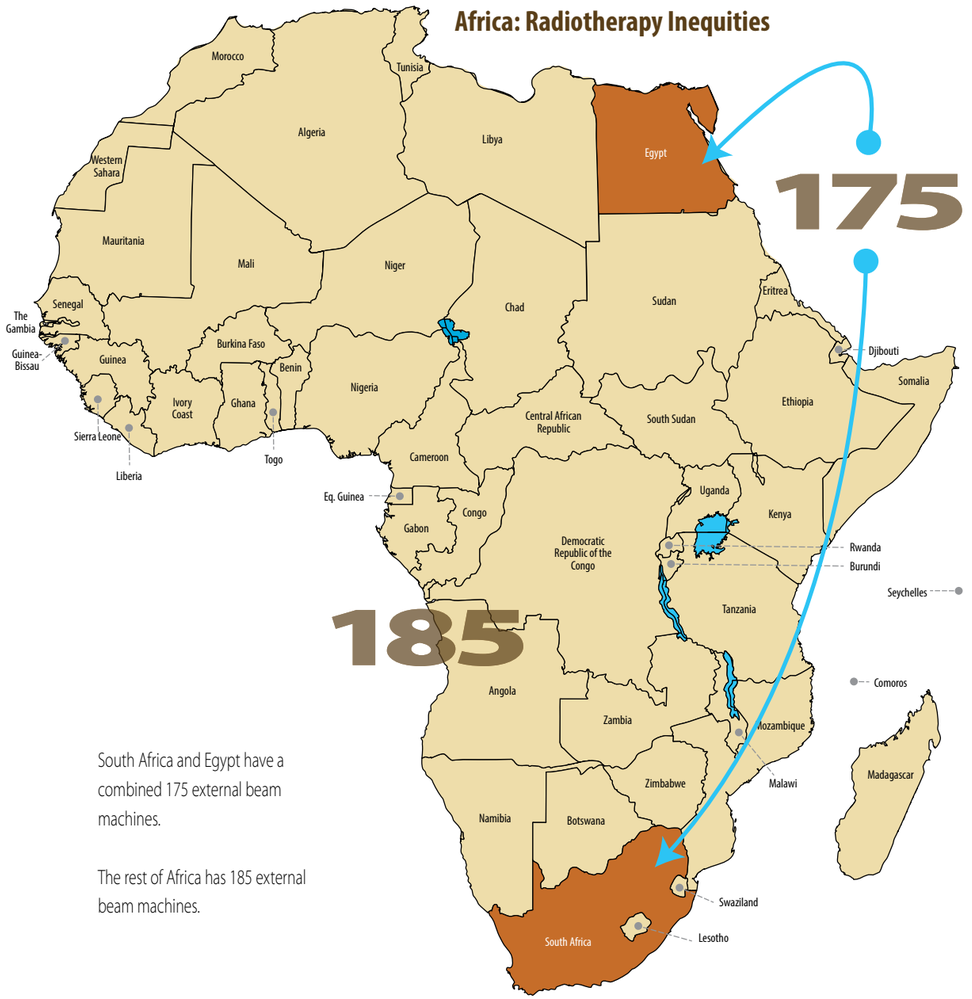

Figure 3: Inequities of Radiotherapy Equipment distribution in Africa

One indicator for radiotherapy equipment availability is the number of teletherapy or megavoltage units per million population. It is a simple calculation with limited application as it does not take into account the sophistication and utilization of the said equipment. A figure of 400 to 500 patients per treatment unit per year has been used as the acceptable standard although up to 1million patients per treatment unit per year has been considered acceptable in low to middle income countries where the number of treatment field per day may be smaller and treatment hours per day longer (Zubizarreta et al, 2015).

Table 1: External beam treatment equipment

Equipment Item	Sub-Saharan Africa (SSA)	SSA Countries Without (n=15)	North Africa (NA)	NA Countries Without (n=6)	Total SSA & NA	South Africa	Total
Linear Accelerator (LINAC)	29	5	164	0	193	81	274
Orthovoltage (kilovoltage therapy)	6	11	6	4	12	6	18
Cobalt Teletherapy Unit	28	2	37	2	65	4	102
Total	63	18	207	6	270	90	394

SSA = Sub-Saharan Countries (n=15 –South Africa excluded) NA = North African Countries (n=6)

Africa with an estimated population of 1.2 billion has only 394 teletherapy units of which 376 are megavoltage units. The best outlook would be to consider this to represent 3 million patients per treatment unit. With the knowledge of the unevenness in the distribution of equipment amongst the countries that have and more than half of the African countries going without radiotherapy facilities at all, the gravity of the situation is very apparent.

Only 16% of this vital equipment is found in sub-Saharan Africa of which over half is either orthovoltage or 60 cobalt technology. Only 2 out of 15 countries with radiotherapy facilities in this sub region do not use 60 cobalt teletherapy units at all.

North Africa has however seen a surge of growth in radiotherapy treatment capacity and technology. More than half of the teletherapy equipment is found in this sub region's 6 countries that have radiotherapy facilities. Less than a quarter of this is orthovoltage and 60 cobalt technology. Similarly South Africa has a high number of teletherapy units with the least proportion of 60 cobalt and orthovoltage units (12%) in Africa.

Utilization of this teletherapy equipment can be partly assessed by simple measures of availability of treatment planning facilities and imaging. As shown on table 2, there are a few countries in sub-Saharan Africa offering radiotherapy treatment that still do not have radiotherapy treatment planning systems and with also a few having 2 dimensional treatment planning capability only thus limited to even do forward planning. Most countries have 3 dimensional treatment planning systems but only 7 countries in the whole of Africa reported to utilize inverse planning modules of which all are in North Africa and South Africa. This shows the relative lack of IMRT usage in sub-Saharan Africa in the public sector. With current trends leading to more and more application of IMRT in radiotherapy and its benefits in sparing normal tissues whilst giving adequate dose to the tumour this situation needs to be addressed. Most published work on radiotherapy in the literature is based on the usage of IMRT as standard.

African radiation oncologists face a possibility of not being able to generate corresponding home-grown evidence-based strategies due to this technological lag.

Table 2: External beam treatment planning equipment

	RT Simulator	Dedicated CT	CT Simulation	No TPS	Only 2D TPS	3D TPS	Inverse Planning Module	SPECT /PET/ CT scanner
SSA	12	9	10	2	4	10	3	10
NA	5	5	5	0	0	6	4	5
Total	16	14	15	2	4	16	7	14

SSA = Sub-Saharan Countries (n=16 –South Africa included) NA = North African Countries (n=6)

Nuclear Medicine

The specialty of Nuclear Medicine is very closely linked to the management of cancer. In Africa a large number of nuclear medicine departments operate in radiotherapy centres of which they are part. Nuclear medicine molecular imaging employing the fluorodeoxyglucose positron emission tomography/computed tomography (FDG-PET/CT) has revolutionized the management of cancer in routine clinical service and is now a key procedure in oncological imaging. PET/CT has had a significant impact on diagnosis, treatment planning, staging, therapy, and monitoring of treatment response and has therefore played an important role in the care of cancer patients, being useful in a large number of common cancers. For cancers which do not have tracer uptake mechanisms suitable for FDG imaging, more specific tracers are used and these are in constant development.

PET/CT imaging can avoid over-treatment where lesions seen on other imaging modalities may be of doubtful significance. PET/CT may make it possible to cure cancer where it was otherwise impossible to do and to detect and effectively treat recurrent disease in a more meaningful way. There is also increasing use of therapeutic radiopharmaceuticals to treat various cancers.

All the reported PET/CT facilities in Africa are located in North and South Africa with the rest of the facilities having SPECT technology as shown on table 2. The need to expand nuclear medicine facilities in support of cancer management and upgrade to newer technologies is therefore very clearly demonstrated.

Brachytherapy

Brachytherapy using remote after loading of a single HDR source was developed in the 1970s. The use of high dose rate brachytherapy (HDR) is advocated for centres with a large number of patients to treat due to shorter treatment times. Another advantage of HDR brachytherapy is the ability to change dwell times (i.e. the time a source remains in one position) of the stepping source, which allows dose distributions that closely match the target volume. Brachytherapy is a major treatment modality in the treatment of common cancers and in Africa it is mainly used to treat cervical cancer as intracavitary treatment, a tumour of very high prevalence in the region.

Table 3 shows that 18/22 countries in Africa have adopted the HDR technology. Medium dose rate (MDR) and low dose rate (LDR) equipment is still very much in use. The increased demand for high dose rate (HDR) brachytherapy equipment has resulted mainly from the discontinuation of the limited production of low dose rate equipment. Whilst the concept of remote after loading was first introduced by Siervet in 1937 to eliminate radiation exposure to personnel, to date, a number of countries, mostly in sub-Saharan Africa are still practicing manual after loading techniques. So far electronic brachytherapy is not available in Africa.

Table 3: Available Brachytherapy Equipment Resources

Brachytherapy	SSA Countries With	SSA Without	NA Countries With	NA Without	Total
HDR after loader	13	3	5	1	18
MDR after loader	2	13	0	6	2
LDR after loader	6	9	3	3	9
Manual Brachytherapy	4	12	1	5	5
Permanent Implants	2	14	0	6	2

SSA = Sub-Saharan Countries (n=16 –South Africa included) NA = North African Countries (n=6)

Transition from 2-D to 3-D brachytherapy is still therefore not an option for most countries as the prerequisites such as access to 3-D volumetric patient imaging modalities including computed tomography and magnetic resonance are still limited. Furthermore potential benefit of implementing 3-D HDR brachytherapy needs to be balanced with the higher cost and more time consuming nature of the imaging and the 3-D treatment planning process particularly in departments that have a high throughput of patients. There is however an improvement in treatment outcome with 3-D HDR that can outweigh the disadvantages stated.

The use of permanent implants is currently not widespread in the continent and where available these are used mainly to treat early prostate cancer.

Human Resources

Quality radiotherapy delivery requires a team of dedicated, well trained staff in the fields of radiation oncology, medical physics, and radiation therapy technology and oncology nurses. The sophisticated equipment requires regular maintenance to eliminate unacceptable down time. In-house frontline service engineers have been advocated for in Africa where maintenance services are mostly poor. Flight of skills is a common occurrence in the continent with all of its consequences. This leads to a chronic inadequate capacity of well-trained staff overall but more so in the field of radiotherapy.

Table 4 shows the level of staffing in the various sub-regions of Africa. Although sub-Saharan Africa is the most affected, the continent as a whole however, falls way short of the ratios expected of staff to patient/population ratios in radiotherapy. Medical physicists have further, the issue of lack of recognition as a stand-alone profession in some countries still. This fuels flight of skills in this field where local training programs are also scarce. Oncology nursing is not yet an established nursing subspecialty in most countries and 6/22 of countries reported as having no trained oncology nurses at all.

Table 4: Human Resources in Radiotherapy

	Sub-Saharan Africa n=15	North Africa n=6	South Africa	Total n=22
Staffing				
Radiation Oncologists	149	565	150	864
Medical Physicists	67	301	115	483
RTTs/ Radiographers	229	671	500	1,400
Radiation Laboratory Technologists/ Mould- room technicians	15	83	12	110
Frontline service engineers	38	26	N/A	-
Radiation Oncology nurses	137	150	??	-
Academic Education Programs for staff:				
Radiation Oncologists	10	5	1	16
Medical Physicists	7	5	1	13
RTTs	12	4	1	17
Clinical Training programs for staff:				
Radiation Oncologists	10	3	1	14
Medical Physicists	8	3	1	12
RTTs	12	3	1	16
Compulsory CPD programs for staff:				
Radiation Oncologists	11	3	1	15
Medical Physicists	8	2	1	11
RTTs	11	2	1	14

CPD = Continuous professional development, RTT=Radiation Therapy Technologist

Development of local training programs is known to be an effective way of ensuring reasonable staff retention generally. This must not, however, be achieved by lowering standards of training if quality radiotherapy services are to be achieved. Most countries reported having academic educational or clinical training programs that will hopefully go a long way in alleviating human resource disparities in the region. This scenario was different a decade ago when most countries relied on external training of professionals. The practice of compulsory continuous professional development mirrors these training programs in that where there are no training programs, continuous professional development is not given priority.

Socio Cultural Considerations in Radiotherapy Practice in Africa

It is well known that cancers in Africa are largely diagnosed late, treatment is often not accessed nor given, there are high rates of default and poor follow up. There are many reasons for this although many socio cultural factors may come into play and in some instances be the major players. The effect of these factors may be more wide ranging than the resultant negatives mentioned. There is also a wide variation from sub region to sub region in this vast continent. It is important that the practitioner fully understands and puts measures in place to minimize negative social impact and capitalize on the strengths of positive perceptions within the local communities served in order to develop an effective radiotherapy service.

In most parts of Africa, illness is associated with pain. It can therefore be easily concluded that a painless lump, as is typical of how early cancer presents, is not associated with illness. As such, health-seeking behaviours are modified and patients tend to decline interventions for early cancers thus tipping the balance towards presentation with late stage disease.

Presenting with late stage disease can also be as a result of alternative beliefs in causation of disease such as witchcraft, whereby other forms of remedy are sought prior to visiting the hospital as a last resort. The effect is more pronounced on vulnerable groups such as minors, albinos, women and poorer members of society (See figure 4). The menace of large, unsightly malignant lesions as commonly seen in Africa needs to be addressed through extensive awareness and educational campaigns that are appropriate for the sociocultural norm of the communities that are targeted.

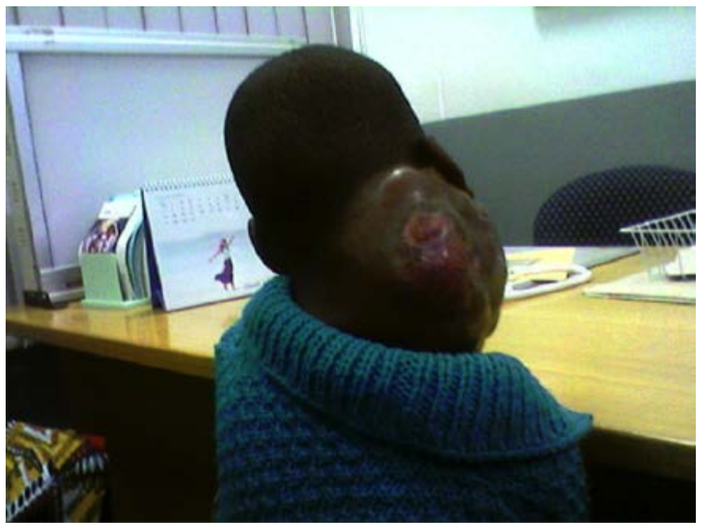

Figure 4: An excessively large lesion from rhabdomyosarcoma in a six-year-old boy presenting at a cancer treatment facility in Africa

Radiotherapy as a form of cancer treatment is not fully understood by patients and their families as well as other medical professionals who do not practice in the field. This can lead to a mystical perception of radiotherapy, which is seen as an experimental, painful, doubtful and even useless intervention in cancer management. It's naming and description in vernacular terms needs to be well thought out and clearly articulated to reduce the levels of treatment refusal and defaulting as is currently seen in some regions.

Radiotherapy is sometimes also misunderstood to be a treatment that is hot and that burns. This perception, apart from its derivation from linguistics, can be attributed to the common use of old equipment technology that has little or no skin sparing effect thus causing severe skin reactions. With patients coming from long distances to get treated and usually having hypofractionated treatments to increase throughput, the full manifestations of skin reactions may occur when the patients have been discharged and are back in the remote areas where knowledgeable

assistance is not as available. This can further the negative perception of radiotherapy within these communities. Avoidance of severe skin reactions may therefore be a case for investing in modern equipment.

The assessment of treatment outcomes is very important for each individual treatment unit and collectively as it can give an indication of the quality of service provided. There are also other good reasons of promoting good follow up strategies that are beneficial to the patients' wellbeing. Follow up of patients in Africa is generally known to be poor not just for post radiotherapy patients alone but is more marked with cancer patients. This has being ascribed to lack of transportation for the usually long journeys back to the tertiary treatment institutions. It is also linked to general poverty and inadequate communication networks. Great attention needs to be given to this, as in such circumstances outcomes of interventions cannot be evaluated for self-assessment, documentation and future planning. With increased uptake of mobile phones and the internet in Africa, these can be vehicles that can be explored to facilitate better follow up in patients treated for cancer and other diseases.

Radiotherapy as a Component of National Cancer Control Plan

It is well known that to fight cancer effectively, a cancer control approach is essential. This involves specific and coordinated activities focused around prevention, early detection, diagnosis, treatment and palliative care. Improving access, affordability, quality and delivery of all these services to cancer patients requires a multidisciplinary set of expertise that can only be made available by the government and different organizations engaged in the global fight against cancer.

It is important for African countries to understand that radiotherapy is a critical and inseparable component of comprehensive cancer treatment and care because in many of the most common cancers in African countries, radiotherapy is essential for effective treatment. Although in these countries, radiotherapy is indicated in more than half of all cases of cancer to cure localized disease, palliate symptoms, and control disease in incurable cancers, in planning and building treatment capacity for cancer, radiotherapy is frequently the last resource to be considered. Consequently, access to radiotherapy is unacceptably low in Africa. This needs to change if cancer care is to improve in Africa.

Since several studies have provided compelling evidence that investment in radiotherapy not only enables treatment of large numbers of cancer cases to save lives, and bring positive economic benefits, African countries are advised to conduct accurate assessment of the available healthcare resources and demand for radiotherapy, so as to the address the shortfall in radiotherapy services. The shortfall in radiotherapy refers to the difference between currently available radiotherapy resources and what would be needed to optimally deliver necessary radiotherapy services to patients with cancer.

In view of the variable patterns of cancer presentation and limited information on the current proportion of patients receiving radiotherapy, estimation of the exact proportion of new cancer cases that will need radiotherapy is challenging. During the past 20 years, several investigators (Borras et al, 2015a,b; Samiei, 2013; Barton et al, 2014; Delaney et al, 2005) have developed evidence-based estimates of desirable radiotherapy use on the basis of the indications for radiotherapy in clinical practice guidelines and the distribution of cancers and different stages of disease at presentation.

These estimates suggest that 50–60% of all patients with cancer will need radiotherapy. Optimum allocation of radiotherapy resources within the framework of a national cancer control plan necessitates monitoring of both the national cancer burden and the population's cancer staging, as well as determination of radiotherapy use by cancer type. Only then can resource requirements be estimated to align radiotherapy-intervention need to cancer burden effectively over time.

Although epidemiological data for worldwide incidence and distribution of cancer are available, the data are not enough because the relations between cancer burden and radiotherapy resources (services, equipment, and personnel) needed to address this burden also depends on factors such as access, levels of use, cancer stage distribution, and the nature of the required radiation treatment. In view of the factors mentioned above the following three approaches are recommended for estimating radiotherapy requirements to meet current and future needs.

Approach 1: Estimation of the Radiotherapy Services Based on the Burden of Cancer in the Country

The first approach is to find out the number of patients with cancer in need of radiotherapy and the radiation treatment resources needed based on the number of individual radiotherapy treatment visits or fractions that should be made available to the population in need of care. There are two approaches that have been used to estimate appropriate radiotherapy use. Criterion-based benchmarking (Mackillop et al, 2015) is an empirical approach, which measures the use of radiotherapy services in population groups privileged enough to have optimum access to services, delivered under optimum conditions. The rate of use in these privileged communities is used as the benchmark for optimum rate of use (Kerba et al, 2007).

The second approach is an epidemiological, evidence-based estimation approach, in which the appropriate level of radiotherapy use is estimated for radiotherapy services by using decision models underpinned by evidence-based guidelines, cancer type, and disease stage, to allocate patients to radiotherapy or no treatment (Barton et al, 2014; Delaney et al, 2005). Comparison of the two methods shows that the latter approach typically predicts higher rates of use than criterion-based benchmarking, raising questions about which approach is more reliable (Mackillop et al, 2015; Asli et al, 2014). A challenge with the criterion-based benchmarking approach is that privileged communities are not easy to define in African countries because of the lack of reliable data

Therefore the best option is to use the epidemiological, evidence-based estimation approach, because this method allows the estimation of the proportion of patients needing radiotherapy and the number of courses and fractions needed for a given population for curative and palliative indications (Wong, 2012)

The difference between evidence-based and observation based approaches is a topic of investigation, and is not unexpected in view of the many factors that affect clinical decision making and access to care. Taken together, the two approaches provide insight into the complexities of designing and ultimately achieving access to radiotherapy.

Approach 2: Estimation of Radiotherapy Services Based on Anticipated Treatment Volumes

The second approach is to translate the number of radiotherapy fractions or courses needed into resources needed to provide the radiotherapy fractions. Several rules of thumb define the number of patients or courses that can be served by one megavoltage machine or per radiotherapy professional (Slotman et al, 2005; IAEA, 2010).

A benchmark of 400–500 patients per radiotherapy treatment unit per year has been suggested for suitable machine throughput, whereas annual numbers of 200–300 patients per radiation oncologist, 300–500 per medical physicist, and 100–150 per radiation technologist have been suggested (IAEA, 2010; IAEA, 2008). There are fewer recommendations, however, for the resources needed to deliver several fractions. Although various studies (Datta et al, 2014b; Rosenblatt et al, 2013) have been done to forecast the number of radiotherapy units and personnel needed on the basis of these figures, other factors affecting resource needs should be considered when estimating required resources. The proportion

of long-course versus short-course treatments will affect the number of fractions needed, which, in combination with the level of complexity of radiotherapy used, will affect the resources needed (Dunscombe et al, 2014).

Thus, when determining investment in radiotherapy, there are many benefits associated with characterizing the demand and the work to be done in terms of delivered fractions rather than courses. To overcome the shortcomings of the guidelines used to estimate resource needs, an activity-based costing model can be used (Lievens et al, 2003). To populate the activity-based costing model, assumptions in relation to facility size and level of complexity, equipment chosen, construction costs, personnel costs, and details of the operating model (i.e., working hours and time needed by staff to do various activities are made. The value of these variables is affected by economic standards, work regulations, and the costs associated with the distance that patients have to travel to treatment facilities.

Approach 3: Estimation of Radiotherapy Services Based on International Recommendations

The International Atomic Energy Agency recommends as reasonable levels of radiotherapy services for developing countries one teletherapy machine per 1,000,000 population and for developed countries one teletherapy machine per 250,000 population. The third approach is easy to use but it does not take into account the variables within and among populations

Investments Needed to Establish Radiotherapy Services in Africa

Human Resources Development Investment

Africa has an acute shortage of health workers in general and lack of qualified staff in radiotherapy specifically. The lack of qualified staff in sufficient numbers is the main obstacle to the development of radiotherapy in Africa. A survey done by IAEA/AFRA in 2012/13 to assess the existence, number and location of education programmes for the five main radiotherapy professions revealed that most African countries had no training programmes (Ndlovu et al, 2013). It is therefore important that investments in radiotherapy education are made to get the required human resources.

Regulatory Body Investment

Radiotherapy can cause substantially harm if it is not delivered safely. Because of this, the International Atomic Energy Agency, International Commission on Radiation Units and Measurements, and National Council on Radiation Protection and Measurements (a United States national association) have been given the mandate to set safety and quality standards for the use of ionizing radiations. However, enforcement of safety and quality standards is the responsibility of national governments, which should incur the cost to establish national regulatory bodies with sufficient authority and independence to undertake assessments and inspections, enforce minimum standards, provide authorization, and issue licenses.

Regulation of occupational, medical, and public exposure to ionising radiation requires adherence to dose constraints, guideline-based therapy, and a commitment to maintaining exposures as low as reasonably achievable. Trained personnel in medical physics and physicians with medical specialization in radiation oncology must oversee this system and participate in organized quality-assurance review (Jaffray et al, 2015).

Technical Investments

The practice of modern radiotherapy requires huge investments in technology that vary substantially with the technological package that is purchased. Treatment machines and simulators typically need a reliable power supply and some degree of environmental control, including specific air-handling requirements. Treatment units that have reduced energy demands, such as Co units, address these issues but can present other challenges, including transporting and replacing the radioactive source amid increased international security and transportation concerns.

Societal Investments

Since radiotherapy is delivered as a daily treatment modality, patients have to find accommodation near the treatment facility or travel back and forth from home each day. Adequate roads, transportation, and financial support for the cost of receiving treatment away from home must be available to encourage adherence to treatment. Furthermore, access to nursing and hospital services to manage radiotherapy side effects during and after treatment is essential.

Civil Society's Investments

The role of national civil societies in engaging in awareness building, policy development, mobilizing support, expanding access, programme implementation, and education is undisputable, Global civil societies ensure that cancer is framed as an integral part of the global commitments to address NCDs and thereby engage a wider range of supporters for expanding worldwide access to radiotherapy to improve treatment outcomes for cancer. The involvement of patients with cancer is essential in the development of civil society's voice and capability. Patients are well positioned to advocate for access to high-quality services and care.

Professional Associations' Investments

Professional associations such as Africa Radiation Oncology Group (AFROG) and Africa Organization for Research and Training in Cancer (AORTIC) have an important role in expanding access to radiotherapy through education, training, setting quality standards, disseminating knowledge and evidence, and planning of human and other resource needs. There is an urgent need for the professional associations in Africa to work together more effectively to accelerate the progress in expanding access to radiotherapy.

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Chapter 6

Africa: Radiotherapy Technology

Radiotherapy Technology for Low and Middle Income Countries

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Per the World Bank, countries are divided in three categories based on gross national income (GNI). Eighty two countries (38% of the established global regulated bodies) operate with a GNI below $4,125 per capita (Nielsen, 2011). The burden inherent in such a discrepancy compared to other countries is dramatic; the highest income economies being more than three times the individual rate as the middle cohort and continue to increase rapidly. No continent suffers the global wealth distribution burden more than Africa. With Africa as the centre not simply of the vast global landscape but its economic disparity, Africa includes 51% of the world's low- and middle income countries (LMIC). Since 76% of African nations are LMIC, requiring a national focus for them on healthcare resourcing and cancer prioritisation may be short-sighted. Strategically, the demands of infrastructure are too tremendous to consider cancer care above basic health reform or development. In the presence of Ebola, basic health needs in education, vaccination, infectious disease control weigh heavily in the minds of leadership. Health infrastructure as currently operationalised is hugely subsidised via beneficiary bodies. Under these circumstances, sadly there is little room for a specialised cancer treatment like radiotherapy, with its host of requirements for a full integrated and operationalised treatment for curative intent or minimal beneficial treatment.

The basic needs for LMIC are to give food, shelter and basic health care. Unfortunately the financial burdens of many counties are so large that they cannot even afford even minimum basic health care. Cancer is treated as an incurable disease and treatment is beyond the reach for most patients due to unavailability, distance, or cost.

There is a silver lining for the United States because of its huge spending on cancer care. The American Cancer Society recently reported the death rate from cancer is falling since 1990 based on the surveillance data in men and women and in every disease site (ACS, 2015). This trend is tribute to the vast amount of resources used in developed countries to combat non-communicable diseases. In general, the *per capita* death rate in these countries also is falling linearly in other diseases such as heart disease and stroke (Ma et al, 2015).

The disparity between Radiotherapy access in high-income and LMIC has been noted by IAEA and WHO for over 2 decades through manpower and resource allocations (Levin et al, 1999; Levin et al, 2002; Tatsuzaki et al, 2001). Since Radiotherapy is capital intensive, in LMIC countries inevitably it ranks low in the list of priorities (Atun et al, 2015). However, the global disparity is so large that now most communities are trying to address this issue (Barton et al, 2006a; Barton et al, 2006b; Levin et al, 2002; Tatsuzaki et al, 2001). Several journals have devoted special issues related to global cancer health where serious concerns about the African continent are clearly explored (Atun et al, 2015; Datta et al, 2014, 2015; Jaffray et al, 2015a; Jaffray et al, 2015b) .

Lost in most of the current Radiotherapy literature is the fact that recent exciting advances in precision and personalized therapies are remarkably limited in geographic scope. To be sure, the developed world boasts remarkable technologies that encompass genomic fingerprints informing Radiotherapy (Torres-Roca, 2012) and proton and carbon ion therapy (Das et al, 2015). Overlooked is the fact that 39 of the world's 214 countries have no Radiotherapy facilities whatsoever (Zubizarreta et al, 2015). Radiotherapy is a critical component of the cancer care continuum in high-income countries where at least 40% of the patients get radiation sometimes in their care during cancer management. From a global cancer control perspective, for an entire nation to have no Radiotherapy access is simply unacceptable. Upon close examination however, there may be many reasons for this to be the case.

Infrastructure Issues

The World Bank data reveals 139 of the world's economies are LMIC (Nielsen, 2011). This equates to about 82% of the world's population: about 5 billion persons in middle-income and 850 million in low-income economies. The challenges to these nations gaining Radiotherapy access are several, including: economic, utility, healthcare, repair, and unique infrastructures. Each will be discussed in some detail below.

Economic

By "economic", we mean to include not simply a stable national currency, but the existence of some sort of state-sponsored health coverage which is vital to the population. In the absence of this, new health technology usually comes on a cash basis via private entrepreneurs. Such assets are not universally available to the population and are distributed unevenly to leadership or richer cadres. The inclusion of state supported coverage implies that high-capital items such as advanced imaging and Radiotherapy might be available on some program for all members of a population, usually accompanied by state support for its acquisition.

In many LMIC countries, widely available healthcare is available only through an uncoordinated patchwork of clinics and hospitals managed by religious and non-governmental organizations (NGO). An example is the Moi Teaching and Referral Hospital in Eldoret, Kenya, supported by AMPATH (Academic Model for the Prevention and Treatment of HIV/AIDS) (Asirwa et al, 2015). Under these circumstances, finances may be available for a cobalt machine or linear accelerator, but given the infrastructure challenges below they may not be used for that purpose.

Utilities

The most critical aspect of using any piece of high technology is stable power supply. In LMIC this is often no existent. Even in highly sophisticated infrastructure countries such as the United States, during heavy load periods in winter and summer, even national electrical grids fail to provide power to critical structures.

We have previously published that, at the Indiana University Cyclotron, one of the major contributors to downtime were power failures (Miller et al, 2012). Importantly, this not only included frank loss of power, but more problematic "brown outs", where a rapid loss and resumption of power causes circuit breakers to trip to prevent damage to sophisticated technology. During a power outage, equipment will not work because of lack of power. After a brown out—even with rapid resumption of stable power—equipment may not work because of damage to the circuitry.

Healthcare

Realistically, while cancer care is an important part of any national health plan, it is far from the most critical. Prenatal care, infant inoculations, distributed vaccinations and infectious disease control all serve as far more basic national responsibilities. Cancer control however should be a focus of a mature national healthcare priority.

Within cancer, Radiotherapy should be an early focus because of its extensive palliative properties. As any country begins to come to grip with cancer within its borders, the vast majority of patients will not be curative but palliative. Radiotherapy has an excellent capacity to palliate the pain and mass effect of primary and metastatic sites, and the cosmetic/toilet issues of skin lesions. While the transition to a national cancer focus on prevention and cure comes far in the future, even in the United States about 2/3 of all cancer patients will receive Radiotherapy during their life (https://www.astro.org/News-and-Media/Media-Resources/FAQs/Fast-Facts-About-Radiation-Therapy/Index.aspx).

Even so, Radiotherapy relies heavily on at least two other sophisticated medical practices that must simultaneously exist in the healthcare milieu. For instance, the ability to obtain and interpret tissue sample is important not simply to provide a cancer diagnosis, but also to determine the histologic type. Radiotherapy fractionation schemes for lymphoma are vastly different than for squamous cell cancers. Physicians and technicians with facility in cytologic interpretation are as important to a radiotherapy practice as are radiation therapists. Similarly, proper Radiotherapy targeting requires adequate three dimensional imaging in most cases. CT is suitable in the vast majority of cases, but even CT is unavailable in many LMIC.

Repair

In high-income countries, managing a clinic of linear accelerators (linacs) is relatively uncomplicated. Most sites have more than one unit, so if a linac breaks down for whatever reason, patients can be moved to another unit, and treatment can be completed. With the exception of catastrophic failure, maintenance agreements available within hospitals or purchased from vendors guarantee rapid repair in most locations. Preventive maintenance (PM) is well defined and based on decades of experience on thousands of identical units. Because of these favourable circumstances, uptime of linac-based oncology departments varies between 92%–98% (Bjärngard et al, 1974; Dawson et al, 1985).

Such is not the case in LMIC. Repair of such sophisticated equipment requires (a) parts and (b) expertise; neither of which are likely to be available. Even in the unlikely event of having availability of many spare parts in-country, the correct part must first be determined and then installed by workers on site. Finally, in today's sophisticated environment, spare part pipelines are assumed in most high-income countries; this is not globally true. It is unlikely that a large collection of spare linac parts are either available or readily accessible from any LMIC.

Radiotherapy-Unique

Just as surgeons require assistants facile with surgical and sterilization techniques, and medical oncologists require specially trained nurses to deliver chemotherapy, radiotherapy presumes several other professional cadres. Medical physicists are critical not simply for commissioning and

preventive maintenance on the equipment, but also for constant and time consuming quality assurance as required nationally (Klein et al, 2009), and sophisticated and complex treatment plans required by the discipline. A recent IAEA survey in Europe uncovered issues in physics or dosimetry in 10% of cases (Gershkevitsh et al, 2014); so in addition to the physics training inherent in being a medical physicist, significant experience is required as well.

Manpower issues are critical in every countries with rapidly developing Radiotherapy technologies (Mills, 2005; Mills et al, 2006), but even bleaker in LMIC countries. IAEA and WHO have been trying to train therapists, physicists and radiation oncologists via an annual program held in Trieste, however such efforts are a drop in the bucket (IAEA, 2008; IAEA Human Health Series No. 14, 2010; WHO, 2002) compared to the need. These issues are being discussed about in many editorials (Coleman et al, 2015; Coleman et al, 2014; Zietman, 2014); to date most training initiatives are with assistance from private and donor institutions from developed countries.

LINAC versus Cobalt?

Once a nation feels comfortable with the challenges inherent in a national radiotherapy presence, the next major issue is what technology to incorporate. This is not a subtle concept. Where linacs are sophisticated and complex to operate, the alternative, cobalt machines, use the gamma rays emitted from radioactive cobalt in the head of the equipment to provide therapy. The relative pros and cons of each have been reviewed several times, including recently (Page et al, 2014). Linacs are usually preferable for dosimetric precision, but cobalt treatment units may be more flexible regarding power sources, simplicity of maintenance, and ease in training.

With surgery and chemotherapy, radiotherapy plays an integral role in the management of cancer. Nearly 40% of patients in high-income countries require radiotherapy at some point in their care (IAEA, 2008). Radiation therapy is divided into 2 categories; teletherapy for broader use using external beam and brachytherapy for internal use. Brachytherapy is cheaper but has limited clinical applicability for lesions of the cervix, vagina, and oesophagus. Teletherapy machines provide the vast majority of radiotherapy usage. Various international reports discuss the planning and management part of radiotherapy in developing countries (IAEA, 2008; IAEA Human Health Series No. 14, 2010; WHO, 2002).

The first Cobalt machine was developed in Canada in 1949 using Co-60, an isotope of cobalt that emits high energy gamma rays of 1.25 MeV (Johns et al, 1983). At about the same time (1950) the linear accelerator was developed in Chicago (Johns et al, 1983). Not surprisingly, the discussion of whether to purchase a Cobalt machine or linac has been ongoing in some fashion for decades especially for LMIC countries.

The following table summarizes these points.

Table 1: Comparison between Cobalt-60 unit and Linear accelerator (LINAC) characteristics

	Cobalt-60 Unit	Linear Accelerator
What diseases are appropriate?	No limitation. If AP/PA treatment, optimum thickness <25 cm	No limitation. Any disease and any depth can be treated. No restrictions. Additionally most units come with electron beams that can be used for superficial tumours.
Duration of treatment?	Variable dose over time due to source decay. Consider source replacement in ~5 years	Dose rate is variable but does not slow over time.
Personnel & Training	2/unit; moderate training required	
	3/unit; extensive training required	
Initial Investment	~$ 800,000. Minimum installation cost.	~ $3-4,500,000 High installation and commissioning cost.
Maintenance	Minimum. Source replacement $200,000	Significant. ~ $120, 000/yr. for service contract
Stability	Highly durable; minimum, maintenance	
	Spare parts may be an issue.	
Water Supply	None	Needs clean water and 15 gal/min flow. Requires a chiller
Airborne Particulates	Minimum risk	Significant. Needs air conditioning to operate. Clean dust free environment
Security (e.g. terrorism potential)	Requires security	None

Based on the data in Table 1, a logical recommendation for LIMC can be made in favour of Cobalt units based on following:

- Cobalt unit is nearly 1/8 the cost of linear accelerator
- Maintenance cost including parts and repairs is nearly 1/10 the cost of linear accelerator
- Manpower and training is less demanding
- Uncertain power supply in most of Africa.
- Less downtime

However, there are some unique features in linac, such as multileaf collimator (MLC), electronic portal imaging (EPID), and on-board imaging (OBI) that are essential for modern and advanced treatment techniques. It is understood that palliation would be the initial need for radiotherapy in any LMIC developing a nascent cancer control program, so such sophistication may not be necessary. In such a case, Co-60 is a good choice. There are new developments in providing such tools on Co-60 thus making it suitable and cost effective treatment (Langhans et al, 2015).

Disruptive Influence and Potential for LMIC

A recent article in the Harvard Business Review is apropos to the circumstances of radiotherapy in LMIC. The discussion begins with a description of a novel wheelchair; 80% faster and 40% more efficient to propel than conventional wheelchairs, though it is manufactured from parts available at a bicycle shop. It can handle the varied terrain found in LMIC as well as being suitable for indoor use. Finally, it costs only about $250.

The background to this product is instructive for radiotherapy vendors. The problem with the current radiotherapy vendor universe is that it is very narrow (fewer than 5 large vendors), highly focused on global partners with sophisticated infrastructures. Such equipment does not well translate or transport or even exist well in countries without. It is encouraging to think what such an entrepreneurial perspective could bring to the table with 18% of the world's economies and 82% of the world's populations at risk.

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Chapter 7

Africa: Medical Oncology

Medical Oncology in Africa

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Cancer chemotherapy is a vital part of effective cancer treatment. In some diseases, among them Burkitt Lymphoma or Acute Lymphocytic Leukemia it is essential for cure. The medical oncologist uses a number of drugs to treat cancer. Often the patient will regularly receive three or four in combination over a period of months. Thirty-eight chemotherapeutic drugs and six hormones are commonly used (Table 1) to treat the common treatable cancers with high population impact (Table 2). (Shulman et al, 2016; World Health Organization, 2015) These drugs have been judged essential for good care. Unfortunately many of these drugs are commonly not available to many cancer patients in Africa.

Table 1: Essential Medicines 19th edition WHO Model List

Cytotoxic and adjuvant medicines	
all-trans retinoid acid (ATRA)	Capsule: 10 mg – acute promyelocytic leukemia
allopurinol	Tablet: 100 mg; 300 mg
asparaginase	Powder for injection: 10 000 IU in vial – acute lymphoblastic leukemia.
bendamustine	Injection: 45 mg/0.5 mL; 180 mg/2 mL – chronic lymphocytic leukemia – follicular lymphoma
bleomycin	Powder for injection: 15 mg (as sulfate) in vial – Hodgkin lymphoma – Kaposi's Sarcoma – ovarian germ cell tumour – testicular germ cell tumour

Cytotoxic and adjuvant medicines	
calcium folinate	Injection: 3 mg/ mL in 10 mL ampoule. Tablet: 15 mg – early stage colon cancer – early stage rectal cancer – gestational trophoblastic neoplasia – metastatic colorectal cancer – osteosarcoma – Burkitt lymphoma
capecitabine	Tablet: 150 mg; 500 mg – early stage colon cancer – early stage rectal cancer – metastatic breast cancer – metastatic colorectal cancer
carboplatin	Injection: 50 mg/5 mL; 150 mg/15 mL; 450 mg/45 mL; 600 mg/60 mL – early stage breast cancer – epithelial ovarian cancer – nasopharyngeal cancer – non-small cell lung cancer – osteosarcoma – retinoblastoma
chlorambucil	Tablet: 2 mg – chronic lymphocytic leukemia
cisplatin	Injection: 50 mg/50 mL; 100 mg/100 mL – cervical cancer (as a radio-sensitizer) – head and neck cancer (as a radio-sensitizer) – nasopharyngeal cancer (as a radio-sensitizer) – non-small cell lung cancer – osteosarcoma – ovarian germ cell tumour – testicular germ cell tumour
cyclophosphamide	Powder for injection: 500 mg in vial. Tablet: 25 mg – chronic lymphocytic leukemia – diffuse large B-cell lymphoma – early stage breast cancer – gestational trophoblastic neoplasia – Hodgkin lymphoma – follicular lymphoma – rhabdomyosarcoma – Ewing's Sarcoma – acute lymphoblastic leukemia – Burkitt lymphoma – metastatic breast cancer
cytarabine	Powder for injection: 100 mg in vial – acute myelogenous leukemia – acute lymphoblastic leukemia – acute promyelocytic leukemia – Burkitt lymphoma

Cytotoxic and adjuvant medicines	
dacarbazine	Powder for injection: 100 mg in vial – Hodgkin lymphoma
dactinomycin	Powder for injection: 500 micrograms in vial – gestational trophoblastic neoplasia – rhabdomyosarcoma – Wilms tumour
daunorubicin	Powder for injection: 50 mg (hydrochloride) in vial – acute myelogenous leukemia – acute promyelocytic leukemia
docetaxel	Injection: 20 mg/ mL; 40 mg/ mL – early stage breast cancer – metastatic breast cancer – metastatic prostate cancer
doxorubicin	Powder for injection: 10 mg; 50 mg (hydrochloride) in vial – diffuse large B-cell lymphoma – earlystagebreastcancer – Hodgkin lymphoma – Kaposi's Sarcoma – follicular lymphoma – metastatic breast cancer – osteosarcoma – Ewing's Sarcoma – acute lymphoblastic leukemia – Wilms tumour – Burkitt lymphoma
etoposide	Capsule: 100 mg Injection: 20 mg/ mL in 5 mL ampoule – testicular germ cell tumour – gestational trophoblastic neoplasia – Hodgkin lymphoma – non-small cell lung cancer – ovarian germ cell tumour – retinoblastoma – Ewing's Sarcoma – acute lymphoblastic leukemia – Burkitt lymphoma
fludarabine	Powder for injection: 50 mg (phosphate) in vial; Tablet: 10 mg – chronic lymphocytic leukemia.
fluorouracil	Injection: 50 mg/ mL in 5 mL ampoule – early stage breast cancer – early stage colon cancer – early stage rectal cancer – metastatic colorectal cancer – nasopharyngeal cancer

Cytotoxic and adjuvant medicines	
filgrastim	Injection: 120 micrograms/0.2 mL; 300 micrograms/0.5 mL; 480 micrograms/0.8 mL in pre-filled syringe 300 micrograms/mL in 1 mL vial, 480 mg/1.6 mL in 1.6 mL vial – As primary prophylaxis in patients at high risk for developing febrile neutropenia associated with myelotoxic chemotherapy – As secondary prophylaxis for patients who have experienced neutropenia following prior myelotoxic chemotherapy – to facilitate administration of dose dense chemotherapy regimens
gemcitabine	Powder for injection: 200 mg in vial, 1 g in vial – epithelial ovarian cancer – non-small cell lung cancer
hydroxycarbamide	Solid oral dosage form: 200 mg; 250 mg; 300 mg; 400 mg; 500 mg; 1 g – chronic myeloid leukemia.
ifosfamide	Powder for injection: 500 mg vial; 1-g vial; 2-g vial – testicular germ cell tumour – ovarian germ cell tumour – osteosarcoma – rhabdomyosarcoma – Ewing's Sarcoma
imatinib	Tablet: 100 mg; 400 mg – chronic myeloid leukemia – gastrointestinal stromal tumour
irinotecan	Injection: 40 mg/2 mL in 2 mL vial; 100 mg/5 mL in 5 mL vial; 500 mg/25 mL in 25 mL vial – metastatic colorectal cancer
mercaptopurine	Tablet: 50 mg – acute lymphoblastic leukemia – acute promyelocytic leukemia
mesna	Injection: 100 mg/ mL in 4 mL and 10 mL ampoules. Tablet: 400 mg; 600 mg – testicular germ cell tumour – ovarian germ cell tumour – osteosarcoma – rhabdomyosarcoma – Ewing's Sarcoma
methotrexate	Powder for injection: 50 mg (as sodium salt) in vial. Tablet: 2.5 mg (as sodium salt) – early stage breast cancer – gestational trophoblastic neoplasia – osteosarcoma – acute lymphoblastic leukemia – acute promyelocytic leukemia
oxaliplatin	Injection: 50 mg/10 mL in 10 mL vial; 100 mg/20 mL in 20 mL vial; 200 mg/40 mL in 40 mL vial. Powder for injection: 50 mg, 100 mg in vial – early stage colon cancer – metastatic colorectal cancer

Cytotoxic and adjuvant medicines	
paclitaxel	Powder for injection: 6 mg/ mL – epithelial ovarian cancer – early stage breast cancer – metastatic breast cancer – Kaposi's Sarcoma – nasopharyngeal cancer – non-small cell lung cancer – ovarian germ cell tumour
procarbazine	Capsule: 50 mg (as hydrochloride)
rituximab	Injection: 100 mg/10 mL in 10 mL vial; 500 mg/50 mL in 50 mL vial – diffuse large B-cell lymphoma – chronic lymphocytic leukemia – follicular lymphoma
tioguanine	Solid oral dosage form: 40 mg – acute lymphoblastic leukemia
trastuzumab	Dose form: – early stage HER2 positive breast cancer – metastatic HER2 positive breast cancer
vinblastine	Powder for injection: 10 mg (sulfate) in vial – Hodgkin lymphoma – Kaposi's Sarcoma – Testicular germ cell tumour – Ovarian germ cell tumour
vincristine	Powder for injection: 1 mg; 5 mg (sulfate) in vial – diffuse large B-cell lymphoma – gestationaltrophoblasticneoplasia – Hodgkin lymphoma – Kaposi's Sarcoma – follicular lymphoma – retinoblastoma – rhabdomyosarcoma – Ewing's Sarcoma – acute lymphoblastic leukemia – Wilms tumour – Burkitt lymphoma
vinorelbine	Injection: 10 mg/mL in 1 mL vial; 50 mg/5 mL in 5 mL vial – non-small cell lung cancer – metastatic breast cancer

Hormones and antihormones	
anastrozole	Tablet: 1 mg – early stage breast cancer – metastatic breast cancer
bicalutamide	Tablet: 50 mg – metastatic prostate cancer
dexamethasone	Injection: 4 mg/ mL in 1 mL ampoule (as disodium phosphate salt) Oral liquid: 2 mg/5 mL [c] – acute lymphoblastic leukemia
leuprorelin	Dose form – early stage breast cancer – metastatic prostate cancer
hydrocortisone	Powder for injection: 100 mg (as sodium succinate) in vial – acute lymphoblastic leukemia
methylprednisolone	Injection: 40 mg/ mL (as sodium succinate) in 1 mL single-dose vial and 5 mL multi-dose vials; 80 mg/ mL (as sodium succinate) in 1 mL single-dose vial – acute lymphoblastic leukamia

Table 2: Priority Cancers for the 19th WHO Essential Medicines List

Adult Cancers
Acute Myelogenous Leukemia
Acute Promyelocytic Leukemia
Breast Cancer, Early Stage
Breast Cancer, Metastatic
Cervical Cancer, Early Stage
Chronic Lymphocytic Leukemia
Chronic Myelogenous Leukemia
Colon Cancer, Early Stage
Colorectal Cancer, Metastatic
Epithelial Ovarian Cancer
Follicular Lymphoma
Gastrointestinal Stromal Tumor
Gestation Trophoblastic Neoplasm
Head and Neck Cancer
Hodgkin Lymphoma
Kaposi's Sarcoma
Nasopharyngeal Cancer
Non-Small Cell Lung cancer
Ovarian Germ Cell Tumors
Metastatic Prostate Cancer
Rectal Cancer, Early Stage
Testicular Germ Cell Tumors

Pediatric Cancers
Acute Lymphocytic Leukemia
Burkitt Lymphoma
Osteosarcoma
Retinoblastoma
Rhabomyosarcoma
Wilms Tumor

Indeed, the effective treatment of many cancers is multi disciplinary, requiring surgery, radiation and cancer chemotherapy. These disciplines and especially cancer chemotherapy, require many other resources for support. Among them, are pathologic and laboratory analysis for diagnosis and receptor assay, radiologic imaging for staging and assessment of response, and supportive care services such as blood banking and nutrition counseling. Supportive care takes the form of drugs including anti-emetics and antibiotics. Some important support for chemotherapy is often not readily apparent. For example, pharmacists and pharmacy technicians are needed to prepare intravenous chemotherapy drugs. Specialized equipment is also needed, for example exhaust hoods are used so that drug preparation can be done safely and infusion lines and infusion pumps are needed for drug administration.

Drugs are often not available in low income and low middle income. A pharmaceutical company invests in a medicine based on its anticipated income. There is little financial incentive to seek approval to sell drugs in many low and middle-income countries. This is especially true in African countries where one dose of a chemotherapeutic can cost more than the average individual income. Availability can be limited due a number of factors beyond cost and profitability. These include issues with a country's drug approval system, the logistics of importation and distribution and the lack of technology needed to support the use of the drug.

Some countries require an application for approval. This is a notoriously slow process in many African countries. It can often take three to four years after approval in the United States or European Union. Some countries will accept United States or European Union approval of the drug, but some require local review and a small number even require local clinical development. Local clinical development is a common requirement of the Japanese government but rare in Africa. It may become more necessary in Africa in the future as drugs become more personalized or tailored.

Drug importation is often laborious and expensive. The company often must pay the receiving country's government inspection fees. Even after drug approval, there are often importation difficulties as the importer must document the chain of custody of the drug and that it has gone through Good Manufacturing Practice. Even with this, many countries do not have the infrastructure to guarantee the quality, efficacy and safety of medicines. In a 2015 survey of the 14 countries of the Southern African Development Community (Lesotho, Swaziland, Seychelles, DRC, Angola, Malawi, Mozambique, Zambia, Botswana, Mauritius, Namibia, South Africa, Tanzania, Zimbabwe), most National Medicine Registration Authorities were unable to perform full regulatory function (dossier evaluations and registration, GMP inspection)

There are other factors that cause pharmaceuticals to be hesitant to file application. In many instances the application has proprietary data. The pharmaceutical company may not have confidence that its intellectual property will remain confidential. Also, in many cases the unlicensed drug is already available on black or gray markets. (Caudron et al, 2008) Counterfeit drugs are a serious problem. (Gautam et al, 2009)

The American or European price of many cancer medicines is unaffordable for most Africans. In many countries the drug cost (not including cost of administration) for one round of chemotherapy is more than the average individual annual income.

Gross National Income per capita is a rough estimate of average annual income for a country's citizens. It is used to classify countries as low income, lower middle income, upper middle income or high income. Most African countries are classified as low income or lower middle income. A low income country has a Gross National Income per capita less than 1,025 USD and a lower middle income country has a has a GNI per capita up to 4,035 USD. A few are categorized as upper middle income (among them: Angola, 5,300 USD; Namibia, 5,820 USD; South Africa 6,800 USD). (World Health Organization, 2016)

Country approval for sale of a drug does not mean all patients have access to medicine. It means a small number of wealthy patients will be able to pay for it in the private sector. Separate from approval, the country's Ministry of Health must adopt the drug to a national formulary of medicines in order for it to be available in the public hospitals. Many Health Ministries consider drugs on the World Health Organization Essential Medicines List for inclusion on formularies for public hospitals.

The WHO publishes the Essential Medicines Lists in an effort to improve quality of care for a number of common diseases. Essential medicines, as defined by the WHO are "those drugs that satisfy the health care needs of the majority of the population; they should therefore be available at all times in adequate amounts and in appropriate dosage forms, at a price the community can afford."

The list is updated every two years. The process of creating the list looks at the population impact of a disease as well as the efficacy of drugs on that disease. The cost and value of a drug is considered when evaluating it as is the support burden required to administer the drug. Preference is given to curative treatments and treatments that can provide palliation. An expensive adjuvant cancer therapy that increases median survival by three months and consumes many hospital resources is not weighted as high as a four-drug combination that can cure a disease.

In developing the cancer drugs for the list, the committee considers regulatory issues, supply chain management, quality assurance, training of personnel, service delivery. Cost and use scenarios are considered. Estrogen receptor testing is relatively simple and inexpensive. The drug tamoxifen and the SERMs are relatively inexpensive drugs that are quite effect in prolonging life. Erlotinib and Gefitinib for Non Small Cell Lung Cancer does prolong life, but were rejected because clinical effect is shorter, they are relatively expensive and there is a scarcity of laboratories capable of doing needed molecular essays.

Health Ministries can trust that a regulatory body has evaluated drugs on the WHO EML to assure efficacy, safety and value. (Doua et al, 2014) Inclusion on the list can provide some assurances replacing need for a formal country specific approval process. It is estimated that 90% of LMIC Health Ministries use the WHO EML to establish a national formulary and for public procurement. Factors in the decision to put a drug on a national formulary include the ability of the local health system to support use of the drug and the amount of resources the use of the drug would take from other clinical activities. In many countries drugs on the national formulary are provided at reduced cost or free of charge in public hospitals.

The EML lists the drug, its commonly used dose, and its formulation. In the case of cancer drugs, those on the EML are traceable to the type of cancer they are used to treat. Dose and schedule is important as it affects the volume estimates for national purchasing. Unfortunately, the limited number of registries and the very rough estimates of the number of cancer cases in Africa make purchase-planning difficulty.

While the EML is good for determining efficacy of a compound, most drugs on the EML are generic. The logistics of importation, storage and custody as well as assuring quality of the drug to be administered are still issues to be dealt with. (World Health Organization, 2016)

The Essential Medicines List has had impact. (t Hoen et al, 2014) It has created pressure to push drug prices downward in some diseases. Several countries have used the EML and bulk or pooled procurement in order to negotiate a lower price for drug. To our knowledge, this has not happened for a cancer drug. Several years ago, Brazil did this with the manufacturers of hepatitis C drugs. Some African countries have bulk ordered anti-retroviral drugs.

Drug companies have also been involved in the effort to make drugs affordable in low and middle income countries. Some pharmaceutical houses have used equity pricing. They have reduced wholesale prices and varied margins, so that there are different retail prices in different countries and sometimes even a public and a private market price for the same drug within country. This can mean parallel importing for the public and the private markets and can create a public relations backlash.

Another approach is for a pharmaceutical company to voluntarily license a drug to a second manufacturer where production costs are lower. The second company can then make the drug, distribute and sell it cheaper in lower income countries. Roche partnered with Emcure, of India, as a second manufacturer of a lower priced Herceptin for sale in lower income countries.

Still other companies have established compassionate use or expanded access programs in which the drug is given away. The Gleevec International Patient Assistance Program is one example. Gleevec (imatinib) has been distributed directly to more than 35,000 patients to treat chronic myelogenous leukemia, acute lymphocytic leukemia, and gastrointestinal stromal tumor in 80 countries. Novartis contracted with Axios International to qualify treatment centers and physicians and the Max Foundation to verify and screen patients for eligibility, do case management and provide patients with emotional support and education. This program has been very successful for distribution of an oral anticancer drug. It is unclear if it can be adapted to more complicated chemotherapy regimens that involve several drugs from several companies.

Even with all this activity, availability of the most essential and necessary drugs is limited in Africa. Of the nearly 600 drugs on the 2015 WHO list of essential medicines, 44 are used to treat cancer (38 chemotherapeutics and six hormones). They are listed in Table 1. The cancers considered treatable with these drugs are in Table 2. A most unsettling fact; among the 37 countries in the African region subscribing to the WHO Essential Medicines List, the median number of chemotherapeutics adapted for national formularies is 15. This means that a substantial number of cancer patients do not have legal, affordable access to very minimal anti-cancer therapies. Cancer can only be a treatable disease if the treatment is available. It is a shame that for many it is not treatable as the treatment is not available for logistical and monetary reasons.

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Chapter 8

Africa: Palliative Care

The State of Palliative Care in Africa

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As clinicians we often forget to take the public health approach as to how we are dealing with the needs of communities. Yet nowhere in the world is this more important than in the African continent where more than 50% of the patients never reach a health worker. This is the stark reality! Yet at conferences, eloquent clinicians often speak as if everyone in Africa had the same opportunities as in the more affluent countries. Thus we teach often from the books published from these advanced countries, expecting our patients to receive the same treatments. In our personal experience, but not yet documented, most cannot afford these treatments and about 80% get better without treatment anyway. Some of these patients are in the 2-3% aged over 65 of most African countries (Central Intelligence Agency, 2015). Between 10 and 20% of those prescribed treatment are unable to pay, either die or are left with terrible suffering and poor quality of life for them and their families.

"But if we zone into cancer care in Africa, surely should we be treating the felt needs of the patient throughout the disease trajectory."

In 1986, the WHO stated and repeated in 1996: "In most parts of the world, the majority of cancer patients present with advanced disease. For them the only realistic treatment is pain relief and palliative care" (WHO, 1996).

How is Africa doing here? For the 5% that reach curative therapy, we need our oncologists to realise the public health approach required for cancer patients and to be focusing on the quality of life for the patient and family, rather than carrying out painful curative therapy up to the last day of life. For the 80-90% who die at home with dreadful suffering we need improved palliative care reaching out to the communities in each country (WHO, 1986) with the backing of the oncologists and Governments.

This chapter will cover the state of palliative care (PC) in Africa by January 2016 as a starting point for a more rapid progress in improving pain control and the quality of life of cancer patients in Africa.

What is Palliative Care?

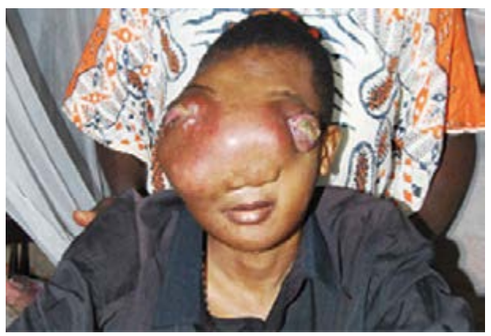
"Palliative care is an approach that improves the quality of life of patients and their families facing the problems associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual" (World Health Organization, 2002).

The reference to suffering includes physical pain but also suffering associated with end of life, including psychological, social (including economic), spiritual and cultural suffering. But these latter areas cannot be even talked about in the presence of severe physical pain. Thus the identification and relief of physical pain through the use of affordable oral morphine has now made palliative care possible in African countries. But the barriers associated with myths regarding morphine must be overcome within our health professionals and our Governments. Sadly those who impose the restrictions on morphine use, from Global to National leaders, have never visited a patient with untreated and advanced cancer trying to cope at home. Thus they cannot have the compassionate approach required, as compassion needs empathy before action.

Case Report: Sam

This is a case reported in the papers in one of our countries:

Sam is 15 years old and about to do his O levels. A year ago he noticed a problem with his left eye. A swelling came across it until he could no longer see. This spread to the right eye and has steadily grown to present size when reported on. He had been to three hospitals supported by good neighbours as he was from a very poor family.



There was only one oncology unit in the country and he lived 50 miles away. He was first referred there, but each time he went early in the morning the doctor who came would leave on the dot of 12 (for his private practice) and he would be told to come the following week. This happened five times until the person supporting them suggested trying another hospital. The second hospital referred him back to the first hospital and the whole saga began again. He never actually saw a doctor there until it was too late. He told his father: "let me just go home, this is too much".

Sam's mother earned a small amount as a carer at a school and his father was a subsistence farmer. He would take him for hospital visits. The local neighbours tried all they could to help him financially, but it was in vain, and cost a lot of money.

He eventually managed to get relief from a palliative care team. This was in one of the 20 countries presently with oral morphine and he died with palliative care workers while at home. This same story is told so many times among the poor in African countries.

Sam would be counted as among the luckier ones who reached hospital care but is the health care system letting down the poor? Are we compounding the "total suffering " described by Dame Cicely? (Saunders, 2005)

Evidence of Outcomes in Oncology vs. Palliative Care: Divided we Fall… United we Stand?

The impression we get from African countries, is that our oncologists are mainly focused on "cure". Cure is success and death is a failure. Cure is measured in the length of time a patient lives after treatment. There is little reference to quality of life. Perhaps we should re-assess our measurable outcomes.

For many years, those in palliative care have recognised that patients who receive palliative care live longer than those who do not. Once pain is relieved and their holistic needs are being met, the patient eats and sleeps better and thus lives longer with a better quality of life, and more likely to die at peace with their family, friends and their God. This is the recommended approach from WHO.

Since the first paper with proven evidence came out in 2010 (Temel et al, 2010), showing that "compared with patients receiving standard care, patients receiving early palliative care had less aggressive care at the end of life AND longer survival", several others have appeared.

One publication in Biomed Central, summarised their advice to oncologists as follows:

"Continuing chemotherapy for advanced non-small cell lung cancer (NSCLC) until very near death is associated with a decreased likelihood of receiving hospice care, but not prolonged survival. Oncologists should strive to discontinue chemotherapy as death approaches and encourage patients to enrol in hospice for better end-of-life palliative care" (Saito et al, 2011).

Two further studies in Journals of Clinical Oncology suggest that early referral to palliative care not only improves quality of life but also reduces costs (May et al, 2015; Sher, 2015). A literature review has indicated that palliative care is most frequently found to be less costly relative to comparator groups, and in most cases, the difference in cost is statistically significant (Smith et al, 2014).

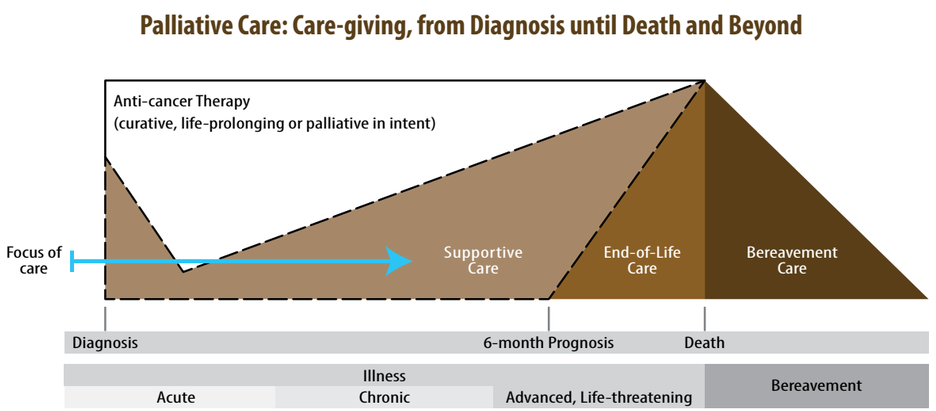


Figure 1: Different types of care-giving, from diagnosis till death, and beyond

The WHO has recommended for many years that palliative care should be introduced at diagnosis and given alongside curative/palliative treatments. Yet many African oncologists, or others using "curative" therapies, tend only to refer their patient when curative therapy has failed, if at all!

Thus affordable palliative care in Africa is particularly important as it can be given in the communities where the patients and families in Africa wish to live and die coming to the end of life (Sepulveda et al, 2003).

History of Palliative Care in the World

Palliative care, was first known as "Hospice Care" from 1967, following the opening of St Christopher's Hospice in London by Dame Cicely Saunders (Cicely Saunders International, 2016; Merriman et al, 2010) – the founder of modern palliative care (left).

There had been Hospices since the "holy woman" Fabiola (right) set up her "homes of rest" for pilgrims en route to the Holy Land in 200AD. Initially they were places of hospitality and later became the places where those who were sick could go and be looked after.

In England before the reformation, the very sick were mainly looked after by religious communities in "Hospices". At the reformation the Catholic religious Communities were disbanded and so there were no longer places to take the sick. The people begged for similar facilities and "hospitals" were commenced. The word "Hospital" came from the same root as "Hospice" but what a different approach has developed today!

The word Hospice comes from the Latin "hospitium" or the Greek "hospes" meaning hospitality. This denotes that those who come to such facilities are treated as guests. But Hospitals are far from guest houses today where patients are expected to do as they are told, and in Africa, often asked to sign themselves out if they are not compliant to doctor's orders!!

The first "Hospice for the dying" was formed in Lyon, France in the 19th century. Today this is a home for the elderly and today in France, Hospice is often understood as a home for the elderly. The hospices which subsequently developed for the very sick, chronically sick and the dying across Europe, then became places that were dreaded. Kind people tried to take care of the inmates, but those in pain had no relief. Thus holistic care was impossible for them and/or their families. Anne Merriman remembers as a medical student in Ireland in the late '50s, that we were encouraged to visit such a "hospice" and adopt one person. It was such a sad place, with a familiar smell of stale dinners and incontinence, while patients carefully wrapped up food and placed it under their mattresses in case someone else would take it, carers or other patients. It was not a happy place to be and not one that we as young medical students wanted to see our loved ones or even ourselves, ending our days!

But hope was round the corner. Dame Cicely who graduated in 1957 as a doctor, had carried out research in St Joseph's Hospice in London on the use of regularly administered oral morphine to control severe pain. This research was to prove to the world that the control of severe pain allowed those with cancer to die in peace. Later this was extended to care for any one dying of chronic or other diseases and palliative care was born, allowing people to die in peace.

But this was a Cinderella specialty and there was slow progress.

As palliative care reached each continent in turn, it was found that the word "hospice" had dreaded meanings. In Canada the Hospice was a building within walls where there was very little true care and people dreaded being admitted there. Thus Dr Balfour Mount, coined the term "palliative care" to take the place of "hospice care" so that Dame Cicely's new approach of holistic care could be embraced in this new specialty. Thus we now hear mainly about palliative care and palliative medicine. The word palliative comes from the word "pall" a Latin word meaning covering or blanket. It has been interpreted by the comfort given in all the multiple symptoms both medical, social, psychological, cultural and spiritual which are present in the critically ill and dying.

In Singapore, Hospice was related to Sago Lane, a road for the dying and the dead. It was unlucky in Chinese culture for someone to die in the house and often the house was abandoned after the death. Thus when a person was considered to be dying they were sent to a house in Sago Lane. Next door was the undertaker and after that the cemetery! The dying were not well cared for and most dreaded this place seeing it as the conveyor belt to the cemetery. When we tried to commence hospice in Singapore there was fear that we were multiplying this form of care. It was the publication of the WHO book in 1986, and the recognition that loved ones were dying in pain in Singapore when the rest of the world knew how to control it, that allowed palliative care to commence and it has since prospered.

Hospice/palliative care from the start covered all ages in need. In recent years paediatric palliative care has become a specialty in its own right and we are getting better at the care of the developing child. Palliative care is also becoming part of geriatric medicine in those countries where dying is mostly among the elderly and has been extended also to psycho geriatric medicine. Initially commenced for patients with cancer, palliative care in the west is now open to all conditions leading to the end of life. The HIV epidemic brought palliative care to infectious diseases and now is becoming a large part of care for those with non-communicable diseases.

The History of Palliative Care in Africa

Modern palliative care commenced when the pioneer Dame Cicely Saunders opened St Christopher's Hospice in London in 1967. It took 12 years to first reach Africa. Zimbabwe commenced with Island Hospice, in 1979 and South Africa commenced with St Luke's Hospice, Cape Town in 1980 (Hickman, 2009). These were then among the most affluent African countries. There was then a gap of ten years before palliative care was to take off again. This was in spite of WHO in 1986 stating that oncology would not be available to all in the resource poor countries for generations to come, and recommending that palliative care was the only affordable and humane approach to the suffering of cancer in these countries.

It was from 1990 with the opening of Nairobi Hospice in Kenya, and the inspiration derived from witnessing the terrible suffering there that inspired Hospice Africa, that palliative care began to move throughout the poorer African countries. Since then 35 African countries (out of 54) know about palliative care but only 20 of these have oral morphine and 15 affordable oral morphine. The morphine story is now part of the history of palliative care in Africa and will be discussed later.

Meanwhile other landmarks in palliative care were occurring worldwide. In 1986 the WHO produced their best seller *Cancer Pain Control* (WHO, 1986) which first discussed the role of the analgesic ladder. The following year, palliative medicine was declared a specialty under the Royal Colleges of Medicine in United Kingdom and Ireland. It took another 20 years for the United States to declare it a specialty. In Africa it is yet to be recognised as a specialty in the majority of countries.

This chapter will look at the state of palliative care in Africa in 2016 (Figures 2 and 3), its relationship to other specialties and the reason for the greater need in resource strapped countries where less than 5% of cancer patients reach oncology and 50% of Africans do not reach health services.

Figure 2: Reach of Palliative Care in Africa 2016 (Timothé Vulin)

Palliative Care: Year by Year

1979+	1990+	2000+	2010+
1979 Zimbabwe	1990 Kenya	2000 Tanzania	2010 Sudan
1980 South Africa	1992 Botswana	2001 Malawi	2011 Gabon
	1993 Botswana	2006 Nigeria	2012 Senegal
	1993 Tunisia	2006 Cameroon (anglophone)	2012 Rwanda
	1994 Sierra Leone	2006 Ghana	2013 Cameroon (francophone)
	1994 Swaziland	2006 Ethiopia	2013 Mauritius
	1994 Zambia	2007 Mozambique	2014 Guinea Conakry
	1996 Congo Brazzaville	2007 Lesotho	2015 Benin
		2008 Cote d' Ivoire	2015 Mauritania
		2009 Gambia	2015 Burundi
		2009 Democratic Republic of the Congo	
		2009 Egypt	

Figure 3: Palliative Care in Africa according to start year

How have Palliative Care Programmes Commenced in African Countries?

Palliative care has usually been commenced by an individual who is inspired by compassion. Having seen the suffering of the African families when a loved one is dying of cancer, in agony, and then having seen that something is being done in other countries, they have brought this idea back to their own country. Initially such persons were inspired from seeing St Christopher's in London where Dame Cicely had started the modern Hospice Movement. Once palliative care had moved to other continents, some were equally inspiring. However coming back to Africa, the greatest obstacle for commencing such a service was the economy. Palliative care had become expensive when compared to medical services allowances in African countries. Examples of this are seen in Nigeria, where Mrs Fatumbi, a Nurse in Lagos, visited St Christopher's Hospice, and returned to Nigeria convinced she might bring this approach to the suffering of her own people, in Lagos. But not only was there no funds, but there was huge opposition to having available opioids or other medications for severe pain. Thus the only patients that she could help were those who returned from treatment in other countries brining their own supply of medications. Some died before medications ran out but others survived beyond the medications and were thrown back into pain.

This experience was repeated as others returned to their countries and realised without funds the United Kingdom or United States model would not work for them either.

Since affordable oral morphine came in and it was possible to create an affordable African model, palliative care is being taken up by many non-governmental organisations (NGOs) supported by governments with policy, but very few with any funding or material support. Uganda, the only country to give free oral morphine and to allow nurses trained in palliative care to become prescribers of morphine, provides encouragement for other countries now taking up the WHO resolution of 2016.

Since 2000, more countries have come forward with a Champion wishing to commence palliative care in their own country and sometimes their own village! Most are not trained in palliative care and need to attend at least the initiators course (International Programmes, HAU) to grasp the multifactorial aspects of this new specialty and carrying it out within their own economy and culture.

How African Services are Started so far

Palliative care commences with the first patient seen and helped holistically, and not with the Government policy. Government policies are important, but they should arise from the knowledge of the needs of patients in that country rather than Government officials. No patient should be allowed to suffer while awaiting a policy. We must all be prepared to learn from our patients!

Some have started by one person with no previous knowledge but have witnessed good palliative care (Figure 8). Others have commenced with inspiration and experience and helped others. Some have been in palliative care and others in other cancer or non-cancer specialities.

- Right: A volunteer prepares to visit a patient
- Left: Typical slum in an African city where volunteers and palliative care teams go to care

In particular anaesthetists who have been involved in pain clinics and post-operative pain and concerned over the lack of pain control, have become involved and are doing very well. This is particularly well in Nigeria.

These are some of the prerequisites for palliative care initiation:

Inspiration

Inspiration to inflame fire in the belly: it is recommended that palliative care commences with someone already trained in palliative care. However seeing the different ways a service has commenced in African countries, we can see that many times a person, with compassion for the suffering seen among cancer/AIDS or other patients has stirred or inspired them to support the commencement of a service to prevent/treat suffering in their own country.

The Public Health Approach

It is useful to have knowledge of the pillars of the public Health approach needed for a new service. These are drug availability (the first priority especially for oral morphine available in the home), a service which reaches out to the community so there is no break in treatment and care once commenced, and a service from which we can teach so that palliative care spreads beyond the scheduled catchment area of this service. The service ideally commences with the blessing of the Government through the Ministry of Health. However some have commenced a support service and later received this support.

Knowing the Difference Between Palliative Care and Support Care

Before 1967, patients who were critically or chronically ill or approaching the end of life were given "support" care. Modern Hospice care later named "palliative care" commenced when management of pain in these patients was researched then taught and practised. Dame Cicely brought this medical knowledge to the world following her personal research in St Joseph's Hospice in London before commencing St Christopher's in 1967. She was the first to recognise "total pain" which meant not just physical pain but so many other aspects of suffering in the time before death. But the other aspects of suffering could not be reached without first controlling severe physical pain occurring in at least 80% of cancer patients.

Some Knowledge and a Willingness to Learn

Every patient is different. They have lived with their bodies all their lives and know if anything does not suit them. They also have beliefs that may prevent them from accepting certain medications or advices. We must respect this, listen to their preferences and trust them as a guest unless their preference is doing them harm, then advise gently, while keeping their confidence. We need to consider the following:

- The needs of patients and the factors that affect care, approach to end of life and customs surrounding death according to culture and religious practice; spirituality and the relevance of this when a person is dying in Africa and locally.
- Health and ill health behaviour affecting use of medical services. The percentage of the population who do not reach a health service and why? Where are they? What are their preferences for this time before death? Understanding how health behaviour is affected by spiritual beliefs, new and old religious and cultural beliefs Alternative health behaviours? Are they using traditional health services: herbal versus witch doctors? Where would they like to be before death?
- The public health needs of each country need to be tailored to knowing preferences, including where patients and families wish to die, how culture and spirituality affect the critically ill and those at end of life, and a recognition as to where patients are, when in Africa at least 50% of patients do not reach hospitals. Our service must reach the patient where he/she is. Remembering that many are too sick to travel.
- The elements of pain and symptom control management and managing these at home: these are simply defined in the "Blue Book" (Merriman et al, 2012) of Hospice Africa, which has been the basis for teaching PC in most African countries today. Other books have been written from different angles and using experiences of more affluent countries, but in training the simpler forms for Africa need to be introduced and understood so that they can apply only what is relevant to their own country and not introduce expensive methods of treatment with no possibility of sustainability.

Counting the Cost

This will depend very much on how you plan to start. The two most successful palliative care services in Uganda commenced with a huge difference in funds available to them. Hospice Africa Uganda, 1993, founded for cancer but taking on AIDS patients by the second year, commenced with enough funding for three months for three team members, relying on Ugandan people to lend them rent free accommodation in which both to live and see patients. Having told people of their work and individual patient stories showcasing the terrible suffering as well as the caring of Ugandan members of the team, funding began to trickle in, mainly from international donors in the United Kingdom and Ireland as well as from individuals and later two charity shops in Merseyside. This allowed Hospice Africa Uganda to expand. In 1998, Mildmay, founded for palliative care and service to HIV patients, commenced but before opening its doors it had received donated land from government of Uganda supported by the British government through the Department for Internal Development and a state of the art facility for their service and training, funded by the British Government for two and a half years. Both have been successful in bringing palliative care to many countries in Africa.

Vision and Mission

It is essential to have a well thought out vision, before commencing and to be committed to see this through. The mission will develop from the vision and objectives can be clearly defined. In resource-restricted countries, there is a huge temptation to move away from the mission in order to access funds from donors who have their own agendas, often diverting away from the founding vision. This has caused many palliative care services in Africa to fail or to become diverted into other areas to please the donors so the palliative care either becomes low standard (away from the "impeccable service" in the definition of palliative care of WHO), or be diverted into another cause altogether.

The founders must be convinced of the need for palliative care in their area and be able to bring this need to the attention of their Government. This needs to be backed up with statistics that prove, and experience which can demonstrate the terrible suffering of the sick their country or area. A situation analysis should be carried out early after the start of the service, reflecting the preferences of patients and families at this time of life. The service should reflect and be assured of the essentials of the public health approach (see below) i.e. service, medications and training with Government approval and later strengthened by policy. If possible a trained person in African palliative care should be one of the initial team. African Palliative care, by economic necessity and special skills and time required, is a nurse led specialty. Their experiences with patients are taken into account before making organisational decisions affecting patients and families.

Teaching can commence immediately, once the team includes palliative care professionals. This begins with teaching of families in caring, training of community volunteers in identifying and referring those in need, to appropriate services as well as basic nursing skills in the home. This training must extend to health professionals and others involved in caring in Governments, Missions and other services. Undergraduate teaching in medical and nursing schools is essential to commence as soon as possible. Local experts in parallel areas, e.g. lawyers in will making, local professionals and others in cultural and spiritual aspects as well as oncology and surgical professionals in the different aspects of treatments.

Knowledge and Willingness to Absorb and Practise the Hospice Ethos

The ethos coined at Hospice Africa Uganda, is really the basis of all medical care, but we have strayed far from it in health care in most countries in the world (Figure 4). As we have developed health care, more and more bureaucracy has crept into our services, and we have moved away from the elements that should guide us as ethical doctors with integrity.

Without the ethos, palliative care becomes just another specialty where the interest is more in the disease than this person with a life, a family who is part of a community and has contributed to this world. This approach is essential for holistic palliative care.

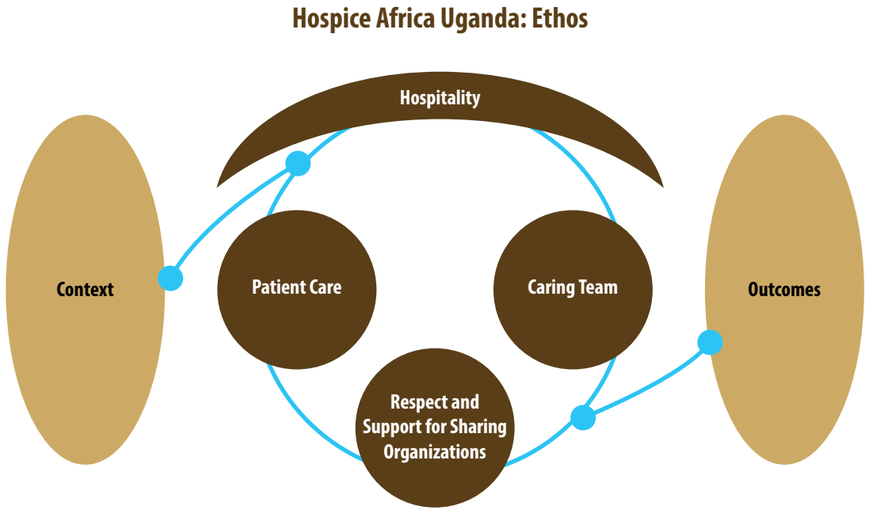


Figure 4: Ethos for Palliative Care services in Africa

African Spirituality

Spirituality is very precious to the dying and a huge need in African palliative care. It is also a large part of the ethos. But our team members must be spiritual themselves. Even if not affiliated to a religion we need to understand human spirituality and be able to relate to it. Relationships with their God are more important when someone is dying than their religion, although they may need to go through religious and traditional rituals.

Nearly all Africans can tell you their commitment to the "modern" religions, Christianity and Islam being the dominant religions given in the national censuses. But it must be remembered that Africans have been spiritual long before these religions were introduced. Their beliefs about life, death and the role of ancestors in their lives today, is entrenched in most Africans. It is also reflected in the traditional beliefs about being human and part of the human race to act human or "Ubuntu" or "Obuntu". Coming towards death, he or she will believe in the mercy of their God, while believing that there are certain rituals they may have to carry out to please the ancestors or to reconcile them with people living or dead, before they leave this world.

Cultural beliefs are different in every tribe and area and some of them affect the approach to the dying process and to the form of burial services. The way a person is buried is very important to the tribe and this caused huge problems during the recent Ebola crises in Western Africa where people were instructed how the bodies should be buried or handled so that the infection would not spread from handling the corpse.

The Role of Religions

Throughout the world many palliative care services have developed from the religious beliefs of the founders. A study of the common denominators between the founder of Christianity, Judaism and Islam found that the common denominator from all was "Compassion" directed towards the suffering (Armstrong, 1994). Their mantra was "Always treat others as you would wish to be treated yourself". Thus we find palliative care services commencing from Christian, Islamic, Hindu and Buddhist beliefs, and religious communities, throughout the world. Those who declare themselves attached to one religion will receive funding through their declared religious affiliation. But although most today will give their services to all, no matter what belief, political persuasion or class, their religious affiliation may give the impression that they are going to convert, or will turn away those of other faiths not prepared to convert. African Hospices must be free from the necessity to evangelise and make converts to their beliefs, because this is a special time of life when our role is to bring the patient to the God they have known throughout Life, not to offend or to make false promises of cure if they convert to the faith of the organisation or other evangelistic members of their team.

But our patients must be able to discuss their spiritual needs with their palliative care team member. No longer as health professionals can we say that this belongs to the priest. This is now as much our domain. Thus we need to reflect on our own spirituality and also what we would need spiritually as we approach our own death. Our patient may want their own spiritual leader, but often they are happy to pray with our team or with neighbourhood prayer groups. Some have had unfortunate experiences with Church leaders, and do not want to be near them, but still will have spiritual needs. We cannot impose and if they do not want to discuss or share, leave them as they wish while caring and praying for them. We also assure him/her that we are there for them throughout this illness and will never leave while he or she needs us.

Other Innovative Models of Hospice and Palliative Care in Africa

Most African countries have drawn lessons for the provision of hospice and palliative care services from Uganda and used these to adapt innovative models in their settings. Kenya and Malawi have for example implemented a model for the integration of hospice and palliative care in public, private and mission hospitals to increase access. Among the various models for service delivery in South Africa is that which has seen the integration of hospice and palliative care in prisons health services. The hospital-based hospice (hospice-in-hospital) model implemented by Bamalete Lutheran hospital (BLH) in Ramotswa, Botswana is allowing for the extension of hospice and palliative care services to patients at home and in the community, through the sharing of resources between the hospice and the hospital. This has made it a sustainable model. The Botswana Retired Nurses Society (BORNUS) has piloted a purely community home based care (CHBC) model for the provision of palliative care to patients and their families, incorporating a day care programme for children. Holy Cross Hospice and Pabalelong Hospices are utilising a stand-alone hospice model that is providing palliative care service through home-based care, in-patient services and day care. In Zambia, Livingstone General Hospital has adapted a model of service delivery that has ensured a strong relationship between St Joseph's Hospice and the hospital and this has strengthened the referral system for palliative care patients. In Tanzania, the reconstitution of powdered morphine to oral liquid morphine has been decentralized to consultant hospitals and more than 65 hospitals are using oral liquid morphine.

The Morphine Story and Innovations in Providing Oral Affordable Morphine

The first two palliative care services in Africa commenced in 1979 and 1980 in Zimbabwe and South Africa. These were the two highest economies in Africa at the time and could afford to import oral morphine and other expensive step 3 analgesics. This was followed by a gap of ten years, when palliative care did not move.

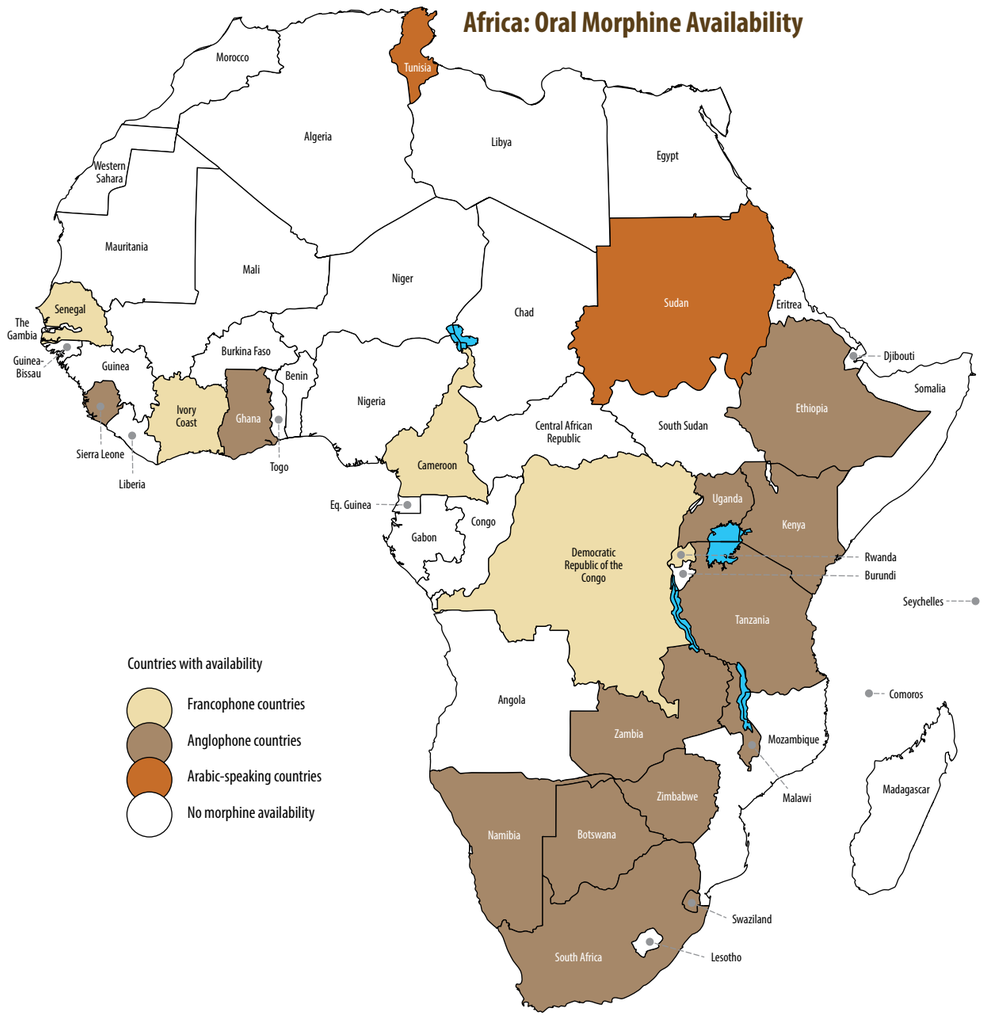


Figure 5: Oral Morphine Availability in Africa 2016 (Timothé Vulin)

During these ten years, the present formula for oral affordable oral morphine was designed to meet the needs of Singaporeans by their new palliative care team working in the homes. This formula was brought to Nairobi Hospice in 1990 and Kenya commenced a service that could move throughout Africa, even within those countries with low economies. Inspired by the need to stop the terrible suffering of cancer patients witnessed in Nairobi, and in order to facilitate the moving of oral morphine throughout Africa, Hospice Africa was conceived in 1992 and the model for all Africa chosen and commenced in Uganda in 1993. Since then the movement has moved throughout Africa now making palliative care available in 20 countries and support care in 15 more (Figures 5 and 6). The African palliative care association (APCA) was conceived to expedite the movement in the continent in 2002. They took this up in 2005 and have been successful in supplementing the coordination and support to Africa countries (Merriman et al, 2010).

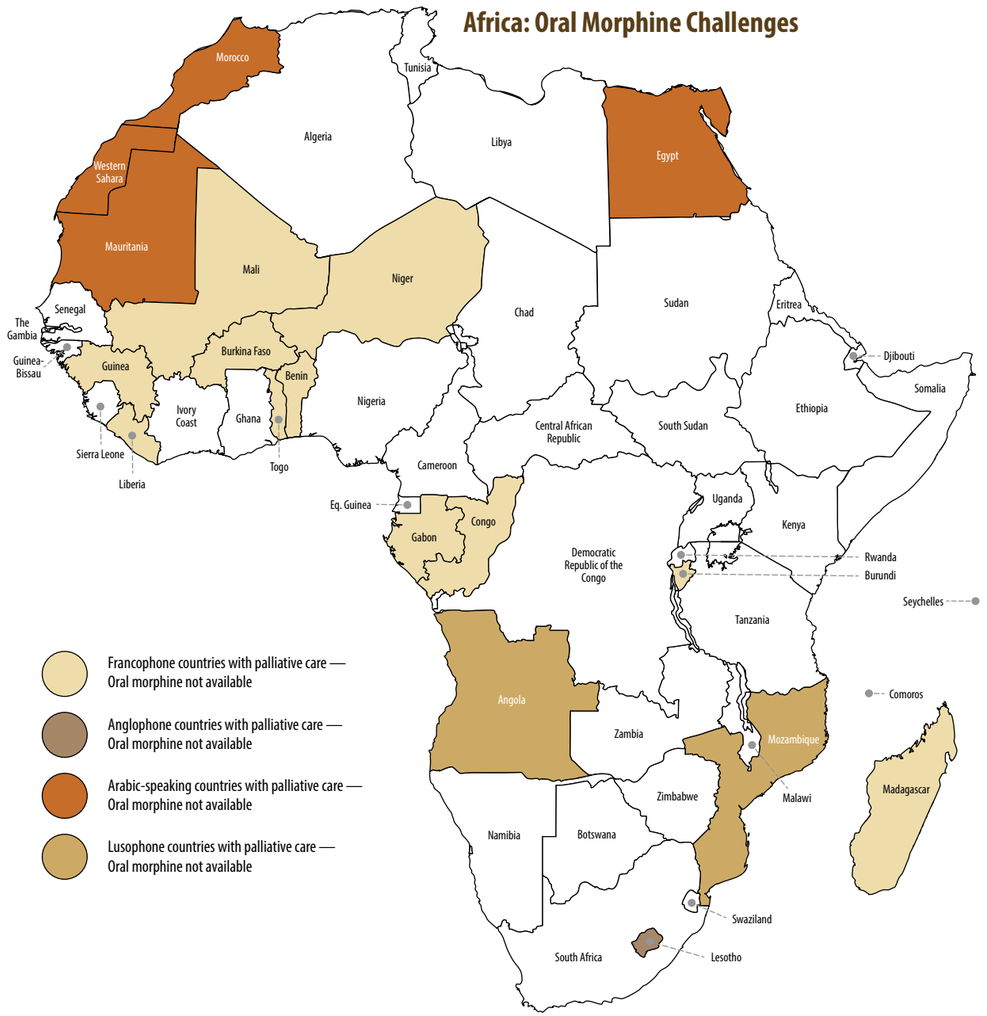


Figure 6: The challenge of oral morphine availability in Africa 2016 (Timothé Vulin)

Estimating Palliative Care Needs in Africa Today

From our work in different African countries, dealing with the 95% who remain in the communities and do not reach a biopsy, necessary to get onto the cancer registry, we realise that the figures given from different sources vary widely and most are inaccurate (Table 1). Most are based on figures for cancer from cancer registries which themselves are the results of biopsies and often confined to a small area, usually around the capital, of the country. But the majority of patients we see cannot afford their fare to hospital, much less the cost of a biopsy.

Thus we have come up with a formula using guestimates, using figures estimated in the past, by the occupying countries working in with cancer.

This formula can be used to estimate a country needs, or a subunit of the country down to village and health centre levels. It is being used to teach initiators and has become referred to colloquially as the "Merriman Formula" (F1).

These calculations at least give us the number of cancer patients in need of PC, but do not include the many others in need suffering and dying from AIDS and non-communicable diseases. Using these formulas, based on the populations, the numbers of people with cancer or in need of palliative care are much higher than the figures given from other sources, but we think they are much more realistic. They also relate to cancer needs only.

Table 1: Examples of four African countries in 2015 showing the expected prevalence of cancer in need of palliative care in 2015, based on population

HDI	Country	Population (millions)	%HIV	Prevalence in need for palliative care (cancer patients)
138	Ghana	26	1.4	78,000
152	Nigeria	177	3	531,000
164	Uganda	38	7.4	114,000
141	Zambia	15	12.5	45,000

Uganda: the Model for Palliative Care in Africa?

Palliative care was introduced to Uganda in 1993 with the commencement of Hospice Africa Uganda. This was to be the model for Hospice Africa, commenced with a vision of Palliative care for all in Africa. It was important that palliative care in Africa should be African palliative care suitable to any culture or economy to make it realistic and sustainable. Transplanting palliative care from the developed world had been tried several times and failed. The founders were adamant that it should commence from a free standing Hospice and NGO, free of the bureaucracy and lack of hospitality found in most hospitals today. Thus with limited resources, the clinical service and education service commenced simultaneously, even reaching the undergraduate medical and nurses students as well as health professionals and all those involved in the holistic management of patients in hospitals and the communities. Facing the reality that the vision could not be achieved without education, thus expanding the provider of palliative care throughout Africa, education commenced with the clinical service in 1993. Today there is training for all Africa up to degree level from the institute which is a major component of the care. There are three sites for Hospice Africa Uganda (HAU) since 1998 and presently 80% of Districts have palliative care available.

Mildmay international commenced for HIV care in 1998 with training and services which included patients with AIDS/cancer and those started on antiretroviral medicines (ARVs). There was a palliative care service for HIV from the start. They have expanded over the years to giving chemotherapy and screening for cervical cancers among the HIV positive clients under their care. They have specialised in children's palliative care from the start and have training up to degree level in their specialist areas.

The Palliative Care Association of Uganda commenced in 1999 at HAU and is independent since 2006. They support those who have been trained at HAU or Mildmay with further support and training throughout Uganda as well as holding quarterly updates which are well-attended and triennial Conferences. They are the main points of information in Uganda.

The African Palliative Care Association was registered in Uganda in 2003 while housed at HAU. It commenced its own offices in 2005. This organisation is the coordinating organisation for palliative care throughout Africa. They support all those who are registered with them both with advice, training and funding. They work with Governments and major donors. They are the main point of information for Africa.

The Palliative Care Unit of Makerere University Department of Medicine and Mulago Teaching Hospital, Kampala was commenced in 2008, this role being held by HAU since 1993. Negotiations with Makerere led to its formation in 2008. Their brief is to set up a sustainable clinical, education and research services within Makerere and Mulago teaching Hospitals. There are two professors of Palliative Medicine for Makerere University appointed six years ago. Professor Julia Downing is Professor of Paediatric Palliative Medicine and Professor Dr Anne Merriman, Professor of Palliative Medicine. Both professors also hold their titles with the Institute of Palliative Care in Africa, at HAU which runs the Bachelor's degree programmes conferred by Makerere University.

Uganda had the most rapid expansion of palliative care in Africa since 1993 and has been found to be the only country in Africa with stage 4 comprehensive palliative care published in the Global Atlas of Palliative Care (Worldwide Palliative Care Alliance, 2014; figures 7 and 8).

Uganda: Global Rank in Palliative Care

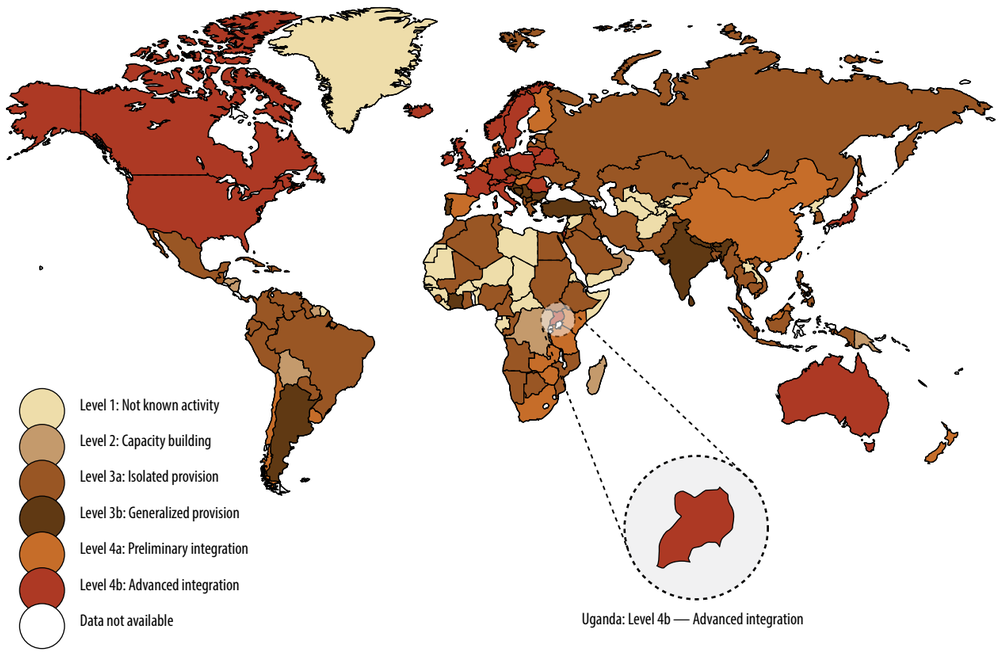


Figure 7: Uganda in the world today – advanced level of palliative care development

Uganda: Palliative Care Today

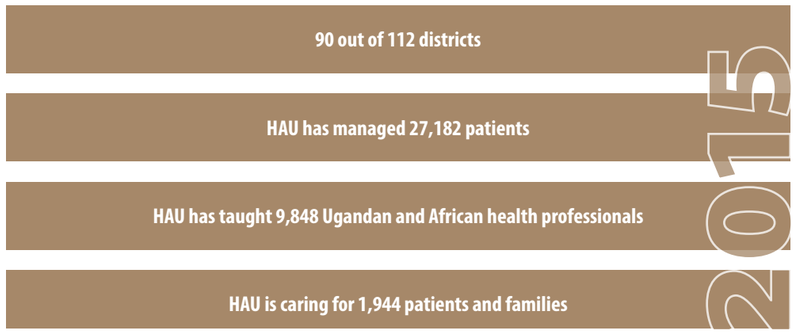


Figure 8: State of palliative care in Uganda today

Uganda was also found to be 35th out of 80 countries measured in the Quality of Death Index 2015 (Economist Intelligence Unit, 2015). In a way this is an accolade but our vision would have expected more countries to have caught up with Uganda by now.

Ethos for Palliative Care Services in Africa

This is best represented in diagrammatic form (Figure 4). Our mainstay is hospitality, where our patients and all who come to our service are welcomed, having choices in all decisions being made so that the patient and family come together. The three pillars of the ethos are based upon the patient and family being the centre of all we do and all our decisions, whether for administration, clinical or teaching. This pillar is supported by the second and third pillars, our caring for each other and recognising that none of us can reach all Africa alone. We need to work together with our partners who we respect and support. This includes working with the oncologists and all who are caring for patients in critical illness or approaching the end of life.

The ethos must be incorporated into every clinical service and into all teaching so that African hospitality becomes a model, not just for palliative care but for the return of health professionals to their caring philosophies more than curing. In a world where death is the only certainty, surely we as carers need to be able to help others to prepare for this even if we too need to be prepared for it?

The African Palliative Care Association (APCA)

The function of a palliative care association is to:

1. Coordinate with the Ministry of Health and civil society organisations all the services in the country, to ensure services are equally distributed throughout the country and supported through network.
2. Update all recent advances affecting their country at regular country meetings.
3. Support education services in the country by supporting teaching in all districts or political divisions.
4. Advocate for palliative care services with the government based on the public health needs of the people. To work with the Government, keeping them up to date with gaps and human resource needs to ensure palliative care reaches all in need.
5. Ensure that medications are available particularly oral morphine.
6. Keep registers of:
   A. All services in the country so that health workers and patients can call them to find the nearest to them.
   B. All registered morphine prescribers, except doctors who are registered with the Medical Council.
   C. Mapping of palliative care services in the country and distribution of same.
7. To produce newsletters and publication so that all keep up to date on the services and to share innovations which can be applied for fund raising and services.

The establishment of national palliative care associations in 23 countries in Africa has also accelerated the development of hospice and palliative care services and well as its integration in main stream health services (Figure 9).

Figure 9. Palliative Care Associations in Africa

Alongside the development of national palliative care associations, Africa birthed its continental association- the African Palliative Care Association. Formally established in Arusha, Tanzania, in June 2004, APCA's aim is to scale-up palliative care across the continent. It promotes a culturally appropriate public health approach that strives to balance quality with coverage. Its broad objectives are to: promote the availability of palliative care for adults and children; encourage governments across Africa to support affordable and appropriate palliative care incorporated into all health care services; promote the availability of palliative care medications for all in need; promote palliative care training programmes specific to the need of African communities; develop and promote quality standards in palliative care training and service provision for different levels of health professionals and care providers; encourage the establishment of national palliative care associations in all African countries.

Palliative Care Development in Africa as Seen Through the Who Health Systems Building Blocks

Palliative care needs to have proper leadership and governance within a national health system that ensures development and retention of good human resource force to effect the required palliative care service delivery. This requires a good health information system with palliative care indicators, good supply of palliative care medicines as part of the essential medicines list and good and sustainable financing.

The Need for Palliative Care in Africa is Difficult to Measure with Accuracy but Nonetheless Significant.

In 2004, the World Health Organization estimated that at least one in every 200 individuals each year in Africa needed palliative care. Because of the prevalence of cancers and Africa's HIV/AIDS epidemic, the WHO projects that at least 50% of patients with HIV and 80% of patients with cancer will experience severe pain during the terminal phase of their disease.

According to the UNAIDS, in 2013 an estimated 24.7 million people in sub-Saharan Africa were living with HIV and AIDS, while cancer rates on the continent are expected to grow four-fold over the next 50 years. More than 50% of Africans do not reach a health facility. Those who do reach a facility, over 80% of cancer cases are in advanced stages at the time of diagnosis because of late presentation to health facilities and poor access to diagnostic technology (Kanavos, 2006). Despite documented successes in cancer treatment and control programmes globally (Ngoma, 2006; Rastogi et al, 2004) large differences in mortality persist, with survival rates in developing countries often far less than half those of developed countries.

Also as people's lifestyle, nutritional preferences and non-sedentary work patterns on the continent are changing Africa is experiencing an increase in the incidence of chronic, life-limiting non-communicable diseases like diabetes, hypertension and strokes which all contribute to the burden of diseases coming to Palliative Care.

The Public Health Approach to Palliative Care in Africa

The public health approach to palliative care highlights that the provision of Palliative Care must be founded on knowledgeable caring teams, clinical care with adequate affordable medications from which appropriate government policies can be written. Implementation and integration of palliative care within the health systems is necessary, at all levels. Research is now recognised as a pillar of the WHO Public Health model, and the immense contribution of this field to patient care and education cannot be overemphasised (Figure 10).

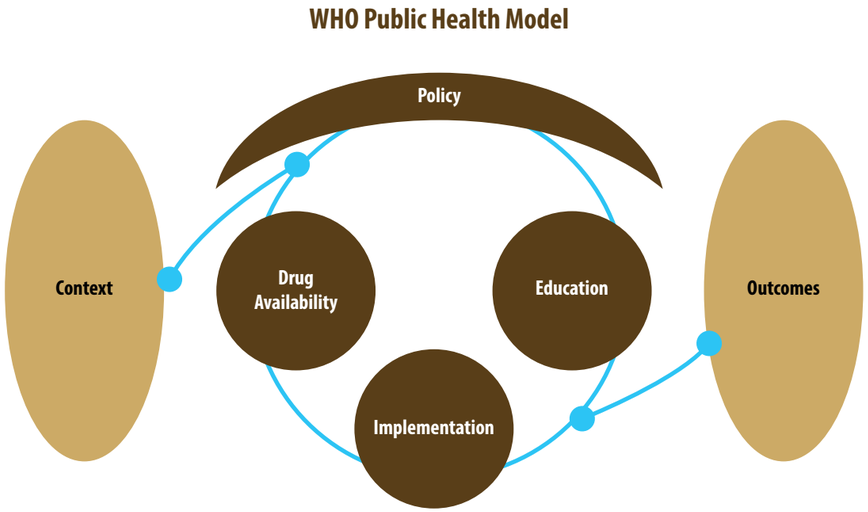


Figure 10: WHO Public Health Model

In Africa it is important to remember that care of the patients must not be put on hold while awaiting a government policy and the components of the WHO public health model (policy, education, medication availability, etc.) must be put in place with the needs of the patient and family in mind and always at the centre.

Also while the International Association for Hospice and Palliative Care (IAHPC) and the WHO have developed lists of essential medicines for palliative care, the entire armoury of medications which are available in the developed world is not available for most African countries and it is crucial that the most affordable medications for palliative care are selected from a country's essential list of medications.

Experience shows that initially, most countries are missing the essential medications for pain control. Palliative care for cancer, cannot be established without pain control being in place (Table 2).

Table 2: Minimum essential drugs required for pain and symptom control in uganda and other African countries, 2012 (Merriman et al, 2012)

Generic Drug	Proprietary	Dose	Form
Amitryptyline	Lentizol	10, 25, 50 mg	tabs
Phenytoin	Epanutin	100 mg	tabs/liq
Acetyl Salacylic Acid	Aspirin	300 mg	tabs
Diclofenac	Volterol	25, 50, 75, 100 mg	tabs
		75 mg/3mL	inj
Codeine		30 mg	inj
Morphine		5 mg & 50 mg/5mL	liq
chlorpromazine	Largactil	10, 25 mg	inj & tab
haloperidol	Serenace	5 mg	tab
dexamethasone	Decadron	0.5, 2 mg	tab
		8 mg/mL	inj
diazepam	Valium	2.5, 10 mg	inj & tab
frusemide	Lasix	20, 40 mg	inj & tab
spironolactone	Aldactone	50, 100 mg	tab
ketoconazole	Nizoral	200 mg	tab
nystatin		100 & 500,000 iu	Tab/susp
magnesium trisilicate			liq
metoclopramide	Placil	10 mg	inj & tab
metronidazole	Flagyl	200 mg	tab
amoxycillin		250 mg	cap
bisocodyl	Dulcolax	5 mg	tab
hyoscine butylbromide	Buscopan	10 mg	inj & tab
chlorpheniramine	Piriton	4 mg	tab

In developing countries often gifts are given of medications at low or no cost from charities. Some of these are similar to the above and can be used. Some are different and if commenced cannot be continued. Medics not wanting to use morphine may use alternative, but not affordable step 3 analgesics but they must be aware that if the patient lives longer than the supply, the patients will be thrown back into severe pain.

Challenges in the Assessment and Management of Pain in Africa

Modern palliative care has spread across Western Europe, North America and Australia, where it is widely integrated into the health system, so it is difficult to imagine that in many African countries palliative care is not integrated into the health system and in many countries medicine for the management of severe pain is absent.

As is the case everywhere a comprehensive clinical assessment is fundamental to successful treatment. In Africa many people are unable to read and write and the comprehension of scales and tools, like the Wong-Baker scales, is sometimes a challenge. This is complicated by the fact that standard pain scales are often developed and validated in non-African settings. It is therefore necessary to develop reliable, culturally-appropriate

pain assessment tools and several are in development and validation in African populations. An example is one based on African cultural familiarity with the jerrycan used to collect water as most homes are not plumbed.

Pain scores on the jerrycan pain scale (JPS) have been found to be well-correlated to standard pain scales (Numerical Hand Scale and the Wong-Baker faces pain scale and many patients have preferred to use the JPS. The jerrycan pain scale is a culturally appropriate, reliable way to assess pain in the Ugandan population and is being used at Hospice Africa Uganda.

Table 3. The jerrycan pain scale

0	1	2	3	4	5
Empty jerrycan or extremely light to carry	Very little water or easily carried	More water or beginning to feel its weight	Jerrycan over half full r heavy	Nearly full jerrycan; Difficult to carry	Full jerrycan; Very heavy
No pain	Mild pain	More pain	Moderate pain	Severe pain	Overwhelming pain

Eighty-six percent of the world's morphine is still used by the 20 richest countries (Spencer, 2003), and according to the International Narcotics Control Board (INCB) South Africa is the highest user of morphine and other licit opioids on the African continent and the only African country whose consumption is above the global *per capita* mean. The other countries which are increasing their morphine consumption are: Uganda, Malawi, Kenya and Cameroon.

Analgesic Ladder

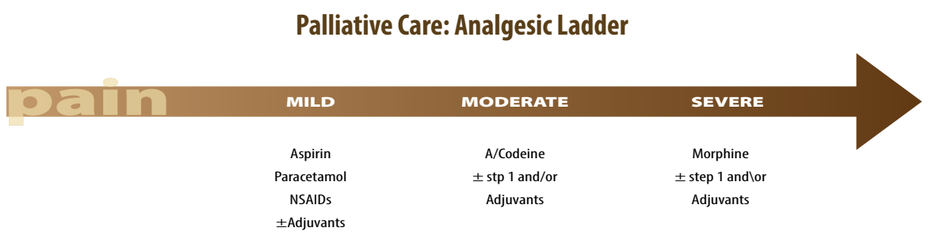


Figure 11. Analgesic ladder (Merriman et al, 2012)

Note: More recently codeine, which has a ceiling and is more expensive than oral morphine, has been skipped and patients move from step 1 to step 3 without step 2. But in countries without morphine, codeine may be the nearest alternative. If codeine is used we do not add in morphine as they use the same receptors.

According to the WHO, pain relief requires the analgesic ladder first described in their booklet "Cancer Pain Relief" in 1986. Severe pain requires step 3 analgesics and the only affordable one in most African countries is morphine. As most wish to die at home and most do die at home, this has to be in an oral form so that the patient and family, fully informed, can administer it using the usual precautions. It must be remembered that oral morphine has never been known to cause addiction. Morphine needs to be given in high concentrations intravenously to give any form of a high and pain is a physiological antagonist to pain. The side effect of drowsiness after the patient is stabilised indicates the dose is too high. The patient should be free of pain and able to concentrate on other pertinent and immediate aspects of leaving life, once he/she is controlled and without pain. The main side effect is constipation and this is managed with simple laxatives or if not affordable, dried and smashed pawpaw seeds given at night also keep the patient comfortable with normal bowel movements.

Besides the lack of availability pain relief in many countries in Africa is hindered by barriers to the accessibility of opioid analgesics. Overzealous drug control by policy makers, and laws and regulations crafted to restrict the diversion of medicinal opioids into illicit markets, interfere with the availability of morphine for the relief of pain. This is compounded by myths and fears which abound among many of the older clinicians though with sensitisation and education this is steadily changing.

In total, 15 African countries have adopted the morphine reconstitution formula, and five other countries have access to some type of oral morphine by end of 2015. Access is especially poor among the Francophone and North African countries. Africa therefore has a difference in outcomes between high-income and lower-income countries for oncology services called the great "cancer divide" (Knaul et al, 2011) in addition there is the disparity in access to pain medication and schism in level of Palliative Care integration- which we can call the "Palliative Care divide".

Other Pains, Other Treatments

It must be remembered that it is important to diagnose the cause of the pain by taking a thorough history of start, the character, severity and frequency of the pain. Neuropathic pain responds more to antidepressants and/or antiepileptic's and bone pain more to step 1 analgesics. But both can be improved by the addition of small doses of oral morphine.

Using the affordable medications, it is possible with experience, to manage 90% of pain in cancer patients without injections. Even when the patients cannot swallow, oral morphine can be absorbed from the buccal mucosa. Hospice Africa Uganda has not used injections or pumps for 20 years. Adjuvant medications also include the use of corticosteroids. The medications affordable, available and suitable for Africa, are discussed in detail in the Blue Book.

Morphine

Why Oral Liquid Morphine?

In Africa most patients have severe pain at time of presenting to the clinician. When available most are given a stat dose of 5mg of oral morphine because it is difficult to give history and be examined if one is in severe pain (Figure 11). It also helps develop trust and confidence in the

practitioner, as many patients have been in pain for a long time. Most of the patients in severe pain have probably already been on simpler analgesics like NSAIDs, and it is often easier to move straight to oral morphine.

For continuous management of severe pain the home with therapy controlled by the patient there is no better option than oral Morphine. It is highly effective for severe pain, is inexpensive (see table below) and has no ceiling, so the dose can be increased to keep the pain controlled. It is also easier to titrate the correct dose with the flexibility of doses from a solution and breakthrough doses can be given. The oral route does not require expert/ nurse availability for its administration, and the entero-hepatic metabolism and modification of the medication without giving a "high" means that unlike parenterally administered opioids there is very little propensity for abuse of oral liquid morphine.

Formula for reconstitution: Simple/ kitchen sink & modern pharmaceutical plant

Because oral liquid morphine is so inexpensive to make up from ingredients and does not require high-tech equipment it can be reconstituted by any service "in a kitchen sink".

The most commonly used formulation of oral liquid morphine is the 5mg in 5mL strength. The simple formula requires 4 ingredients:

1. Morphine sulphate powder 80g
2. Bronopol powder BP 16g - This preservative gives the product a longer shelf life of six months compared with parabene which gives three months.
3. Green colour powder (Tartrazine) 4.8 g
4. Purified water 80L

Colour Coding of Morphine Solutions

This is a safety measure. Clear fluid can be misinterpreted for water and large amounts swallowed. In Africa many sick patients cross borders to receive treatments for cancers and other painful conditions, not available in their own country (Table 4).

Table 4: Recommended Colour Coding of Morphine Strengths in African Countries (Merriman et al, 2012)

Strength	Colour
5 mg / 5 ml	GREEN
50 mg / 5 ml	PINK / RED
100 mg / 5 ml	BLUE

Step by Step: The Morphine Production Method

Check the balance scales
Weigh the morphine powder.
Measure 80L of purified water and pour into a clean calibrated 100L bucket.
Dissolve morphine powder in this water by continuous stirring.

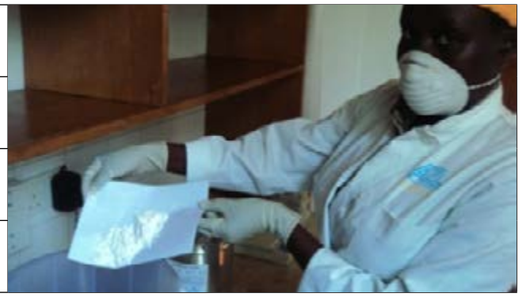


Figure 12: Morphine production step by step

1. Measure the Bronopol powder and dissolve into the morphine solution in the bucket while continuously stirring
2. Measure and dissolve the green colour into the solution in the bucket while continuously stirring.
3. Ensure the solution is 80L and stir to homogeneity/uniformity.
4. Measure out product into bottles
5. Bottle the product and label appropriately, including expiry date

Comparative Cost of Morphine

In Africa many patients are commenced and are on much lower doses of opioids than patients in developed countries. It is possible that there is a genetic basis for this difference. Most adult patients who are not emaciated are on an average of 5 to 7.5mg of morphine every 4 hours and a 500mL bottle of morphine of strength 5mg in 5mL lasts about ten days, including break through doses. The cost of this bottle made up using the simple formula above in Uganda is 8,190 UGX (1.66 UK pounds or 2.36 USD). A 500mL bottle of Oramorph morphine sulphate 10mg/5mL solution costs 8.50 UK pounds. For the same amount of analgesia the oral morphine solution made in Uganda costs less than one third of Oramorph and is probably the cheapest opioid preparation in the world! The combination of being inexpensive and the fact that it can be made up low-tech is the reason why the Uganda government is able to ring-fence funds for pain relief for all its citizens in need. Several African countries are now using the simple formula to reconstitute oral morphine solutions from powder for their patients and this has been shown to be a sustainable way towards pain relief for all.

Myths and Fears Around Morphine in Africa

Some people and communities in Africa have superstitious beliefs and these sometimes impact on the administration of care and the use of medications including morphine. "Opiophobia" which is the unfounded fear of opioids including morphine is rife and is not restricted to lay persons but is also there among health professionals who have not received training in Palliative care and for whom education in the medical and nursing school emphasised the toxicities of morphine rather than its rational use for management of severe pain by trained professionals.

The main myths and fears around morphine are:

- Respiratory depression- which is unknown in our experience when using small doses of oral morphine titrated against pain. Pain is a physiological antagonist to respiratory depression.
- Tolerance: Increasing dosage of morphine is the accepted method of titrating morphine against the pain until the pain is controlled. The only upper limit is the dose that controls the pain while the patient is still alert.
- Addiction- Addicts are looking for a "high", which cannot be obtained when morphine is taken by mouth. This is only obtained with stronger concentrations given intravenously.
- Cognitive impairment: there may be some sedation when morphine is first commenced, but this is temporary, lasting two-three days at the most.
- Lethality- Morphine does not kill when properly prescribed and gradually increased according to need. As many Palliative Care patients in severe pain will be taking morphine when they die some family members mistakenly ascribe the death to morphine rather than to the patient's advanced disease.

Table 5: Barriers to morphine importation and use in African countries

Courtesy of Dr J Jagwe, personal communications Jan 2016; (Berterame et al, 2016)

	BARRIER	REASONS	SOLUTION
1	Overly restrictive laws governing use of narcotics — Greatly exaggerated fear of addiction — Inadequate knowledge about morphine	Too much bureaucracy (and in country regulations) — Anti-Narcotic Drug Enforcement Agencies	Education, Sensitization, Advocacy — Revisiting and amending restrictive and outmoded laws on the use of narcotics — Demystifying concerns about addiction
2	Morphine not reaching outlying areas in country — Low priority for pain management in health care systems	Problems of importation and distribution of Opioids to remote rural areas — Shortage of prescribers, pharmacists and dispensers e g: the poor (Doctor: Population ratio)	Facilitating distribution to remote rural areas — Expanding the prescribers of opioids (HAU/MOH) — Encouraging use of affordable and effective oral morphine (WHO/HAU initiative)
3	Severe Opiophobia and Morphinephobia	Drs and health workers ignorant of recent advances in pain control — They advise Governments and patients	Advocacy and Education of health workers, narcotic police and others
4	Recommended changes already incorporated in some countries are not acceptable in others	Each country wants to make its own regulations and not willing to learn	Health Sector Strategic Plan should include Palliative Care continuously. — Enlist WHO support through the influence of WHO representative in the country.
5	Morphine produced at non user friendly strengths and packages for needs of patients in country	Governments independence but danger in measurements and when patients cross borders	User friendly Recommended strengths and colouring: — Green: 5mgs /5mls — Pink: 50mgs/5mls — Blue: 100mgs/5mls

But in spite of the exhortations from WHO and WHA to Governments, some African Governments still refuse to import powdered morphine for reconstitution. Keeping in mind that injectable morphine is available in strengths of 10 or 15 mg per mL per ampoule, and are still rarely used and out of date, some initiators have managed to get around this by using injectable by mouth:

- Example 1: One country has taken the ampoules and made it up into oral solutions of the recommended strengths. As there is already a preservative in the injection, there are only three ingredients required, leaving out the Bronopol. But this is labour intensive as the morphine in each ampoule has to be withdrawn and placed into a receptacle to add water and colour.
- Example 2: another country is giving an ampoule to the patients and asking them to add the required dose, having withdrawn it into a syringe, puts it onto a sugar or a food like yogurt and swallows it.
- Example 3: BE WARNED: Some well wishers in the developed world have brought in tablets or other oral preparations of morphine into an African country and given them to palliative care teams. This is dangerous! It is a criminal offence to carry class A medications unless prescribed for the person carrying it. This practise could have a huge effect on the legal importation to all African countries. This also throws the patient back into pain when the limited supply finishes.

The Pain-Free Hospital Initiative

This is an initiative commenced with the help of the American Cancer Society through their programme "Treat the pain" (American Cancer Society, 2016) in 2014.

The American Cancer Society has partnered with government health agencies in Nigeria, Uganda, Kenya, and Ethiopia to assist them in improving access to high-quality pain relief as part of the Treat the Pain programme.

This programme augments the efforts of HAU and APCA by initially focusing on getting morphine into a country and making it affordable for patients. All the above countries already had morphine through the efforts within Africa. Treat the Pain have taken on the initiative commenced within Uganda and carried it forward. They have now introduced in each of the above countries, a training programme in five hospitals, which focuses on pain control and ensures that oral morphine is available.

They have developed a very helpful "Morphine Framework" which can be accessed from their website, indicating the steps to pain free countries, from Government advocacy to hospital level. The next step is to reach the communities where most of those in pain are suffering. Organisations and countries need to work together in a harmonised fashion to make this a reality.

Up to now they are not involved with patients after discharge but these hospitals are encouraged to be involved with a home care service or if not available, to commence one themselves.

Policy and Legal Frameworks

Worldwide adequate relief of cancer pain is now considered to be a human right. Policy and legal frameworks to remove unnecessary suffering and to promote cheap and effective palliative care is seen as both a public health and a human right issue.

In most African countries, palliative care services have started before the development of national palliative care policies. Delaying the start of palliative care service provision until completion of national policy frameworks for palliative care causes delays and untold suffering for patients. Most African countries, successful in palliative care so far, have used existing international conventions and frameworks to avail opioids and palliative care as they waited for the complete adoption of national palliative care policies. This has helped to develop home grown best practices

and service delivery models that have in turn informed national palliative care policy development. Countries that have waited for palliative care policy development before starting palliative care services have experienced time lag in service development. On the contrary countries that started palliative care service provision as they worked on policy have had the opportunity to pilot practices and approaches that have in the end augmented policy development.

Uganda is the first African country to practice using the WHO guidelines developed from such services, and prioritised palliative care as an Essential Clinical Services in its National Health Plan of 2001–2005. Previously in 1998, after years of lobbying, the Ministry of Health invited Hospice team members to be technical experts in a pilot study in 15 (out of 56) districts to assess the feasibility and safety of using morphine for chronic pain in the community. In 2002–3, the districts, including mission hospitals, underwent extensive initial training involving local dignitaries, police, and senior health officials. Uganda has passed laws to allow nurses and clinical officers with training in palliative care to prescribe oral morphine (Ministry of Health, 2003), an essential step as at a ratio of 1:20,000 doctors are scarce in rural areas. Palliative care is included in the mission of the Ministry of Health, the National Health Policy, and the Health Sector Strategic and Implementation Plans.

National Cancer Control Plans and Palliative Care

It is now recommended that palliative care should be part of the continuum of cancer approaches starting with promotion of life styles that prevent cancer, using cancer prevention approaches such vaccination, early detection and treatment of cancer as well as rehabilitation and palliative care.

Service Delivery and Models

Most PC services in this world have commenced from one person, usually inspired by their compassion, inspired by the founder of their religion based on their love of their God. Hence many have been developed from religious groups of different persuasions. Dame Cicely herself, having grown as an agnostic, was a deeply committed Christian when she conceived the idea of St Christopher's and pain free care for the dying (Clark, 2005). It was in 1948, as an almoner, that her patient David Tasma told her before he died "I will be a window in your home" (for the dying) and left her £500 in his will for this window which still inspires many visitors to St Christopher's today. His other words "I want what is in your mind and in your heart" reflect how different palliative care is to other specialties in medicine. As Balfour Mount says in his forward to the same book, "Compassion cannot be tabulated in columns, nor are we yet able to assign a p value to the significance of diminished suffering". Care of the spirituality of the patients, families and team members in palliative care was a priority for Dame Cicely from the start. This is more than relevant in Africa today.

Dame Cicely researched the use of oral morphine in pain control from St Joseph's Hospice in Hackney, London after graduating as a doctor in 1957 and St Christopher's opened in 1967. Cicely recognise that holistic care of "total pain" was impossible without the control of the severe pain of cancer. In Africa, where the chance of cure is minimal, it is even more important that pain control is affordable and available to all even to those who cannot reach a hospital, in the home.

Sadly, pain control is often the last thing sought by those caring in hospitals, even though it is often the biggest problem for the patient and the family. Yet, Human Rights Watch considers doctors who neglect pain control, when methods have been known for more than 50 years, should be considered as torturers! Pain control can be commenced immediately even before the diagnosis has been confirmed and curative therapy commenced.

Service Delivery Models

Development of palliative care service delivery models needs to be directed by patient needs. Each country is different. Thus situation analyses, political will and direction and emerging evidence from research and audits have contributed, but the heart comes from relationships and experiences with our patients.

Over the years several service delivery models have been developed in Africa and below are experience to date, using case studies:

A Model of Public Private Partnership for Oral Morphine Procurement, Reconstitution and Distribution in Uganda

Public Private Partnerships (PPP) are moving in health systems today. The recognition that the voluntary sector has the knowledge and expertise and the Governments through their Ministry or Health's have the funding, brought this about. This partnership worked well, particularly in palliative care.

While Hospice Africa Uganda (1993) was the fourth Hospice in Africa it was the first with a vision for all of Africa. It commenced from the need to address the extreme suffering witnessed in cancers. A year after commencement the suffering of AIDS patients was addressed, due to a high prevalence of HIV in Uganda at the time and the lack of knowledge of pain control in the AIDS support organisations. Hospice Africa was encouraged to come to Uganda, supported by the commitment of the Ministry of Health, for the relief of the suffering among its citizens. Hospice Africa Uganda (HAU) imported the first kilogram of morphine powder in 1993. This was reconstituted into a solution together with a preservative and cake dye used to differentiate strengths. The solutions were put into recycled mineral water bottles. This simple formula of making liquid morphine at the "kitchen sink" produced an affordable form of oral morphine which was appropriate for use in the patients' home.

Since 2011 HAU entered a public-private partnership with the Ministry of Health/Government of Uganda to scale-up morphine production for all the country. HAU has the expertise and with ring- fenced finance from the government, affordable pain relief is available for all citizens who need relief from severe pain. This model entailed the setting up of a more sophisticated production facility. In 2015 the unit was further modernised so that a local morphine reconstitution facility is now in place at Hospice Africa Uganda. The PPP is the joining of an NGO hospice with the Uganda government, which provides the funding.

After the reconstitution, the liquid morphine is sent to the National Medical Stores (NMS,) a national medicines procurement and distribution parastatal company. The NMS then distributes to all government facilities at no cost to the patient. The morphine is also distributed to the non-government and faith-based hospitals through the Joint Medical Stores an entity owned by the Uganda Catholic and Protestant Medical Bureaus, to serve their constituent health units across the country.

Some countries have commenced with a free standing Hospice based on the experiences of hospice Africa Uganda. However, with the problems of funding, many have commenced within hospitals so that some of their care can by supported financially by the health system of the country. But this has its drawbacks, particularly due to the bureaucracy which controls our care of patients more than the patients' needs controlling what we do.

Models of Hospices or Palliative Care Units Within a Hospital

A large number of patients are admitted to hospitals for uncontrolled pain and symptoms from HIV/AIDS, cancers and other illnesses. The need for hospital palliative care is therefore well recognized. Palliative Care needs are more profound among oncology patients and it is imperative that palliation is available to patients in addition to specialised oncologic treatments. Few hospitals however have the ethos for palliative care and this is often strangled by the bureaucratic demands on health workers to hit targets more than meet their patient's needs.

Sadly, most palliative care units do not have dedicated beds, so patients are admitted to other wards and often not referred to the PC team. Dedicated beds would ensure that patients were screened in palliative care, before being transferred to other units for specialised treatments.

A model of palliative care in a public hospital helps to ensure integration of palliative care services within the hospital. The hospital maybe in a public hospital as is the case in many of the hospitals in Kenya where the Kenya Hospice Palliative Care Association (KEHPCA) works with public hospitals to establish these units in government facilities. It could also be in a mission or church hospital as is the case of Ramotswa Hospice in Botswana. Other examples include Malawi, Tanzania. Mulago Teaching Hospital in Uganda and Livingstone General Hospital in Zambia.

Such models can help avoid duplication of services and ensures smooth and timely referrals for palliative care as well as utilisation of hospital doctors to support opioid prescription which would have been difficult with hospices that cannot hire full time doctors. But to give patients smooth relief throughout the illness they all need to have their own palliative care team in the community or have another service to refer patients to on discharge as they will deteriorate and be unable to attend hospital out patients departments.

In Uganda the national referral hospital at Mulago has a Palliative Care unit based within the Department of Internal Medicine through which specialist physicians and nurses offer support and consultative services to the entire hospital complex through a system of "link nurses" who are from the different wards and specialities. The link nurses are trained at a generalist level and are able to manage basic palliative care needs of their own patients and through a liaison service have access to specialists to manage the most complex palliative care needs.

Stand-Alone Hospices

As most of those in dire need of palliative care are unknown to health services and in the communities, the vast majority of hospice care in Africa consists of non-governmental and faith-based organizations. This model consists of an independent hospice and in most cases, not-for-profit, set up to provide palliative care to the community in a defined geographical area with links to other health care units within that geographical area for two-way referral.

The simplest does do have in-patient facilities, giving consultations within hospitals and caring for patients and families in their own homes. Some have come with the Western model based on inpatient beds, and most have failed because of expense. However some that have home care models have more recently added a few beds for emergencies only, more for social than medical emergencies.

Free-standing Hospices are a good model for the promotion of the ethos and spirit of Palliative care in Africa. They are able to raise their own finances, craft their strategic plans and supplement government health systems. Being autonomous they fill an important void, for home-based care within catchment boundaries, which is rather expensive for many countries' health systems. These are key to palliative care in Africa where the majority of cancer patients remain in the community with extreme suffering. Valuable partnerships between Hospices and hospitals create a

system for continuity of care for patients. Many stand-alone Hospices maintain high palliative care standards and become centres of excellence in their regions/ countries.

Such examples include the Island Hospice in Zimbabwe, Holy Cross Hospice in Botswana. Ndi Moyo in Salima, Malawi and Hospice Africa Uganda among others.

Service Delivery Organisations

Many studies have emphasized the importance of the home as part of the African identity. Studies in Uganda and five other Africa countries (Kikule, 2003; Sepulveda et al, 2003) have shown that most patients and their own family members prefer home, when support services are available, to hospitals for their end of life phase. Here they are close to their relatives and ancestors, and in an environment which is familiar to them. Many service delivery organisations therefore also offer out-patient services, with day care services and outreach clinics into the communities. This also is sustainable in a resource-limited setting as in-patient care is very expensive. Community based services appropriately utilise the social fabric of large and extended families which are common in many African countries.

The service may be organised around a non-residential hospice, with teams that offer services to patients in the homes in the community or in the local hospitals, as is the case with Hospice Africa Uganda and Island Hospice in Zimbabwe. This may also be offered by an inpatient hospice as found in Pabalelong Hospice in Botswana and several others in South Africa.

Medicines and Technologies

Access to opioids has developed in Africa progressively through inclusion of palliative care medicines and opioids in the national essential medicines lists. This has happened in several countries including Uganda, South Africa, Rwanda, Botswana, Malawi, Kenya and Zambia. According to the 2015 Quality of Death Index, Uganda has made huge advances in availability of opioids.

The use of mobile phones to monitor morphine stocks has been piloted in Uganda and is an area of potential development. Health services including the use of mobile phone technology to monitor medicines access and procurement, as well as reporting, is therefore an area that many countries can explore.

Local and national reconstitution of powder morphine into liquid morphine takes place in Kenya, Uganda, Tanzania, Malawi, Ethiopia, Nigeria, Cameroon, Swaziland, Rwanda, and several others are still working with their Governments, with the help of Hospice Africa and APCA, to ensure the importation of powdered morphine.

Human Resources Management and Education

Human Resources

Palliative care is a specialty, but also a special calling or vocation. Supporting others at the end of life is not easy and often requires a higher commitment based on the compassionate and spiritual nature of the candidate. This cannot be assessed from applicants to Institutes or centres but should be assessed by employers and those deciding on who to send for palliative care training. Training is essential for all PC teams.

Also the graduate of palliative care needs to return to a unit where the medications for pain control are available, so that the holistic care can be given both in hospitals and the community.

The palliative care team is made up of several cadres. These include clinicians and educationalists but all the clinicians need to be trainers and teachers. In a free standing Hospice the organogram needs to be cemented together by administration and accounts. All these sectors heed to have trained team members as well as untrained members, who are trained on the job. Those who exceed will be sent for further education. The team spirit is held together by the ethos.

Palliative care and oncology need to be more closely associated within education programmes. Thus all palliative care programmes should have oncology sessions or modules and all oncology palliative care sessions or modules.

But all this takes money. Rarely can Africans find the funding for a long programme so scholarships from donors have supported most to date. With the funding going down due to the donors being hit recently by the recession, it is becoming more difficult to obtain funding.

The palliative care teams were initially small and widely dispersed but as PC training improves and expands, more units are able to have trained teams, but there are not enough trained to meet the needs of the millions in need.

The following are the programmes that have developed within Africa since early 1990:

- Short courses up to a week are really sensitisation and not training but they are essential to get the approach out there. These short courses are available in many countries. These include courses held for the teams as well as different cadres such as health professionals, allied health professionals, community volunteers and carers in the home, traditional healers where most patients have attended before presenting, spiritual advisors, counselling for counsellors on end of life care etc.

- Intermediate courses are held for special cadres e.g. clinical officers in PC and prescribing, tutors, teachers in health institutions, training of trainers, and so on. These last between five and nine weeks. Many who attend those programmes will not be working full-time in palliative care but need palliative care knowledge and skills to be incorporated into their every day work and to know when and how to refer.

- International Initiators programmes are a minimum of five weeks. These are for health workers who have just commenced or about to commence a new service. They include sharing with other countries as well as learning the basics of African palliative care, clinical care in hospital and the home and finally, TOT so they can return to their own countries and train others. Presently these are from International Programmes of HAU and are held mainly in Uganda but have also been held in Nigeria and Malawi, after assessment of services and on request. The clinical component of this training is essential to be of highest quality. Thus it is essential that countries requesting this programme are first assessed for high quality palliative care service and enough training sites for the students to receive experience in different settings.

- Training of Undergraduate health workers in medicine, nursing and other health professions take place in Universities and institutes of Higher education. These are most important because on this training depends the knowledge for the future of medical services in which palliative care will be incorporated. Also as more and more doctors are trained as undergraduates, the more influence they have as advocates on Governments to ensure the medications and services as well as policies are carried through. However as palliative care in this world, and particularly in Africa, is mainly based on the caring nurse, undergraduate and post graduate training of nurses is possibly the greatest need.

- International Degrees and Diplomas are held in Institutes of Higher Education, and presently held in Cape Town University, South Africa in conjunction with Cardiff University, United Kingdom and IHPCA/Makerere at Hospice Africa Uganda. Diplomas are also available in Nairobi Hospice with Oxford Brookes University, and Mildmay in Uganda. Institutes of Higher Learning in other countries are in the planning stages

Many countries are finding it difficult to employ the palliative care trained personnel. Thus we find that some who are trained are then placed in areas not requiring palliative care but to fill places in the health systems. This means that they are de-skilled and their higher degrees are a waste of time and money, and only used to boost their CVs. It is important that those trained are placed in positions to match their skills.

Like all education, training should be matched to the positions available after training. This is particularly important for expensive degree and diploma programmes. After completing training it is important that the candidate serves in a palliative care post for at least two years so as to internalise and practise the ethos and the specialty.

There should be at least one specialist nurse in palliative care attached to each oncology and/or radiotherapy unit in each country. This multi-purpose Nurse can ensure continuing medical education (CME) for the teams so that no patient is left in pain or without holistic care in parallel with their treatments and followed up into their communities.

Informal education programmes were commenced in South Africa and Zimbabwe early on. Hospice Africa Uganda commenced the service alongside clinical teaching and advocacy in 1993 and this has progressed since to a degree awarding Institution with degrees and Diplomas available for all in Africa. Education has been well established alongside clinical services in Zimbabwe, South Africa, Kenya and Uganda since they were founded. Uganda was the first to introduce palliative care in the undergraduate curriculum for doctors in 1994 and this became examinable in 1998. Training undergraduate nurses was done in parallel, while training of those working in the community including volunteers, carers in the home, traditional healers, spiritual advisors and para-medicals including lawyers and teachers, as well as short courses for health professionals in practice, were also introduced. Education alongside an impeccable clinical service was seen as the most effective way to follow the vision of "palliative care for all in Africa".

In August 2004 Uganda introduced statutory instrument 24 which authorises appropriately trained nurses and clinical officers/ medical assistants to prescribe certain forms and strengths of morphine without requiring the signature of a medical doctor. This has made it possible to improve palliative care access in the country as stated in both the Quality of Death Index Report (2015) and the Global Atlas on Palliative Care (Worldwide Palliative Care Alliance, 2014).

Palliative care has also been integrated into health worker training at pre-service levels in Uganda, South Africa, Kenya, Botswana, Ghana and development of the specialist palliative care courses at diploma and degree levels has been achieved in South Africa, Kenya and Uganda while Malawi is in the process of developing its own local courses.

The following countries have developed palliative care education at different levels: South Africa, Uganda and Kenya have Degrees and Diplomas as well as shorter courses. Nigeria has short courses in several geopolitical zones, mainly from Universities, but few services and training reaching out to communities.

Health Information and Health Management Information System (HMIS)

The development of palliative care indicators and integration of these into national health information systems is also progressively taking off. Uganda has included two palliative care indicators in the national HMIS and these are the morphine consumption data and the number of patients requiring palliative care.

Finance for Palliative Care

The biggest challenge facing palliative care provision in Africa is funding. Palliative care in Africa has historically been funded by donors. These include trusts and foundations such as the Diana Princess of Wales Memorial Fund, the True Colours Trust, the Open Society Foundation (OSF) through the International Palliative Care Initiative (IPCI), the Open Society Institute of Eastern Africa (OSIEA) and Open Society Institute of Southern Africa (OSISA), the American Cancer Society, Livestrong Foundation, Global Partners in Care and the World Prevention Alliance (African Palliative Care Association Annual Report 2013/14).

The western governments have also funded palliative care and the United States Government through the President's Emergency Plan for AIDS Relief in Africa (PEPFAR) gave palliative care development a very significant financial boost since 2004 though this has come to an end. Other western governments and their agencies have included the Department for International Development (DFID) of United Kingdom, the Danish International Development Agency (DANIDA) of Denmark and some European Union funding.

With the dwindling of some of these western government funds, the burden of palliative care funding is carried by the trusts and foundations as well as some of the African governments that are starting to invest some money into the discipline. The governments of Botswana, Namibia, South Africa and Malawi are covering the costs of the medications as well as Uganda which has ring-fenced the money for oral morphine so that patients whether in government or NGO facilities get it free of charge.

More needs to be done to safeguard the lives of Africans and reduce unnecessary suffering especially when faced with life threatening illnesses such as cancer, Multi-resistant drug tuberculosis, HIV and others and especially at the end of life.

Sustainability

The cost of health care is high but Palliative care in Africa presents even bigger challenges because health insurance is rare, families are often impoverished by their illness, and in many cases a breadwinner is the unfortunate victim of a life-limiting illness needing Palliative Care. Few insurance companies include Palliative care as a benefit in their packages and when pre-existing chronic illnesses are discovered by underwriters the premiums are made unaffordable. Insurance schemes providing for Palliative care have started in some African countries including Ghana, Rwanda and Mauritius- albeit slowly and with minimal packages. Patients are rarely able to pay out of their own pockets as this catastrophic expenditure bankrupts families. Palliative Care therefore remains largely funded through the generosity of donors. As this is in a setting of a global economic crunch the need for Palliative Care units, Hospices and teams to attend to cost-effective models of service delivery, obtain value for money and ensure programme sustainability has never been as critical as it is today. Some of the most cost-effective models of service delivery which consider the peculiarities in Africa are out-patient rather than in-patient services, home-based care, use of community volunteer workers to identify patients and be part of the care system, private-public partnerships and the use of innovative models like roadside palliative care clinics and day outreaches into the community and into institutions like prisons and slums.

Governance

A proper governance framework is critical for sustainable palliative care development. At the global level the World Health Assembly at its 67th sitting adopted a unanimously agreed palliative care resolution 67.9 that commits WHO member states to follow through with the nine roles that embrace palliative care integration into health systems, palliative care policy development, access to pain medications including narcotic medicines, palliative care education and research, partnerships and funding at country level. This resolution envisages the implementation and provision of palliative care through the life course. At the global level therefore countries have a guiding framework.

In Africa a number of governments have either passed or are in the process of developing national palliative care policies and frameworks. As at December 2015, national overarching palliative care policy development and adoption has been successfully done in Swaziland, Rwanda, Tanzania, Malawi, Mozambique, and Zimbabwe. Uganda and Botswana have also developed their draft policies and are awaiting final approvals and adoption at the highest level in government.

Inclusion of palliative care in National Cancer Control Plans has been done in Kenya and Zimbabwe. In Uganda, Botswana and Swaziland palliative care is included in the national Health Sector Strategic Plan as well as in the NCDs and HIV strategic plans.

Country Palliative Care Teams or task forces hosted by the ministries of health have been established in Uganda, Zimbabwe, Tanzania, Botswana, Namibia, Kenya, Swaziland and Mozambique.

The Ministries of Health in Swaziland, Botswana, Namibia, South Africa, Uganda, Kenya, and Rwanda as part of strengthening palliative care governance at the ministry of health level have established palliative care desks to coordinate the palliative care initiatives in their countries.

Crosscutting Issues

The role of Governments and doctors in availability of oral morphine

"States must recognize they have an obligation under international law to ensure access to controlled medicines for their populations. This obligation is implied in the cornerstone treaty of the international drug control system, the Single Convention on Narcotic Drugs, and is firmly rooted in the right to the highest attainable standard of health in international human rights law" (Global Commission on Drug Policy, 2015).

There continues to be resistance to the importation of morphine powder in many African countries. This dates back to the myths still held by many doctors due to the negative messages instilled into them as medical students re the dangers of addiction to morphine and the need to avoid it at all costs. This teaching had been changed in most medical schools in the world as the recent advances regarding this were published to governments from WHO in 1986, but many Schools of Health Care Sciences in African Universities still teach this. Governments take their advice from the medical professionals and thus doctors continue to give this message

Research and Advocacy

The World Health Assembly recently passed a resolution on strengthening palliative care as a core component as a component of comprehensive care throughout the life course (World Health Assembly, 2014). The resolution outlines responsibilities of WHO member states which are based on nine thematic areas of evidence based palliative care policies; funding and allocation of human resources; basic support to all care givers

including families, volunteers and others; education and training at all levels; assessing basic palliative care needs including pain medication requirements; revision of national and local legislation and policies for controlled medicines to improve access; updating national essential medicines lists; fostering partnerships; and implementing and monitoring palliative care actions in the included in WHO's global action plan for the prevention and control of NCDs 2013–2020. To support comprehensive integration of palliative care, the need for evidence is critical and indeed WHO's commitment to strengthening palliative care highlights commitment to more targeted research;

- monitoring global palliative care access and evaluating progress made in palliative care programmes
- encouraging adequate resources for palliative care programmes and research, especially in resource-limited countries
- building evidence of models of palliative care that are effective in low- and middle-income settings
- building evidence models of affordable oral morphine use in Africa without diversion or addiction

The African Palliative Care Association in partnership with various academic institutions in Northern, Western, Eastern and Southern Africa as well as Europe and North America has established the African Palliative Care Research Network (APCRN) to train palliative care researchers, nurture a research culture and developments on the continent. The APCRN also coordinates international student placement scheme to support international researchers who wish to undertake research in Africa.

Through joint effort and collaboration, evidence base for palliative care in Africa has greatly improved over time; research conducted include a clinical trial evaluating the nurse led model of palliative care for HIV patients (Lowther et al. ,2015) and another trial assessing the potential use of Amitriptyline for Analgesia in Painful HIV-Associated Sensory Neuropathy (Dinat et al, 2015). Research has also been conducted on understanding models of models of palliative care in Africa (Downing et al, 2015; Harding et al, 2014), appraisal of palliative care services in Africa (Wright et al, 2006). Studies have also been conducted on needs assessments for palliative care in Africa (Jacinto et al, 2015; van Niekerk et al, 2014; Herce et al, 2014) and this will inform planning for service delivery in the region.

Other research in the region has focused on opioid and other medicine availability and general practices in Africa (Harding et al, 2014; Cherny et al, 2013; Cleary et al, 2013; Harding et al, 2010a; Merriman et al,2010a) , outcome measurement in palliative care (Siegert et al, 2014; Blum et al, 2014; Besley et al, 2014; Downing et al, 2012; Harding et al, 2010b), pain and symptom burden in malignant and non-malignant diseases (Simms et al,2011; Harding et al, 2012;, Harding et al, 2014; Namisango et al, 2015; Lazenby et al, 2016), focus on heart failure (Harding et al, 2014; Selman et al, 2015; Lokker et al, 2015 ; Kimani et al, 2016), focus on delirium in the sub-Saharan Africa (Paddick et al, 2015). There is also context specific literature on symptom burden and care practices for specific cancers (Shimakawa et al, 2015; Zeeneldin et al, 2014; Mubiligi et al, 2014; Ogundiran et al, 2013; Mwaka et al, 2013; Distelhorst et al, 2015) .

Recently research has also been conducted in other areas like telemedicine and e-learning in palliative care use of telemedicine in palliative care (Rawlinson et al, 2014; van Gurp et al, 2015), costing of palliative care services (Hongoro et al, 2011), community palliative care (Frank et al, 2015; Murray et al, 2015), caring for care givers (Repar et al, 2014), place of death and end of life care preference (Downing et al, 2014; Powell et al, 2014) , education in palliative care (Rawlinson et al, 2014) and views of health professionals about palliative care (Lofandjola et al, 2014).

The evidence base for palliative care for children remains limited but several studies have been conducted documenting the experiences in developing children's palliative care (Downing et al, 2013), mapping priorities for research in children's palliative care (Downing et al, 2015b) children's palliative care needs assessment (Connor et al, 2014) status of paediatric palliative care in Africa (Harding et al, 2014), malignancies in children (Davidson et al, 2014; Weaver et al, 2015), community based palliative care services for children living with cancer (Tamannai et al, 2015) and recent development of an outcome measure for children.

Institutions engaging in palliative care research include academic institutions, hospital based palliative care units, hospices, APCA, National Associations with an anchor into collaborations and partnerships in institutions based in Europe, North America, and New Zealand. It is encouraging to note that most regions in Africa are actively participating in the dissemination of best practices through publication. This evidence is informing policy (Nabudere et al, 2014). Uganda, Rwanda, Swaziland and Malawi currently have standalone evidence palliative care policies. The evidence has also informed policy dialogues that have led to improved access to Opioids for pain management in countries like Uganda, (Merriman et al, 2010b), where trained nurses and clinical officers can now prescribe morphine and where local production has been embraced. More countries like Rwanda are talking local production which is cheaper and reduces waiting time between medicine ordering and delivery. There is however more need for capacity building and engagement in knowledge translation to increase use of evidence for informing policy, service development, delivery and general palliative care practice.

APCA has also established a triennial palliative care conference which is held every three years in different parts of the continent. This helps to create a forum where palliative care providers, researchers, educators, donors, governments, patients and the general public have an opportunity to meet and share best practices and research evidence. The previous conferences were held as follows, Arusha 2004, Nairobi 2007, Windhoek 2010, Johannesburg 2013 and the next one will be held in Kampala in August 2016.

As part of the palliative care conference of 2013 in Johannesburg, a minister of health palliative care session was held and this brought together delegations from 34 countries with ministers of health from Kenya, Uganda, Malawi and South Africa attending in person. The ministers' session came out with a statement urging for integration (Jackson, 2013).

Partnerships and Coordination

The achievement of progress in palliative care implementation and training in Africa has been possible because of the north-south partnerships that exist between African ministries of health, training institutions and civil society players and their partners in Europe and North America. South-to-South partnership have also been useful especially as regards training where other African countries have utilised facilities in Cape Town South Africa and Hospice Africa Uganda and Makerere University in Uganda to develop palliative care human resources (African Palliative Care Association Annual Report 2012/13). However African palliative care needs a greater input from African academics and the communities. There is so much in Africa that Western countries could learn from, particularly in keeping costs down, which African teams are forced to do in order to have an affordable service.

Other key role players include the legal and human rights players in supporting the unique challenges of palliative care patients as professional councils for medical, nursing, allied health professional as well as legal practitioners in ensuring accreditation of palliative care training and recognition.

Too often oncologists view their role in cancer care as ending when cure cannot be achieved, but this approach leaves most cancer patients in resource-limited countries with no care at all.

Role of Community Volunteer Workers in African Palliative Care

In Africa there is a shortage of doctors and even nurses especially in rural areas. The need for community-based resources to complement Hospice and Palliative Care teams is therefore necessary. Community Volunteer Worker (CVW) (Jack et al, 2011) programmes have been developed by some countries (Uganda, Kenya, Malawi etc) to train lay people who are identified by their own local villages to help by providing support to

patients in their own homes. The CVWs are the Palliative Care team's "eyes and ears" in the community whose hands bring basic nursing care into the home. CVWs assist collect patient medications from the health centre/ hospital, and promote adherence to treatments. There has been much value shown by these programmes with CVWs acting as a 'bridge to the hospice' in identifying patients who would otherwise not have received any care (Jack et al, 2011).

Traditional Healers and Remedies in Palliative Care

Traditional healers have been part of the fabric of care in Africa since time immemorial and many molecules purified in the laboratory into tablets have their origins from plants and other natural materials found in the forests. The biggest challenge with traditional remedies is that some have not been well researched and without standardisation it is difficult to specify doses and combine treatments for the concern of side effects. It is nonetheless important to recognise that many patients will concurrently use traditional remedies during their Palliative care and the clinician will need to watch for drug interactions and side effects. Palliative Care however recognises that herbal remedies may represent valid local alternatives to the scarce and unaffordable modern medicines for the treatment of pain and symptoms. In some countries like Uganda and Malawi Palliative Care practitioners are working with traditional healers to identify useful remedies and there are training courses in PC for traditional healers who in turn invite the professional interdisciplinary teams to learn about herbal remedies in and from their forests. There is increasing interest in traditional medicine becoming an integral part of health policy through collaboration or integration. With research more remedies, like frangipani sap for the treatment of pain of herpes zoster vesicles as well as post herpetic pain, will become regularly used treatments.

Sap from the frangipani tree when topically painted on herpetic vesicles, and post herpetic area of pain, brings pain relief.

Figure 13: Pain relief for herpes can be obtained from the sap of the frangipani tree

Complementary Therapies in Africa

Unless overtly harmful it is important that anything which improves the quality of life of the patient should be encouraged. The psychological support which many complementary therapies offer must be appreciated. Complementary therapies used together with conventional treatments offer a more holistic approach to care and promote pain relief as a relaxed patient has a higher pain threshold. Acupuncture, aromatherapy, reflexology, massages, and distraction techniques are being increasingly used including in oncology units when added on therapies to benefit patients. The placebo effect is real and must not be scorned.

Role and Influence of Religions and Spirituality

Religion and spirituality are part and parcel of the fabric of the people of Africa and in offering holistic care health workers must recognise this and address issues of patient's spirituality. Everyone has a spiritual dimension to his/her being, and spirituality is about what gives us meaning in our lives, our beliefs and values, and our ultimate concerns particularly when patients are facing life-limiting illnesses like cancer. At the end of life spiritual issues become increasingly important and it is often at this stage that patients can often experience significant spiritual growth and gain meaningful fulfilment.

Although spirituality is important in care of cancer and other palliative care patients talking about spirituality is a very personal matter, and good listening and communication skills and a trusting relationship needs to be developed in order to bring the discussion to a greater depth. A patient's experience of physical pain may be worsened by spiritual distress, and sometimes spiritual pain is diagnosed after the failure of the patient's physical pain to respond to increased doses of analgesia.

It is important that clinicians are not judgemental, do not try to convert patients to another faith but recognise that it is a time to listen to the person facing death, and respect his or her wishes and needs. Some oncologists and health workers find caring for people with cancer in the end stage of life challenging, and all too often when faced with difficult questions or situations there is a tendency to give false reassurances to try to make the patient feel better. It is also important to remember that in Africa some religions and faiths may interfere with the continuation and completion of cancer treatment and palliative care, for example when miraculous cure is sought by patients and their families.

Each professional has a role to play in dealing with spiritual issues and an interdisciplinary model of oncologic and palliative care that includes spiritual support is intended to ensure that patients receive the best care. Referral to a religious leader or pastoral worker should always be considered for patients, but in our experience most patients have developed their own way of supporting their relationship with their God and are grateful if the health care professional shows empathy and understanding of this. Therefore a section on spirituality is included in patient assessments in palliative care in Africa.

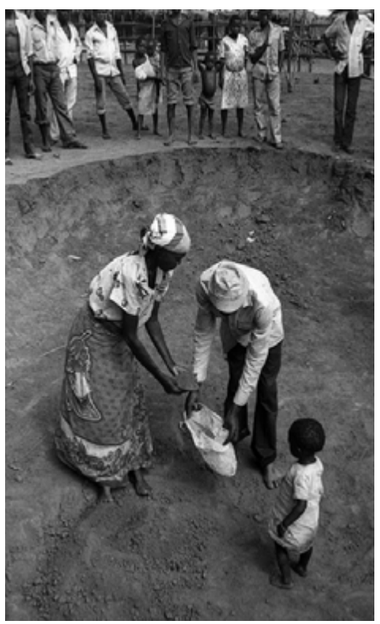


Figure 14: Therapies for the desperate - Nanyonga's "garden soil cure" for HIV/ AIDS - With permission from Prof Peter Mugyenyi

Legal and Human rights approaches to palliative care

Legal, ethical and Human Rights issues are now a recognised field within palliative care and countries such as Kenya, Uganda, and Malawi have developed guidelines on this topic for health care workers as well as families.

Leveraging the policies and system for cancer, HIV, tuberculosis, for palliative care delivery

Because of the decline in funds for palliative care over time and given the burden, all funds for the various disease programmes such as tuberculosis, HIV and cancer ought to be used to offer palliative care as part of an integrated approach to suffering.

The Future?

Many HIV organisations have been trained in palliative care although few were able to practice it fully due to pressure from donors for numbers, which are reduced when time is given to those in need of palliative care. However as the epidemic is reducing in the countries above the South of Africa, these people are a rich source of palliative care human resource in the future.

Working closely together with oncologists, sharing resources according to patient's needs and expertise in our clinical professions and in education and training programmes, we will bring relief to those with total suffering in Africa, and in the words of Hippocrates:

"Cure sometimes, treat often, comfort always."

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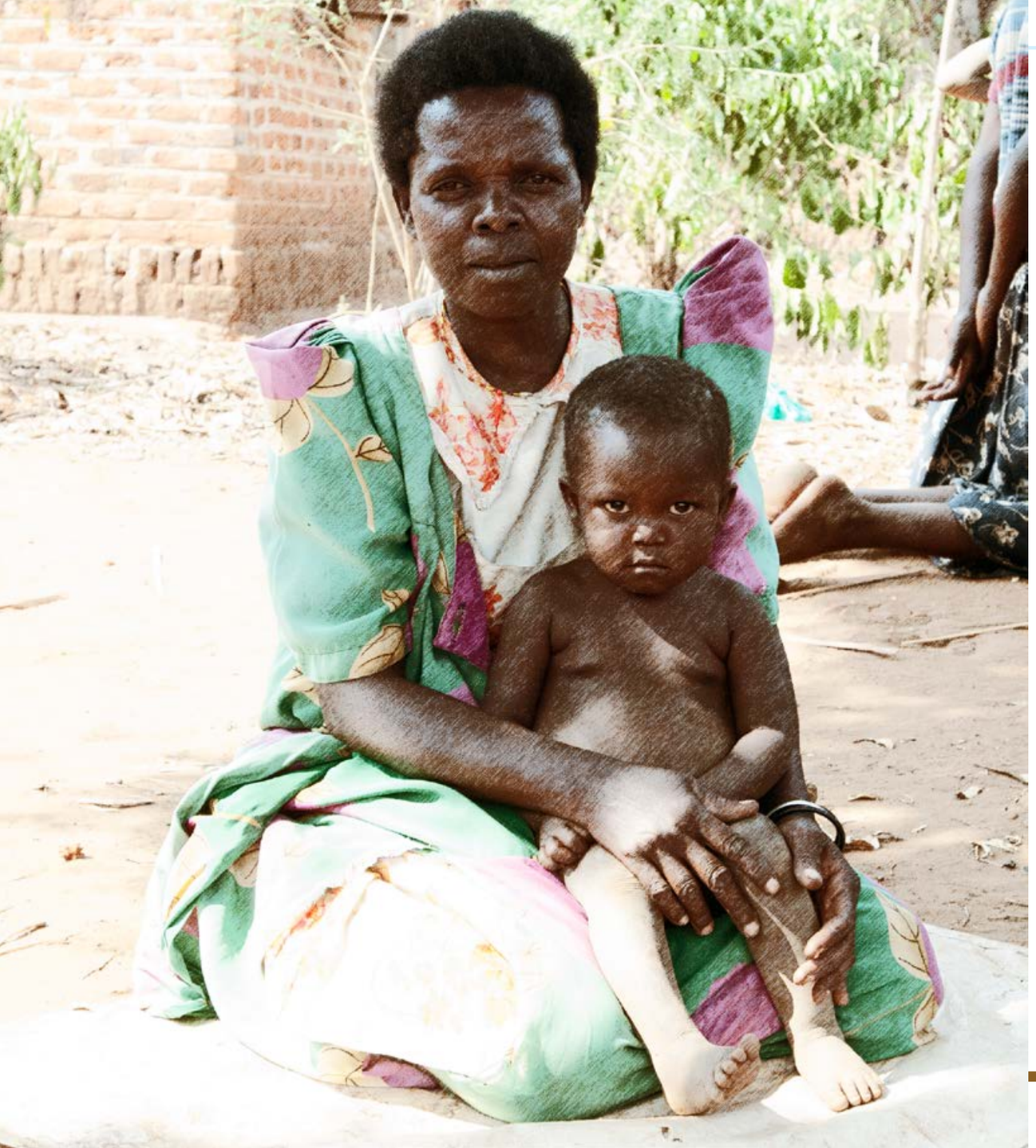

Chapter 9

Africa: Liver Cancer

Pierre Hainaut*

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Liver cancer is the first cause of death by cancer in men (13% of all cancer deaths) and the third in women (6%) across the African continent (Jemal et al, 2012). Incidence and mortality rates are almost equal, underlining the lack of curative treatment options. Based on clinical case series, the majority of African liver cancers are hepatocellular carcinomas (Umoh et al, 2011), a cancer that develops from the cells of the liver parenchyma (the hepatocytes), often as a sequel of a chronic infectious and inflammatory liver condition. Other forms of liver cancer are rare, including intra-hepatic cholangiocarcinoma (CC), a cancer of the epithelial cells lining the bile ducts (the cholangiocytes). In high-resource countries, CC represents about 10-15% of all cases of liver cancer and its incidence is rising (Bruix et al, 2015). CC occurs at high rates are in regions of South East Asia where infections by liver flukes (flatworms) are widespread. In Africa, CC is relatively frequent in Egypt but represents less than 5% of the cases documented in clinical series in sub-Saharan Africa (Otegbayo et al, 2006). These figures, however, should be taken with caution since histological diagnosis is available for only a fraction of the liver cancer cases detected on the continent.

The main causes of liver cancer in Africa are chronic infections with Hepatitis B Virus (HBV) and to a lesser Hepatitis C Virus (HCV), compounded by exposure to aflatoxins, a class of carcinogenic mycotoxins that contaminate food commodities in Western and Central African countries (Franceschi and Raza, 2009; Hall and Wild, 2003; Hoshida et al, 2012; Kirk et al, 2006; Montesano et al, 1997). The main form of aflatoxin in the food is aflatoxin B1 (AFB1), a demonstrated mutagen in hepatocytes. HBV and HCV have strong and multifactorial oncogenic properties. Aflatoxins, chronic HB and chronic HC infections are all classified as Group 1 carcinogens by the International Agency for Research on Cancer (IARC) (Pearce et al, 2015). Together, these factors account for well over 75% of the risk of hepatocellular carcinoma across sub-Saharan Africa. Preventive strategies to reduce the effects of these factors are available: a safe and efficient neonatal HBV vaccine has been introduced in the mid-eighties and reduction of aflatoxin exposure is achievable through several methods, including improved agricultural processes and diversification of the diet towards non-contaminated diets. However, these measures will take decades to reveal their full impact and, to date, their effect on the reduction of the rates of liver cancer is not yet perceptible. In the meantime, the population of Africa is expanding at an unprecedented pace, from about 1.2 billion in 2016 to a predicted 2.5 billion in 2050, with an increase of over 200% of those aged over 60 years, the age at which HCC most frequently occur in the rest of the world (https://populationpyramid.net/africa/2050/). Thus, the death toll by liver cancer in Africa will continue to increase at least until circa 2050-60, when most subjects aged 60 would have been vaccinated against HBV at birth. Therefore, we must be prepared to

see at least a doubling of African liver cancers death until 2050 with dramatic human, social and economic consequences, making it one of the worst cancer epidemics worldwide.

In 2008, we proposed an action plan of 36 measures to curb the African liver cancer epidemics in the period 2010-2050 (Hainaut and Boyle, 2008). These measures included four domains for action: rolling out and assessing sustainable vaccination against HBV, reducing exposure to aflatoxins, monitoring and preventing the spread of HCV, and developing early detection, diagnosis and treatment of chronic liver disease and cancer. In this chapter, I briefly summarize the current situation and knowledge on liver cancer in Africa, highlighting the few progress made since 2008, and I review the progress made in implementing the the "36 steps against liver cancer in Africa".

Geography and Ecology of Liver Cancer in Africa

The burden of liver cancer is not uniform across the African continent. The GLOBOCAN database of the International Agency for Research on Cancer (http://globocan.iarc.fr/Default.aspx) provides estimates of incidence and mortality for all African countries, showing over 10-fold variations between highest (parts of Western Africa) and lowest (parts of Northern and South-Western Africa) incidence regions (Figure 1 A). These estimates should be seen as conservative, in particular for Central Africa. The lack of clinical infrastructure in many regions precludes accurate diagnosis and it is likely that a number of cases are neither diagnosed nor systematically reported. Rigorous data on incidence and mortality are scarce and incomplete for most African countries. There are only 5 national cancer registries and less than 50 regional registries, the latter mostly covering urban areas, altogether covering about 5% of the African population, with a quasi-absence of formal data for Central Africa. The highest incidence rates are observed in The Gambia, the only country where liver cancer is actively registered in the context of the Gambia Hepatitis Intervention Study (Bah et al, 2013). Moreover, incidence rate estimations by country do not accurately reflect the differences that may exist across regions in large countries with contrasted populations and ecological patterns, such Mali, Niger, Sudan, RDC Congo or South Africa. In countries of the Sahel, liver cancer occurs at much higher rates in the semi-tropical South than in the arid North.

According to GLOBOCAN, the estimated overall incidence for liver cancer across the continent was 11.3 per 100,000 in men and 5.3 per 100,000 in women in 2012, roughly corresponding to about 50,000 cases in men and 25,000 cases in women. Broadly speaking, three areas with contrasted incidences can be distinguished. Areas of high-incidence cluster into an "African liver cancer belt" that forms a crescent-shaped zone running across Western and Central Africa but leaves out most of eastern Africa (Figure 1).

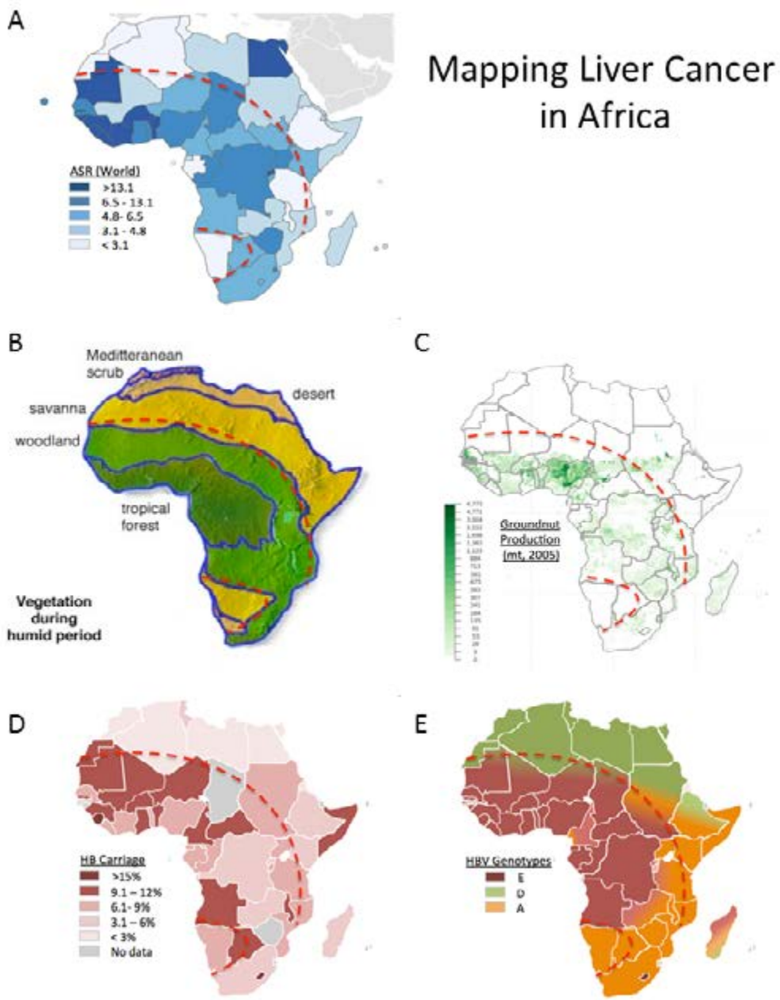

Figure 1: Mapping the African liver cancer belt

Dotted red lines delineate an area encompassing countries with incidence rates > 5 per 100,000 (both genders), excluding Egypt (see text).

(A) Age-Standardized Rates (ASR) of incidence according to GLOBOCAN 2012 (http://globocan.iarc.fr/Pages/Map.aspx; both genders). (B) Ecological zones and vegetation during the humid period (source: Berkeley Library, http://guides.lib.berkeley.edu/VegMaps/Africa); (C) Areas of rainfed groundnut production (millions of tons, 2005; source: HarvestChoice, 2015. "Groundnut Rainfed Production (mt, 2005)." International Food Policy Research Institute, Washington, DC., and University of Minnesota, St. Paul, MN. Available online at http://harvestchoice.org/data/grou_r_p.). (D) Estimates of Hepatitis B chronic carriage in adult population (source: Schweitzer et al, The Lancet 2015; http://dx.doi.org/10.1016/S0140-6736(15)61412-X, SCHWEITZER); (E) Estimated distribution of the main genotypes of Hepatitis B Virus (data from Pujol et al. 2009, adapted).

The northern limit of the belt forms an arc that runs from the coast of Mauritania in the west to central Chad and South Sudan, then plunges southwards across the Lakes region to reach the eastern coast of Africa at the level of Mozambique, engulfing Western, Central and parts of southern Africa, with the exception of desertic areas of Namibia. Within this belt, incidence rates for liver cancer are consistently above 10-20 per 100,000 in men and 5-10 per 100, 000 in women. In the Gambia, where nationwide cancer registration is continuous since 1986, liver cancer is the most frequent cancer in men, representing 62% of all cancers with an age standardized rate (ASR) of 32.84 (95% CI, [30.97–34.70]) per 100,000. In women, it represents 28% of all cancers, with an ASR of 14.90 (95% CI, [13.62–16.17]) per 100,000, ranking a close second to cancer of the cervix cancer (15.45 (95% CI, [14.18–16.66]) per 100,000) (Bah et al, 2013; Viviani et al, 2008) (Figure 2).

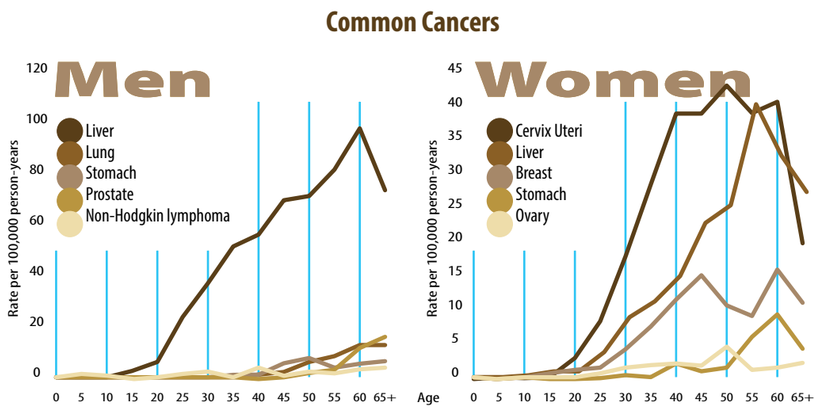

Figure 2: Cancer burden in The Gambia

Age-specific incidence rates of the most common cancers in men in The Gambia: 1987 to 2002. B. Age-specific incidence rates of the most common cancers in women in The Gambia: 1987 to 2002. Figure adapted from Viviani et al, 2008.

Lower incidence rates are observed in regions north, south and east of the belt, with a few notable exceptions. In northern Africa, rates are in the range of 3-5 per 100,000 in both man and women, except in Egypt, where an unusually high burden of chronic liver disease and HCC has been caused by the iatrogenic spread of Hepatitis C Virus (HCV) during mass intervention campaigns against liver flukes (Shistosoma haematobium), a parasitic infection causing bladder and pancreatic cancers (Strickland, 2006). In Eastern Africa, low rates are reported in Ethiopia, Tanzania, and Malawi (< 2 per 100,000), whereas rates are lower than the African average in Eritrea, Somalia, Kenya and Mozambique.

Trends in incidence suggest that the burden of liver cancer has remained practically unchanged over the past 30 years. However, there is evidence for an increasing trend in women. In The Gambia, comparison between cancer registration data from 1986-1997 and 1998-2006 revealed that rates remained relatively stable in men (from 38.36 to 32.84 cases per 100,000 in the first and second period, respectively) whereas in women rates increased from 11.71 to 14.9 cases per 100,000, with an Annual Percentage Change (APC) of 3.01% and increase in the absolute number of cases of 80.28% (compared to 26% in men) (Sighoko et al, 2011). This trend may underlie the growing impact of risk factors for liver cancer such as metabolic disorders associated with obesity, physical inactivity and/or diabetes type 2. Indeed, time trend analyses indicate that the prevalence of obesity in urban West Africa had more than doubled (114%) over 15 years, accounted for almost entirely in women (Abubakari et al, 2009).

Most of the African liver cancer belt coincides with the hot and humid climates that characterize the inter-tropical zone. Within this zone, the highest incidence rates appear to be at the junction between humid and semi-arid climates in West and Central Africa, in the regions of maximal amplitude of change in the vegetal cover between humid and dry seasons (Figure 1 B). The map of this high-incidence area overlaps with that of production of groundnuts (peanuts), one of the main sources of contamination of the diet by aflatoxins (Figure 1 C). This area also shows the highest levels of endemicity for Hepatitis B Virus (HBV) carriage (Figure 1 D). Strikingly, the regions of highest incidence within the belt correspond to countries where the major form of HBV in chronic carriers is Genotype E, whereas incidence rates are lower in regions with dominant Genotypes A (Southern and Eastern Africa) or D (Northern and Eastern Africa) (Figure 1 E). Outside the belt, the most prevalent cancers are cancers of lung (Northern Africa), oesophagus (Eastern Africa) and prostate (South- Western Africa) in men and breast cancer in women. The maps presented in Figure 1 show illustrate the strong ecological correlations between climate, vegetation, agriculture and viral infections, characterizing the African liver cancer ecosystem. Together, these characteristics not only determine the prevalence of exogenous risk factors for liver cancer: they also shape the infectious, immunological and inflammatory patterns affecting the people living in these areas.

Diversity of HBV Genotypes and Risk of Liver Cancer

HB carriage is endemic throughout sub-Saharan Africa and is not restricted to the zones of the African liver cancer belt. Rates of carriage are consistently above 8% not only in the high-incidence regions of Western and Central Africa, but also in regions of Eastern and South-Western Africa where the rates of incidence of liver cancer are substantially lower (Figure 1, map C). In The Gambia, chronic HB carriage is detected in about 15% of the subjects born before the initiation of the neonatal vaccination program in 1986. In Mali, a recent study in a cohort of volunteers from Bamako city has detected a rate of carriage of 18% in (non-vaccinated) adults aged over 18 years (Traore et al, 2015). There are, however, considerable local variations in the rate of HB carriage. For example, in The Gambia, rates of 36% and 17% have been observed in the children of two rural villages located less than 5 km apart (Whittle et al, 1990). Overall, the prevalence of chronic HCV carriage appears to be low in Western Africa (1-2%). In The Gambia, successive case-control studies conducted between 1986 and 2000 have shown a cohort effect for HC carriage (Kirk et al, 2004), suggesting a possible iatrogenic spread due to unidentified interventions. In Northern and Southern Africa, sub-endemic rates of HB carriage are observed, together with a higher prevalence of HC carriage, culminating in Egypt, where HC carriage is detected in over 20% of the male population (see above).

HBV (and HCV) are genetically diverse groups of viruses that occur as distinct genotypes, each prevalent in defined geographic areas (Figure 1, map D). HBV genotypes are defined as forms that differ between them by at least 8% of viral DNA sequence (Pujol et al, 2009; Sunbul, 2014). Genotype E is by far the most prevalent form in the regions of high incidence of Western and Central Africa. This genotype is rarely detected in other parts of the world (with the exception of limited regions of African immigration in the Caribbean's and in Latin America) and represents up to 90% of the virus circulating in the populations of The Gambia, Senegal and Southern Mali. It differs from other HBV genotypes by its homogeneity – there are no defined sub-genotypes- and by the relatively mild course of the acute hepatitis it causes in children and adolescents. Genotype D is the main genotype in North Africa and its region of high prevalence extends across the Middle East, Central Asia and India. Genotype A is a genotype of Western European origin, which dominates in Southern and Eastern Africa. Genotypes B and C, the most prevalent genotypes in south Eastern Asia, and the less common genotypes F, G, H, I and J are virtually absent in Africa (Pujol et al, 2009; Sunbul, 2014). HB genotypes show differences in their mode of transmission, their rate of carriage acquisition and the characteristics of acute and chronic diseases they cause in infected subjects (Kao, 2002). They all infect newborns and children, either through vertical transmission from carrier mothers during delivery, or horizontal transmission by saliva or blood contacts in the first months of life. Younger age at infection increases the risk to become HB carrier (Kirk et al, 2006). Transmission of Genotype E appears to be predominantly horizontal, with only few children becoming infected at birth from carrier mothers with high viral loads (Viviani et al, 2008).

Clinical Patterns of Liver Cancer and Trajectories of Chronic Liver Diseases

In high-resources countries, HCC typically develops at an average age of 65-70 years in patients with clinical history of chronic metabolic and immuno-inflammatory liver disorders characterised by progressive liver fibrosis and/or cirrhosis. Over 80% of the patients diagnosed with HCC have a previous diagnosis of cirrhosis (Bruix et al, 2015). In regions of high incidence of Africa, the situation appears to be quite different. First, most liver cancers develop at a much earlier age than in industrialized countries, in particular in patients with chronic HB. In a case-control study in The Gambia, the mean age at diagnosis was 48.1±15.2 years (Kirk et al, 2004). A recent survey in 1552 histologically confirmed patients from 14 centres across sub-Saharan Africa has reported that the mean age at HCC diagnosis was 42 years (Interquartile range, IQR: 34-55) in patients with chronic HB and 55 years (IQR: 46-65) in patients with chronic HC. The most frequent age range for HCC diagnosis in HB carriers was 32.5-37.5 years and 43% of HB-related HCC cases occurred before age 40 years (Yang et al, 2015). Second, cirrhosis does not appear to be an obligate precursor for HCC. In a case-control study in The Gambia, histological signs of cirrhosis were present in 62% of the patients at the time of HCC diagnosis (Umoh et al, 2011) but only a minority of the patients had received a diagnosis of cirrhosis prior to HCC. In particular, cirrhosis was seldom detected as precursor in young patients (<35 years). The majority of the patients presented with advanced HCC (84% of the cases), with multiple lesions (64%), the largest of which had more than 10 cm in diameter (53%) and affecting 20-70% of the volume of the liver (56%). Portal hypertension (dilated splenic vein), a common sequel of cirrhosis, was detected in only 10% of the cases. The main symptoms at presentation were abdominal pain (95%), weight loss (95%), and hepatomegaly (93%), whereas jaundice was observed in 22% of the cases. The median self-reported duration of the symptoms prior to diagnosis was 8 weeks (IQR: 4-16) and the median level of alpha-fetoprotein (AFP), a common biomarker for HCC, was 500 ng/ml (IQR: 266-5000) (Umoh et al, 2011). There were no treatment options for these advanced cancers and survival did not exceed 3-6 weeks post-diagnosis. These observations suggest that in high incidence areas of sub-Saharan Africa, many patients with early HB-related HCC (<45 years) show a rapid, almost explosive disease trajectory, with a lag of about 3 months between first symptoms and death from advanced liver cancer and no prior diagnosis of cirrhosis. This explosive trajectory is uncommon in regions outside the liver cancer belt, even in those with high incidence of HCC. For example, in Egypt, a retrospective study on 290 patients reported that HCC occurred at a mean age of 56.6±7.7 years in a context of cirrhosis due to HCV in 71% of the cases (Abdelaziz et al, 2014).

Current knowledge on the burden of chronic liver diseases in Africa is scarce. There is little information on the prevalence of liver fibrosis and liver cirrhosis in the general population or in at-risk groups of HB or HC chronic carriers. The 2010 Global Burden of Disease study analysed liver disease mortality based on mortality estimates mostly from verbal autopsy given the lack of publicly available vital registration data in most regions. This study found that the number of death by of cirrhosis doubled between 1980 and 2010 (53,000 to 103,000 deaths) and that cirrhosis mortality rates per 100,000 were 50% less in Southern (12.9) as compared to Central (24.2), Eastern (23.1) and Western Africa (23.5) (Spearman and Sonderup, 2015). In a clinical series of 57 patients with severe chronic liver disease and treated in a main referral centre in Bamako, Mali, the mortality was 82.5% over 1 years, due to HCC in 33% of the cases, the other causes of death being abdominal bleeding and hepatic encephalopathy (Diarra et al, 2010). Due to lack of awareness and of systematic screening, most chronic HB or HC carriers are unaware of their status and are not being followed-up for liver functions and symptoms. In a recent study in Bamako, chronic HB carriers were identified in a cohort of 1466 adult volunteers without diagnosed liver dysfunction. Among these carriers, 32.9% had plasma HBV loads > 104copies/mL, indicative of active viral replication. Furthermore, 35.6% had Fibrotest scores ≥ 2, indicative of moderate to severe liver fibrosis (Traore et al, 2015). These results suggests that about one-third of adult HB carriers in this group show signs of active hepatitis and might benefit from anti-HB treatment (e.g. Tenofovir) for reducing the risk of progression towards severe liver disease and liver cancer (Howell et al, 2015).

These fragmentary data suggest that the burden of chronic liver disease (chronic hepatitis, fibrosis, cirrhosis) is largely under-estimated and unnoticed in sub-Saharan Africa. Because of the lack of awareness and the poor access to treatments, it is possible that many patients with severe chronic liver disease do not survive long enough to progress to HCC, causing an over-representation of the "no cirrhosis" pattern among HCC cases. On the other hand, the fact that the majority of patients with early HCC (<45 years) do not show sign of pre-existing cirrhosis supports the hypothesis that there is a specific pattern of occurrence for early HCC that does not require obligate precursor cirrhosis.

Africa: The Most Lethal Form of HCC

Recent pan-genomic studies using exome sequencing have identified the core oncogenic pathways often targeted by mutations or epigenetic modifications in HCC (Lee, 2015; Schulze et al, 2015; Shibata and Aburatani, 2014). In high-resource countries, the mutational landscape of HCC is dominated by alterations in three major genes and pathways, each occurring in over 30-35% of the cases: TERT, encoding the catalytic subunit of the telomerase, TP53, encoding the tumour suppressor protein p53, and CTNNB1/APC/AXIN1, encoding three regulators of the WNT signalling pathway. Additional recurrent somatic alterations occur in a large number of other genes are commonly observed, occurring each in 5-10% of the cases. .

The telomerase is an enzyme that is physiologically silenced in most normal cells but is required for indefinite replication of cancer cells. Mutations in the promoter of TERT are found in up to 50% of some HCC series and are also detectable in a significant proportion of cirrhotic nodules, thus probably representing a molecular adaptation to the strong repression of liver cell regeneration that prevails in a context of severe chronic liver disease. The importance of TERT activation is further stressed by the frequent integration of HBV DNA in its vicinity, highlighting the role of integrated HBV DNA as an insertional mutagen in liver carcinogenesis (Kawai-Kitahata et al, 2016). The tumour suppressor protein p53 plays multiple roles in preventing abnormal cell proliferation in response to a wide range of endogenous and exogenous signals. The loss of p53 through deletion or inactivating mutation is a frequent event in carcinogenesis. TP53 mutations are more frequent in HCC that develops in relation with chronic HBV than with other aetiologies (HCV, Non-Alcoholic Fatty Liver Disease) (Amaddeo et al, 2015; Nault et al, 2013). A subset of HBV-related HCC displays mutations in IRF2, a tumour suppressor controlling p53 protein activation. Consistent with their functions, TP53 and IRF2 mutations are mutually exclusive in HCC (Amaddeo et al, 2015). The WNT pathway is an essential growth factor signaling pathway that controls the maintenance, motility and differentiation of hepatic stem cells. This pathway is commonly activated by oncogenic mutations of CTNNB1, encoding beta-Catenin, or inactivating mutations of AXIN1 or APC, two tumour suppressors that negatively regulate beta-Catenin. These mutations appear to be more frequent in HCV-related HCC than in HCC of other aetiologies.

Overall, these molecular characteristics allow distinguishing between two main classes of HCC. Class I consists of poorly differentiated tumours associated with HBV, occurring early (age <60 years) and containing inactivating alterations in the TP53 pathway. Class 2 includes well-differentiated tumours associated with HCV and/or other aetiologies, occurring mostly at age >60 years and containing activating alterations in the WNT pathway (Figure 3). Further integration between genomics and transcriptomics allows subdividing these two broad classes into 6 subgroups of HCC (G1-G6), each associated with specific clinical and genetic characteristics. This classification has potential therapeutic implications since it identifies molecular targets that may be actionable using targeted therapies in about 50% of HCC.

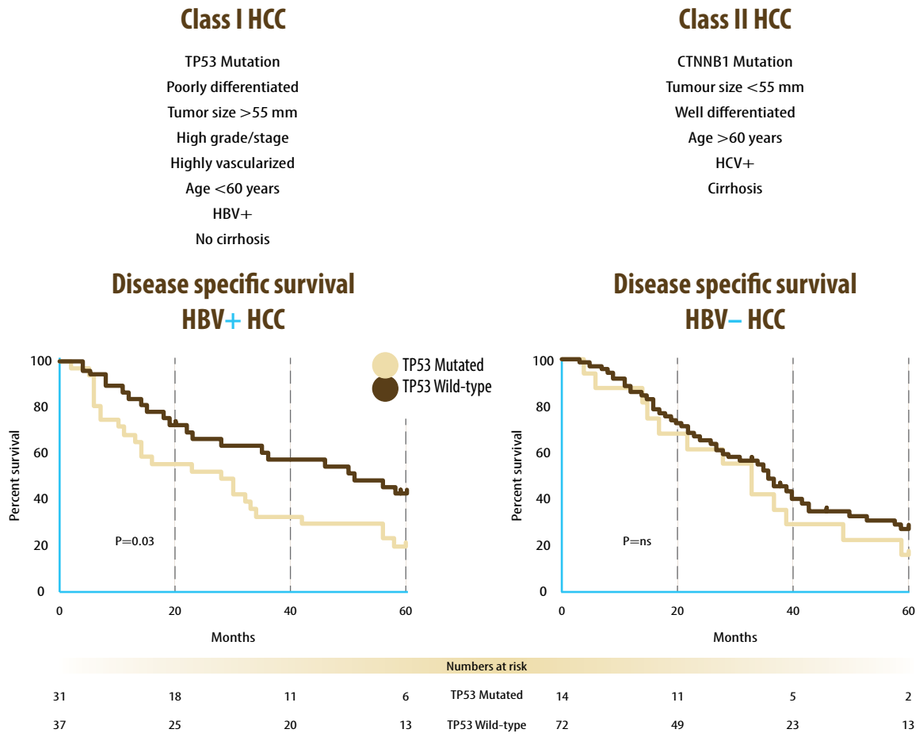

Figure 3: Two distinct classes of Hepatocellular Carcinomas (HCC) based on molecular and clinical patterns

Top boxes: molecular and clinical patterns of Class I (left, orange), and Class II (right, green) HCC. Bottom: impact of TP53 mutations on HCC survival in HBV-positive (mostly Class I) and HCV-positive (mostly Class II) HCC. Schematic pictures represent multifocal liver cancer without cirrhosis (more frequent in Class I than Class II HCC) and liver cancer developing on liver cirrhosis (most frequent presentation of Class II HCC). Survival curves from Ammedeo et al, 2015.

To date, there is no published report on the mutational landscape of liver cancer in Africa. In series of HCC from patients recruited in Europe, Shultze et al. (2015) and Amaddeo et al. (2015) have identified a subgroup characterized by a recurrent mutagenic signature, with many transversions from C:G to A:T base pairs (Amaddeo et al, 2015; Schulze et al, 2015). Most of these patients were of African or Asian origin, and their cancer tissues frequently contained a C:G to A:T transversion at the third base of codon 249 in TP53 (leading to the substitution of arginine to serine, p.R249S). This mutation has been extensively described as a specific target of mutagenesis by aflatoxin B1, which binds at the third base of codon 249 to form an adduct in TP53 DNA which, if not properly repaired, induces a specific mutation rarely found in other cancers (reviewed in (Gouas et al, 2009)). Initially independently reported in HCC from South Africa and Mozambique, the mutation was subsequently found in almost all HCC case series from sub-Saharan Africa that have been analysed to date (including cases from The Gambia, Senegal, Guinea, Nigeria, and several other countries in West Africa). In Senegal, Mozambique and The Gambia, the mutation has been reported in 30-50% of the patients. In Egypt and other Northern African countries, the mutation is found in only 1-5% of the cases. In case series from western and southern Europe, the mutation is detected in only 1-2% of the cases and the few patients who carry this mutation are of African origin. The molecular characteristics of HCC cases with p.R249S place them among the worst forms of HCC, characterized by early onset, early relapse, large size, multiple nodules, high grade, high genomic instability, vascular invasion and overall extremely poor survival (Amaddeo et al, 2015). These characteristics are consistent with the clinical features of HCC in sub-Saharan Africa, indicating that countries of the African liver cancer belt are confronted with the most lethal form of liver cancer.

Ecological Correlation Between Aflatoxin and TP53 Mutation

The majority of the cases in Western and Central Africa occur in a context of joint chronic HB carriage and lifelong exposure to aflatoxins. Overall, the two factors interact with a multiplicative effect (Montesano et al, 1997). The maps in Figure 1 demonstrate the remarkable geographic overlap between high exposure to aflatoxins, HB chronic carriage and high incidence of liver cancer.

Since aflatoxins cause specific mutations in the tumour suppressor gene TP53, it may be assume that these mutations may occur very early in the natural history of the disease, and that its occurrence may reflect the intensity of exposure to aflatoxins. Ongoing mutagenesis by environmental agents can be detected by measuring mutation load in cell-free blood DNA. The plasma or serum contains small amounts of DNA shed by cells from normal or damaged tissues. The use of sensitive methods allows detecting very low levels of mutations using simple blood sampling strategies. To address whether the aflatoxin-induced p.R249S mutation is detectable in African subjects who consume contaminated foodstuffs, we have applied a sensitive method to detect trace levels of mutant TP53 DNA circulating in the serum of subjects participating in annual surveys of chronic HB carriage in two villages in rural Gambia (Lleonart et al, 2005; Villar et al, 2011). Results showed that a low but significant number of mutant DNA copies (1-500 copies/mL) were detectable in the serum of healthy subjects, whereas much higher copy numbers were detected in the serum of HCC patients (2,500-15,000 copies/mL) (Kirk et al, 2005; Villar et al, 2011). These results suggest that high levels of mutant DNA in the blood of HCC patients are caused by the constant shedding of tumour cells containing TP53 mutation into the bloodstream. In contrast in healthy subjects, low levels of mutant DNA might occur through the occasional shedding of DNA from cells damaged by ongoing consumption of aflatoxin-contaminated foodstuffs.

In The Gambia, the culture of arachides (groundnuts) occupies >50% of harvested land. Data from the eighties showed that the vast majority of the population was exposed to AFB (Wild et al, 1990). Groundnuts are harvested at the end of the rain season (September/October) and kept into storage for consumption during the following months, until their availability decreases in February-March of the following year. Aflatoxins

are already present at harvest but further accumulate during the storage period, causing a peak of dietary exposure to occur between December and March. Studies on children from The Gambia have documented that levels of AFB-albumin adducts in the serum showed a strong seasonal variation, with the highest levels corresponding to the period of highest exposure to aflatoxins (Turner et al, 2000). Interestingly, copy numbers of mutant TP53 DNA also showed a seasonal variation between dry and wet seasons, but with different trends in HB carriers and non-carriers (Villar et al, 2011). These seasonal variations are summarized in Figure 4.

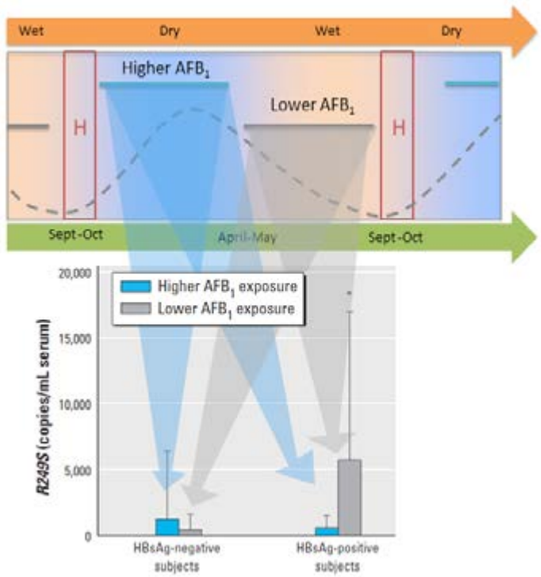

Figure 4: Seasonal cycles of exposure to aflatoxin and of mutant TP53 DNA release in the plasma in subjects from a rural area in The Gambia.

Top: Time chart representing the succession of wet (orange background; June-September) and dry (blue background, October- May) periods in West Africa. The red boxes marked "H" identifies the period of groundnut Harvesting. Blue and grey bars delineated the documented periods of higher and lower exposure to aflatoxin, respectively. The dotted line represents an estimate of the seasonal variation in exposure to aflatoxin. Bottom: detection of mutant TP53 DNA (aflatoxin-induced mutation, p.R249S, in copies per mL serum) in HB carriers (HBsAg-positive) and non-carriers (HBsAg-negative) subjects. Blue and grey arrows linking the top and bottom parts of the figure emphasize the contrasted patterns of mutant TP53 DNA variations between periods of high and low exposure to aflatoxin in both groups of subjects. Figure developed using data from Villar et al, 2011.

In non-carriers (HBsAg-negative subjects), the seasonal variations in copy numbers of mutant TP53 DNA was consistent with the seasonality of aflatoxin exposure: copy numbers were high during the period of high exposure to AFB (October-March) and low in the period of low exposure (April-July, no data were available for August and September). In HB carriers, however, the seasonal variation pattern was discordant, with low copy numbers in period of high exposure to aflatoxin (October-March) and very high copy numbers in the period of low exposure to aflatoxin. Overall, these results show that TP53 mutation by aflatoxin occurs in subjects who are exposed to the toxins. The mutant DNA detected in the blood may originate from liver cells that have acquired the mutation and may therefore reflect the turnover of these cells. In non-HB carriers, cells with the mutation are rapidly cleared, leading to the release of their DNA in the bloodstream. In HB carriers, however, cells with the mutation may persist, replicate and accumulate in the liver, so that DNA is released in the bloodstream only several months later. Interestingly, the April-July peak coincided with a period of seasonal flare (exacerbation) of chronic HB, during which hepatocytes may undergo an accelerated turnover (Villar et al, 2011) at the beginning of the wet season (Figure 4). These observations suggest that synergistic interactions between aflatoxin-induced TP53 mutation and HB chronic carriage take place well ahead of cancer occurrence and that chronic infection may enhance the persistence in the liver of cells with aflatoxin-induced mutations, which have an increased risk of neoplastic transformation.

Interactions Between Mutant TP53 and HBV: Adaptive Response for Survival to Chronic Liver Disease?

The mechanisms by which chronic HB contributes to hepatocarcinogenesis are complex and multiple. These mechanisms can be broadly divided into two types, specific and non-specific mechanisms. Non-specific mechanisms include liver damage caused by viral replication, leading to fibrosis, a wound-healing process characterized by the progressive replacement of hepatocytes by components of the extracellular matrix (Wallace et al, 2015). Specific mechanisms include the direct molecular effects of the virus itself, such as insertional mutagenesis by integration of viral DNA into the genome of host cells or oncogenic effects exerted by viral proteins, among which the HBx antigen. HBx is a multifunctional protein that controls the replicative life cycle of the virus by interacting with a multitude of cellular regulators involved in controlling entry into cell cycle, cell proliferation, mitotic spindle formation, transcription, DNA methylation and bioenergetics metabolism (Dai et al, 2014; Hodgson et al, 2012; Levrero and Zucman-Rossi, 2016; Slagle and Bouchard, 2016). By targeting these proteins, HBx accomplishes a wide series of molecular tasks geared at adapting hepatocytes to the requirements of HBV replication and production. The combined effect of the interference of HBx with these pathways may confer HBx the properties of a genuine dominant viral oncogene. However, the molecular biology of HBx is far from being understood. It has been proposed that distinct domains of the HBx protein may carry different functions, with some domains promoting cell replication whereas others may cause cell suppression, depending upon the cellular factors they interact with. Thus, the ultimate effect of HBx on cell fate may depend upon the balance between these two effects (Gouas et al, 2010; Gouas et al, 2012; Ng et al, 2016).

In chronically infected cells, HBx undergoes multiple mutational events, highlighting the rapid evolution of the gene under strong selective pressure. This adaptive evolution may enable HBx to exert different functions, depending of the stage of the natural history of infection. A number of reports have indicated that HBx is the most commonly integrated HBV open reading framed into the genome of liver cancer cells. In many instances, HBx is integrated in a truncated form, missing the C-terminal part of the protein that may be critical for its suppressive effects. This truncation may therefore activate the oncogenic properties of HBx. In HCC with aflatoxin-induced TP53 mutations, HBx is often integrated without truncation and the C-terminal part of the protein seems to form a stable complex with the mutant p53 protein (p.R249S) (Gouas et al, 2010; Jiang et al, 2010). Thus, presence mutant p53 and its binding to HBx may neutralize growth suppressive effects associated with the C-terminus of HBx, dispensing for the need of truncating that domain upon integration of HBx into the host cell genome.

Taken together, these results support the hypothesis that TP53 mutation and chronic HB cooperate together to shape the trajectory of liver disease and cancer in African patients who are exposed to both factors. This hypothesis implies that the aflatoxin-induced mutant p53 neutralize

the growth-suppressive effects of HBx while promoting its capacity to activate cell proliferation and liver regeneration. In principle, the short-term consequence of this effect is to alleviate HBV-induced liver damage and prevent fibrosis/cirrhosis, thus reducing the severity of HB-related chronic disease. The long-term consequence, however, is to give cells a head-start on the road to carcinogenesis by dramatically increasing their risk of neoplastic transformation. Figure 5 illustrates two distinct trajectories of progression towards liver carcinogenesis that may occur in different contexts.

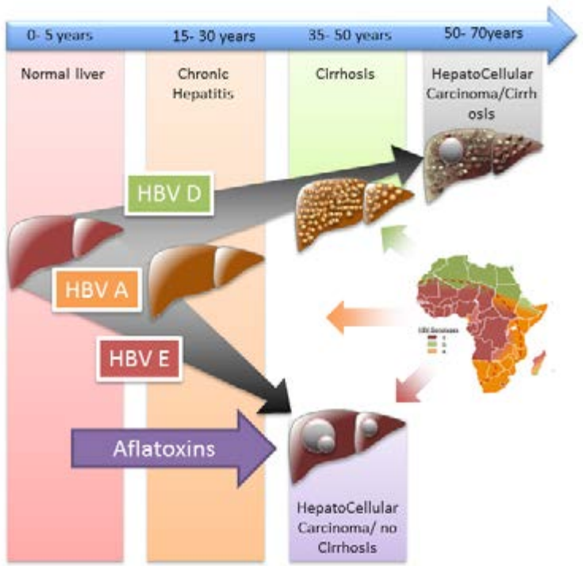

Figure 5: Trajectories of liver carcinogenesis in Africa

The figure illustrates the lifelong development of liver conditions that ultimately lead to Hepatocellular Carcinoma (HCC), starting with normal liver (left) and ending with liver cancer (right). Following HBV infection and acquisition of HB carriage in infancy (0-5 years), two distinct trajectories are highlighted. One trajectory encompass the development of progressive chronic liver disease (chronic hepatitis and cirrhosis) and culminate with the development of HCC at age >50 in a context of pre-existing cirrhosis. This trajectory is commonly observed in HB carriers from North and East Africa who are infected with Genotype D or A of HBV. The other trajectory is characterized by the early occurrence of large and multi-focal HCC at age <50, without clear evidence of pre-existing cirrhosis. This trajectory is characteristic of early HCC in HB carriers from Western and Central Africa who are infected with the Genotype E of HBV and are exposed to aflatoxin.

The first trajectory involves chronic infection, chronic liver disease developing over several decades and liver cancer occurring at age >60 in a context of liver cirrhosis and fibrosis. This trajectory is commonly seen in patients from Northern Africa, in particular in those with chronic HBV Genotype D or with chronic HCV infection. The second trajectory involves chronic infection by HB and cooperation between aflatoxin-induced

TP53 mutation and chronic HB to maintain a healthy liver until the third or fourth decade of life, when patients develop very aggressive liver cancer without conspicuous pre-existing liver disease. This trajectory is commonly observed in patients from Western and Central Africa, in particular in those with HBV Genotype E and, to a lesser extent, Genotype A. It may have evolved as an adaptation for survival in the conditions of viral infection and aflatoxin exposure that prevail in Western and Central Africa.

Curbing Liver Cancer in Africa: the Impact of Prevention

Vaccinating Against HBV

The two main risk factors for HCC in Africa, HB chronic carriage and exposure to AFB, are in principle preventable. Given the intractable nature of HCC, prevention is currently the only achievable approach to curb the liver cancer epidemics in Africa. A safe and efficient HB neonatal HB vaccine is available since the early eighties and its introduction in the WHO expanded immunization program (EPI) has been initiated in 1986 in The Gambia. The Gambia Hepatitis Intervention Study (GHIS) is an intervention trial jointly developed by The Government of the Republic of The Gambia, the Medical Research Council of United Kingdom, and the International Agency for Research on Cancer, in which 125,000 children born during the period of introduction of neonatal HB vaccination (between 1986 and 1990) are followed for 40 years through nationwide cancer registration to compare the incidence of HCC in vaccinated versus non-vaccinated subjects (Viviani et al, 2008). Since 1990, neonatal HB vaccination is available for the entire population of The Gambia. In the past 25 years, neonatal HB vaccination has been progressively rolled out in most African countries. By 2000, 7 countries had implemented nationwide HB vaccine coverage. By 2011, neonatal HB vaccination was available in 45 African countries, with reported coverage estimates varying between 22% in Chad to 99% in Eritrea (http://apps.who.int/immunization_monitoring/globalsummary/timeseries/tswucoveragebcg.html). However, vaccine coverage is at best partial for the largest and most populated countries of the African liver cancer belt (Nigeria: 50%; RDC Congo: 75%; South Africa: 76%; Sudan: vaccination started in 2014, Ivory Coast: 62%; Cameroon: 66%; Niger: 75%; Mali: 72%; Mozambique: 76%). These estimates indicate that probably less than 60 to 70% of the population of the high incidence areas is currently covered by neonatal HB vaccination, and that in most places vaccinated subjects are currently less than 15 years old.

Although the evaluation of neonatal HB vaccination against liver cancer is still pending, data on protection against chronic carriage are extremely encouraging. Most children vaccinated at birth are efficiently protected against chronic carriage at least until early adulthood. Although antibody titres wane quickly during the first 5-10 years of life, subjects develop a robust immune memory and do not become chronic carriers when in contact with the virus at adolescence, even in the absence of a booster dose (van der Sande et al, 2007). Furthermore, given the predominant horizontal pattern of transmission, only a few vaccinated children become carrier from infection at birth, suggesting that there is no systematic need for post-exposure prophylaxis using anti-HB immunoglobulins (HBIG) (Viviani et al, 2008). Despite sporadic reports of HBsAg mutants, there is no evidence for outbreaks of escape HBV mutants in vaccinated populations. Thus, neonatal vaccination against HB seems to be a realistic and efficient measure to prevent chronic HB carriage and possibly its life-threatening sequels, chronic liver disease and liver cancer. A re-evaluation of the GHIS trial in 2008 design has indicated that the first results of this intervention against cancer should be available in the years 2017-2020 (Viviani et al, 2008).

Results from Taiwan, where HCC commonly develops in adolescents and young adults, have demonstrated that neonatal HB vaccination causes a strong and sustained decrease in the incidence of early liver cancer (Ni et al, 2016). This success has led to the general belief that neonatal HB vaccination will dispose of the long-term risk of liver cancer in high incidence areas of Africa and South Eastern Asia. However, a close examination of the data from Africa should dampen this enthusiasm, at least in the short and middle term. First, whereas the risk of HCC attributable to HBV is over 90% in subjects <45 years, the lifetime risk is in the range of 70%, with the majority of cancers occurring in subjects >60 attributable to HCV and/or other aetiologies such as alcohol and chronic metabolic liver disorders. Second, as explained above, vaccine coverage was still

very incomplete in 2011. Combining these numbers predicts that neonatal HB vaccination may cut the incidence rates of liver cancer by up to 40-50% in high incidence areas by the year 2050. Since the population of Western and Central Africa is in expansion, with an exponential increase of those aged >60 years by 2050, it is predicted that the number of annual HCC cases detected by mid-XXIst century will more than double as compared to current numbers. Thus, HCC will remain at the top of mortality by cancer in sub-Saharan Africa. Therefore, the reliance on neonatal HB vaccination as the main, if not only method, to curb the African liver cancer epidemics is not warranted, and other companion measures must be identified and implemented.

Preventing Dietary Aflatoxin Exposure

Decreasing the contamination of common crops by aflatoxins is a major economic goal in most sub-Saharan African countries, in which levels of contamination of many commodities such as cereals, dried fruits and nuts by aflatoxins are above the European (4 ppm) and United States (20 ppm) accepted limits. Aside of liver diseases and cancer, exposure to aflatoxins causes severe poisoning (aflatoxicosis; in cases of acute exposure), fetal and neonatal toxicities, stunted childhood development and dysfunctions of the immune and digestive systems (Wild et al, 2015). In Nigeria, a country-wide assessment commissioned in 2012 evaluated that contamination by aflatoxins affected about 10% of the total calorie intake of the population (mainly through maize and groundnuts) and that the combined monetized burden of aflatoxin on trade and on human health in the country amounted to up to 0.5% of the GDP (http://www.aflatoxinpartnership.org/).

In 2014, the International Agency for Research on Cancer convened a working group to evaluate the effectiveness of various intervention strategies to reduce human exposure to mycotoxins (aflatoxins and fumonisins) (Wild et al, 2015). These measures include the selection of genetically resistant seeds, improved post-harvest processing (manual sorting of visibly contaminated crops, storage and packaging in controlled conditions that reduce fungal growth), primary prevention with mycotoxin-trapping enterosorbents (clay-based products, chorophyllin) and opportunities for chemoprevention. The first two approaches have been shown to cause significant reductions of aflatoxin levels in commodities. Post-harvest measures, in particular, can result in a marked decrease in the levels of biomarkers of aflatoxin contamination in subjects participating to these interventions (Turner et al, 2005). Primary prevention using enterosorbents is useful for intervention against severe aflatoxicosis. Preclinical and clinical trials of chemoprevention have been developed in high HCC incidence areas of China using Oltipraz, a dithiolethione that activates enzymes involved in carcinogen detoxification, sulphoraphanes (broccoli sprouts), a potent activator of the NRF2-KEAP1 pathway of anti-oxidant cell response, and green tea polyphenols. However, their long-term impact in preventing the health effects of aflatoxin exposure remains to be established.

All these measures require developing the awareness of the risk caused by aflatoxin in the population and making aflatoxin mitigation a joint and coordinated priority action for health, agriculture and trade ministries. Perhaps the most efficient and direct aflatoxin mitigating effect is the one that spontaneously take places through dietary diversification associated with changes in the lifestyle of African populations. In urban areas, the reliance of populations on traditional supplies of local crops is decreasing and a growing part of the food sources are commercial products containing lower levels of aflatoxins. In West Africa, in particular, there has been a constant increase in the consumption of rice in the past two decades. Over the same period, the cultivated surface of groundnuts has not increased despite the fact that the population has almost doubled. This suggests that the overall aflatoxin exposure per capita is decreasing, thanks to the diversification of food sources. Evidence from the area of Qidong, in southeast China, demonstrates that a switch from high to low aflatoxin-contaminated foodstuffs may result in a sharp and rapid decrease in the incidence of liver cancer (Chen et al, 2013). Unpublished data from the population-based cancer registry of the district of Bamako-Kati, in Mali, have shown an unexpected and continuous drop in liver cancer incidence rates over the past 15 years, perhaps related to changes in dietary habits in this mostly urban population (D. Sighoko, P. Hainaut and S. Bayo, unpublished data). It should be kept in mind, however, that exposure to aflatoxins will remain high in rural populations who essentially rely on locally produced crops for their subsistence.

Early Detection: A Stepping-stone for Curative and Palliative Treatment

Curbing the liver cancer epidemics implies curbing its mortality by improving cancer detection, diagnosis, management and therapy. To date, treatment of liver cancer in Africa is barely feasible because of the late presentation of most cases and because of the lack of clinical infrastructures. The only potentially curative option for patients with such advanced cancers in liver transplantation, which is not feasible in most clinical centres and will, in any case, never represent an option for mainstream therapy. Other treatment options include surgery, percutaneous injection of alcohol or other cytotoxic agents into the tumour, radio-ablation or therapy using specific drugs. These options require that liver cancers be detected early, at a stage where therapy is still possible. Currently, less than 20% of the patients present with early disease potentially amenable to therapy (Umoh et al, 2011).

Diagnosis of HCC in the resource-constrained context of many African countries relies on the combination of clinical signs, ultrasonography findings and detection of elevated levels of alpha-fetoprotein (AFP). In The Gambia, the use of these criteria with an AFP cut-off level of 200 ng/ml showed an overall specificity and accuracy of 99.6% and 92.3% respectively, when compared with histologically confirmed diagnosis (Umoh et al, 2011). However, even these simple criteria are not systematically used. Data from the National Cancer Registry from The Gambia indicate that, during the period 1998-2006, AFP testing was performed in less than 25% of the cases of liver cancer and that half of the tested cases were negative at a cut-off level of 200 ng/ml (Bah et al, 2013).

The short lag between the self-reported onset of first symptoms and diagnosis of advanced liver cancer (a few weeks) suggests that the disease may be present in a clinically occult form for a much longer period before its manifestation. This, in principle, provides a good opportunity for early detection. Screening is standard of care for patients at risk (e.g. patients with severe chronic liver disease) in high-resource countries, with ultrasonography at 3–6 monthly intervals as the current method of choice (Bruix et al, 2015). There is no demonstration of the efficacy of ultrasonography screening in a low-resource African context. Thus, the best option for anticipating diagnosis to potentially treatable stages of the disease is to identify specific biomarkers for early detection using simple and robust laboratory methods.

The current reference biomarker, alpha-fetoprotein (AFP), is of limited interest for screening since low levels of AFP are poorly specific for HCC. A number of other potential biomarkers have been proposed in recent years but none of them has demonstrated its applicability in low-resources contexts (Hu et al, 2013). Screening for the aflatoxin-induced TP53 mutation in DNA from the serum is not a reliable option since variable levels of mutant DNA are found in healthy subjects who are exposed to the mycotoxin and since only about half of HCC patients have the mutation in liver cancer cells (Villar et al, 2011). With this in mind, we have initiated an international collaborative effort aimed at discovering and assessing new serum biomarkers tailored for optimal applicability in detecting early HB-related HCC. Using deep-plasma proteomics, two markers have been identified as performing better than AFP in discriminating cancer against chronic liver disease and cirrhosis, with sensitivities and specificities >90% for HCC associated with HBV (da Costa et al, 2015; Shang et al, 2012). These two markers are Osteopontin (OPN) and Latent-TGFbeta Binding Protein 2 (LTBP2), two components of the extracellular matrix of the liver. A recent evaluation of circulating OPN levels in a prospective European cohort revealed that an increase in serum levels of OPN was predictive of HCC up to 2 years ahead of diagnosis. After adjusting for all variables such as AFP and liver enzymes, each 10% increment in OPN levels was associated with a significant increase of developing HCC after 2 years (OR multivariable=1.30; 95%CI: 1.14-1.48) (Duarte-Salles et al, 2016, in press). Testing of OPN and LTBP2 can be performed using robust and low-cost immunoassays. Therefore, combining these two markers offer attractive characteristics for the screening of HCC in at-risk population groups but their efficacy remains to be evaluated in an African cohort.

Perspectives: 36 Steps Against Liver Cancer in Africa

In 2008, we proposed a set of 36 steps for reducing the mortality by liver cancer in Africa by the year 2050 (Hainaut and Boyle, 2008). These steps fall into 4 main areas: preventing HB carriage, mitigating aflatoxin exposure, treating HB and HC chronic infections and chronic liver disease, and improving liver cancer detection, diagnosis and therapy. None of these measures on its own will be sufficient to significantly decrease the number of death by liver cancer in the next decades. To have a realistic chance of limiting the natural increase in liver cancer cases due to population expansion and ageing, several of these measures need to be combined into an organized and structured action plan for Africa. Table 1 lists these 36 steps and discusses the progress towards their implementation since 2008, highlighting that much remains to be done to fully implement them.

Table 1: 36 steps against liver cancer in Africa

Recommendations, Hainaut & Boyle 2008	Comments and remarks, 2016
Development of sustainable childhood vaccination strategies	Based on current estimates, we are still only half-way in implementing this objective
Bring current vaccination trials to final assessment on basis of their disease endpoints	Not done yet
Monitor long-term protection (vaccine effectiveness) of people vaccinated in childhood and assess need for booster vaccines	Current evidence shows that vaccine is effective against carriage despite loss of protection against infection itself
Monitor breakthrough infections; detect new mutants in vaccinated individuals Study interactions with other infections (e.g., HBV, hepatitis δ virus, HIV) and their effect on vaccine protection	There is still a dramatic lack of knowledge on these interactions
Establish whether vaccine efficacy varies according to viral genotype	Not done yet
Work out sustainable vaccination regimens applicable in areas with poor coverage by vaccination teams	Remarkable progress have been achieved since 2008, but this needs to be extended and consolidated
Inform and educate stakeholders, obtain participation in vaccination programmes	This is a permanent need, also taking into account changing perceptions of vaccination.
Assess the effect of occult (seronegative) infections	Not done yet
Develop infrastructure for both vaccine storage and distribution	Remarkable progress since 2008
Work out and implement economically sustainable programmes for permanent inclusion of HBV vaccination in state-sponsored vaccination programmes	This task is piloted through the GAVI alliance
Assess the effects of individual genetic susceptibility on risk of HBV carriage and on responses to vaccination	Not done yet
Reduction of exposure to aflatoxin (AFB)	Recent results support the feasibility and effectiveness but a global action plan still need to be rolled out
Develop and communicate recommendations on behavioural methods to reduce exposure	The lack of awareness on aflatoxin risk in the population is still enormous
Understand mechanisms of synergistic effects between HBV and aflatoxin	New molecular studies have revealed important clues but there is still a lack of studies using next-generation sequencing in African patients
Assess the effect of genetic susceptibility to mutagenic effects of aflatoxin	There is no significant progress on this aspect
Develop ready-to-use field biomarkers to monitor individual exposures	Current biomarkers remain relatively complex to implement.
Develop monitoring methods to assess contamination of crops and foodstuff	Markers and methods for AFB dosimetry are available
Assess mutagenicity of aflatoxin in childhood, in relation to acquisition of chronic HB infection	There is still a lack of understanding on the long –term effects of early exposure to AFB
Stimulate research on substitute crops with less contamination by aflatoxin	Remarkable progress are being made thanks to structured efforts to support agricultural research and development
Work out economically sustainable models to phase out most contaminated food supplies	New socio-economic studies are needed to assess whether changes in lifestyles and diet diversification will result in significant mitigation of aflatoxin exposure
Understanding the spread of HCV	The availability of new treatments for HCV provides unprecedented opportunities for controlling and reducing HCV-related chronic liver disease

Recommendations, Hainaut & Boyle 2008	Comments and remarks, 2016
Understand mechanisms of transmission of HCV in Africa	This is still not well understood
Assess interactions between HBV and HCV	Whether occult HBV remains a driver of carcinogenesis in patients who are seropositive for HCV is an open question.
Assess interactions between HCV and aflatoxin	Data suggest that the interaction is of similar magnitude as for HBV; however the mechanism of this interaction remains unknown
Monitor the effect of HCV in population vaccinated against HBV	This remains to be done
Promote safe injections and develop awareness of possible HCV transmission mechanisms	Remarkable progress have been made, in particular in implementing intervention and in developing transfusion
Developing registration, early detection, and treatment of hepatocellular carcinoma	Registration still covers less than 5% of African population and mortality remains unabated
Develop operational definition of disease on basis of simple and robust biomarkers	The standard diagnostic algorithm still relies on the clinical/ulstrasound/alfa-foetoprotein (AFP) "triad" and its still not systematically implemented.
Identify new biomarkers useful as pre-diagnostic and diagnostic markers for screening	New promising biomarkers have been identified but still require extensive validation
Study natural history of early disease, and its association with other chronic liver diseases	The mechanisms of occurrence of cancer in patients with no precursor cirrhosis need to be extensively studied
Understand environmental or genetic basis, or both, for familial clustering of disease	There is evidence of familial clustering; however the genetic basis have not been identified
Support training, teaching, and education of health field workers to better detect and assess liver diseases	This remains an essential task. Remarkable efforts have been made to train laboratory personnel in west Africa.
Support dissemination of simple and robust imaging technologies	Access to ultrasonography remains dramatically poor
Develop central pathology resources to assess the variability of cancer presentation throughout continent; develop biobanking	Access to pathology remains poor in most areas of high incidence. Commendable efforts are underway to develop biobanking
Improve population-based cancer registration; Develop and coordinate network of chronic liver disease registries	Support to existing registries should be maintained and expanded. Registries should provide a tool to assess the impact of HB vaccination and AFB mitigation measures.
Develop experimental model systems to assess novel pharmacological targets on basis of molecular hallmarks of disease in Africa	No relevant model is yet available for HCC in Africa
Assess the effects of antiviral treatment	Several studies have started to examine the effect of anti –HB therapies.
Develop appropriate infrastructures for therapeutic clinical trials	There is a dramatic lack of clinical resource to pilot the development of treatment trials
Develop awareness of liver disease and support patients and families	Information on liver cancer risk is poor, with many misperceptions. There is a need for advocacy and patient-oriented actions
Develop and provide palliative and pain control interventions	There is no systematic access to palliative care. The majority of patients still die with excruciating pain.

To date, only infant HB vaccination has been rolled out as a structured program, thanks to the efforts of WHO, Unicef and the Gavi Alliance (http://www.gavi.org/). Since 2014, the vaccine is available in all African countries but population coverage remains insufficient to sustain hopes of decreasing liver cancer mortality in the next three decades. Active mitigation of aflatoxin exposure requires a multi-level action plan but passive reduction will spontaneously occur through diversification of the diet as African countries move up from low- income towards middle-income status. However, this diversification is likely to take place at different paces in more affluent areas as compared to poorer (mostly rural) areas, which will continue to rely on local production of traditional foodstuff for their subsistence. Since the very few cancer registries operating in West or Central Africa are mostly based in urban areas, it is possible that we may record in the coming year an apparent decrease in liver cancer rates that may not reflect the continuing burden of the disease in rural areas.

Economic growth and dietary diversification are expected to cause many changes potentially impacting on the incidence rates of liver cancer. On the one hand, better awareness and access to care will improve the prevention and management of chronic liver diseases. On the other hand, a switch towards westernized hypercaloric diet and lifestyles may result in a rapid rise in obesity, metabolic syndromes and diabetes,

thus contributing to increase the prevalence of risk factors for liver cancer in both HB carriers and non-carriers, including individuals in whom carriage has been prevented by neonatal vaccination. Monitoring these trends will be essential to sort out positive from negative impacts of these changes.

Access to diagnosis, treatment and palliation is dramatically constrained by economic resources. Yet, the trajectory of liver cancer in Africa suggests that a good window of opportunity exists for screening, early detection and early intervention. Achieving this requires developing biomarkers and drugs specifically designed to target the liver cancers in Africa. Indeed, these cancers appear to correspond to specific subgroup of severe liver cancers, different from the most common molecular subtypes occurring in industrialized countries. Another concern is that these biomarkers and drugs should be pitched for usage in low resource contexts and that their efficacy should be demonstrated in clinical trials involving African patients.

According to WHO, health is defined as "a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity". In the case of liver cancer in Africa, the pathogenic process starts in the first weeks of life with HB infection and acquisition of chronic carrier status, and further develops over lifetime under the joint influence of chronic HB and aflatoxin exposure. Subjects exposed to these two risk factors carry a silent time bomb in their liver cells. They may remain in an apparently healthy state with no clinical signs until a few weeks before being diagnosed with advanced liver cancer. Yet the advanced status of the disease indicates that it had been developing undercover for a long duration. Thus, liver cancer in Africa is the perfect paradigm for an alternative definition of health as "the expression in a person's body of the characteristics of the ecosystem in which the person lives". Indeed, the main risk factors for liver cancer are, so to speak, built in the ecosystems of West and Central Africa. Curbing the liver cancer epidemics will require careful and rational management of African ecosystems, taking into account economic growth, changes in agricultural practice, reduction of endemic diseases, in a context of population expansion and migration, and considering that climate change and deforestation may dramatically modify the ecology and economy of the countries in the area of high incidence of HCC.

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Chapter 10

Africa: Cervical Cancer

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Cervical cancer is a preventable and curable disease, preventable by vaccination and screening and curable if identified at an early enough stage. Despite evidence for its high preventability, cervical cancer remains the first common cancer among women in Eastern Africa and the second most common in the other parts of Africa (Arbyn et al, 2011; Ferlay et al, 2015).

Brief Description of the Uterine Cervix Anatomy

The cervix is the lower part of the uterus that opens into the vagina. The lower opening in the vagina is called the "external os". The cervix is divided in two distinct anatomical entities, the exo-(or ecto-) cervix that extends from the external os to the vaginal wall, and endocervix which is the canal between the external to the internal os that ends into the uterine cavity. The epithelium covering the exocervix are squamous keratinocytic cells arranged in multiple layers similar to the vaginal epithelium. The epithelium covering the endocervix consists one layer of columnar exocrine cells. The transformation zone (TZ) is the transition between multilayer squamous and one-layered cylindrical epithelium. The anatomical position of the TZ changes with age: in young women (puberty to 20 years of age), the TZ is located on the ectocervix and is completely visible at colposcopy or other technique that enables visualisation of the cervix. With aging, the TZ migrates into the endocervical canal and after menopause, the TZ is no longer or only partly visible.

The Two Types of Cervical Cancers

There are two types of cervical cancer that have different cellular origins is squamous cell carcinoma (SCC: 80 to 90% of all cervical cancers) and adenocarcinoma (ACC: 10 to 20% of cervical cancers). The SCC develops from the transformation zone (TZ). Nearly all cervical cancers originate from carcinogenic processes induced by long-lasting, persistent infection of the TZ by oncogenic HPV (human papillomavirus) types (mainly HPV 16 and 18 which cause approximately 70 % of all cervical cancers). In this respect, it is the presence of a HPV virus in the cervix of women 30 years of age or more that represent the key risk factor for cervical cancer.

Pre-Malignant Lesions of the Cervix

Cervical intra-epithelial neoplasia (CIN) represents pre-malignant (or precursor) lesions, a fraction of which may evolve into invasive SCC if left untreated. CIN lesions are classified in three categories during the histology examination of cervical biopsies, CIN 1 being small and mild abnormalities that generally regress spontaneously; CIN 2 are larger lesions more susceptible to progress in CIN3 lesions, a fraction of which may progress into an invasive SCC. CIN lesions that are not too large can be treated with cryotherapy that is freezing of lesions at very low temperature with e.g., liquid nitrogen, which destroys the abnormal tissue. For larger CIN lesions, more aggressive treatment is needed, like local surgical excision under colposcopic control. Adenocarcinoma-in-situ can be considered as the precursor lesion of adenocarcinoma.

The Burden of Cervical Cancer in Africa

Available Data on Cervical Cancer Incidence and Mortality

Egypt and South-Africa are the two African countries that have reported cervical cancer mortality data for several years (World Health Organization, 2013). In Egypt, from 1955 to 1962, age-adjusted cervical mortality rates were stable at around 0.2 per 100,000 women. From 2000 to 2011, age-adjusted rates were stable around 0.3 per 100,000 women. In South-Africa, from 1993 to 2013, age-adjusted rates remained stable at around 12.1 per 100,000 women. Hence, according to these mortality data, the burden of cervical cancer over the last 10 to 20 years would have remained stable. However, one should bear in mind that the quality of death cause certification for cervical cancer is questionable since for a major part of deaths due to cancer of the uterus the anatomical origin (cervix or corpus uteri) is not specified. Hence trend analysis of mortality from cervical cancer is somewhat biased by the inclusion of deaths due to cancer of the corpus uteri (Arbyn et al, 2009). However, according to the Kampala cancer registry, cervical cancers would represent about 92% of all cancers of the uterus, and the remaining 8% would be the cancers of the corpus uteri (Wabinga et al, 2014).

Several cancer registries have reported incidence data from African countries to "Cancer in Five Continents", volumes I to X (Ferlay et al, 2014) and in publications (Wabinga et al, 2014). All age-adjusted (World standard population) incidence data from 1953 to 2010 have been displayed in Figure 1. No registry covers an entire country. No data have been reported for Central African countries. Few registries have reported data for periods exceeding 10 years without interruption. Despite these huge limitations, Figure 1 clearly shows the very high incidence of cervical cancer in Eastern Africa, the intermediate position of Western Africa, and the lower incidence in Northern Africa (Figure 2). Regarding trends, from 1991 to 2010, 30% increases in incidence over 20 years have been reported by two population-based registries in Uganda. Similar increases were observed in Bamako (Mali) from 1989 to 1996. In Harare (Zimbabwe), steady drops in incidence took place from 1990 to 2002, followed by a steep increase in 2003-06. A publication by the same Zimbabwe National Cancer Registry suggests a continuing increase in incidence, from 62 per 100,000 women in 1991-95 to 104 in 2006-10 (Chokunonga et al, 2013). However, incidence trends of other cancers in women were more pronounced, such as for corpus uteri (5.2% annual increase), colorectal cancer (3.8% annual increase) or pancreas cancer (4.2% annual increase). It is uncertain whether increases were real or due to better ascertainment and reporting of cancer cases.

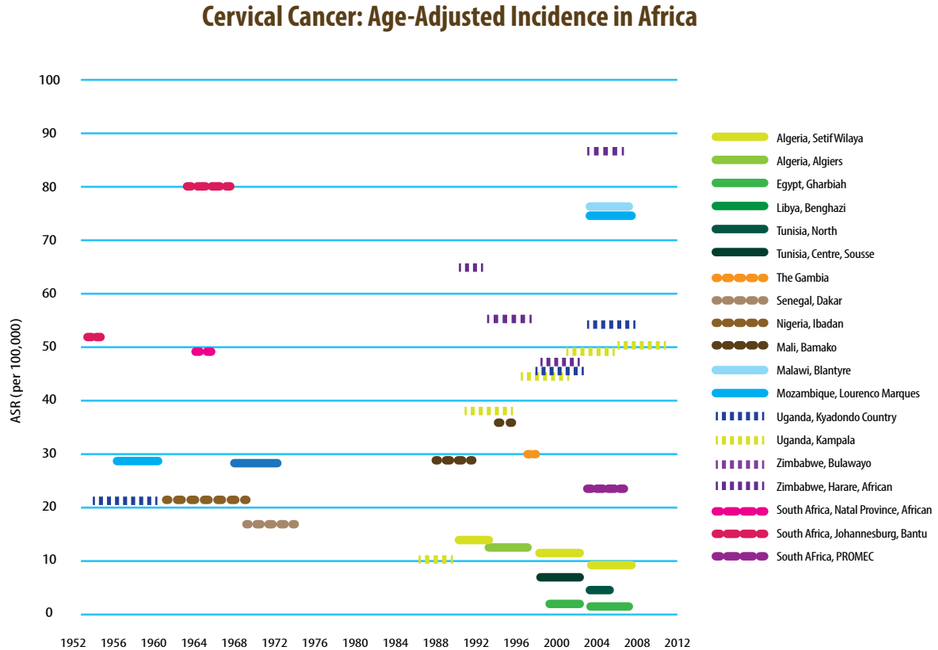

Figure 1: Age-adjusted cervical cancer incidence in Africa, reported to "Cancer Incidence in Five Continents", volumes I to X ((Ferlay et al, 2014))

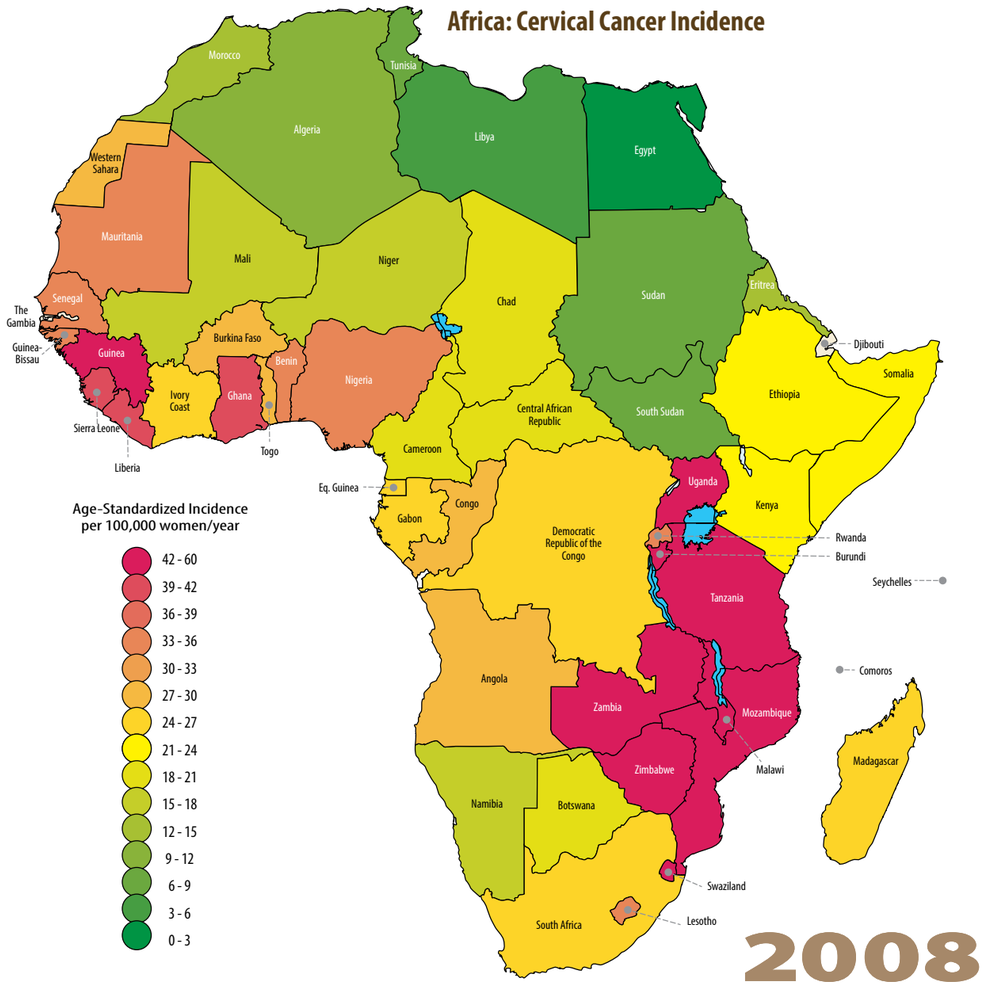

Figure 2: Geographic distribution of the world-age-standardised incidence rate (ASIR) of cervical cancer in Africa, by country, estimated for 2008 (per 100,000 women-years). Extracted from Arbyn et al, 2011

Because of the paucity of data on cancer incidence and mortality, the burden and evolution of cervical cancer in Africa are difficult to appreciate, and one needs to have recourse to statistical modelling exercises for estimating these rates.

Limitations of Statistics of Cancer Incidence and Mortality

One of the challenges to estimate the global burden of cancer is in the availability of death statistics. Only around 25% of the world population lives in countries with registration of more than 90% of births and deaths. Regions with mostly high income countries such as Europe, North America, and a few countries in East Asia and Oceania are fully covered by death statistics. In contrast, regions with low and middle income countries are poorly covered, and in Africa, very few data are available on causes of death or on cancer incidence.

There are two main sources for estimates of the global burden of cancer: the Global Burden of Disease (GBD) project (Institute for Health Metrics and Evaluation; http://www.healthdata.org/gbd) (Fitzmaurice et al, 2015; Forouzanfar et al, 2011) and the Globocan project of the International Agency for Research on Cancer (IARC) (Ferlay et al, 2010; Ferlay et al, 2012b). Unfortunately, estimates of the cancer burden from these two sources are not congruent because of the differences in methods used for estimating incidence and mortality rates in countries that do not collect the appropriate statistics.

The Global Burden of Disease project provides the most comprehensive estimate of global mortality and disability data. This study uses a wide range of data sources including death registration data, disease registry data, health facility data, and data from surveys and studies. Potential problems with this type of data include incomplete ascertainment, non-representativeness, instrument bias, misclassification and distortion. Adjusted health statistics correct for known biases in order to enhance the likelihood of generating valid, reliable and comparable health statistics. There is a need to extrapolate data for populations with no information, and to make extensive use of cause of death and epidemiological models to arrive at estimates for those countries without useable data (approximately 20% of all countries, mostly in Africa).

Globocan estimates are based on cancer registries which provide the data for cancer surveillance. In 2006, there were 449 different populations covered by population-based cancer registries in the world producing cancer incidence data covering approximately 22% of the world's population (Curado et al, 2009). Although only about half of these registries (in number and coverage) produce data of sufficiently high quality for inclusion in the periodic volume of standard comparative statistics ('Cancer Incidence in Five Continents'), the remaining registries, especially in low- and middle-income counties, nevertheless provide valuable data for the purpose of making estimates.

In many low- and middle-income countries, cancer registration faces significant challenges, including the low priority given to cancer control, lack of trained personnel, lack of expertise in data processing, lack of personal identifiers, unstable populations and lack of census data.

Alternatives to population-based registries such as hospital registers, pathology registers and hospital episode statistics are second-best solutions. Hospital-based cancer registries are common but suffer from the inability to estimate the denominator in any analysis, and this may lead to serious biases. Moreover, in low-resource settings, many people with highly fatal cancers, such as liver and pancreatic cancer, do not go to hospital and therefore are not counted.

There is still much to be done to ensure better coverage of vital statistics at the global level and more consistent and accurate estimates of specific causes of death, including cancer.

The Estimated Incidence and Mortality of Cervical Cancer

For both Globocan and the GBD project, the highest rates of incidence and mortality of cervical cancer are observed in Sub-Saharan Africa. The Globocan project has estimated an age-adjusted (World population) average of 28 cases and 18 deaths per 100,000 women in 2012, peaking to 43 and 28 per 100,000 women in Eastern Africa (Table 1). It was estimated that 57,400 women died from cervical cancer in Sub-Saharan Africa in 2012 which represents 23% of all cancer-related deaths in women (Ferlay et al, 2012a). Breast and liver cancers were the cause of death for 17% and 5% of all cancers, respectively.

Table 1: Incidence and mortality of cervical cancer by regions and sub-regions in the world and in Africa (estimations for 2012)

	Incidence			Mortality		
	N cases	Crude rate	ASR	N cases	Crude rate	ASR
World	52,800	15.1	14.0	265,700	7.6	6.8
Less developed regions	444,500	15.6	15.7	230,200	8.1	8.3
More developed regions	83,100	13.0	9.9	35,500	5.6	3.3
Africa*	99,000	18.5	27.6	60,100	11.2	17.5
Northern Africa	5,800	5.6	6.6	2,700	2.6	3.2
Sub-Saharan Africa	93,500	22.0	33.1	57,400	13.5	21.7
Eastern Africa	46,000	25.8	42.7	28,200	15.9	27.6
Central Africa	11,600	17.2	30.6	7,900	11.8	22.2
Southern Africa	8,900	29.3	31.5	4,700	16.0	17.9
Western Africa	27,000	17.2	29.3	16 600	10.4	18.5
Americas	83,200	17.2	14.9	35,700	7.4	5.9
Asia	284,800	13.7	12.7	144,400	7.0	6.4
Europe	58,400	15.2	11.4	24,400	6.4	3.8
Oceania	2,200	11.7	10.2	1,100	5.6	4.5

Rates are per 100,000 women; ASR: age-standardised rate (World standard population)

* Countries part of the different sub-areas are in the chapter annex.

Ref: Ferlay, J., et al. (2014). "Cancer incidence and mortality worldwide: Sources, methods and major patterns in GLOBOCAN 2012". Int J Cancer 136(5): E359–E386

http://globocan.iarc.fr/Pages/summary_table_pop_sel.aspx, accessed on 28/10/2015

The epidemiological picture is quite different in Northern African countries, where cervical cancer accounts for 4% of all cancer-related deaths in women, well below breast cancer that accounts for 23% of all cancer deaths, and liver and colorectal cancers that account for 8% and 6% of all cancer deaths, respectively.

According to Globocan, the incidence of cervical cancer in sub-Saharan Africa steadily increases after 20 years of age, and peak ages are between 50 and 65 years of age, which is later than in other parts of the world where the peak incidence is between 40 to 54 years of age. After 65 years of age, the incidence somewhat decreases with age.

The Globocan and the GDB project have estimated the cumulative risk of cervical cancer in women (Table 2). The estimates for the years 2010 (GBD project) and 2012 (Globocan) are comparable. However, the GBD project has estimated that overall, the lifetime risk that a woman would be diagnosed with a cervical cancer has decreased from 1980 to 2010, and these decreases are observed in all the World including in Africa (Fitzmaurice et al, 2015; Forouzanfar et al, 2011). In contrast, the Globocan estimates suggest decreasing cumulative risk for the world, but not for Middle, Eastern and Southern Africa, where cumulative risks would be on the rise (Ferlay et al, 2010; Ferlay et al, 2012b). These contrasting trends may be due to the known tendency of models used by the GBD project to obtain overoptimistic predictions. As a matter of fact, the GBD estimates for the burden of cervical cancer are systematically below what is observed by population-based cancer registries (Bray et al, 2012). It is expected that in the near future, access to HPV vaccination will become more widespread in Africa. The evaluation of the long-term impact of vaccinations on cervical cancer incidence will critically depend on methods used for estimating the burden of cancer in these countries. Population-based cancer registries should have the lead in these evaluations.

Table 2: Estimated cumulative risk of being diagnosed with a cervical cancer

GBD project					Globocan		
Cumulative risk, age 15-79					Cumulative risk, age 0-74		
	1980	1990	2000	2010		Ferlay 2008	Ferlay 2012
Africa*					Africa		2.0
North Africa and the Middel East	0.5	0.4	0.3	0.3	Northern Africa	0.5	0.4
Central sub-saharian Africa	3.2	3.6	3.9	2.8	Central Africa	1.9	2.6
Eastern sub-saharian Africa	3.6	3.4	3.4	2.7	Eastern Africa	3.0	3.1
Southern sub-saharian Africa	3.4	3.0	2.7	2.2	Southern Africa	1.7	1.9
Western sub-saharian Africa	2.0	1.9	2.0	1.7	Western Africa	2.9	2.1
Developing regions of the world	1.5	1.3	1.1	0.8	Developing regions of the world	1.1	0.9
Developed regions of the world	0.9	0.7	0.6	0.5	Developed regions of the world	0.3	0.3
World	1.2	1.0	0.9	0.7	World	0.9	0.8

GBD: Global burden of diseases

* no data for all Africa,

(Ferlay et al, 2010; Ferlay et al, 2015; Forouzanfar et al, 2011)

Risk Factors for Cervical Cancer

Risk Factors for CIN Lesions and for Cervical Cancer

The persistence of oncogenic HPV types in the cervix is a necessary cause for the occurrence of cervical cancer (World Health Organization, 2007) and therefore the epidemiology of HPV in humans strongly correlates with risk factors for cervical cancer. A number of epidemiological studies have studied risk factors for CIN 2/3 lesions and for cervical cancer within the African context (Sudenga et al, 2015; ter Meulen et al, 1992).

Most factors that increase both HPV acquisition, transmission and promote the oncogenic effect of the virus are widespread in Africa. These are:

- young age at marriage or first sexual intercourse (i.e., before age 15 or 16 years)
- a high number of sexual partners
- polygamy
- a partner that has sexual intercourses with other partners
- unprotected sexual intercourses (e.g., non or infrequent use of condoms, diaphragms or gels)
- a history of sexually transmitted infections or diseases
- low education, deprivation
- non-attendance or non-access to cervical cancer screening

In women infected with HPV, several co-factors further increase of the risk of progression to cervical cancer. These are parity (number of full-term pregnancies –see below), the use of oral contraceptive for 5 years or more, and tobacco smoking (Appleby et al, 2006; International Collaboration of Epidemiological Studies of Cervical Cancer, 2006).

Tobacco smoking is relatively uncommon in African women. According to the World Bank statistics for Africa in 2012 (World Bank, 2012), the smoking prevalence in women was less than 1% in 11 countries, 2 to 4.9% in 12 countries, and 5 to 10% in 9 countries.

Other factors have been associated with a higher risk of being HPV infected. For instance, in Morocco, a history of abortion was associated with a 4-fold increased rate of HPV infection (Bennani et al, 2012).

Infection with the Human Papilloma Virus (HPV)

Genital HPV infection is thought to be the most frequent sexually transmitted infection (STI). The infection is acquired during sexual intercourse with penetration and also, in the absence of penetration, just by skin-to-skin contact of genital organs. In most HPV infected subjects, the infection is silent. The prevalence of HPV infection is highest in adult women less than 25 years of age, with a worldwide estimate of 24% (Bruni et al, 2010). This age-related higher prevalence may be linked to the greater exocervical position of the TZ, which makes this zone highly exposed to repeated HPV infections. In a large proportion of infected women, the HPV infection progressively clears with age due to cellular immunity. The lower prevalence in older women may be due to the more endocervical position of the TZ and the lower frequency of sexual intercourse.

Risk factors for persistent HPV infection of the cervix are repeated HPV infections and increasing viral load (Grabowski et al, 2014; Gravitt et al, 2007), and these factors are strongly correlated with the younger age at first sexual intercourse, having more than one lifetime sexual partner, and having a high-risk partner (Fukuchi et al, 2009). In addition, oncogenic types of HPV are those more likely to persist in the cervical epithelial

cells (Jaisamrarn et al, 2013). Reasons why in some women the oncogenic HPV strains can escape recognition by the host immune system is still unclear (Grabowska et al, 2012).

Worldwide regularly updated reviews of HPV strains found among women with normal cytology results are maintained by the ICO (Institut Català d'Oncologia) Information Centre on HPV and Cancer (Bruni et al, 2015). According to these reviews, the prevalence of HPV infection in adult women adjusted for age using the world reference population is 24% in sub-Saharan Africa with a peak of 34% in Eastern Africa, compared to a prevalence of 9% for Northern Africa and 12% for all less developed countries (Bruni et al, 2010).

Of more than hundred known HPV types, there are thirteen oncogenic HPV (i.e., HPV capable to induce malignant transformation), the two most frequent being the HPV types 16 and 18 that are found in 50% of CIN 2/3 lesions and in 70% or more of all cervical cancers in Africa (Li et al, 2011; Ramogola-Masire et al, 2011). A large study in women with histologically confirmed cervical cancer in Ghana, Nigeria and South Africa found HPV 16 in 51% of cases, HP 18 in 17% of cases, HPV 35 in 9% of cases and HPV 45 in 7% of cases (Denny et al, 2014). HPV35 and HPV45 are more frequent in Africa than other parts of the World (Li et al, 2011). Of note, a large review of biological materials archived in biobanks found that the predominance of HPV 16 and 18 strains in cervical cancer occurrence is retrieved among HIV-infected women (Ogembo et al, 2015)

Genital warts are mainly caused by types 6 and 11.

The Role of Parity

Parity is the number of children born alive to a woman. Parity is a known risk factor for cervical cancer (Castellsague et al, 2003). Reasons why high parity would favour the occurrence of this cancer are still debated. High parity could be a surrogate measure of more sexual contacts and of low socio-economic status, factors that are themselves associated with a higher risk of cervical cancer. However the other explanation maybe mechanical. As women age, the transformation progressively climbs up into the endocervical canal, and after menopause, it is no longer, or only partially visible during colposcopy. A study in a large sample of women using cervicography (an optical system resembling to colposcopy) has demonstrated that the higher the number of livebirths, the longer the transformation zone stays on the external part of the cervix (Autier et al, 1996). And the longer the transformation zone remains on that external part, the more it keeps being exposed to infectious agents, including repeated HPV infections, all factors that maintain high levels of inflammatory processes in the cervix which contribute to the occurrence of cancer (Adefuye et al, 2012).

Of all world areas, parity is highest in sub-Saharan Africa. While from 1950-55 to 2007, parity has dropped by 40 to 60% in all continents, it has decreased by only 18% in sub-Saharan Africa, from a mean 6.7 live births in 1950-55 to 5.5 in 2007 (United Nations, 2007). In 2014, of the 50 countries with highest parity rates above a mean of 4 live births per woman, forty were sub-Saharan countries (Population Reference Bureau, 2015). In this regard, the permanence of a high parity may contribute to the high burden of cervical cancer in sub-Saharan Africa.

Impact of the HIV-AIDS Epidemic

The AIDS epidemic that erupted in 1982 mainly affected sub-Saharan populations. The immune suppression caused by the HIV infection is at the origin of a greater susceptibility to infectious agents, including HPV. Studies in all parts of the World have documented ten to thirty-fold increased risk of HPV-related lesions and cancers (e.g., genital warts, CIN lesions, anal and vulvar cancers) in AIDS patients or in HIV-infected subjects without AIDS (Denslow et al, 2014; Six et al, 1998). In Africa too, HIV-positive women have a 2 to 12-fold higher risk of CIN lesions compared with

HIV-negative women (Chirenje, 2005; Seck et al, 1994). However, the prevalence of CIN in HIV-infected women may be overestimated because cytologists tend to find more CIN lesions when they know that a woman is HIV-infected (van Bogaert, 2014).

HIV and HPV infections influence each other, because both are associated with a same sexual behaviour, and because HIV-induced immune depression increases the tolerance to HPV infection. Longitudinal studies have shown that being HIV-infected is associated with a 7-fold increased risk of persisting HPV infection (Adler et al, 2015) and with a broader range of HPV types. In their turn, women and men with genital HPV infection have a nearly two-fold increased risk of being infected with HIV (Smith-McCune et al, 2010; Smith et al, 2010).

The risk of cervical cancer in HIV-positive women in Europe and the USA is 3 to 9 times greater than in non-HIV-infected women (Chaturvedi et al, 2009; Clifford et al, 2005; Engels et al, 2008). Higher rates of cervical infections with HPV are found among HIV-infected African women. Some case-control studies in Africa demonstrated a higher risk of cervical cancer among HIV-infected women, for instance the odds ratio was 6.5 (95% CI: 2.1 to 19.8) in Dakar, Senegal (Holmes et al, 2009). However, other studies in Africa found a less increased risk of cervical cancer associated with HIV-infected African women, like a relative risk of 1.6 (95% CI: 1.3 to 2.0) in South-Africa (Stein et al, 2008).

Cervical cancer occurs at a younger age among HIV-infected women, and the aggressiveness of the cancer (as measured by the mitotic rate) is greater than in non-HIV-infected women (Gichangi et al, 2003).

The highly active antiretroviral therapy (HAART) represent an efficient treatment of HIV infection. According to the UNAIDS, between 20 and 23 million HIV infected patients in Africa would be eligible for HAART (UNAIDS, 2013). Despite marked progress after 2000, in 2012, 69% of eligible patients had still no access to HAART. Also, the massive introduction of HAART in high income countries the mid 1990's and the greater access to these therapies in the 2000's in Africa has not influenced the incidence of CIN and of cervical cancer among HIV infected patients (Ahdieh-Grant et al, 2004; Atashili et al, 2012; Heard et al, 2006). This is probably due to the impairment of the immune system that is still present when HAART is taken, or to resistance of the HIV to treatments. Thus it is far from being clear that the greater access to HAART of HIV-infected patients would affect the incidence of cervical cancer in Africa.

Socio-Economic Impact of Cervical Cancer

Because cervical cancer mainly affects women at a relatively young age, the socio-economic consequences are enormous. Women in sub-Saharan Africa lose more years of life to cervical cancer than to any other type of cancer. Many women with cervical cancer can no longer take care of their family, and their death leaves many orphans. From the GBD project data (Fitzmaurice et al, 2015), one can estimate that cervical cancer in Africa led to the loss of 1510 DALYS (disability-adjusted life years) per million women in 2013, for 880 DALYS per million women in the rest of the World.

Management of Patients with Cervical Cancer

The mortality to incidence ratio of cervical cancer in Africa is high, around 66%, which means that two-thirds of women with cervical cancer die from the disease. Several causes concur to the high fatality of cervical cancer in Africa (Anorlu, 2008):

- Most (about two thirds of cases) occur in areas where access to adapted anti-cancer treatment is rare
- Most case are diagnosed at a late stage
- Poor nutritional status and anaemia (due to cancer bleeding)
- Frequent concomitant HIV infection

- Deprivation: if treatment exists, it is not affordable
- Inadequate management of patient
- No availability of adequate therapy (e.g., radiotherapy)

Most women with cervical cancer present with late stage disease, for which the only possible modality treatment is radiotherapy for treatment or (more frequently) for palliative purposes). Radiotherapy facilities are rare in Sub-Saharan Africa and supportive care (e.g., morphine-based pain killers) is rarely available.

Some publications provide a vivid illustration of the abysmal deficiency in the capacity to adequately manage cervical cancer patients in most countries of sub-Saharan Africa. For instance, in Ethiopia, only one single medical centre can provide cobalt 60 therapy (Kantelhardt et al, 2014). Of 2300 cervical cancer patients that attended the centre between September 2008 and September 2012, about 900 received no treatment at all. Of those treated, 1059 received radiotherapy. Forty percent of them had advanced cancer (FIGO stage IIIb or more) when they were first seen by a doctor. Unfortunately, because of a waiting time of several weeks to 2 or 3 months between first visit and radiotherapy, a substantial proportion of patients with stage IIIa or less cancer had progressed to stage IIIb or more, with the consequence that when radiotherapy was delivered, 64% of patients had an advanced cancer stage IIIb or more. One quarter of radiotherapy regimens were for curative purpose and three quarter for palliative purpose.

In such circumstances, the survival of cervical cancer patients is poor. In a study in Nairobi's teaching hospital (Kenya) on 335 patients that received cobalt 60 therapy with curative intent, the median survival was 15 months (Maranga et al, 2013).

An economic study in Morocco estimated that direct costs of cervical cancer diagnosis, treatment and one-year follow-up amounted to about US$ 7,000 in 2012 (Berraho et al, 2012), and costs increased with late stage at diagnosis. This means that the management of the 100,000 cervical cancer cases in year 2014 in Africa would cost US$ 700 million (Berraho et al, 2012).

Primary Prevention

Prevention of Sexual Transmitted Infections (STI)

The primary prevention of cervical cancer largely overlaps with the primary prevention of STIs, including that of HIV.

In Africa, many studies were conducted on behaviours and methods associated with lower prevalence and transmission of STIs. Because STIs in general are associated with numbers of sex partners and unprotected sexual intercourse, prevention policies first focused on reductions of sex partners and on the provision of "barrier methods" such as the condoms.

Information on the need to reduce high risk sexual relationships has proven effective in Uganda where this policy has contributed to the control of HIV transmission (Green et al, 2006).

The regular use of condoms may reduce HPV transmission between partners. Occasional use of condom may confer no protection, mainly if partners have multiple sexual relationships. Also, because HPV-infected skin areas in the genitalia other than those covered by a condom may come into contact, condoms do not provide complete protection against the infection (Manhart et al, 2002).

Condom use has never been popular in most African countries and factors influencing utilization patterns are unclear (Hearst et al, 2004). Intervention studies have revealed constant risk of HIV infection despite increased condom use (Kajubi et al, 2005). Distribution campaigns of condoms to men and to women, although massive in some countries (e.g., in South Africa), have not been sufficient for ensuring use during most events of sexual intercourse. Inconsistent (i.e., not at all high risk sexual intercourse) and incorrect (e.g., re-use of damaged condom) use of condom is common. In South Africa, the incidence of STIs and HIV infections remain very high despite apparent marked raises (57 to 87% in men and 46 to 73% in women 14-24 years of age) in the uptake of condom use signalled by population surveys done from 2002 to 2008 (Beksinska et al, 2012). Decreases in the use of condoms has been noticed after 2010 because the fear about HIV and AIDS epidemics were waning in the general population.

A main finding of studies was that circumcision and regular condom use were associated with reduced risk for oncogenic and overall HPV (Baldwin et al, 2004). Similar findings were observed for HIV. An ecological study of 118 developing countries showed that the higher the prevalence of male circumcision, the lower the incidence rates of cervical cancer and of HIV infection prevalence (Drain et al, 2006).

In view of these observations, three randomised trials were conducted between 2002 and 2006 in South Africa, Kenya and Uganda including men from the general population tested the hypothesis that circumcision could reduce the incidence of STIs. The three trials provided strong evidence that medical male circumcision reduces the acquisition of HIV by heterosexual men and a Cochrane review estimated that reductions of HIV transmission were between 38% and 66% over 24 months (Siegfried et al, 2009). One trial in Uganda found that male circumcision reduced by about 25% the incidence of oncogenic HPV infections in women (Wawer et al, 2011). In addition, male circumcision would reduce the incidence of other STIs in women (e.g., bacterial vaginosis and trichomonas's). Circumcision of men when they are 20 to 30 years of age would be the most effective option (Londish et al, 2008).

The prevalence of male circumcision in less developed countries, especially in Africa has been the subject of scrutiny (Drain et al, 2006). It appears that circumcision rate are quite high in most Western and Northern countries, and uncommon in Eastern and Southern Africa (Figure 3). In the recent years, some countries have implementend ambitious large scale circumcision programmes, like in Rwanda where novel non-surgical modalities have been adopted for circumcising adult men (Mody et al, 2015; Mutabazi et al, 2014).

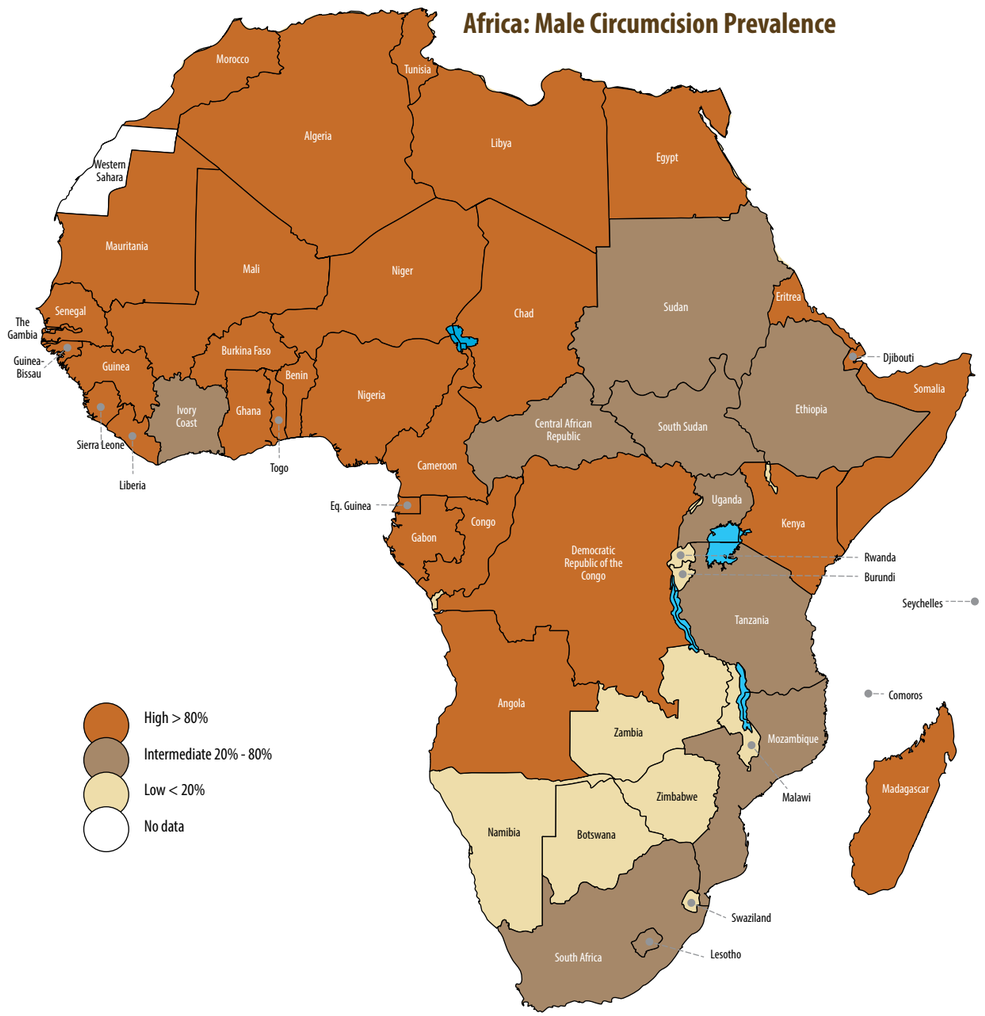

Figure 3: Male circumcision prevalence in Africa (figure created with data from Drain et al, 2006; serperate data for Northern and Southern Sudan were not available)

In conclusion, male circumcision seems to represent a practical and affordable method for controlling the transmission of HIV, HPV and other STIs. Nonetheless, circumcision does not confer a complete protection against HIV and HPV transmission and this method needs to be supplemented with other prevention methods. The role of condom use and the effectiveness of projects promoting regular condom use is still debated.

Reproductive Factors

Family planning programmes intended to reduce woman's parity may contribute to reducing the HPV transmission (e.g., improving sexual hygiene, promoting regular use of condoms) and lower the duration of exposure of the cervical TZ to the vaginal cavity and thus to repeated HPV infections.

HPV Vaccination

The advent in the 2000's of prophylactic vaccines able to trigger immunity via the production of antibodies against certain types of HPV represents a considerable progress in the prevention of cervical cancer. There are at present three commercially available vaccines, a bivalent vaccine against HPV 16 and 18 (Cervarix® - approved in 2007), a quadrivalent vaccine against HPV 6,11,16,18 (Gardasil® - approved in 2006) and a nonavalent vaccine against HPV 6,11,16,18, 31, 33, 45, 52, 58 (Gardasil 9®). In theory, approximately seventy per cent of cervical cancer cases could be prevented by vaccines against HPV 16 and 18 and 90% by the nonavalent vaccine (Arbyn et al, 2014a). Trials have shown that vaccines prepared against specific types have some capacity to protect against lesions caused by other strains (Malagon et al, 2012). Vaccination against HPV 6 and 11 also prevents genital warts. HPV vaccination in HIV+ subjects has been demonstrated to be safe and immunogenic. Efficacy results from ongoing trias are waited for (Toft et al, 2014).

Considerable attention has been given to the safety of HPV vaccination. To date, no randomised trial or pharmaco-epidemiology study has reported side effects serious enough for questioning the large scale immunisation of young adolescents. Nation-wide studies that specifically examined the possibility of thrombo-embolic and neurologic adverse events (e.g., multiple sclerosis) found no increased risk associated with HPV vaccination (Arnheim-Dahlstrom et al, 2013; Scheller et al, 2015). In 2014, the WHO has stated that the two commercially available HPV vaccine "continued to have an excellent safety profile" (World Health Organization, 2014a).

The immunogenecity and safety of HPV vaccines has also been studied in Africa and appears to be similar to studies done in other parts of the World, and the endemicity of malaria and of helminth infestation does not affect that immunogenicity (Nakalembe et al, 2015).

Anti-HPV vaccination is unable to eradicate present HPV infection (Hildesheim et al, 2007). Therefore, vaccination needs to be done preferentially before the start of sexual activity. In Africa, because a large proportion of women have their first sexual intercourse before age 15 years, HPV vaccination should start at around ten years of age (Sudenga et al, 2015). Large scale vaccination of young women and boys is likely to bring dramatic changes in the burden of cervical cancer in sub-Saharan Africa. Indeed, such vaccination represent an investment for the future given that at least twenty years would be needed before observing significant drops in the incidence of cervical cancer among younger women (i.e., women 20 to 40 years of age). However, HPV screening and vaccination of HPV-negative women is a new concept of integrated prevention that may accelerate impact on cervical cancer incidence (Bosch et al, 2016).

The trend is to incorporate HPV vaccines in national vaccination programmes. Uganda was the first sub-Saharan country to adopt national HPV vaccination in 2012. However the costs of these vaccines and their administration remain a serious barrier to the implementation of large scale vaccination campaigns in most African countries (Hutubessy et al, 2012). Furthermore, other diseases preventable through vaccination like

gastro-enteritis due to the rotavirus, meningitis, and pneumonitis are competing for the same public money. One way to reduce costs is suggested by randomised trials that indicated that two doses instead of three doses of HPV vaccines had similar immunogenicity, and that different vaccination schedules did not affect immunogenicity (Lamontagne et al, 2013; LaMontagne et al, 2014). Reviews indicate that 2 doses of HPV vaccine in girls aged 9–14 years have immunogenic properties comparable to when 3 doses are administered in girls of the same age group (World Health Organization, 2014a). A pooled analysis of two trials showed also protection against HPV16/18 infection (Kreimer et al, 2015).

In addition to cost issues, the vaccination of girls 9 to 12 years of age is challenging in view of the low attendance to schools in many areas. Other barriers include religious and cultural beliefs (Bello et al, 2011).

Worldwide health programmes like the Global Alliance for Vaccine Initiative (GAVI) have the necessary dimension for helping countries to introduce HPV vaccines in national programmes as well as for negotiating the price of vaccines. In 2015, the cost for one dose of HPV vaccine accessed through the GAVI programme was US$ 4.50, when such dose cost at least US$ 100 in developed countries (see www.gavi.org).

Despite the numerous economic and logistic barriers, a wealth of studies are on-going for determining best strategies for delivering HPV vaccination and for overcoming beliefs and cultural habits that could alter the feasibility and success of HPV vaccination programmes (Ezeanochie et al, 2014; Mugisha et al, 2015; Poole et al, 2013). A major priority for Africa would be the demonstration of long-term protection of currently available HPV vaccines, allowing integration of HPV vaccination in the traditional expanded immunisations programmes targeting infants.

Socio-Economic Condition and Women's Education

Improvements in socio-economic status, encouraging the education of women and the progress in the adoption of women's rights may make a substantial contribution to cervical cancer prevention (and probably also other preventable conditions). The preventive properties of these actions are linked to the multiplicity of influences they exert on factors involved in cervical cancer occurrence. For instance, wealthier families tend to have less children. Educated women tend to adopt healthier behaviours like attending screening (when available). The defence of women's rights may contribute in prioritizing the funding of cervical cancer screening and HPV vaccination campaigns.

Early Detection and Screening Programmes

Cytology

From 1970 onwards, cytology screening has been highly effective in reducing the incidence of and mortality from cervical cancer in developed countries (Arbyn et al, 2009; Cox et al, 1992; Watson et al, 2008). However cytology screening requires trained cytologists, a high level of quality control, has to be repeated regularly and involves multiple patient contacts with health services for the detection, diagnosis and treatment of pre-cancerous lesions. For these reasons, cheaper screening methods, which are more adapted to low and middle income countries have been recently proposed and evaluated (Tsu et al, 2005).

Visual Inspection

Three randomised trials in India showed that naked eye visual inspection of the cervix after application of diluted acetic acid (VIA) can reduce the risk of being diagnosed with an advanced cervical cancer and the risk of cervical cancer death (Sankaranarayanan et al, 2007; Sankaranarayanan

et al, 2009; Shastri et al, 2014). Although VIA is less efficient than cytology or HPV screening (Sankaranarayanan et al, 2009), this technique has been proposed as a screening modality adapted for African countries (Sankaranarayanan et al, 2003).

Swabbing the surface of the cervix with vinegar (i.e., 3-5 % aqueous solution of acetic acid) turns the neoplastic epithelium into a white area that keeps the whitening for at least one minute. This aceto-whitening may contain one or several pre-cancerous cervical lesion(s) that can be treated with cryotherapy (i.e., the so-called 'see and treat strategy'). When inspection indicates the possible presence of an invasive cancer, the patient needs to be referred to a hospital for oncological treatment.

Although, VIA has been demonstrated to have good sensitivity and reasonable specificity for cervical pre-cancerous lesions in some studies (Sankaranarayanan et al, 2004), these findings could not be reproduced in other study settings (Zhao et al, 2010). In fact, it is increasingly clear that evaluation of VIA accuracy depends much on the experience of the assessor and on the type of gold standard test against which the VIA technique was evaluated (Arbyn et al, 2008).

The meta-analysis, in Figure 4, on the accuracy of VIA for CIN-2 or more lesions derived from studies with limited verification bias, obtained sensitivity estimates varying between 37% and 91% with an average value of 77%. Also the specificity for excluding presence of high-grade CIN was highly variable, between 49 and 98%. Visual inspection after application of lugol iodine (VILI) is another visual inspection technique based on the principle that neoplastic tissues do not absorb the iodine and stay yellow. A large multi-centre large study, conducted in India and five African countries, showed that VILI is on average 10% more sensitive than VIA for CIN-2 lesions or worse without loss of specificity (Arbyn et al, 2008; Sankaranarayanan et al, 2004).

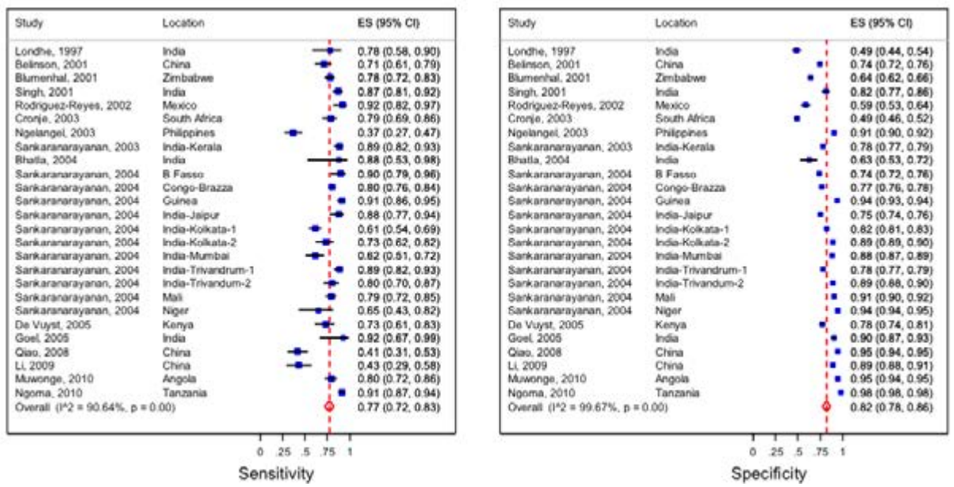

Figure 4: Meta-analysis of the sensitivity (left) and specificity (right) of visual inspection using acetic acid to detect underlying cervical intra-epithelial neoplasia or worse.

Testing for Presence of High-Risk Human Papillomavirus Infection

The detection of nucleic acid sequences of the genome of high-risk HPV types is another option for cervical cancer screening potentially applicable in Africa. Screening with clinically validated hrHPV assays, usually is very sensitive and shows a sensitivity (generally > 90% for CIN2+ and CIN3+) that is significantly greater than VIA and cytology (Arbyn et al, 2012; Cuzick et al, 2012). Nevertheless, the sensitivity of HPV testing was surprisingly low in ten studies conducted in low and middle income countries that compared HPV assays to VIA: the sensitivity could vary between 50% and 95%, with an average 82% (Figure 5). On the other hand, in ten Chinese studies, the sensitivity of hrHPV testing was uniformly very high (pooled value of 97%, p for inter-study heterogeneity=0.49, see figure 5). The lower sensitivity of HPV testing estimated in certain developing countries may be attributed to gold standard misclassification correlated with visual inspection findings (Arbyn et al, 2008), as shown in Figure 6). The higher efficacy of once-in-life time screening with HPV-testing compared to screening with cytology or VIA was evidenced in a large Indian randomised trial (Sankaranarayanan et al, 2009). In the HPV arm, the incidence of advanced cervical cancer (stage II+) was 53% (95% CI: 31-68%) lower and the cause-specific mortality was 48% lower (95% CI: 19-67%) compared to the women in the control arm where no screening was offered. No significant reductions were seen neither in the VIA nor cytology arms. Another advantage of HPV-based screening is that it can be performed on vaginal samples taken by the women herself (Arbyn et al, 2014b) and strategies based on HPV-testing in self-samples may increase population coverage rates (Arrossi et al, 2015; Verdoodt et al, 2015). About ten HPV assays are currently clinically validated for cervical cancer screening (Arbyn et al, 2015; Meijer et al, 2009). Given recent recommendations from USA, Australia, Europe and WHO, HPV will probably become the main test for cervical cancer screening world-wide. However, the challenge for Africa and other developing countries, is to identify an hrHPV assay that is clinically validated, low-cost, easy-to-use and adapted to the field circumstances prevailing in Africa, preferentially in a point-of-care format and applicable on self-samples.

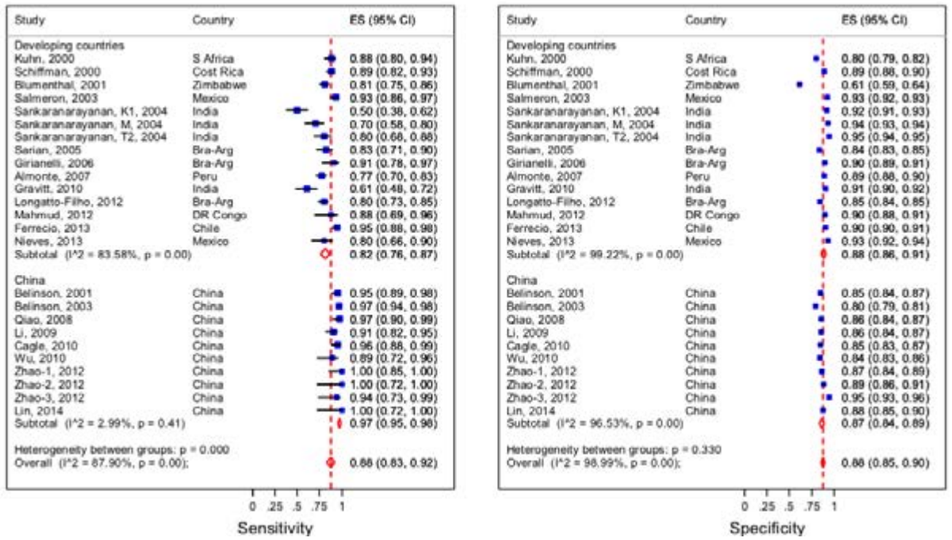

Figure 5: Meta-analysis of the sensitivity (left) and specificity (right) of high-risk HPV DNA testing using the Hybrid-Capture-2 assay to detect underlying cervical intra-epithelial neoplasia or worse, observed in studies conducted in developing countries and China. Updated from (Arbyn et al, 2012).

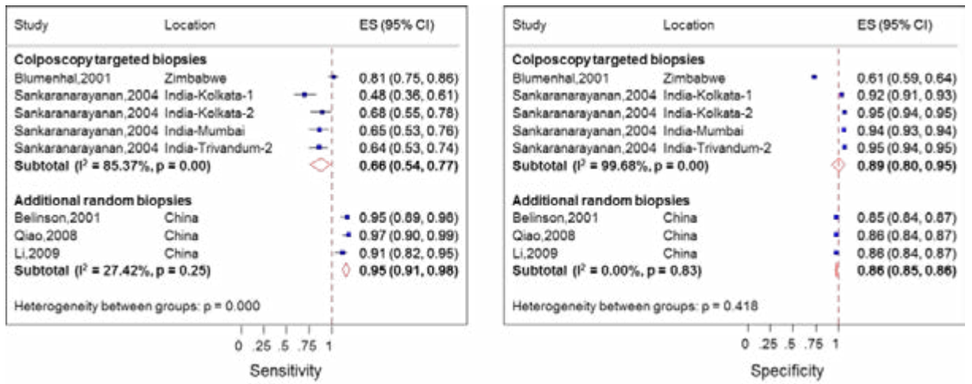

Figure 6: Meta-analysis of the sensitivity (left) and specificity (right) of high-risk HPV DNA testing with Hybrid Capture-2 to detect underlying cervical intra-epithelial neoplasia of grade 2or worse, stratified by method of gold standard, in studies, where also VIA was applied.

Discussion on Cervical Cancer Screening

Cytology, VIA and HPV detection are the three methods currently recommended for secondary prevention of cervical cancer screening by the World Health Organization (2014b). But only the latter two (VIA and HPV testing) seem feasible for population-wide programmes in Africa. Decisions about whether to screen or not, and about the test to be used are to be taken by national health authorities on the basis of the burden of cervical cancer, the prevalence of other health conditions, and the available resources. It must be stressed that screening should only be offered when facilities for appropriate treatment of screen-detected cancer precursor lesions are made available to screened populations (World Health Organization, 2014b). Curative and palliative facilities in tertiary hospitals should be available for screen-detected cancer cases. VIA or VILI have the advantage of being cheap, simple tests that provide immediate result (allowing the implementation of "see-and-treat" strategies. Unfortunately, VIA and VILI have a variable accuracy which requires regular quality monitoring and training. HPV testing is highly sensitive and reliable but requires laboratory infrastructure and adequate logistics. Moreover, the tracking of women who tested positive for further management may be problematic. An interesting scheme is to screen with a point-of-care HPV test, followed by triage with VIA of hrHPV positive women and treatment of aceto-white lesions in one single visit. Use of a low-cost clinically validated HPV assay run in an equipped laboratory in urban areas with rapid transport communication and logistics might be a plausible alternative in the near future. Mechanisms to assure sufficient procurement in accurate screening tests for major target diseases at affordable prices, such as GAVI assures procurement of vaccines for developing countries, could become part of the agenda of international funding agencies. HPV vaccination of girls of 12-15 years combined with the screening of women aged 30-45 once-a-life-time might be an effective strategy that could reduce substantially the burden of cervical cancer in African countries.

Discussion and Conclusions

A key question is about the likely future burden of cervical cancer in sub-Saharan Africa.

Some scientists predict a nearly doubling of the number of cervical cancer cases from 2008 to 2030 on the basis that the prevalence of HIV and HPV infections are the highest in the world, combined with low access to HPV vaccination and screening, and also to population aging and growth (De Vuyst et al, 2013).

A current trend is to integrate sexual, reproductive health (SRH) and HIV policies, with the perspective that all these topics would be delivered by the same providers (Cooper et al, 2015). This integration could also encompass the prevention of cervical cancer, including screening. HPV vaccination is less amenable to integration because of age groups concerned (girls 9 to 12 years of age).

Challenges for research are the development and demonstration of effectiveness of a point of care HPV screening assay followed by triage by an accurate biomarker assay assuring good sensitivity and specificity for precancerous lesions. Such a combined test tandem should be made widely available.

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Chapter 11

Africa: Raposi's Sarcoma

Kaposi's Sarcoma: Uganda's Experience

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Kaposi's Sarcoma is a multifocal angioproliferative disorder of vascular endothelium, primarily affecting mucocutaneous tissues with the potential to involve viscera (Lynen et al, 2005). The disease was first described by Moritz Kaposi, a Vienna-based Hungarian dermatologist, in 1872. He described it as a rare multifocal angioproliferative tumour involving the blood and lymphatic vessels in elderly men of Jewish origin (Kaposi, 1872). To date, there are four clinical variants of Kaposi's Sarcoma; classic, endemic, iatrogenic and epidemic Kaposi's Sarcoma (Schwartz et al, 2008); and each has a distinct natural history, site of predilection and prognosis (Mohanna et al, 2007).

In sub-Saharan Africa (SSA), Kaposi's Sarcoma is endemic, and its incidence has increased substantially with the advent of the AIDS epidemic. In Uganda, Kaposi's Sarcoma is the second commonest cancer among HIV patients and it is the third commonest cancer seen in either men or women in Uganda (Ferlay et al, 2013). According to data from the Kyadondo cancer registry, in 2012 alone, the rate of new cases of Kaposi's Sarcoma was 13.3% and mortality was 12%, with a 5 year prevalence of Kaposi's Sarcoma at 12.2% (Ferlay et al, 2013). In Uganda, despite of the observed decrease in HIV/AIDS prevalence since 1992, a decrease in Kaposi's Sarcoma incidence was observed in only men younger than 50 years but not in men aged > 50 years nor in women (Chaabna et al, 2013). In a survey of over 12, ,600 participants of The AIDS Support Organization (TASO) in Uganda, the risk of developing Kaposi's Sarcoma in the first 4-27 months after signing up with the non-governmental organization was increased significantly compared to the general population, with a standardized incidence ratio of 6.4 (95% CI (4.8, 8.4)) (Mbulaiteye et al, 2006).

While AIDS-associated Kaposi's Sarcoma is the most common variant of Kaposi's Sarcoma in Uganda, among the other forms of Kaposi's Sarcoma; the African or endemic Kaposi's Sarcoma is fairly common in clinical practice. The African or endemic Kaposi's Sarcoma is a variant of disease affecting human immunodeficiency virus (HIV) –seronegative children and young adults in sub-Saharan Africa (Bunn et al, 2012; Dedicoat et al, 2003). The clinical course of endemic Kaposi's Sarcoma is variable and includes indolent skin disease, locally infiltrative lesions of the extremities, and aggressive visceral involvement with potentially fatal sequel. Generalized lymphadenopathy is a common feature of endemic Kaposi's Sarcoma (Hengge et al, 2002), and oral mucosa is infrequently affected (Bunn et al, 2012). In children with Kaposi's Sarcoma, endemic forms are not uncommon in Uganda. The main presentation is of extensive lymph node involvement, with minimal cutaneous involvement.

Pathogenesis: What is the Role of Human Herpes Virus 8?

For decades, the aetiology and pathogenesis of Kaposi's Sarcoma was unknown. Chang et al. (1994) reported the discovery of the Kaposi's Sarcoma-associated herpes virus (KSHV), also known as human herpes virus-8 (HHV-8), and demonstrated an aetiological link between the virus and Kaposi's Sarcoma (Chang et al, 1994). HHV8 induces angiogenic and inflammatory cytokines, as well as gene products implicated in angiogenesis (Kang et al, 2008); and its viral load correlates with the clinical progression of Kaposi's Sarcoma from patch/plaque to the nodular stage (Feller et al, 2008; Johnston et al, 2009) (Chang et al, 1994; Hengge et al, 2002). HHV8 is also the aetiologic agent for primary effusion lymphoma (PEL), and Multicentric Castlemans disease (MCD) (Baresova et al, 2013).

HIV infection further potentiates the development of Kaposi's Sarcoma through the transactivation (Tat) protein, which acts as a growth factor for Kaposi's Sarcoma (Guadalupe et al, 2011; Hassman et al, 2011). The Tat protein induces endothelial cell proliferation and facilitates the invasion of extracellular matrix (Hassman et al, 2011). Further on, there is a synergistic relationship between the HIV and HHV8. HHV-8 infects the endothelial cells and increases its viral load by reactivating it from latent state (Guadalupe et al, 2011). This activation occurs with an increased HIV-1 Tat protein (Guadalupe et al, 2011), thus HIV and HHV-8 infection is associated with increased risk for Kaposi's Sarcoma.

However, it is important to note that other factors play a role in the pathogenesis of Kaposi's Sarcoma. This is supported by observations where the incidence of HHV-8 infection was only found in few cases (Ablashi et al, 1999). In addition, the regression of iatrogenic Kaposi's Sarcoma with the cessation of immunosuppressive therapy indicates that HHV8 may be an essential but insufficient cofactor in the pathogenesis of Kaposi's Sarcoma (Feller et al, 2006). For instance, gender plays a role in the pathogenesis of Kaposi's Sarcoma; women tend to present with lower CD4 T-cell counts at diagnosis, frequent orofacial Kaposi's Sarcoma, and were less likely to have tumour-associated oedema or nodular lesions than men (Phipps et al, 2010). In HIV-seropositive patients, the presence of HHV8 DNA in peripheral blood had been shown to predict the onset of Kaposi's Sarcoma (Cannon et al, 2003; Johnston et al, 2009; Whitby et al, 1995). It is postulated that HIV-mediated immune suppression/deregulation promotes T-helper type-1 cytokines, such as TNF-alpha, interleukin-1b (IL-b), and IL-6 (Feller et al, 2008; Krown, 2003; Papagatsia et al, 2009)

Clinical Presentation

Nearly all patients with Kaposi's Sarcoma present with a lesion in the oral cavity; however, oral lesions are more frequent in the epidemic variant of the disease (Bottler et al, 2007; Dreyer et al, 2009; Lager et al, 2003; Lebbé et al, 2008; Mohanna et al, 2007; Mwakigonja et al, 2007). The oral cavity is the first clinical site of disease in 22% of patients with Kaposi's Sarcoma (Ficarra et al, 1988; Flaitz et al, 1997; Lager et al, 2003; Mohanna et al, 2007) and up to 71% of HIV patients may have concurrent cutaneous and visceral involvement (Lager et al, 2003; Mohanna et al, 2007). The most frequently affected oral sites include hard palate, gingiva and dorsal tongue (Figure 1)(Feller et al, 2007; Lager et al, 2003; Papagatsia et al, 2009). The oral cavity examination should cover the lips; examine for the colour, texture and any surface abnormalities of the upper and lower lip; the labial mucosa, the buccal mucosa and vestibules, the hard and soft palate, the tongue; inspect for any swellings, ulceration, coating or variation in size, colour or texture, and any changes in the papillae covering the surface of the tongue; the floor of mouth and gingiva. Oral Kaposi's Sarcoma may present as solitary, multifocal or multicentre macules, plaques or nodules of different sizes, varying in colour from deep red to bluish purple (Fatahzadeh, 2012).

Figure 1: Patient with extensive oral cavity Kaposi's Sarcoma lesions involving the soft and hard palate

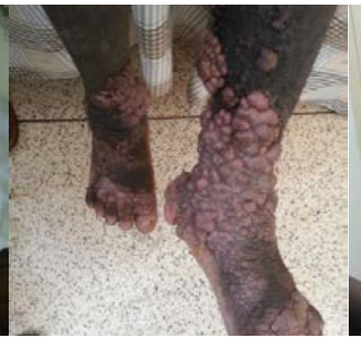

Figure 2: Patient with extensive nodular Kaposi's Sarcoma lesions involving both lower limbs

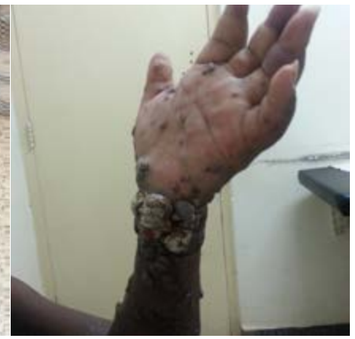

Figure 3: Patient with extensive nodular Kaposi's Sarcoma lesions on the upper limb

Cutaneous Kaposi's Sarcoma is frequent in patients with Kaposi's Sarcoma; however, its absence does not exclude visceral Kaposi's Sarcoma. A wide spectrum of lesions is seen in patients with AIDS-Kaposi's Sarcoma, often in the setting of advanced immunosuppression (Vanni et al, 2006). Lesions of AIDS-Kaposi's Sarcoma tend to enlarge, multiply in number, become more nodular, or coalesce in association with immune deterioration (Petit et al, 1986). Epidemic Kaposi's Sarcoma presents as multifocal plaques, patches, and nodules with a predilection for the face and lower extremities (Figure 2 and 3) (Henderson, 2009; Lynen et al, 2005; Vanni et al, 2006). The lesions should be evaluated for the number, nodularity, size, the diameter, location, and presence of oedema.

The presence of tumour-associated oedema, its locations and severity should be documented. Oedema signifies advanced disease and this constitute sa criterion for the high risk group for both relapse and poor response to treatment. Some patients present with gross oedema of the lower limbs mimicking other tropical diseases like filariasis, elephantiasis and lymphedema.

More than 50% of patients with AIDS-Kaposi's Sarcoma may have visceral involvement (Martellotta et al, 2009). Gastrointestinal Kaposi's Sarcoma manifests as abdominal pain, diarrhoea, weight loss, bleeding and vomiting (Lynen et al, 2005; Martellotta et al, 2009). Pulmonary Kaposi's Sarcoma manifests as cough, dyspnoea, chest pain and haemoptysis. The radiological findings of pulmonary Kaposi's Sarcoma on chest x-ray include pleural effusion, the "ground glass appearance" or the "cotton-wool appearance" of the lung parenchyma, and hilar adenopathy, as shown in Figure 4 (Henderson, 2009; Papagatsia et al, 2009). In paediatric Kaposi's Sarcoma, over 50% patients present with lymph node involvement, followed by cutaneous involvement and visceral involvement in that order (Gantt, 2008).

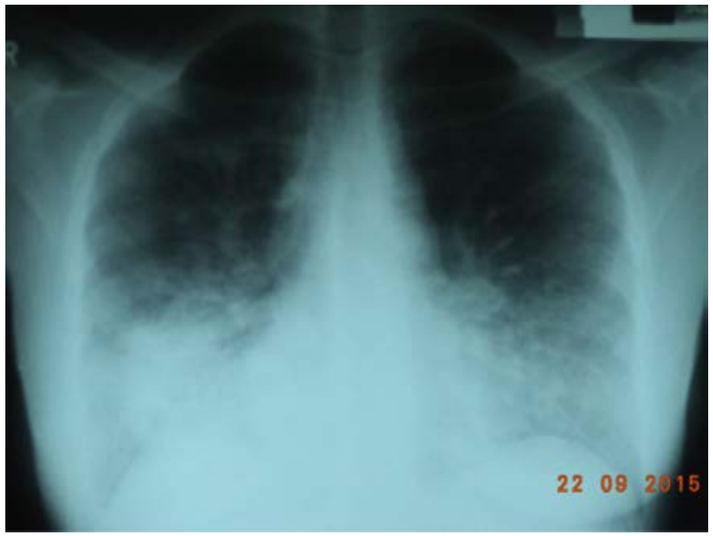

Figure 4: Chest x-ray showing extensive pulmonary Kaposi's Sarcoma. There are bilateral ground glass opacities in the mid and lower lung zones suggestive of PKS

Diagnosis

The most common differential diagnosis of cutaneous Kaposi's Sarcoma lesions in Uganda is bacillary angiomatosis; hence histological tissue evaluation is important for definitive diagnosis (Mohanna et al, 2007). The microscopic features include an abundance of proliferating mononuclear inflammatory and spindle cells, ill-defined vascular channels, haemorrhage, and oedema (Dreyer et al, 2009; Kang et al, 2008).

The clinical and microscopic features of Kaposi's Sarcoma mimic the clinical and microscopic features of bacillary angiomatosis (BA) caused by *Bartonella henselae* (Lynen et al, 2005); and therefore additional test to identify HHV8 DNA improves the quality the diagnosis (Feller et al, 2007; Hammock et al, 2005).

The diagnosis of Kaposi's Sarcoma mandates evaluation for the presence of co-existing HIV. The HIV sero-positive patient requires a detailed history about the HIV infection including duration since diagnosis, opportunistic infections, nadir and current CD4-T cell counts, HAART regimen and its durations, and the response of the skin lesions to the HAART. Initial workup for staging AIDS-associated Kaposi's Sarcoma involves a complete physical examination that includes evaluation of skin, oral cavity, and rectum, a chest x-ray, an abdominal ultrasound scan, a stool faecal occult blood test, a CD4 T-cell count, complete blood count, liver function tests and renal function tests. When pulmonary or gastrointestinal disease is suspected, lesions may be visualized by bronchoscopy or endoscopy, respectively (Vanni et al, 2006).

Prognosis

The AIDS Clinical Trial Group (ACTG) classification was developed in the pre-HAART era to predict survival for patients with AIDS-associated Kaposi's Sarcoma. The criteria is defined using the tumour (T), immune system (I) and systemic illness (S) (Krown et al, 1997) as shown in table 1. Tumour is defined as T0 if disease is confined to the hard palate, or T1 if there is pulmonary or gastrointestinal involvement, tumour associated oedema or ulceration, or extensive oral involvement. Patients with the combination of poor stage (e.g. tumour-associated oedema) and constitutional symptoms (T1S1) were found to have an unfavourable prognosis (Okuku et al, 2012) with a 3-year survival rate of 53% (Nasti et al, 2003). In contrast, HIV patients on HAART with none or only 1 prognostic criteria (T0S0, T0S1, T1S1), were found to have a good prognosis with a 3-year survival rate of 88%, 80%, and 81%, respectively (Nasti et al, 2003). Other prognostic factors include; number of Kaposi's Sarcoma containing anatomic sites, and haemoglobin (Okuku et al, 2015).

Table 1: AIDS Clinical Trial Group classification criteria for Kaposi's Sarcoma

	Good prognosis	Poor prognosis
T – Tumour extent	Localized skin lesions	Ulcerated lesions
	Lympadenopathy	Edema
	Minimal nodular disease	Oral lesions
I – immunosuppression	CD4 > 200 cells/mm3	CD4 < 200cells/mm3
	Cd4 > 15%	CD4 < 15%
S – Severity systemic illness	No B symptoms	Presence of B-symptoms
	Karnofsky score > 70%	Karnofsky score < 70%
	No Opportunistic infections	Opportunistic infections
	No AIDS defining illnesses	Oral candidiasis
	No Oral ulcerations	

In contrast to AIDS-Kaposi's Sarcoma, classic and endemic Kaposi's Sarcoma do not have a universally accepted staging classification. The most widely used criteria was proposed by Brambilla et al, 2002; the classification is composed of four stages based on cutaneous lesions: location, presence or absence of complications and visceral involvement as shown in Table 2 (Brambilla et al, 2003)

Table 2: Staging of Classic Kaposi's Sarcoma

Stage	Cutaneous lesions	Location	Behaviour
I-Maculonodular	Macules or nodules or both	Lower limbs	Non-aggressive
II-Infiltrative	Plaques	Lower limbs	Locally aggressive
III-Florid	Angiomatous nodules and plaques	Extremities, particularly the lower ones	Locally aggressive
IV-Disseminated	Angiomatous nodules and plaques	Extremities, trunk, head	Disseminated, aggressive.

Treatment

Currently, Kaposi's Sarcoma has no cure. The goals of treatment are to control disease symptoms and prolong life, and therapy is tailored to the clinical variant of Kaposi's Sarcoma and disease stage. The majority of patients with Kaposi's Sarcoma in Uganda present with advanced stage of the disease, and hence the aim of treatment is to control symptoms, palliate pain and improve quality of life. All patients with AIDS-associated Kaposi's Sarcoma should initiate HAART as soon as the diagnosis is made, regardless of the CD4 T-cell counts. Treatment with HAART may induce complete remission in patients with good immunological response and limited disease (Bassett et al, 1995; Martellotta et al, 2009). The patients with T1 disease with a performance status ≥ 40%, adequate bone marrow function, renal, and hepatic function tests should be given concurrent systemic chemotherapy and this will reduce morbidity through alleviating the pain, oedema, lymphadenopathy and skin lesions; and slowing the progression of systemic disease. In Uganda, our preferred first line chemotherapy is a combination of Bleomycin and Vincristine, given every three (3) weeks for six to nine cycles to achieve very good partial response or clinical remission. In contrast, liposomal doxorubicin is the preferred first-line regimen for AIDS-associated Kaposi's Sarcoma in high income countries due to its higher efficacy and reduced toxicity (Cooley et al, 2007; Samad et al, 2007), but the cost and access are limiting factors in Uganda.

In patients with localized disease, localized treatment modalities are recommended and these include radiotherapy and topical therapy with alitretinoin gel or imiquimod gel. Other local therapies like cryotherapy, laser therapy, and intra-lesion interferons are not readily available in a country such as Uganda.

Following systemic chemotherapy, Kaposi's Sarcoma patients are reviewed monthly for three months and thereafter every three months for six months, then bi-annually for one year and annually for life. At every visit, the clinician should take record of the lesions: size, number, location, characteristics, severity of oedema and location of tumour-associated oedema, and number of raised and flat lesions. The clinical features of lesions, such as colour, surface, and presence of nodularity should also be documented (Vanni et al, 2006). Radiological and other imaging or endoscopic investigations should be requested in patients with suspected non-measurable lesions including ascites, pleural and pericardial fluid, lymphatic lung disease, and abdominal masses/abdominal organomegaly.

Table 3: Systemic chemotherapy for patients with Kaposi's Sarcoma in Uganda

Regimen	Drug	Dosage	Route/Time	Frequency/Duration
First line treatment	Vincristine sulfate	2 mg/2mL solution	IV over 1minute	Every 3 weeks for up to 6 cycles
	Bleomycin sulfate	15 units/m2 in 50 mL 0.9% Sodium Chloride for injection	IV over 10 minutes	Every 3 weeks for up to 6 cycles
Second line treatment	Paclitaxel	100 mg/m2 in 200 mL, 250 mL, or 500 mL of 5% dextrose or 0.9%Sodium Chloride for injection	IV over 1 hour using non-PVC administration set and ≤0.22 micron inline-filter	Every 3 weeks for up to 6 cycles

Response evaluation in patients with AIDS-Kaposi's Sarcoma is guided by the ACTG criteria where; complete response (CR) is defined as the absence of any detectable residual disease, including tumour-associated oedema persisting for at least four weeks. Partial response (PR) is defined as ≥ 50% decrease in the number or size of previously existing evaluable lesions lasting for at least four weeks without the appearance of new lesions or tumour-associated oedema. Stable Disease (SD) is defined as any response that does not meet the criteria for progression or PR. Overall response rate is defined as both complete and partial rates. Progressive Disease (PD) is defined as ≥ 25% increase in the size of previously existing lesions or the appearance of new ones or the development of new or increasing tumour-associated oedema or effusion. Relapse is defined as the development of progressive disease in the presence of a documented CR, or PR.

Conclusions

Kaposi's Sarcoma is a vascular tumour of endothelial origin that is associated with HHV8 infection. In sub-Saharan Africa, AIDS-Kaposi's Sarcoma remains the most common HIV-associated malignancy and hence it poses a huge burden to the already constrained health-care systems. Kaposi's Sarcoma has four clinical variants: classic, endemic, iatrogenic, and epidemic Kaposi's Sarcoma. The histopathology in these different Kaposi's Sarcoma forms is essentially identical; however they have different clinical patterns. HHV8 DNA identification in tissue biopsies of patients helps confirm the diagnosis and distinguishes Kaposi's Sarcoma from its mimics. Even though, there is no cure at present, the expanding knowledge of Kaposi's Sarcoma biology increases hope for rational therapies and hence better quality of life among patients with Kaposi's Sarcoma.

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Chapter 12

Africa: Breast Cancer

Breast Cancer in Africa: Screening, Diagnosis and Treatment

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The continent of Africa is made up of 55 states, the majority of which are classified as Low- and Middle-Income Countries (LMICs)(The World Bank, 2015). Forty-eight are categorized as sub-Saharan, and the remaining seven are in North Africa. These countries are linguistically, culturally, demographically and ethnically diverse. Unfortunately, one area of commonality shared by African women regardless of their nationality is poor outcomes from breast cancer with associated high mortality rates. The recent CONCORD-2 study of 5 year breast cancer survival rates from 1995-2009 based on the analysis of individual data from 279 population-based registries in 67 countries, reported that in High Income Countries (HICs) age-standardized net-survival rates were in excess of 85% (Allemani et al, 2015). One country in Africa, Mauritius, a HIC island nation off the coast of Madagascar, had similar 5-year survival rates of 87.4 (78.1–96.7) and North African countries had somewhat less favourable outcomes including 59.8 (48.6–71.1) in Algeria; 76.6 (55.5–97.7) in Libya (Benghazi registry); and 68.4 (64.5–72.2) in Tunisia. By contrast, data are available from only 2 sub-Saharan African countries: South Africa, 53.4 (35.5–71.3); and Mali, 13.6 (0.0–30.1) both of which are significantly inferior to other regions around the world (Allemani et al, 2015).

The reasons for these disparities are varied. Cancer remains a low priority for much of the population in Africa, with many barriers impeding women's access to affordable effective breast health care, including gaps in the receipt of accurate, culturally appropriate information on breast health including signs and symptoms of breast cancer; access to breast cancer early detection and to appropriate and timely diagnosis and treatment. These barriers can be cross-cultural such as endemic poverty, a lack of infrastructure, inadequate training and expertise, inequitable distribution of services in urban vs. rural areas, and poverty (Harford, 2015). Barriers, which are rarely encountered in HICs such as major transportation deficits, are common in Africa. A study in the Republic of South Africa reported that increasing residential distance from hospitals was associated with risk of late stage diagnosis (Dickens et al, 2014), and a study in Cameroon reported that 23% of patients seen over 2 months in 2010, travelled for more than 7 hours to reach the hospital to receive treatment for cancer (Price et al, 2012). Unfortunately, many countries in the region also have a history of military conflict and political instability which contribute to fragmented health infrastructure, and often disrupt established health care practices (Spiegel et al, 2014). Finally, other more culturally specific barriers also limit women's ability to seek care even

where it is available and include such as sociocultural influences as use of traditional medicines, discrimination, stigma, and cultural taboos, along with fears mastectomy and of abandonment after a diagnosis of breast cancer (Daher, 2012; Nour, 2003). For example, a Nigerian study of 2154 breast cancer patients where 87% presented with stage III or IV disease reported that the most common reasons for delay in seeking treatment were preference for prayer houses or spiritual healing homes (13.5% of patients); a belief that the lesion was due to inflammation (8.5%); preference for native doctors or herbalists (23.1%) and economic reasons (10.2%)(Ajekigbe, 1991). A Rwandan report of 144 breast cancer patients seen at rural hospitals, reported that seeing a traditional healer first were significantly associated with a longer delay in seeking treatment, a risk factor for late stage diagnosis (Pace et al, 2015).

Investment in healthcare overall in the region is limited. Total expenditure on health per capita (US$) in 2013 in counties classified by the World Bank as low income averaged US$36, compared to $277 in middle-income countries, and $4,687 in HIC (Table 1)(The World Bank, 2015). Competing burdens of communicable diseases, and high child and maternal mortality rates, make it difficult for many countries to prioritize health spending on cancer, especially as rates of cancer have historically been lower than in HICs (Galukande et al, 2010). Despite the increase in breast cancer incidence and the concomitant increase in breast-cancer related mortality, spending on all cancers averaged only 5% of the total expenditure on health (Farmer et al, 2010). In addition, the lack of cancer registries and access to appropriate statistics on incidence and mortality rates in many African countries, may contribute to a lack of awareness about the magnitude of the current and future cancer burden among policy makers and the general public.

Table 1: Characteristics of North African and Sub-Saharan countries

Source:

(1) The World Bank, 2015 (2) World Health Organization, 2015 (3) African Cancer Registry Network (AFCRN), 2015; Gakunga et al, 2015 (4) Adesina et al, 2013 (5) Adbdel-Wahab et al, 2013

Country Name	Region	Income Group[1]	Health expenditure per capita (current US$) (2013)[1]	Existence of operational policy/strategy/ action plan for cancer (2013)[2]	Existence of Cancer registry[3]	Number of pathologists (2010-2012)[4]	Teletherapy units[5]	Teletherapy per million people[5]
Algeria	Middle East & North Africa	Upper middle income	313.52	Yes	Yes		20	0•58
Angola	Sub-Saharan Africa	Upper middle income	267.22	No data received			1	0.06
Benin	Sub-Saharan Africa	Low income	36.69	No	Yes	1	0	0
Botswana	Sub-Saharan Africa	Upper middle income	397.32	No	Yes	9	1	0.52
Burkina Faso	Sub-Saharan Africa	Low income	45.68	No		7	0	0
Burundi	Sub-Saharan Africa	Low income	21.46	No		1	0	0
Cabo Verde	Sub-Saharan Africa	Lower middle income	164.69	No data received			0	0
Cameroon	Sub-Saharan Africa	Lower middle income	67.17	Yes		12	3	0.16
Central African Republic	Sub-Saharan Africa	Low income	13.05	No			0	0

Country Name	Region	Income Group[1]	Health expenditure per capita (current US$) (2013)[1]	Existence of operational policy/strategy/ action plan for cancer (2013)[2]	Existence of Cancer registry[3]	Number of pathologists (2010-2012)[4]	Teletherapy units[5]	Teletherapy per million people[5]
Chad	Sub-Saharan Africa	Low income	37.20	No data received			0	0
Comoros	Sub-Saharan Africa	Low income	51.49	No			0	0
Congo, Dem. Rep.	Sub-Saharan Africa	Low income	15.91	No data received		8	0	0
Congo, Rep.	Sub-Saharan Africa	Lower middle income	130.71	Yes	Yes	2	0	0
Cote d'Ivoire	Sub-Saharan Africa	Lower middle income	86.76	Yes	Yes	8	0	0
Djibouti	Middle East & North Africa	Lower middle income	137.36	No			0	0
Egypt, Arab Rep.	Middle East & North Africa	Lower middle income	151.26	No	Yes		76	0•93
Equatorial Guinea	Sub-Saharan Africa	High income: nonOECD	713.86	No			0	0
Eritrea	Sub-Saharan Africa	Low income	16.51	Yes		1	0	0
Ethiopia	Sub-Saharan Africa	Low income	24.52	No data received	Yes	40	2	0.02
Gabon	Sub-Saharan Africa	Upper middle income	441.39	No			0	0
Gambia, The	Sub-Saharan Africa	Low income	28.91	No	Yes	1	0	0
Ghana	Sub-Saharan Africa	Lower middle income	99.53	Yes	Yes	30	2	0.09
Guinea	Sub-Saharan Africa	Low income	24.75	Yes	Yes		0	0
Guinea-Bissau	Sub-Saharan Africa	Low income	31.84	No			0	0
Kenya	Sub-Saharan Africa	Lower middle income	44.51	Yes	Yes	40	2	0.05
Lesotho	Sub-Saharan Africa	Lower middle income	123.42	No		1	0	0
Liberia	Sub-Saharan Africa	Low income	44.37	No			0	0
Libya	Middle East & North Africa	Upper middle income	432.84	No			5	0•79
Madagascar	Sub-Saharan Africa	Low income	19.63	Yes		8	1	0.05
Malawi	Sub-Saharan Africa	Low income	26.21	No	Yes	6	0	0
Mali	Sub-Saharan Africa	Low income	53.29	Don't know	Yes	3	0	0
Mauritania	Sub-Saharan Africa	Lower middle income		Yes		3	1	0.31
Mauritius	Sub-Saharan Africa	Upper middle income	462.54	No data received	Yes		3	2.36
Morocco	Middle East & North Africa	Lower middle income	189.20	Yes	Yes		28	0.89
Mozambique	Sub-Saharan Africa	Low income	40.26	Yes	Yes	8	0	0

Country Name	Region	Income Group[1]	Health expenditure per capita (current US$) (2013)[1]	Existence of operational policy/strategy/ action plan for cancer (2013)[2]	Existence of Cancer registry[3]	Number of pathologists (2010-2012)[4]	Teletherapy units[5]	Teletherapy per million people[5]
Namibia	Sub-Saharan Africa	Upper middle income	422.58	Don't know	Yes	2	1	0.47
Niger	Sub-Saharan Africa	Low income	27.23	No	Yes	3	0	0
Nigeria	Sub-Saharan Africa	Lower middle income	114.97	No	Yes	158	7	0.05
Rwanda	Sub-Saharan Africa	Low income	70.51	Yes		5	0	0
Sao Tome and Principe	Sub-Saharan Africa	Lower middle income	109.98	No			0	0
Senegal	Sub-Saharan Africa	Lower middle income	45.55	No		6	1	0.08
Seychelles	Sub-Saharan Africa	High income: nonOECD	550.85	No	Yes			
Sierra Leone	Sub-Saharan Africa	Low income	95.83	No data received		2	0	0
Somalia	Sub-Saharan Africa	Low income		No		0	0	0
South Africa	Sub-Saharan Africa	Upper middle income	593.45	No data received	Yes	170	92	1.89
South Sudan	Sub-Saharan Africa	Low income	18.07	No data received		2		
Sudan	Sub-Saharan Africa	Lower middle income	114.95	Yes			7	0.17
Swaziland	Sub-Saharan Africa	Lower middle income	256.11	No		1	0	0
Tanzania	Sub-Saharan Africa	Low income	49.32	No data received	Yes	23	3	0.07
Togo	Sub-Saharan Africa	Low income	54.45	Yes			0	0
Tunisia	Middle East & North Africa	Upper middle income	308.56	No	Yes		16	1.55
Uganda	Sub-Saharan Africa	Low income	59.12	No	Yes	30	1	0.03
Yemen, Rep.	Middle East & North Africa	Lower middle income	74.47	No				
Zambia	Sub-Saharan Africa	Lower middle income	92.81	Yes	Yes	10	2	0.16
Zimbabwe	Sub-Saharan Africa	Low income		No	Yes	5	2	0.16

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Statistics

Breast cancer is the second most common cancer worldwide, and the most common cancer in women (1.7 million cases, 11.9% of total cases); incidence rates vary nearly fourfold across the world regions, with rates ranging from 27 per 100,000 in Central Africa to 96 in Western Europe (Ferlay et al, 2015). However, it is the most frequent cause of cancer death in women in LMICs (324,000 deaths, 14.3% of total deaths).

While breast cancer incidence is lower in LMICs, its incidence is increasing rapidly compared with HIC, where rates have been stable or have declined since the early 2000s. Between 1990 and 2013, age-standardized incidence rates (ASIR) per 100 000 have increased by 17% globally (44.36 to 51.73), by 46% in developing countries (27.74 to 40.40) and by 8% in developed countries (69.75 to 74.98)(Fitzmaurice et al, 2015). For breast cancer in 2012, Globocan reported that more cases occurred in less developed (883,000 cases) than more developed regions (794,000) (Ferlay et al, 2015). In addition, the burden of breast cancer is greater in LMICs: breast cancer caused 13.1 million disability-adjusted life-years (DALYs) s in 2013; 63% occurred in developing countries and 37% in developed countries (Fitzmaurice et al, 2015).

Similar to other countries with previously low incidence rates of breast cancer, incidence rates of, and mortality from breast cancer are rapidly increasing in the Arab countries in North Africa (Libya, Tunisia, Morocco, Algeria and Mauritania). Breast cancer in Arab women is often diagnosed at a younger age and at a more advanced stage (El Saghir et al, 2006; El Saghir et al, 2002; Ezzat et al, 1999; Salhia et al, 2011) compared to other populations. The ASIR of breast cancer in North Africa for example is currently 2-4 times lower than in western countries (Corbex et al, 2014) but is expected to double in the next 15 years as risk factor exposure increases (including that related to population aging).

In sub-Saharan Africa, the proportion of the disease burden attributable to cancer is rising, and the region is projected to have more than an 85% increase in cancer incidence by 2030, solely based on demographic changes (i.e., a larger and older population than exists presently)(Morhason-Bello et al, 2013). Unfortunately, the overall case fatality from breast cancer, as estimated by the ratio of mortality to incidence (MIR) in a given region or country, is consistently higher in LMICs (Table 2) (Ferlay et al, 2015; Ferlay et al, 2013). Overall cancer mortality in sub-Saharan Africa is high because of poor infrastructure, insufficient numbers of health-care workers, advanced stage at presentation, reliance on traditional therapies, few treatment choices, and poor compliance with treatment regimens (Kingham et al, 2013).

Table 2: Estimated cumulative risk to age 75 (percent) for Incidence and Mortality* by region. North America and Europe are included for comparative purposes.

Source: Ferlay J, Soerjomataram I, Ervik M, et al. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Available from: http://globocan.iarc.fr, accessed July 7, 2014. 2012

	Incidence (%)	Mortality (%)	MIR
Africa	3.7	1.8	0.49
Eastern Africa[1]	3.2	1.7	0.53
Central Africa[2]	2.8	1.6	0.57

	Incidence (%)	Mortality (%)	MIR
Northern Africa[3]	4.4	1.9	0.41
Southern Africa[4]	4.1	1.7	0.41
Western Africa[5]	3.9	2.1	0.54
North America	10.0	1.6	0.16
Europe	7.6	1.8	0.24

[1]Eastern Africa (Burundi, Comoros, Djibouti, Eritrea, Ethiopia, Kenya, Madagascar, Malawi, Mauritius, Mozambique, Rwanda, Somalia, Tanzania, Uganda, Zambia, and Zimbabwe), [2]Central (Angola, Cameroon, Central African Republic, Chad, Democratic Republic of Congo, Republic of Congo, Equatorial Guinea, and Gabon), [3]Northern (Algeria, Egypt, Libya, Morocco, Sudan, Tunisia, Western Sahara), [4]Southern (Botswana, Lesotho, Namibia, the Republic of South Africa, and Swaziland) and [5]Western (Benin, Burkina Faso, The Gambia, Ghana, Guinea-Bissau, Guinea, Liberia, Mali, Mauritania, Niger, Nigeria, Senegal, Sierra Leone and Togo)

Late Stage Diagnosis

Late stage diagnosis is a principal barrier to improving outcomes in women with breast cancer in LMICs. Down staging of disease is one of the more important strategies in areas where limited treatment will have the most chance of success. However the women in this region with symptoms of breast cancer do not seek medical attention, leading to late stage presentation, and poor prognosis. Barriers to reducing stage at diagnosis include lack of screening and early detection services, poverty, limited awareness of early signs and symptoms of cancer among both the public and health care providers, reliance on traditional beliefs and treatments, and stigma associated with a diagnosis of cancer (Daher, 2012; Keusch et al, 2006).

Delayed presentation is common: for example one study reported a mean delay of 11.2 months between the onset of symptoms and presentation in Nigerian women diagnosed between 1996 and 2003, (Adesunkanmi et al, 2006) and a second study found that 65% of women waited more than 3 months after symptoms appeared before seeking treatment (Adisa et al, 2011). A study of 66 Ghanaian patients with breast cancer found that while 14 (21.2%) of the breast cancers were discovered through breast education and clinical breast examination (CBE) as offered through outreach programs, women commonly waited between 6 weeks to 2 years before seeking formal diagnosis and treatment (Clegg-Lamptey et al, 2009). Two Cameroonian studies found significant delays in seeking care: one study examined 531 women seen over a 10 year period, and found that the mean delay before presentation at hospital was 10.4 months, and 54.9% had used traditional medicine before medical evaluation. Metastasis and locally advanced breast cancer at diagnosis were present in 8.1% and 62.8%, respectively (Kemfang Ngowa et al, 2011b). A second study reported that 35% percent of patients waited >6 months to speak to a health care provider after the first sign of their cancer (Price et al, 2012). A report of 200 Libyan women diagnosed with breast cancer between 2008 and 2009 found that 56% were diagnosed within a period more than 6 months after presentation of symptoms (Ermiah et al, 2012). One hundred and forty-four breast cancer patients in 2 rural hospital in Rwanda had a median total delay between symptom presentation and treatment of 15 months, resulting from a combination of both patient delays in seeking treatment, and health system delays (both a median of 5 months); patient and system delays of ≥6 months were significantly associated with diagnosis at more advanced-stages (Pace et al, 2015). Finally, an Eritrean study of 82 newly diagnosed breast cancer patients, reported that more than 60% presented after >2 years following onset of symptoms, and 66% of patients had late stage disease (Tesfamariam et al, 2013). These delays in seeking care result in diagnosis at a more advanced stage compared to other populations.

The African Cancer Registry Network (AFCRN) encourages registries to record stage at diagnosis, although a recent review found that less than half were recording TNM status (Gakunga et al, 2015). Thus, the majority of reports at the present come from retrospective reviews of breast diagnoses at individual cancer hospitals or treatment centres. Nonetheless, the reported stage of diagnosis from a variety of studies is broadly

consistent, with the majority of women presenting with late stage disease: approximately 70-80% of tumours were diagnosed as stage III or IV. A review of 225 breast cancer cases diagnosed at the Angolan Institute of Cancer Control in 2009, reported 176 (77.8%) were classified as stages III or IV (Lopes et al, 2015). Data on tumour size and stage of breast cancer from a random sample of women diagnosed with breast cancer between 2008-2009 from population-based cancer registries in Abidjan (Côte d'Ivoire; 141 cases) and Brazzaville (Republic of Congo; 139 cases) reported that in the Côte d'Ivoire, 68% of tumours were ≥5cm in diameter and 74% were stage III or IV; in the Republic of Congo, 63% were ≥5cm and 81% were stage III or IV (Islami et al, 2015). More than half of all histologically confirmed breast cancer patients (N=385) seen between 1991 and 2005 at the Obafemi Awolowo University Teaching Hospital in Nigeria had metastatic disease and more than two-thirds had more than one secondary site on initial evaluation. The 1-year survival rate was 27%.(Adisa et al, 2011) Of 297 patients with breast cancer seen at a hospital in Uganda between 1996 -2000, 77% presented with stage III or IV disease (Gakwaya et al, 2008a), and 85.2% of 330 Ghanaian breast cancer patients had stage III or IV tumours (Ohene-Yeboah et al, 2012). Similar results were found in a review of characteristics of women with breast cancer in several countries in Western Africa (Sighoko et al, 2013).

Infrastructure

Cancer care in any country is a costly, complex and multi-step endeavour, particularly for breast cancer, a heterogeneous disease, where effective treatment is dependent on early detection and diagnosis. Given that the majority of African countries spend less than 6% of their GNP on all healthcare, which also must cover communicable diseases, the scale of the problem can be overwhelming (Strother et al, 2013).

While some middle income African countries, such as South Africa and Ghana have several cancer centres, others have none (Stefan et al, 2013; Stulac et al, 2015). Among existing facilities, there are a lack of trained personnel and technology. For example, a 2013 review of teletherapy units in Africa found that the average number of units was 0.22 per million people in sub-Saharan Africa, with the majority being located in urban referral hospitals. Many African countries have no radiotherapy machines at all (Abdel-Wahab et al, 2013).

With a history of profound lack of investment in breast health care, the question of 'where to start' is difficult to answer. However a number of African countries in partnership with international agencies are making significant strides in improving components of breast health care. In addition, tools such as the Breast Health Global Initiative's (BHGI) 'evidence-based, economically feasible, and culturally appropriate' guidelines for breast health care can allow countries to implement programs that are most appropriate to their resource level. These guidelines were developed according to a 4-tiered system, depending on the availability of resources, and classified as 'basic', 'limited', 'enhanced' and 'maximal' level services. For example, for early detection programs, basic level services are appropriate where mammography services are unlikely to be available, and encompass breast health awareness campaigns emphasize obtaining a history of symptoms suggestive of breast cancer and CBE in women who seek medical care. Limited level services are intended for areas with resources for diagnostic imaging, such as ultrasound and mammography, but not for mammographic screening (Anderson et al, 2008; Anderson et al, 2011; Smith et al, 2006).

The International Atomic Energy Agency (IAEA) Program for Action for Cancer Therapy (PACT) carries out comprehensive cancer control capacity and needs assessments, known as 'imPACT' review missions, and in 2014 completed reviews in 10 countries, including Mozambique, and Rwanda. In Mozambique, key challenges identified were (i) human resource needs for different disciplines related to cancer care and control; (ii) capacity requirements in infrastructure, equipment and workforce at the tertiary level to ensure access to timely and efficient treatment for early detection programs; and, (iii) lack of radiotherapy services. A National Strategic Plan (July 2014 – June 2019), addresses cancer policies, including a national plan to allocate resources to all cancer care components (including radiation therapy) at eleven provincial hospitals and one centre of excellence (IAEA, 2015b).

A critical barrier to providing cancer care in LMICs is the profound shortage of health professionals. According to WHO, 57 countries worldwide including 36 in sub-Saharan Africa, are experiencing a critical shortage of health professionals including surgeons, radiologists, nurses and oncologists (IAEA, 2015b; Kingham et al, 2013; Stulac et al, 2015). In order to achieve sustainable breast cancer control capacity in developing countries, and in Africa in particular, a large increase in professionals trained locally or regionally is needed. IAEA-PACT has called for measures to strengthen local recruitment and ensure retention of graduates from national training programs, and is currently supporting Virtual University for Cancer Control network (VUCCnet) and the Regional African Cancer Training network (RACT): A training program on-site at several cancer centres in sub-Saharan Africa, in collaboration with WHO, IARC, the Union for International Cancer Control (UICC), the United States National Cancer Institute (US NCI), the African Organization for Research and Training in Cancer (AORTIC), and with private sector funding from Roche (IAEA, 2015b). VUCCnet and RACT are part of the EDUCARE (EDUcation for Cancer in African REgions) Initative. Ghana, Uganda, United Republic of Tanzania and Zambia comprise the initial intervention countries with South Africa and Egypt acting as mentor countries.(IAEA, 2015b) In 2010 PACT and BHGI developed an initiative in Ghana to implement a learning lab with a focus on breast cancer control, using the VUCCnet platform (IAEA, 2015a).

Policy: Cancer Control Plans

The World Health Organization developed guidelines for regional and national cancer control programs stratified by national economic development. The WHO recommends cancer control programs in Africa begin in a stepwise approach by implementing one or two key priorities in a demonstration project. The WHO stated that 'projects could be sustainable only when African countries take the initiative and make the political commitment to invest in the programs with a dedicated budget and required staff (World Health Organization, 2005). A 2013 WHO survey assessing non-communicable disease (NCD) capacity found that of 55 African countries, only 16 had an operational policy/strategy/action plan for cancer.(World Health Organization, 2015a) While some countries lack specific policy program or plan for the prevention or control of breast cancer (WHO: African Health Observatory, 2014), some are attempting to implement a variety of interventions including free health care initiatives, and some have described specific programs from breast cancer control. Country specific examples of breast cancer early detection status include the following:

- In Kenya, a report by the Kenyan Ministry of Health called for enhanced health promotion and education, and to improve early detection of cancer by introducing or expanding screening programs, and by developing guidelines for screening and early detecting of cancer (Ministry of Public Health and Sanitation and the Ministry of Medical Services, 2012). However, many of these have yet to be implemented (Matheka, 2014). No formal guidelines for breast screening for the country are currently available.

- In Malawi, mammographic screening is available in only one private hospital (Msyamboza et al, 2012) and there are no governmental guidelines on breast cancer screening.

- The Republic of Mauritius developed a National Cancer Control Program for 2010-2014, and recommended that breast health awareness campaigns encouraging BSE and yearly CBE to women >40 years . Population based screening mammography was not thought to be advisable, given the relatively high proportion of cancers in women younger than 45 years (Republic of Mauritius, 2014).

- There are no formal screening guidelines in Zimbabwe, but a number of non-profit organizations such as the Cancer Association of Zimbabwe and Breast Cancer Alleviation of Zimbabwe recommend breast health awareness and regular BSE (The Cancer Assocaiton of Zimbabwe, 2014). A recent report by the Zimbabwean Ministry of Health on a strategy setting out national goals for cancer prevention and control from 2014-2018 identified a series of barriers to breast and other cancers screening. These included lack of access to early detection; inadequate resources, equipment and technology, lack of education and awareness of the importance of regular cancer screening, prohibitive costs of screening services, and lack of referral of patients. The goals of this strategy included a reduction of late stage breast cancer presentation from 80% to 50% by 2018 (Ministry of Health and Child Care of Zimbabwe, 2013).

- Since 2011, Rwanda has been proactive in developing a national cancer program (Stulac et al, 2015). The national cancer plan was developed by a technical working group of clinicians, civil society representatives, NGOs and international partners to create a program integrating components of the WHO National Cancer Control Plan framework while incorporating experiences of partners from South Africa, the U.S. and Europe. The first national cancer control protocols were first endorsed in 2012 and provide guiding principles on cancer diagnosis and treatment at the Butaro Cancer Center of Excellence (BCCOE), which is the first rural cancer center to deliver comprehensive cancer services in the country through a decentralized health system that prioritizes equitable access to all levels of care. BCCOE was created and is supported through a unique twinning partnership between the Rwandan Ministry of Health (MOH), the NGO Partners in Health and Harvard Medical School. While no breast screening program has yet been instituted, the MOH has supported education of community health workers in supportive care and provided information to women to support breast health awareness. The feasibility screening with the use of CBE at initial point of contact has been evaluated as a national initiative at the request of the MOH (Abdalla et al, 2013), but the program has not yet been implemented.

- In Egypt, cancer has become a national priority with the publication of the 2014–20 national cancer plan (Hamdi Cherif et al, 2014), but it is unclear whether any progress has been made. No data on breast screening policies or practices are published.

Pathology

Accurate diagnosis is a cornerstone of effective breast cancer control. BHGI guidelines emphasized the importance of a pathologic diagnosis before initiation of treatment (Shyyan et al, 2006; Shyyan et al, 2008). However, the process is complex and requires specialized training correct tissue preparation and consensus diagnoses. The capacity and infrastructure necessary to perform adequate pathological assessment of breast cancers is lacking in the majority of African countries. A recent informal survey which aimed to capture the number of pathologists working in African countries reported that, with the exceptions of Botswana and South Africa, all countries in the region have fewer than one pathologist (including all practice sub disciplines) for every 500,000 people, with many having fewer than one per million. One country (Somalia) did not have any active pathologists (Table 1) (Adesina et al, 2013; Awadelkarim et al, 2010). Adesina et al recommended 3 necessary components to ensure provision of effective pathological services including meeting system needs, quality assurance needs and workforce needs (Adesina et al, 2013; Adeyi, 2011).

A major limitation to breast cancer care in sub-Saharan Africa is the shortage of pathologists, resources and infrastructure. BHGI guidelines stratified diagnostic and pathology methods into basic, limited, enhanced, and maximal. Minimal requirements at the basic level include obtaining a medical history from patients, performing a CBE, a tissue diagnosis, and maintaining high quality medical records. The latter is not an insignificant issue: a Cameroonian retrospective study of 531 patients with breast cancer reported that 33% of medical files were incomplete, or missing, and stated that the 'problem of medical records is a big concern in developing countries, and it represents a major handicap for medical statistics and research in this setting (Kemfang Ngowa et al, 2011b).

At the limited level, with increasing availability of resources, several approaches are proposed for improving breast pathology, including training pathologists, establishing pathology services in centralized facilities, and organizing international pathology services (Shyyan et al, 2006). The importance of the development of optimal breast pathology services has been identified by the BHGI as a fundamental requirement for the

delivery of quality breast healthcare with an emphasis on patient outcome (Masood et al, 2008). Immunohistochemical marker assessment is necessary to determine oestrogen receptor (ER) status, but the resources needed are beyond the scope of available resources in some situations (Anderson et al, 2003). While the 2005 BHGI guidelines included assessment of HER-2/neu oncogene status and IHC detection of metastases in axillary lymph nodes including sentinel lymph nodes, it was classified as appropriate for high level resource settings where trastuzumab is available for treatment of HER-2/neu positive cancers.

Several promising international collaborations to improve diagnostic pathology services are in place. One between the Ghanaian Komfo Anokye Teaching Hospital (KATH), and University Hospital of North Norway (UNN), resulted in development of a 5-year plan to re-establish surgical pathology at KATH, where hematoxylin and eosin (H & E) stained slides have been sent to UNN for review and Ghanaian pathologists received training at UNN (Stalsberg et al, 2008). Since that collaboration, KATH has improved cancer surgical pathology diagnosis from 35% in 2004 to >80% in 2010; and pathology services were extended to cover Regional and District Hospitals in northern Ghana (Awuah, 2012).

A collaboration between the Malawi Ministry of Health, Kamuzu Central Hospital, and the University of North Carolina at Chapel Hill in the United States (U.S.), resulted in the opening of the first diagnostic pathology laboratory in Lilongwe in 2011. The authors cited virtual microscopy or 'telepathology' as an important aspect in building a collaborative relationship between pathologists and clinicians in Malawi and the U.S., allowing exchange of ideas, and professional development activities. Over the first two years of operation, the laboratory described an increasing workload, a transition away from reliance on telepathology, and the return of a number of Malawian pathologists to the laboratory from other countries (Gopal et al, 2013). Similar collaborations to develop capacity have been described in Uganda (Stulac et al, 2015). Finally a variety of volunteer organizations have coordinated the efforts of volunteer pathologists to improve and provide affordable pathology services to underserved patients in LMICs, by establishing pathology laboratories, providing diagnostic pathology services, and training local physicians as pathologists. As of 2011 projects have been completed or are currently active in Kenya, Eritrea, Madagascar, and Ghana (Hoenecke et al, 2011).

Cancer Registries

Over 70% of the burden of the increasing incidence of breast cancer will fall on LMICs who are ill-equipped to deal with this burden. The availability of high-quality population-based cancer registration system is a vital component for any evidence-based cancer control program, since it provides direct evidence of changes in outcome following policy changes and interventions. Adequate data on breast cancer incidence and mortality and associated demographics is essential for assessing the burden of cancer, prioritizing health spending, and evaluating the effectiveness of cancer prevention and control programs. In the recent CONCORD-2 analysis, the authors commented that the absence of civil registration and cancer registry systems in participating countries in Africa made the assessment of recent survival trends from available data almost impossible (Allemani et al, 2015).

In an attempt to address the dearth of cancer registries across the continent, The African Cancer Registry Network (AFCRN) was inaugurated on 1st March, 2012, has 22 members, and aims to improve the effectiveness of cancer surveillance in sub Saharan Africa (African Cancer Registry Network (AFCRN), 2015). ACRN partners with IARC within the framework of its Global Initiative for Cancer Registry Development (GICR) in LMICs to provide a network Regional Hub for cancer registration in Sub-Saharan Africa (World Health Organization, 2015c). ACRFN provides technical and scientific support to countries seeking to establish population based cancer registries, advocating for cancer registration in this region, and coordinating research projects and disseminating findings and guidelines. Based on past knowledge and existing opportunities, an initial set of starter countries has been selected for each region. The ACRN and GIRC aim to have initiated work on registry-related activities in 20 low- and middle-income countries by 2020 and a further 30 by 2025 (World Health Organization, 2015c).

While the *Cancer Incidence in 5 continents* (C15, Volume IX) utilized data from only 6 registries which had data of sufficient quality for its estimates; Volume X utilized 8: Algeria (Sétif), Egypt (Gharbiah), Libya (Benghazi), Tunisia, Malawi (Blantyre), South Africa, (PROMEC), Uganda, (Kyadondo County), and Zimbabwe, (Harare) (Forman et al, 2013). A recent paper describing the results of a survey of 23 of the 25 active registries in Africa 2014 (Gakunga et al, 2015) pointed out that while few African registries have meet the high standards of completeness and validity required for inclusion in these analyses, many are functioning well to agreed ACRN standards, and can be used for national cancer control planning. This survey found that the 23 registries who responded had catchment populations ranging from 87,000 (Seychelles) to 48,235,000 (South Africa), with a corresponding range in numbers of cases registered (164–52,706 per year). The majority of data collection was active, and the timeliness of the registries was comparable to that of registries in Europe (Gakunga et al, 2015). Despite these promising changes, however, 19 countries in Sub-Saharan Africa (23% of the population) have no available information on cancer incidence or mortality (Ferlay et al, 2015).

Two relevant recent publications include a case study which described the barriers and facilitators to the implementation of a system for representative nation-wide cancer registration in Nigeria (Jedy-Agba et al, 2015), and a report on the current status of cancer surveillance activities including a pilot project in South Africa and use of the GICR framework to propose the development of four population-based cancer registries (Singh et al, 2015b). The Kumasi Cancer Registry in Ghana, in collaboration with AFCRN, successfully transitioned from a hospital-based cancer registry (initiated in 2004) into a population-based cancer registry in 2012 providing data on cancers in the Ashanti Region (Laryea et al, 2014). Within the past 10 years a number of other countries have either re-established or scaled up cancer registries. For example in 2011, South Africa's Department of Health instituted compulsory cancer registration. While the National Cancer Registry was established in 1986, it had become almost inactive after 2004 because of a lack of resources (National Cancer Registry of South Africa, 2015; Singh et al, 2015a; Stefan et al, 2013). In Egypt, a National Cancer Registry Program of Egypt was established in 2007, and now has a network of population-based registries that contribute data to the national cancer registry (Ibrahim et al, 2014; National Cancer Registry Program of Egypt; Stefan et al, 2013).

Access to Treatment

As discussed earlier, many women do not seek appropriate care when breast cancer symptoms arise, resulting in late stage diagnoses. When women do seek care, treatment is often unavailable due to lack of access to trained personnel, lack of available treatments and economic barriers. For example, a study in Yaoundé General Hospital (YGH), the only hospital in Cameroon where cancer patients can receive chemotherapy from trained medical oncologists, interviewed 79 consecutive patients with a diagnosis of breast cancer, Kaposi's Sarcoma, or lymphoma in 2010. The delay between first consultation with a health care provider and receipt of a cancer diagnosis was >3 months for 47% of patients. The total delay from the first sign of cancer to receipt of the correct diagnosis was >6 months for 63% of patients. 40% of patients interviewed spent >$200 on a single round of chemotherapy (Price et al, 2012). The latter highlights a significant barrier to receiving treatment in many African countries: the prohibitive cost (Kingham et al, 2013). A Ghanaian retrospective study reported that 79.4% of patients with advanced breast cancer cited economic barriers to treatment (Scherber et al, 2014).

Appropriate treatment for breast cancer includes surgery, radiotherapy and systemic therapy. Systemic therapy for breast cancer can include chemotherapy, hormonal therapy and targeted agents and can be administered pre-operatively (neoadjuvant therapy), as a treatment of locally advanced breast cancer, or post-operatively (adjuvant therapy) for metastatic disease. A retrospective study from 2007-2010 identified the majority of cancer treatments in Malawi as palliative in nature (Kendig et al, 2013).

Radiotherapy

Radiation therapy is an important component of breast cancer treatment programs. Nigerian women with breast cancer diagnosed between 2005 and 2008 and who received a combination of receiving surgery/chemotherapy/radiotherapy had a significant increase in survival outcome compared to those receiving surgery/chemotherapy alone (Makanjuola et al, 2014). However like many other breast cancer services associated with improved outcome, many African countries are at a significant disadvantage with respect to availability of radiotherapy resources. The IAEA Program for Action for Cancer Therapy (PACT) estimates that there is a lack of at least 5,000 radiotherapy machines in developing countries, and that up to 70% of patients in these countries who may benefit from radiation medicine do not receive it (IAEA, 2015c). The African Regional Cooperative Agreement for Research, Development and Training Related to Nuclear Science and Technology (AFRA) agreement, in cooperation with the International Atomic Energy Agency (IAEA) which funds approximately 75% of AFRA's budget, provides a framework for its 39 African Member States to collaborate on programs and projects focused on their specific shared needs. AFRA described significant barriers to improving access to nuclear science and technology including lack of adequately skilled and trained personnel and lack of basic nuclear infrastructure in some member states. However, AFRA did identify a number of positive points such as local and international collaborations; implementing AFRA best practices in the region; and African stakeholders focusing on enlarging the scope and sustainability of a number of nuclear programs (AFRA, 2013).

A recent review of the status of radiotherapy in Africa examined the Directory of Radiotherapy Centers (DIRAC), a database by the IAEA, which is estimated to include 90% of existing radiotherapy facilities worldwide, and contains information about external beam radiotherapy, brachytherapy, dosimetry, ancillary equipment, and trained personnel. The review was a longitudinal assessment of the state of radiation oncology resources in from 2002-2012, and found a direct correlation between gross national income per capita, and average number of teletherapy machines per million population: 8.6/106 population for high-income countries; 1.6 for upper-middle-income countries, 0.71 for lower-middle-income countries; and 0.21 for low-income countries. The 160 radiotherapy centres in Africa have 277 radiotherapy machines (88 cobalt60 units and 189 linear accelerators). However the majority of the machines were located in South Africa (33%) and Egypt (27%), and approx. 20% of the African population live in one of the 29 countries that do not have any teletherapy facilities (Table 1) (Abdel-Wahab et al, 2013; Grover et al, 2015).

A 2011 paper arising from the International Conference on Advances in Radiation Oncology (Salminen et al, 2011) discussed new and existing technologies that may be suitable for LMICs, and identified barriers to establishing basic radiation therapy services in LMICs, including a global shortage of skilled professionals and lack of education and training programs. It also cited recommended that a series of conditions be met before advanced technologies are introduced into a target country, including identifying that a need for advanced technology exists (i.e. patients with curative potential); experience with 3D conformal radiation therapy and advanced treatment planning; adequate imaging services are available; personnel have adequate training in planning, implementation, and QA in advanced technology; continuous medical education system is in place; and that an adequate QA/QC program has been established. Finally it recommended that clinical studies should be undertaken to demonstrate clinical and cost-effective benefits to the advanced technologies (Salminen et al, 2011).

It should be noted that, where radiation therapy services do exist, patients may chose or be prevented from attending radiotherapy clinics. A Nigerian study of 385 women diagnosed with histologically confirmed breast cancer, where over 50% had metastatic disease, found that only 30% of women referred to a local centre for radiotherapy attended their first appointment (Adisa et al, 2011).

Chemotherapy

Access to treatment for breast cancer in LMICs is limited (Kingham et al, 2013). A recent report which reviewed national essential medicines lists based on the WHO 2013 list, from LMICs found significant variation in available treatments for different types of early breast cancer in their National Essential Medicines Lists (NEML): over 80% of the American countries included all therapy components for all types of early breast cancer (except for HER2 overexpressed tumours). In comparison, over 40% of the countries in Africa did not have all treatment components for any subtype, and guideline-recommended treatments were less frequently included in the NEMLs of low-income countries than in middle income countries. Treatments for late stages were more frequently selected as essential medicines in LMICs compared to early stages,(Bazargani et al, 2015) reflecting the presentation at late stage of disease by the majority of women in these countries.

As part of Target nine of the Global Action Plan, the WHO aims to have an 80% availability of the affordable basic technologies and essential medicines, including generics, required to treat major non-communicable diseases in both public and private facilities. It provides tools to implement this action plan include guidelines on pricings, storage distribution of drugs (World Health Organization, 2015b). The 2015 WHO essential medicine list now includes five chemotherapy medications commonly used to treat breast cancer (World Health Organization, 2015d). However, a commentary on the essential medicines list pointed out that labelling a medicine as essential does not guarantee patient access, especially in LMICs, and should be regarded as a first step in the policy process towards assuring access to these medicines, as part of broader global health and sustainable development goals (Gray et al, 2015).

The BHGI guidelines stratified by disease stage and resources level recommend classic cyclophosphamide, methotrexate, and 5-fluorouracil (CMF), doxorubicin and cyclophosphamide (AC), epirubicin and cyclophosphamide (EC) and 5-fluorouracil, doxorubicin, and cyclophosphamides (FAC) for adjuvant chemotherapy for stage II breast cancer, and pre-operative chemotherapy with AC, EC FAC or CMP for stage III. In limited resource settings, additional stage I adjuvant therapy with classic CMF, AC, EC or FAC, and classic CMF and anthracycline monotherapy or combination treatment for Stage IV metastatic and recurrent breast cancer treatment, are added to the model. Finally, in enhanced settings taxanes for stages I-III, and sequential single agent or combination treatments with Trastuzumab and Lapatinib for stage IV breast cancer are recommended (Eniu et al, 2008).

In Ghana a retrospective study of medical records for 597 breast cancer patients seen in 2008-2011 examined patient management and treatment patterns. Late stage at diagnosis was common, treatment plans of the study hospital were relatively standardized according to disease severity, and defaulting/interrupting treatment in the records was also common. Patients diagnosed with late stage cancer who received adjuvant therapy and patients with known hormone status evaluation were more likely to have complied with treatment guidelines and continued oncotherapy compared to those who never had hormone status requested or reported (Scherber et al, 2014). A small Sudanese study of 98 breast cancer patients with locally advanced disease (Stage IIIa-c) observed with locally advanced breast cancer and treated with neoadjuvant chemotherapy using therapies appropriate for basic level resources, observed a good clinical response rate with 11.2% with a complete clinical remission and 72.4% had a partial remission (Alawad, 2014).

However financial barriers to completing chemotherapy regimens where they are available have been reported. A small Nigerian study found that number of patients on neoadjuvant chemotherapy declined to 46% by the last cycle during a six-course treatment regimen, principally due to financial reasons as treatment was an out-of-pocket expense (Anyanwu et al, 2010). In Eritrea, a resource-poor country, a small study of 82 breast cancer patients where over 66% were diagnosed with late-stage disease between 2007 and 2008, only 1 patient received chemotherapy; the remainder were managed by surgery only. In comparison a cross-sectional study from the Egyptian Gharbiah population-based cancer

registry, located in a middle-income country, identified 5348 cases of breast cancer: 78.1% received radiotherapy; 92.8% adjuvant chemotherapy and 56.9% hormonal therapy (Zeeneldin et al, 2013).

Information, Awareness and Education

In the absence of breast early detection or screening programs, culturally appropriate education and awareness campaigns have been widely supported as a method to improve awareness of breast cancer symptoms among women in LMICs, and to encourage them to seek early diagnosis and treatment (Anderson et al, 2008). While education and awareness campaigns are of vital importance in LMICs, there are a variety of unanticipated barriers to implementing them. These include lack of awareness, knowledge and poor health literacy. For example, while there have been some efforts to provide education to women on the importance of breast health in Sierra Leone (Shepherd et al, 2006), a study of 3,645 women identified minimal education, poverty and reliance on traditional healers as barriers for women with breast masses (Ntirenganya et al, 2014). A Nigerian study identified a number of economic and cultural barriers to implementing education about basic screening programs including lack of both specialized health personnel and breast cancer screening facilities, the absence of biomedical terminology in local languages, gender inequality and the prevailing influence of traditional health practitioners (Asobayire et al, 2014).

A lack of knowledge of the importance of breast health awareness and of the importance of breast cancer early detection leads to a lack of screening practices, even at the basic level. In an Egyptian study in 2000, only 10.4% of 565 newly diagnosed breast-cancer patients, had practiced BSE, and 2.7% reported monthly BSE (Abdel-Fattah et al, 2000). In Morocco, a study of 136 female doctors found that while 75% of study participants practiced BSE once a month, only 15% ever had a mammogram (Ghanem et al, 2011). A cross-sectional study in Tunisia of 900 women reported poor knowledge of specific risk factors for breast cancer and of breast screening modalities, with only 14% of women performing any type of breast screening (El Mhamdi et al, 2013).

Non-governmental organizations (NGOs) are important resources for many countries in this region, as they partner with governments with a goal of reducing cancer mortality in this region, often by promoting early detection, diagnosis and treatment and reducing the stigma that often surrounds a cancer diagnosis (Oluwole et al, 2013). A number of pilot projects by governmental and non-governmental organizations have attempted to increase breast cancer awareness in urban and rural areas across Africa, with a variety of success. For example, in North Africa the Algerian government, in partnership with Roche and a patient advocacy group El Amel (Hope) launched a mobile mammography unit in 2013, which brings trained nurses, and other healthcare workers to remote regions within Algeria, with a goal of combining breast cancer education with screening facilities. Other countries such as Tunisia are focusing on prevention and early detection of cancer as part of their national strategy in the fight against cancer (2010-2014).

In the absence of formal guidelines in many West African countries, a number of awareness and educational campaigns have been initiated. In Ghana, a cross-sectional survey assessed the impact of an education program on knowledge, attitudes and practices toward breast cancer and breast cancer prevention among women from rural communities, and found that knowledge about breast cancer symptoms improved, and the number of women who reported beginning BSE increased (Mena et al, 2014). There have been multiple studies of awareness, attitude and practice of breast examination in Nigerian women. Knowledge and practice of BSE and CBE vary widely, but women who have received a tertiary education are consistently more likely to be aware of and the conduct BSE. The Free Breast Cancer Awareness and Screening program launched in Nigeria in 2006 in collaboration with the Ministry of Women Affairs and Poverty Alleviation educates women about BSE (Lagos State Ministry of Health, 2011) and performs free counselling and referral services. While there are no governmental guidelines on breast screening in Cameroon, there are periodic mass campaigns for breast health awareness and CBE organized by the Ministry of Health (Kemfang Ngowa et al, 2011a). A number of cross-sectional surveys in African women found that knowledge of preventive measures and risk factors was poor in women

in Cameroon (Suh et al, 2012). An NGO, SOCHIMIO (Solidarite Chimiotherapie) is a Cameroonian NGO affiliated with the UICC, based in Yaoundé that has initiated several cancer research projects in Cameroon. While these are primarily aimed at providing therapeutic care to cancer patients, they have also implemented educational outreach programs (Solidarite Chimiotherapie (SOCHIMIO), 2014).

In South Africa, the government and a variety of NGOs provide community outreach and educational materials to increase awareness of breast cancer signs and symptoms. These include mobile breast check units which travel to semi urban and urban areas offering free CBE, education in BSE and other awareness campaigns (Cancer Association of South Africa, 2014). In Swaziland, the SBCN's educational programs aim to increase awareness on aspects of breast cancer including the promotion of BSE annual medical examinations and the importance of early diagnosis and treatment (Swaziland Breast Cancer Network, 2008).

In an Ethiopian study designed to improve health workers' knowledge and awareness using an abbreviated training intervention reported that initial knowledge and practice skills related to CBE were low, but improved significantly post-intervention (Mutebi et al, 2013). A number of NGOs in Kenya such as Cancer Free Women support a variety of awareness and education campaigns including g teaching BSE and symptoms of breast cancer to Kenyan women (Cancer Free Women, 2013). In Madagascar a variety of NGOs provide preventive care initiatives, and education and awareness campaigns (4aWoman, 2014). In Rwanda, an NGO Breast Cancer Initiative East Africa (BCIEA) launched a month-long campaign in Kigali, Rwanda, to provide free CBE for women and to persuade both women and their partners of the importance of cancer awareness (Kigali, 2014). Finally, NGOs in Zimbabwe perform a variety of awareness programs to inform women about cancer prevention strategies and cancer screening procedures (The Cancer Association of Zimbabwe, 2014).

Breast Cancer Early Detection

Successfully down staging breast cancer in populations is dependent on successful early detection programs. Unfortunately, many African countries have limited resources to allocate to early breast-cancer detection resulting in late diagnosis, which is more difficult to treat effectively, and is associated with increased morbidity and mortality (Coleman et al, 2008). Even if breast cancer awareness increases among African women, access to mammography is limited to wealthier women living in large urban areas. Hence, current early detection efforts focus on promoting BSE, teaching women to recognize the early symptoms of breast cancer, and encouraging them to present for early medical evaluation when necessary. Most women presenting with breast symptoms receive a CBE; those with positive findings are referred to larger hospitals for diagnostic interventions such as fine needle aspirations and biopsies. The effectiveness of CBE depends on the examiner's training and experience and is potentially limited by a high false positive rate, in some cases up to 85% (McDonald et al, 2004; Trapp et al, 1999). Nevertheless, CBE is currently used as the primary method for breast cancer detection in most regions of Africa because of its availability and low cost. Therefore, efforts to downstage breast cancer should include improving provider CBE training with the aim of reducing the number of false positive CBEs which require referral and expensive diagnostic interventions.

Ultrasound is available in many facilities, even those located outside large urban areas, and it is less expensive than mammography. The capacity already exists among midlevel providers (sonographers and midwives) at these facilities to use this equipment to diagnose common medical problems, such as identifying potential complications related to pregnancy (McClure et al, 2014). With appropriate additional training, ultrasound use could expand to include evaluating women with positive CBEs to reduce the number of women requiring referral and diagnostic interventions. Efforts to improve breast ultrasound training and use in Africa are currently in progress (Scheel et al, 2015).

North Africa

A number of countries in North Africa have developed recommendations for breast cancer screening, and several are making strides in scaling up successful pilot projects. WHO EMRO published guidelines on breast cancer screening in 2006, and in line with the BHGI, suggested that screening could be implemented in centralized cancer facilities where breast cancer treatments are available (Khatib, 2006). While these programs will only provide screening to a limited proportion of the population, they could act as pilot programs with the ultimate aim of expanding them to cover the entire population as more resources become available. Recommendations for screening frequency vary considerably in this region. A report by the Algerian National Institute of Public Health in 2003 identified a variety of issues in the prevention and diagnosis of late stage breast tumours including a delay between presentation and diagnosis, and lack of observance of screening and treatment protocols (Hammouda et al, 2003). While cancer has become a national priority with the publication of the 2014–20 National Cancer Plan (Hamdi Cherif et al, 2014), it is unclear whether any progress has been made. No data on breast screening policies or practices were found. Some opportunistic pilot projects are in place such as a partnership between the Algerian government, Roche and a patient advocacy group El Amel (Hope), which launched a mobile mammography unit in 2013.

Similar to other countries in the area, women in Egypt present frequently with advanced breast cancer (Omar et al, 2003; Salhia et al, 2011). The Women's Health Outreach Program recommends monthly BSE starting at age 20, and offers free annual breast screening for all Egyptian women above the age of 45 years (Salem et al, 2008; Women's Health Outreach Program, 2014). The program was made up of 5 phases with a 1-year pilot phase (2007-2008) to identify barriers in implementation. Each implementation phase will address a number of governorates. The target of the 5-year implementation plan is to provide coverage for the entire population. Screening is delivered in an opportunistic fashion through mobile units equipped with digital mammography units which serve rural and less affluent regions. Asymptomatic women are invited to return in a years' time for a repeat mammogram (Women's Health Outreach Program, 2014). However the program was criticized as being both expensive and ineffective and not the most effective use of resources: fewer than 90 true cases of cancer were found as a result of 20,000 mammograms (Harford, 2011; Stefan et al, 2013). More effective alternative methods of breast screening have also been explored, including training women resident in a Cairene slum in breast health awareness and BSE (Kharboush et al, 2011). Another study which randomized 14,807 women to CBE vs. a control arm demonstrated high acceptance, with 85–91% of the women targeted enrolling in the study. Initial results demonstrated that stage distribution was significantly better in the intervention arm compared to the control arm (Miller, 2008). The Egyptian National Screening Program, the Women's Health Outreach Program (WHOP), was launched 2007: prior to this, a study conducted by United States Agency for International Development reported that only 1.7% women aged 40 and above had had a mammogram within the past 12 months (Corbex, 2009; El-Zanaty et al, 2009).

Morocco set up a National Cancer Prevention and Control Plan (NCPCP), comprising a coordinated breast cancer awareness campaign and a program aimed at developing breast cancer screening was in 2010, aimed at targeting half-a-million women. A new breast and uterine cancer screening and early detection center was opened in 2013 in Mohammedia, which provides screening facilities for more than 40,000 eligible women. Mobile mammography units travel to remote areas to provide opportunistic screening to those without access to centralized screening facilities. The NCPCP in Morocco has developed a 3-tiered system for increasing screening coverage. Level 1 health care clinics with general practitioners and nurses who provide breast health education and CBE to women; Level 2, specific reproductive health clinics who receive referrals from Level 1 clinics and perform diagnostic ultrasound and mammography; and Level 3, oncology centres. Breast cancer screening is recommended for women between the ages of 45-69 (The Foundation Lalla Salma, 2014). The Tunisian Ministry of Health has stated goals of focusing on prevention and early detection of cancer as part of their national strategy in the fight against cancer (2010-2014), and currently recommends annual CBE for women aged 40-69 years, with mammography reserved for high-risk women and those referred after primary screening via CBE. The State has implemented a number of pilot programs examining the efficacy and feasibility of mammographic screening in the general

population. Based on the results of these programs the Tunisian government will consider moving toward population-based mammographic screening (Association Tunisienne pour la Recherche et les Etudes en Pharmacie, 2014). One of the first pilot studies in 2003 was a large scale population-based mammographic screening in urban areas, but participation rates have tended to be low (Bouchlaka et al, 2009; Zaanouni et al, 2009). The most recent evaluated three rounds of mammography screening as part of a pilot program, carried out between 2004-2010 in Sfax, Tunisia. Biennial screening was offered to women aged >45 years, and 17.4% of the target population underwent screening, resulting in 12,657 mammograms (Frikha et al, 2013).

Sub-Saharan Africa

A number of countries lack either guidelines and/or data on screening guidelines or practices including: Libya, and Mauritania, in North Africa; Angola, Cameroon, Central African Republic, Chad, Democratic Republic of Congo, Republic of Congo, Equatorial Guinea, and Gabon in Central Africa; Republic of Benin, Burkina Faso, Gambia, Guinea, Ghana, Guinea-Bissau, Liberia, Mali Mauritania, Namibia, Nigeria or Senegal, or Togo in western Africa; Eritrea, Ethiopia, Kenya, Malawi, and Zimbabwe and in Eastern Africa. Where mammography does exist in these countries it is often limited to private hospitals, (Msyamboza et al, 2012) and are centralized in major urban centres (Ly et al, 2012). For example, the Lagos State Ministry of Health reported there are only 4 functional mammography units in Lagos, utilization of mammography is rare and most women are unaware of its use as a screening tool (Lagos, 2014). However, many countries in the region are developing innovative low-cost early detection methods that can be used effectively in low resource settings. While Sudan lacks guidelines on age at which cancer screening should begin (Abuidris et al, 2013b) it established a National Cancer Control Program in 1982, which focuses on prevention, early detection and screening. Unfortunately, a lack of resources has hampered implementation of breast cancer screening and the majority of efforts have been focused on public awareness campaigns and education of medical professionals (Hamad, 2006). However, a Sudanese study trained female volunteers to detect breast abnormalities while visiting households in 56 villages in an intervention county, while the control county received no intervention. The volunteers screened women >18 years for breast abnormalities, and referred those with suspected breast cancer for medical diagnosis and, if necessary, treatment at a district hospital. From 2010-2012, 10 309 (70%) of 14 788 women in the intervention county were screened; 138 women were identified as having breast abnormalities and were referred for diagnosis and treatment; of the 118 women attended the hospital, 101 were diagnosed with benign lesions, 8 with carcinoma in situ, and 9 with malignant disease. In the control villages, only four women attended the hospital for diagnosis: one was diagnosed with a benign lesion and three with advanced disease (Abuidris et al, 2013a).

In recognition of the need to develop formal guidelines, a report by the Kenyan Ministry of Health called for enhanced health promotion and education, and improved early detection by introducing or expanding screening programs, and by developing guidelines for screening and early cancer detection (Ministry of Public Health and Sanitation and the Ministry of Medical Services, 2012). However, many of these have yet to be implemented (Matheka, 2014). Health workers have been proposed as a link between the general population and access to care, especially in rural areas (Mutebi et al, 2013).

There are no formal screening guidelines in Zimbabwe, but a number of non-profit organizations such as the Cancer Association of Zimbabwe and Breast Cancer Alleviation of Zimbabwe recommend breast health awareness and regular BSE for women aged 18 and older (The Cancer Assocaiton of Zimbabwe, 2014). A recent report by the Zimbabwean Ministry of Health on a strategy setting out national goals for cancer prevention and control from 2014-2018 identified a series of barriers to breast and other cancer screening. These included lack of access to early detection; inadequate resources, equipment and technology, lack of education and awareness of the importance of regular cancer screening, prohibitive costs of screening services, and lack of referral of patients. The goals of this strategy included a reduction of late stage breast cancer presentation from 80% to 50% by 2018 (Ministry of Health and Child Care of Zimbabwe, 2013).

Breast cancer incidence rates have increased over the last 20 years in Uganda (Wabinga et al, 2014). The average age in Uganda is low (Uganda Bureau of Statistics (UBOS), 2002), with a peak age at diagnosis of between 40 and 50 years. The limited health care budget and resources in Uganda are directed towards fighting communicable diseases (Galukande et al, 2010). In 2012, there were 4 mammography units in Uganda, (2 in government and 2 in private health units) and 42 radiologists (Monu et al, 2012). Galukande and Kiguli-Malwadde commented on the greater availability and lower cost of ultrasound as a potential breast cancer screening tool in Uganda. Although there is some government subsidized healthcare, the majority of the population has to self-fund care. Consequently, in the Breast Cancer Guidelines for Uganda (written by a team of oncologists, surgeons and radiologists from Kampala) BSE is recommended for its practicability and affordability (Gakwaya et al, 2008b).

No data were found on breast screening policies or practices for countries in Southern Africa, with the exception of the Republic of South Africa. The public-sector health service emphasizes community level healthcare complimented by a hierarchical referral system through district hospitals: breast cancer symptoms are usually detected by cancer patients rather than via screening, who then attend primary health care clinics. They are then referred to secondary and tertiary level clinics and hospitals for diagnosis and treatment. The NGO Cancer Association of South Africa (CANSA) recommends monthly BSE for all women and regular CBE. Yearly mammograms are recommended for women over the age of 40, however these are not free (Cancer Association of South Africa, 2014). CANSA provides education about the importance of early detection and performs opportunistic screening via CBE through mobile health clinics and CANSA care clinics throughout South Africa (Cancer Association of South Africa, 2014). Mammograms are offered though public hospital breast clinics.

In 2010, the Swaziland Breast Cancer Network (SBCN) operated three breast cancer clinics, which offer free consultations, examinations, diagnosis and referrals. SBCN recommends monthly BSE, and annual CBE by a trained provider, and has developed a referral tool for further diagnostic work for patients who report suspicious findings. It is unclear whether the SCBN is affiliated with the Swazi Ministry of Health: no formal guidelines on breast screening were found on the Ministry of Health's website. While the SBCN recommends that all women over 40 should undergo mammography, it recognizes that mammography is used only very occasionally by those who can afford this service (Swaziland Breast Cancer Network, 2008).

Finally unlike many countries in the region, Mauritius is a HIC with a 5-year survival rate from breast cancer that similar to other HICs (Allemani et al, 2015). The republic developed a National Cancer Control Program for 2010-2014, and recommended that breast health awareness campaigns encouraging BSE and yearly CBE to women >40 years. Population based screening mammography was not thought to be advisable, given the relatively high proportion of cancers in women younger than 45 years (Republic of Mauritius, 2014). Diagnostic procedures such as MRI and CAT scans are available as is radiotherapy and chemotherapy (Mauritius, 2015). The Republic of Mauritius is one of the few countries in the region with formal guidelines on breast cancer screening.

Screening Practices and Behaviours in Africa

In Ghana, the majority of women are diagnosed between the ages of 40-49 (Wiredu et al, 2006). In a small cross-sectional study, the rates of breast screening practices was poor, with the self-reported BSE rate of 32%, CBE 12% and mammography, 2%, with higher levels of education strongly associated with screening behaviours (Opoku et al, 2012). A Senegalese cross-sectional study in 2006 interviewed 300 patients attending 5 hospitals in Dakar for a medical or surgical consultation for breast-health related issues, on knowledge and practice of BSE. Study participants were young, with an average age of 34 years, uneducated and living in poverty. Participants were aware of BSE (42.7%) and 29% regularly practiced BSE. Practice of BSE was associated with income and educational attainment (Gueye et al, 2009).

In Cameroon, a 2011 retrospective study examined the medical records of 531 breast cancer patients diagnosed at Yaoundé Medical Hospital between 1989 and 2009: self-detection was the mode of detection in 95.3% of patients, and only 2.9% of patients were diagnosed via mammography or CBE. Seventy-one % of patients presented at late stage (Kemfang Ngowa et al, 2011a). A study interviewing women appearing at Yaoundé General Hospital with Stage IV cancer, found that the main reasons for delay in seeking medical care was inability to pay; inadequate diagnosis by general doctors; beliefs, fears, cultural factors including a fatalistic attitude after a diagnosis of cancer, and lack of knowledge about breast cancer (Ekortarl et al, 2007). A cross-sectional survey in Cameroon of 120 women in 2012 reported that while 74.2% of women had heard of BSE, 40% had never performed it. In Nigeria, a study of 221 undergraduate students reported that 85.1% were aware of BSE; 37.3% were knowledgeable about BSE; but only 11.8% aware of the ideal age to start BSE (Gwarzo et al, 2009). A second Nigerian study of 393 students reported that 67.9% of those who had heard of breast cancer knew that there were screening methods available; of these 91.6% were aware of BSE, 93.2% were aware of CBE and 32.8% were aware of mammography as a screening method. However only 50% of respondents who were aware of breast cancer practiced BSE, and only 7.6% of respondents had ever undergone any form of clinic-based screening (Olugbenga-Bello et al, 2011).

A national population-based cross-sectional study of 2202 women in the Republic of South Africa, found that only 15.5% ever reported having a mammogram; screening was associated with White or Indian/Asian population group, greater wealth, and having health insurance (Peltzer et al, 2014). In an analysis of performance data of screening mammography at a breast centre in South Africa, of 10 000 women screened, 55 cancers were detected. In women aged 40-49 years the detection rate was 3.8/1000 exams, and in women 50-69 years 9.7/1000 (Apffelstaedt et al, 2008).

A 2012 study of 390 health workers in northwest Ethiopia found that 37% of respondents had ever practiced BSE and 14.4% practiced it regularly. The main reasons for not performing regular BSE were not having problems with breasts (53.2%), not knowing the technique (30.6%), and not knowing its importance (21.4%); having knowledge of the importance of BSE was a predictor of BSE practice (Azage et al, 2013).

Qualitative studies of women in this region report a variety of barriers to seeking early diagnosis, or participating in screening. Data from 69 Ethiopian breast cancer patients found that even among women who are aware of breast cancer, early signs/symptoms are frequently ignored, traditional healers are preferred, and study participants indicated that stigmatization and social isolation complicate discussion and action around breast cancer (De Ver Dye et al, 2011). A qualitative study of Kenyan women reported differences between rural and urban women with respect to knowledge of symptoms and the importance of breast screening. The majority of women was fatalistic about the disease and assumed it to be incurable (Muthoni et al, 2010).

Despite the lack of governmental guidelines on breast cancer early diagnosis, and low levels of awareness about the importance of breast self-awareness, a number of countries are implementing pilot studies in an attempt to reach underserved populations. A recent paper from the Democratic Republic of Congo reported use of BHGI guidelines in implementing a breast cancer awareness campaign in Kinshasa from 2010-2012, based on BSE and CBE by trained healthcare workers (Luyeye Mvila et al, 2014). Participating women underwent CBE and in the case of suspicious findings, received a mammography and ultrasound, and where necessary FNA. A total of 4,315 women were screened, of whom 1,113 underwent mammography screening. A pilot screening program using a mobile mammography unit in the Western Cape province in the republic of South Africa in women aged 40 years and older between 2011-2012, performed 2,172 screening mammograms, with a 9.6% recall rate (Apffelstaedt et al, 2014). The authors reported multiple problems, both technical (such as poor quality images) and administrative (e.g., images not reaching the referral centre) and a low cancer detection rate, concluding commencement of a screening program using this model was not justified in this setting.

Conclusions

While the situation in many African countries paints a bleak picture for breast cancer care, due to over-burdened or non-existent health care infrastructures, poverty and increasing rates of breast cancer, which are commonly diagnosed at late stages, the outlook on some fronts calls for optimism. Some African nations are working to create national and international networks to improve aspects of breast cancer care. Governmental initiatives through cancer control planning, public/private partnerships, institutional twinning, and the use of available tools such as the BHGI resource-stratified guidelines can allow local stakeholders to develop novel and innovative methods for improving breast health care. The use of awareness education and distributed models of care to facilitate breast cancer down-staging is essential for most of Africa in order to decrease the number of patients who are unrealistic or inappropriate candidates for curative treatment and instead should be the focus of palliative efforts. Diagnostic services based on tissue sampling is essential, both for making cancer diagnoses, but also for determining proper treatment planning. The prolonged time from initial diagnosis to instigation of treatment is so lengthy as to be a measurable aspect of worsened breast cancer outcome. In addition, healthcare systems in Africa need to be expanded and supported such that patients who begin a treatment regimen are likely to complete it. Through this type of systematic approach to breast cancer care delivery in Africa, we can realistically anticipate seeing improvements in breast cancer outcomes given resources for organizational restructuring and time for realistic implementation.

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Chapter 13

Africa: Childhood Cancer

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The African continent ranks second in the world in terms of area, covering about one-fifth of the whole land surface of the Earth. The continent is divided among 54 countries (Western Sahara, although a member of the African Union, has its statehood disputed by Morocco (CIA, 2015)). Africa ranks second also with regard to its population size, amounting, in 2015, to an estimated 1.17 billion inhabitants (United States Population Reference Bureau, 2015). Out of these, 486 million (43%) are children, aged between 0 and 14 years.

Over the last decade, the economy of the continent has grown at an annual rate of over 5% (Middle East and Africa, 2015) and this growth has reflected, among others, in an improvement of the health of its inhabitants. The progress is not, however, in proportion with the economic growth, and is definitely short of the targets of the UN Millennium Development Goals (MDG). For example, the children under-five mortality rate has indeed decreased in Northern Africa from 73/1000 births in 1990 to 24/1000 in 2015, which means that the region has attained the target set according to the MDG. But the situation in Sub-Saharan Africa is far worse: from 180/1000 in 1990, the child mortality has decreased only to 83/1000 in 2015, whereas the proposed target was 60 (Unicef et al, 2015).

Similarly, with regard to the control of childhood cancers, Africa registered relatively little progress. According to the estimations of the International Agency for Research in Cancer (IARC), the incidence of paediatric (0 to 14 years of age) malignancies on the continent is 8.0/100,000. This incidence rate, together with the mortality rate of childhood cancer (of 4.6/100,000) is comparable with the average estimates for the world as a whole (see Table 1) (Ferlay et al, 2013). A comparison of the same parameters with those recorded in the very high human development (VHHD) nations, as defined by The United Nations (United Nations Development Programme, 2015), indicates that, even if the incidence of childhood cancer in Africa is almost half that of the VHHD areas, the mortality is twice as high (Table 2).

Table 1: Cancer incidence in Africa compared with World incidence

Source: Ferlay J, Soerjomataram I, Ervik M, et al. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Available from: http://globocan.iarc.fr, accessed July 7, 2014; figures per 100,000 population aged 0-14 years

Cancer type	World	Africa
All cancers excl. non-melanoma skin cancer	8.8	8.5
Bladder	0.0	0.0
Brain, nervous system	1.1	0.5
Colorectum	0.0	0.0
Gallbladder	0.0	0.0
Hodgkin lymphoma	0.4	0.4
Kaposi's Sarcoma	0.1	0.5
Kidney	0.5	0.8
Larynx	0.0	0.0
Leukaemia	2.7	1.1
Lip, oral cavity	0.1	0.1
Liver	0.2	0.2
Lung	0.0	0.0
Melanoma of skin	0.0	0.0
Multiple myeloma	0.0	0.0
Nasopharynx	0.1	0.1
Non-Hodgkin lymphoma	0.9	1.6
Oesophagus	0.0	0.0
Other pharynx	0.0	0.0
Pancreas	0.0	0.0
Stomach	0.0	0.0
Thyroid	0.1	0.0

Table 2: Incidence and mortality of pediatric cancers in Africa versus Very High Human Development countries (VHHD)

Source: Ferlay J, Soerjomataram I, Ervik M, et al. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Available from: http://globocan.iarc.fr, accessed July 7, 2014; figures per 100,000 population aged 0-14 years

Cancer type	VHHD incidence	Africa incidence	VHHD mortality	Africa mortality
All cancers excl. non-melanoma skin cancer	14.8	8.5	2.4	5.0
Bladder	0.0	0.0	0.0	0.0
Brain, nervous system	2.7	0.5	0.7	0.3
Colorectum	0.0	0.0	0.0	0.0
Gallbladder	0.0	0.0	-	-
Hodgkin lymphoma	0.6	0.4	0.0	0.1
Kaposi's Sarcoma	0.0	0.5	0.0	0.3
Kidney	0.9	0.8	0.1	0.7
Larynx	0.0	0.0	-	-
Leukaemia	4.9	1.1	0.8	0.7
Lip, oral cavity	0.1	0.1	0.0	0.0
Liver	0.2	0.2	0.1	0.1
Lung	0.0	0.0	0.0	0.0
Melanoma of skin	0.1	0.0	0.0	0.0
Multiple myeloma	0.0	0.0	0.0	0.0
Nasopharynx	0.0	0.1	0.0	0.0
Non-Hodgkin lymphoma	0.9	1.6	0.1	0.8
Oesophagus	-	0.0	-	0.0
Other pharynx	0.0	0.0	0.0	0.0
Pancreas	0.0	0.0	0.0	-
Stomach	0.0	0.0	-	0.0
Thyroid	0.3	0.0	0.0	-

Patterns of Geographic Distribution of Paediatric Cancers in Africa

Estimates of incidence of various malignancies in African children (see Table I) depict a pattern which appears to differ from that of the world as a whole: non-Hodgkin lymphoma is the dominant cancer, whilst in the world leukaemia is the most frequent one. Additionally, kidney tumours are in the third place in Africa, whilst in the world they do not appear among the three most frequent cancers. However, in the VHHD areas, renal malignancy also appears in the third place.

The excess of NHL in Africa is the consequence of the high (Orem et al, 2007) incidence of Burkitt lymphoma over a vast area in Sub-Saharan Africa, spanning from The Gambia in the west to Kenya in the east and descending over Malawi, northern Zimbabwe and Mozambique in the south: "the lymphoma belt". This very same area is where malaria is endemic, and a co-operation between malaria and Epstein – Barr virus infection probably plays a role in the pathogenesis of Burkitt lymphoma (Sugden, 2014).

The HIV epidemic plays a similar role, of enhancing the oncogenetic properties of the Epstein – Barr virus, as the incidence of Burkitt lymphoma (and that of other NHL) is augmented in areas of widespread HIV infection. With regard to the kidney tumours, consisting in around 90% of cases of nephroblastoma, their slight predominance on the African continent is not yet completely explained.

Without detracting from the value of the IARC estimates of the incidence of various cancers in the world, it is important to realise that in many geographical areas there are no reliable registers of cancers, let alone of paediatric cancers. In such situations, the epidemiologist is reduced to extrapolating data obtained in a limited area to the whole country or even to use figures obtained in the neighbouring countries, in order to evaluate the incidence of malignancies.

A recent study (Stefan, 2015a) collated data on childhood cancer obtained from 21 registries situated in 18 countries across Sub-Saharan Africa, mainly from the year 2000 to 2010, but in some cases from as far back as 1985 to as recent as 2012. Among the participating registries, the incidence of childhood cancers is known to differ substantially, from 5.5/100,000 in Congo (Brazzaville) to 12/100,000 in Zimbabwe and 4.5/100,000 in South Africa (Chokunonga et al, 2013; Nsonde Malanda et al, 2013; Stefan et al, 2015).

The study also reflected differences, among countries, with regard to the most frequent childhood cancer (see Table III). NHL, consisting mainly of Burkitt lymphoma, was confirmed to be on top of the list of childhood cancers in those countries forming the "lymphoma belt". Kaposi's Sarcoma, known to exist endemically in large areas of Sub-Saharan Africa and which, additionally, has soared to even higher incidence due to the HIV epidemic, appears in first place among children's cancers only in Uganda and Mozambique. Leukaemia has the highest incidence in South Africa, Zimbabwe and Namibia. A number of other malignancies were reported to be most frequent among childhood cancers in several countries: brain tumours in Lesotho, retinoblastoma in Congo (Brazzaville), nephroblastoma in Senegal and rhabdomyosarcoma in Central Nigeria (Jos regional registry). The above data differ in places from the IARC estimates. However, it would be futile to discuss the veracity of one or another finding, from any of the two sources. What this study illustrates is that we are still far from having a true representation of the incidence of various paediatric malignancies on the continent. It is imperiously necessary to institute national cancer registries there where they do not yet exist, if we are to have a realistic basis for devising effective policies to control cancer in children.

Table 3. Most frequent pediatric cancers in various African countries as reflected in available registers

Modified from Stefan DC: Patterns of distribution of childhood cancer in Africa. J Trop Pediatr 2015, 61:165-73

Country	Most Frequent Pediatric Cancer (Percentage Of All Pediatric Cancers Registered)
Congo (Brazaville)	Retinoblastoma (20.1%)
Ghana (Accra)	Lymphomas (63.6%)
Ivory Coast	Burkitt lymphoma (73.6%)
Kenya	Non-Hodgkin (22.6%)
Kenya	Burkitt lymphoma (18.8%)
Malawi	Burkitt lymphoma (46.7%)
Mali (Bamako)	Non-Hodgkin lymphoma (32.7%)
Mozambique	Kaposi's Sarcoma (16.8%)
Namibia	Leukemia (22.7%
Nigeria (central)	Rhabdomyosarcoma (31.0%)
Nigeria (northern)	Burkitt lymphoma (-)*
South Africa	Leukemia (27.4%)
Sudan	Lymphomas (36 – 42%)**
Uganda	Kaposi's Sarcoma (23.0%)
Zambia	Non-Hodgkin lymphoma (22.7%)

*Percentage not communicated

** Percentages from two separate registers

Findings from the South African Children's Cancer Registry

The South African Children's Tumor Registry (SACTR) was established more than 25 years ago, with the purpose of estimating the general burden of cancer among children in the country, while also giving an indication on the distribution of malignancies in terms of relative incidence, ethnic group and region. All paediatric oncology units in the country contributed their data to the registry and reports were circulated at regular intervals, while all the registry content was available to contributors for research purposes. Ninety-four per cent of all diagnoses were confirmed by histology. Similar data quality is yet unmatched in Africa.

An extensive analysis of the records accumulated in the SACTR over the last 21 years (Stefan, 2015a) has highlighted a number of facts. Even if they might not apply to the whole of Africa, the review of the main findings may contribute to a better insight into the epidemiology of childhood cancer. To start with, the observed overall age – standardized (ASR) rate was 4.5/100,000, which is considerably lower than the Globocan estimation of 8/100,000 for the whole Africa, but indeed only marginally lower than 4.9/100,000 which was the estimation for South Africa. The difference may originate in the fact that Globocan data are obtained mainly from registries situated in urban centres, while the cancer rates in rural areas are lower.

The malignancies with the highest incidence rates observed were, in decreasing order, leukaemia (1.19/100,000), renal tumours (0.6/100,000) and lymphomas (0.58/100,000). These figures are close to Globocan estimations. A substantial difference in cancer ASRs was observed between white (11.6/100,000) and black children (3.7/100,000). A number of explanations were proposed for this: firstly, such differences were observed also in the United States, even if not of the same magnitude; it is therefore possible to find an explanation in ethnic or genetic particularities of the two groups. Secondly, it is possible that a number of cancers in black children are either misdiagnosed or are never entering the health system. Most of the white children live in urban setting, where they have better access to health institutions and where the quality of care is higher.

Moreover, the rates for black children observed by SACTR are considerably lower than those recorded elsewhere in Africa: for example, the Harare registry in Zimbabwe recorded a rate of 11.1/100,000 from 1990 to 1994. The explanation might lie with the lower incidence of Kaposi's Sarcoma and Burkitt lymphoma (BL) in South Africa, by comparison with countries situated to the north of it, where the prevalence of infections with the human herpes virus 8 (HHV-8) and Epstein-Barr virus (EBV) – the respective infectious agents associated with the two diseases – is much higher.

The HIV Epidemic and Children's Cancer in Africa

The above considerations introduce a different facet of this analysis. The incidence rates of cancers with a recognised infectious origin have increased considerably in Africa with the advent of the human immune deficiency virus (HIV) epidemic. As the epidemic was much more severe in Sub-Saharan Africa than in the Northern Africa, its effect on cancer was proportionally more powerful in the southern half of the continent. The most evident change associated with HIV infection in children was the drastic increase in the incidence rates of Kaposi's Sarcoma. In Uganda, for instance, the incidence of Kaposi's Sarcoma increased by a factor of 40 after the onset of the HIV epidemic (Ziegler et al, 1996). Another study in the same country found an odds ratio of 94.9 (95% CI 28.5-315.3) for acquiring Kaposi's Sarcoma and of 7.5 (95% CI 2.8-20.1) for acquiring BL in children with HIV compared with controls (Newton et al, 2001). Comparable changes were seen in other Sub-Saharan countries.

This surge in the incidence of Kaposi's Sarcoma and BL due to HIV infection was not observed in the rest of the world. The explanation resides with the pre-HIV endemic rates of infection with HHV-8 and EBV in numerous countries in the Sub-Equatorial area of Africa. These infections are sporadic in the rest of the world.

Existing Resources for Childhood Cancer Control in Africa

At the present, there is no publication describing a continent-wide inventory of the available resources for the treatment of childhood cancer. In an attempt to shed some light on the matter, a questionnaire was administered to professionals working in 38 hospitals located in 29 African countries (Stefan, 2015b). The resulting analysis of the answers was published in 2015. The survey included 24 teaching hospitals and 14 regional hospitals. Out of the 38 centres surveyed, 17 had no paediatric oncologist. There, children with cancer were cared for by general oncologists or paediatricians, assisted in some places by general practitioners. Surgical treatment was available on site in 28 centres, with the remaining 10 referring their patients for surgery elsewhere.

The survey found a complete absence of specialised oncology nurses in the responding units. Moreover, the nurses were usually rotating between the existing wards, which made it even more difficult to train or employ a specialised (paediatric) oncology caregiver. In 14 centres, probably due to the small number of childhood cancer cases, there was no dedicated ward for this category of patients.

All centres surveyed were able to perform the usual laboratory tests, including bone marrow aspiration, but just one unit was offering bone trephine biopsy. Echography was widely available and so was basic radiology too, however not all hospitals had computed tomography scanning (present only in 31 out of 38) or magnetic resonance imaging (23 out of 38). With regard to chemotherapy, in 8 centres the treatment had to be paid for, in part or in full, by the patient. This might not be affordable for all: covering the cost of cancer drugs was found, in a Tanzanian study, to require spending between one month and seven months of household income (Yohana et al, 2011). Radiotherapy was limited to 21 out of 38 centres. Palliative treatment was offered in 27 hospitals, but in 12 of them Morphine was not available free of charge.

The situation of the pathology diagnostic support was not evident from the study summarised above. Other authors (Adesina et al, 2013) found recently that in Sub-Saharan Africa, for the same population number, there were ten times fewer pathologists than in high-income countries. These specialists were not supported by enough technicians, had to work with inadequate equipment and were confronted with shortages of laboratory supplies (African Pathologists' Summit Working, 2015) and infrastructure problems.

Last but not least, the survey quoted above looked at the contribution of parent support groups. For children with cancer, a parent support group is of major significance, as it may make the difference between accessing and remaining with the oncology programs or not. These non-profit organisations raise funds to facilitate transporting and lodging the children and their accompanying parent and often volunteer for various cancer related activities. Yet such parent groups were active in only in about half of the centres surveyed.

Conclusions

Statistic data on childhood cancer on the African continent are imprecise, as the existing cancer registries have limited coverage and are of variable quality. IARC estimations indicate an ASR of incidence of 8 cases/100,000 and a mortality of 4.6/100,000. While comparable with the average figure of the whole world, the incidence rate is half as high and the mortality rate is actually double when compared with similar indicators from very high human development countries. In terms of incidence, NHL appears to be the dominant cancer in children in Africa, while leukaemia prevails in the rest of the world. This difference can be attributed to the endemic infection with EBV in an extensive area around the Equator, descending to the Tropic of Capricorn, corresponding also to the area of high prevalence of malaria. Epstein-Barr lymphoma is highly incident in this area, which is known as "the lymphoma belt".

The HIV epidemic has exacerbated especially the incidence of another malignancy of viral aetiology, the Kaposi's Sarcoma, whose rates in children have been found to increase between 30 to 90 times. Again, this increase, which was not seen in the rest of the world, was grafted on an endemic infection with HHV-8 in a number of African countries.

Facing this burden of disease, the manpower, skills, facilities and funds allocated to child cancer care need to increase considerably. This is even more justified by the fact that malignancies in children are highly curable, as proven in other regions of the world.

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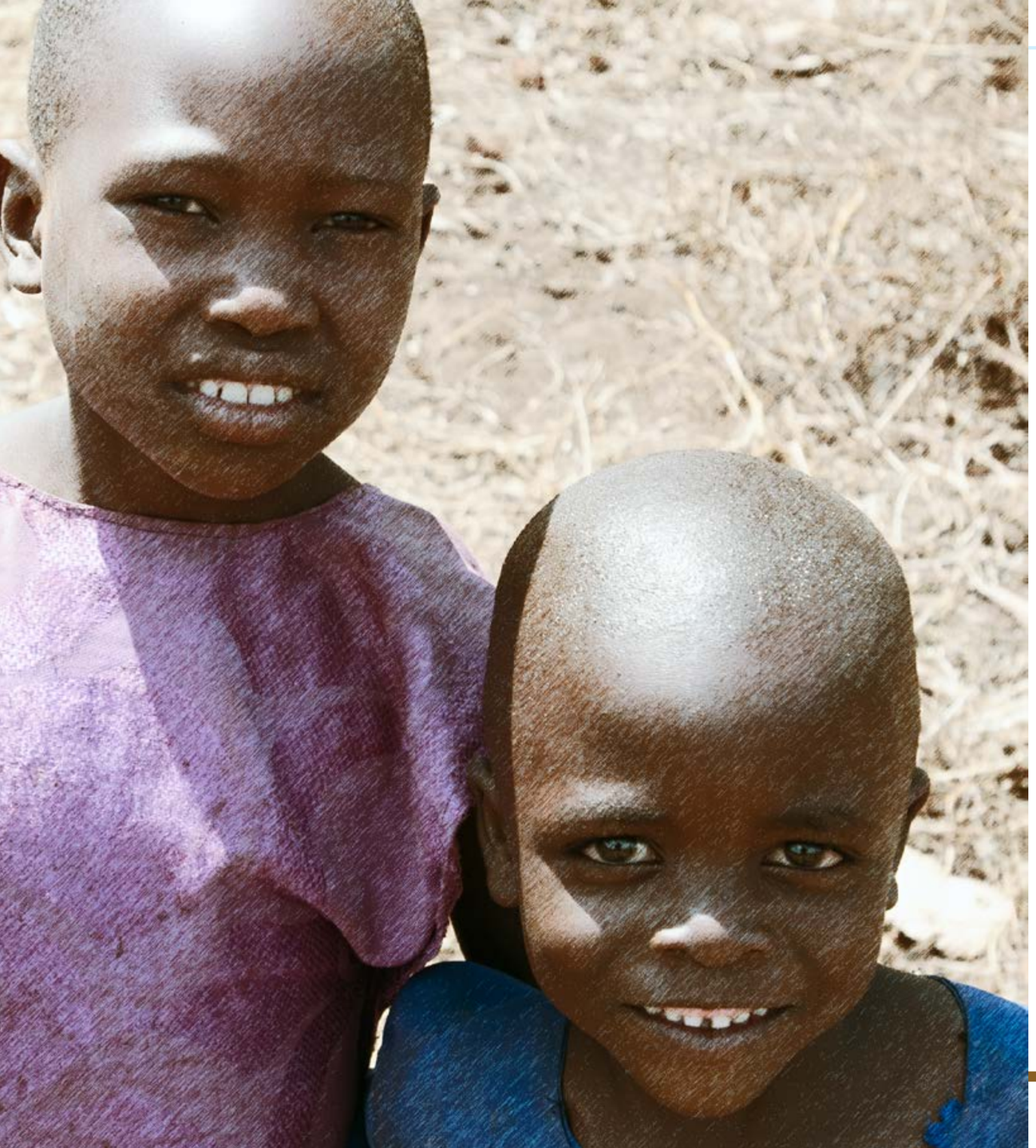

Chapter 14

Africa: Skin Cancer

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The landscape of skin cancer in Africa has been dominated by the problem of Kaposi's Sarcoma (see "Chapter 11" on page 213), occurring sporadically for many years, and more recently commonly found in HIV positive individuals. There has been less information available concerning other forms of skin cancer, which, although less common in Africa, are nevertheless causing significant concern. Ultraviolet radiation is the primary cause of skin cancer and skin pigmentation is partly protective. However there are particular problems in those predisposed to develop skin cancer such as African patients with oculo-cutaneous albinism. The commonest skin problems seen in Africa to date, have been skin infections and inflammatory dermatoses, but there is an increasing prevalence of malignancies (Kiprono et al, 2014). Given the scarcity of information in Africa, parallels with skin cancer in Afro-Americans are informative of the nature of skin cancer in African skin.

Global Picture of Skin Cancer

There are two major groups of skin cancers: melanoma and non-melanoma skin cancers. Melanoma results from malignant change in melanocytes: the colour producing cells of the skin and eye. (Figure 1) Melanoma is the 9th most common cancer in Europe (Ferlay et al, 2013) and the 19th most common cancer worldwide with the highest incidence rates in Australia/New Zealand and the lowest in South Central Asia (Ferlay et al, 2012). In contrast with many cancers, rates are lower for both men and women living in the most deprived areas than the least deprived (National Cancer Intelligence Network, 2014). There is no doubt that skin cancer is increasing worldwide. In Europe age-standardized incidence rates increased more than 6 fold between the end of the 1970s and 2011-13, greater in men than women, which probably results from change in exposure to risk factors. Rates for Asian and African men and women are however significantly lower than white men and women.

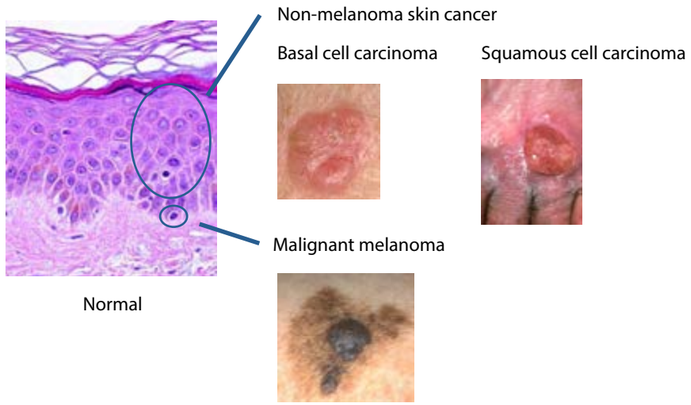

Figure 1: Melanoma derives from melanocytes in the basal layer and basal cell carcinoma histologically resembles basal keratinocytes. Squamous cell carcinomas also derive from keratinocytes but bear a pathological resemblance to suprabasal keratinocytes. Representative clinical pictures of melanoma, basal cell carcinoma and squamous cell carcinoma.

Non-melanoma skin cancers (NMSC) account for three quarters of skin cancers world-wide again with the incidence rising steadily, where this can be ascertained. The majority of NMSCs arise from keratinocytes and so are now being termed keratinocyte skin cancers (KSC) (Figure 1). The commonest, basal cell carcinoma (BCC), is locally invasive but not metastatic, whereas the cutaneous squamous cell carcinoma (cSCC) is both invasive and potentially metastatic. Although metastasis occurs only in around 5% cases of cSCC, this constitutes around a quarter of skin cancer related deaths because of the high number of cases (Karia et al, 2013). Under-recording of non-melanoma skin cancer is a major problem given the frequency of this tumour group, which is excluded from many cancer registries. However this is undoubtedly the commonest cancer in the United States and United Kingdom and equal in numbers to the total of other major cancers. Recent estimates suggest that there are probably around 250,000 NMSC annually across the United Kingdom (Leigh, 2014). In the United States more than 5 million cases of non-melanoma skin cancer are treated each year with more new cases than lung, breast, prostate and colon cancers combined. This means that one in five Americans will develop a skin cancer in their lifetime. More than 1 million cases of cSCC alone are estimated to occur in the United States per year, which has major implications for health costs and service provision (Guy et al, 2015).

There are few population-based studies in Africa but skin cancers do appear among the leading cancers. This varies across African countries related to the racial (i.e. skin colour) mix. In Africa, Sub-Saharan Africa (SSA) is dominated by Black populations and Northern Africa by Arab ethnic groups, with white Europeans forming a significant population in some countries (e.g. 8.8% South Africans). The South African cancer registry documented 44,176 cases of skin cancer between 2000 and 2004, with the highest incidence in Whites, followed by Coloureds, then Asian/Indian, then Black according to the historic racial classification (Norval et al, 2014). Most published studies from Africa comprise small numbers of individuals living in geographically defined areas. For example a retrospective pathological study of skin cancer in Oshobogo Nigeria (Oseni et al, 2015) analysed 98 cases (61% male) and found malignant melanoma, particularly lower limb in men, was commonest followed by cSCC, DFSP and BCC, in that order. This is comparable with figures in other studies (Ochicha et al, 2004; Rafinddadi, 1998). In North Africa, as illustrated in a study from

Egypt, where people of Arab ancestry predominate with brown/olive skin, the picture differs with BCCs being the most common skin cancer, followed by cSCC with melanoma uncommonly (Hussein, 2005). It was estimated that 60% of the risk of developing NMSC could be attributed to sun exposure and 45% to skin colour (el Khwsky et al, 1994).

Role of Ultraviolet Radiation (UVR)

The electromagnetic spectrum of emissions from the sun produces three wavebands of UVR: UVA (long wave), UVB (medium wave) and UVC (which does not reach the earth's surface). UVB (290-320nm) is the major cause of skin cancer. The level of ozone in the earth's atmosphere influences how much UVA and UVB can reach the earth's surface. Ozone holes over South Africa and New Zealand, for example, increase UVA and UVB at the earth's surface and cause easier sunburning. Africa spans latitudes 40oN and 34oS with very high levels of UVR throughout the year. The effects on humans are exacerbated with a largely rural population (>60%) being out of doors for most of the day. There is overwhelming evidence that exposure to ultraviolet radiation is the most important environmental carcinogen for skin cancer, although the patterns of exposure differ with different skin cancers. It is generally thought that cutaneous melanomas arise after intermittent intense UV exposure, whereas cSCC and the precursor actinic keratoses are associated with frequent chronic UV exposure. Combined acute intermittent and chronic UV damage induce BCCs. An individual's response to sunburn and suntan is classified by the Fitzpatrick skin phototype (FSPT): initially, types I-IV represented white skin and types V and VI were brown and black skin, respectively. This has been modified to include self-reported tendency to burn or tan after sun exposure (Andreassi et al, 1987; Fitzpatrick, 1988) (Table 1).

Table 1: Fitzpatrick Phototype

Phototype	Sunburn	Suntan
I	Always burns	Never tans
II	Always burns	Sometimes tans
III	Sometimes burns	Sometimes tans
IV	Occasionally Burns	Always tans
V	Rarely burns	Heavy tan
VI	Never burns	Heavy tan.

The end result of UVR on a skin cell depends on the balance between UVR induced damage and the cell's defence mechanisms. UVB induced direct DNA damage with the productions of cyclobutane-pyrimidine dimers and 6-4 photoproducts and characteristic CC-TT mutations in DNA, combines with indirect DNA damage from UVA-induced guanine oxidation products. The mutagenic effects are exacerbated by UV induced immunosuppression which alters the balance of a Th1 helper to Th2 suppressor response; additionally altering Langerhans cell function and increasing expression of immunosuppressive neuropeptides, melano-cortins and inflammatory mediators by epidermal and dermal cells.

Other Harmful Effects of Sun Exposure

Sunburn is the best known acute effect of sun exposure (Kennedy et al, 2003) and although white skin is at greatest risk, it can be experienced by those with pigmented skin (Battie et al, 2013). 42% of 11-14 year olds with brown /black skin surveyed in a South African school had experienced sunburn the previous year (Wright et al, 2015). Photo-conjunctivitis and photo keratitis are also prevalent due to sunburn of the eye and eyelids. Chronic ocular UVR exposure can cause a pterygium (wing shaped growth) of the conjunctiva, which can grow over the cornea and impair vision.

This can progress into an SCC of cornea or conjunctiva (SCCC) especially in dusty environments, in outdoor workers or those with HIV infection. UVR is also a major cause of cortical cataracts, which begin earlier in life in Africa and contribute to the high levels of blindness in SSA (20% world blindness).

Beneficial Effects of Sun Exposure

Apart from reported benefits of well-being from holidays in the sun, ultraviolet B radiation is a major source of vitamin D in the skin. Recent attention has focused on the association between low vitamin D concentrations and many disorders, such as cancer, cardiovascular disease, autoimmune disease, dementia and diabetes (Autier et al, 2014; IARC, 2008). Observational studies suggested that high serum levels of vitamin D might be protective but randomized controlled trials have failed to support this and this suggests that low level vitamin D is a result rather than cause of ill health. There has been significant adverse publicity to sun avoidance campaigns but evidence is still needed that increasing vitamin D levels decreases the risk of cancer given the well-established link of skin cancer risk and ultraviolet radiation. Endogenous vitamin D production occurs rapidly on UVB exposure: maximum pre-vitamin D3 in white skin can be produced in 5-10 minutes of UVB exposure to face and forearms on a sunny day two or three times a week (Gilchrest, 2008). Thus there is currently no justification for altering sun avoidance advice nor routine supplementation with vitamin D.

Sunbeds and Tanning Booths

A suntan is a signal of DNA damage and provides little protection against further damaging effects of UVR. Sunbeds emit both UVA and UVB and there is good evidence that sunbed use increases the risk of melanoma and skin ageing which increases with the number of sunbed sessions and an earlier age (Boniol et al, 2012). More than 400,000 cases of skin cancer a year in the United States are linked to indoor tanning. This appears to be particularly important in young women who have an increased risk of melanoma by 75% if they use sunbeds before age 35. As a result IARC includes tanning devices in its group 1 cancer causing agents and the recommendation of the 4th edition of the European Code Against Cancer for ultraviolet radiation is: "Avoid too much sun, especially for children. Use sun protection. Do not use sunbeds."There has therefore been widespread legislation to restrict the use of indoor tanning ranging from a total ban (Australia and Brazil) to a ban for under -18s (many European countries including France, Germany and United Kingdom, and many United States' States).

Skin Colour and Susceptibility to Skin Cancer

Skin colour is determined by the number and activity of melanocytes, which live in the basal layer of the skin. They transport the pigment melanin in packages called melanosomes along their long dendritic processes into adjacent keratinocytes to protect their nuclear DNA. There are two types of melanin: the black-brown eumelanin and the yellow-red phaeomelanin. As melanin helps to protect the skin cells from the UV damage and provides a sun protection factor of 13.4 in black compared to white skin. This is why white skinned individuals have the highest rates of skin cancer and the prevalence of skin cancer is highest in Australia and New Zealand. Differences in the amount and type of melanin affecting the final skin colour is determined by a number of important genetically determined factors. These include genes encoding: the melanocortin-1 receptor (MCIR) on the surface of the melanocyte and its ligand alpha-melanocyte stimulating hormone (a-MSH) and the enzyme tyrosinase (TYR) involved in its synthesis.

Much of the information regarding the effects of colour come from communities with mixed racial background, such as United States and here the data on African Americans is relevant given the difficulties in skin cancer registration in Africa. In the United States, BCC is the most common skin cancer in Caucasians, Hispanics, Chinese and Japanese Asians and 2nd most common in African Americans and Asian Indians (Gloster et al, 2006). cSCC is the most common skin cancer in African Americans and Indians (Halder et al, 2003). Melanoma is the least common major skin cancer in all racial groups. There are many rarer cancers of the skin such as Merkel Cell Carcinoma and dermatofibrosarcoma protruberans, which are not considered further.

Genes Involved in Skin Colour

Cloning of the MC1R revealed an association between MC1R variants and red hair, blue eyes and fair skin (particularly Arg151Cys, Arg 160Trp and Arg 294His (Binstock et al, 2014). When MC1R signalling is inactive there is lower melanin production in skin and a tendency to pheomelanin pigmentation in hair. MC1R variants are common in Caucasian populations. Screening Asian and African populations (small numbers) also found prominent variants within populations with high frequency (70%) of Ag163Gln in East and Southeast Asian populations and Amerindians but with a lack of variation from the consensus sequence in African and Indian populations (Rana et al, 1999). This fits with a theory that as populations migrated out of Africa to areas of lower UVR exposure, dark skin was a disadvantage because reduced vitamin D was synthesized in the skin and therefore lighter skin colour had a selective advantage (Cavalli-Sforza et al, 1994). Other polymorphisms in genes that affect skin colour include POMC, ASIP KITLG, SLC24A5, TYR, TYRP1 HERC2/OCA2 and IRF 4. MC1R variants are also associated with an increased skin cancer risk for both cutaneous melanoma (15% cases) and keratinocyte skin cancers. These variants increase the risk of UV induced skin cancer as pheomelanin is less protective than eumelanin. However impaired MC1R function not only affects pigmentary mechanisms but also non-pigmentary mechanisms (reduced DNA repair and effects on cell proliferation and immune function).

Other Risk Factors for Skin Cancer

Patients on long term immunosuppressive drugs for organ transplantation (organ transplant recipients (OTR)) are at greatly increased risk of cSCC (up to 150 fold) with a reversal of the usual BCC:cSCC ration(5:1) (Harwood et al, 2013). This also affects those who receive long-term immunosuppressive drugs for immune mediated disorders, such as inflammatory bowel disease and rheumatoid arthritis. In addition to effects on immune function, some drugs have direct carcinogenic effects, such as azathioprine, which predisposes to UV oxidative damage. Where a disease process results in immune dysfunction, such as chronic lymphoid leukaemia, skin cancer can also a problem. A possible role for beta and gamma papilloma viruses has been extensively examined in OTRs (Bouwes Bavinck et al, 2010) and much is being established about the molecular mechanisms of skin cancer in such patients (Harwood et al, 2016). This is an obvious paradigm for untreated HIV infection. Other risk factors for skin cancer include exposure to chemical carcinogens, notably arsenic in ground water; previous exposure to ionizing radiation and chronic inflammation or injury to the skin such as thermal burns; chronic ulcers; scarring discoid lupus erythematosus; recessive dystrophic epidermolysis bullosa; graft versus host disease, and lichen planus.

Genetic Susceptibility to Skin Cancer: Syndromes Important in Africa

There are a number of genetically determined syndromes which predispose to skin cancer of particular importance In the African context: oculo-cutaneous albinism (OCA) and xeroderma pigentosum (XP) (Figure 2). These are both autosomal recessive conditions, which contributes to the cultural and societal problems experienced by sufferers, particularly albinos. The appearance of a white child of two black parents in Africa can be attributed to witchcraft or adultery of the mother in community health beliefs that are very difficult to counter. The fact that patients can go out more easily at night because of their exquisite sensitivity to sunburn also adds to the belief systems, which ostracise sufferers. In some cultures body parts of an albino are sought for witchcraft and in some countries it is believed that having sex with an albino women can cure AIDS.

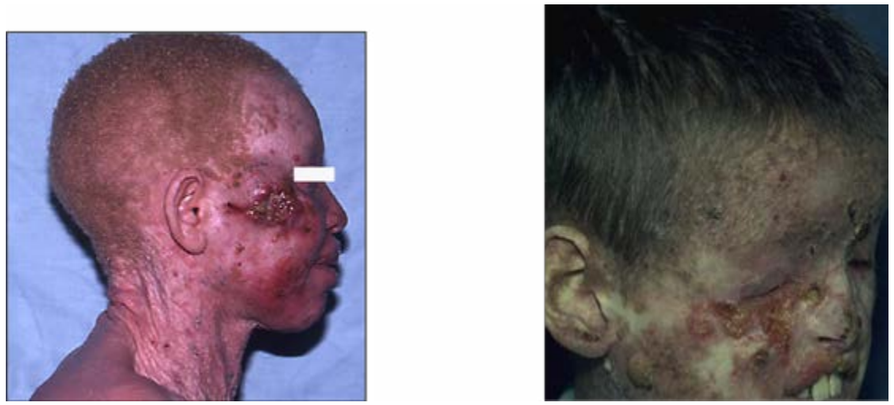

Figure 2: Left: Cutaneous squamous cell carcinoma in African Albino. Right: Multiple tumours in a child with xeroderma pigmentosum

Oculo-Cutaneous Albinism (OCA)

There are 5 types of oculo-cutaneous albinism: the commonest being OCA1 and 2. Affected individuals have a light skin tone but may develop freckles and fleshy pink moles on sun exposure. Their hair colour varies from white to light brown but tends to be yellow or reddish in Africans. The eye colour also varies from very light blue to darker but may appear red or pink due to reflection from the retina. This lack of pigment causes photosensitivity and is always associated with effects on vision such as nystagmus, strabismus and amblyopia.

OCA1, the most frequent variant, is caused by a mutation in the tyrosinase gene (TYR) which means that no or very little melanin can be synthesized. Affected individuals have milky skin, white hair and blue eyes but skin can darken with age. The frequency of this type of albinism is 1/40,000 worldwide (Oetting et al, 1993).

OCA2 occurs most often in sub-Saharan Africa, African-Americans and Native Americans with a similar clinical picture to OCA1. OCA2 is therefore the most common form affecting Black South African albinos (1 in 3,900) but the prevalence is estimated to range from 1 in 15,000 in the East-Central State of Nigeria (Okoro, 1975) to 1 in 1,000 in the Tonga tribe of Zimbabwe (Lund et al, 1997).OCA2 is caused by mutations in a "p" protein which is involved in several aspects of melanin production (Stevens et al, 1995). Although eumelanin cannot be synthesized by affected skin, pheomelanin may be produced with age

The OCA3 (mostly black South African) and OCA4 (Mostly East Asian) variants are due to mutations in genes for tyrosinase related protein 1 (TYRP1) and membrane associated transport protein (MATP) respectively. The search for the other OCA genes is ongoing. OCA particularly predisposes to squamous cell carcinoma of the head and neck, which is aggressive and has a high rate of recurrence (de Vijlder et al, 2013). The risk of cSCC in Black albinos is 1000x the risk in the general population and usually occurs by the age of 30 with a late presentation and poor prognosis (Luande et al, 1985). Head and neck cSCCs are commoner than BCCs and melanoma is relatively rare. Actinic cheilitis and lip cancers are also

common. The regional dermatology training school in Moshi, Northern Tanzania (RTDS), supported by the International League of Dermatology Societies (ILDS) and the International Foundation for Dermatology (IFD) has had an established programme of cancer prevention and treatment for Albinos since 1993, in Northern Tanzania (Lookingbill et al, 1995) where the prevalence is estimated to be 1 in 2,500. A retrospective study of 134 biopsies from 86 patients showed head and neck tumours in 56% and cSCC was the commonest cancer (53.7%) with only one case of melanoma. Patient outcome is affected by a delay in seeking medical care 14.4 months in comparison with 26 months in Nigeria (Yakubu et al, 1995). African albinos living with stigma of the disease present late and the cSCCs are often advanced and have a poor prognosis (Cruz-Inigo et al, 2011; Hong et al, 2006; Lund et al, 2002). Also many patients do not complete their treatment for financial or geographical reasons (Mabula et al, 2012).

Xeroderma Pigmentosum

Xeroderma pigmentosum (XP) where DNA repair is impaired following UVR, is caused by mutations in 8 genes encoding proteins involved in nucleotide excision repair pathways. As it is an autosomal recessive inherited disease, it is commoner in communities with high levels of consanguinity and is a particular problem in Northern Africa and the Middle East. There are 7 subgroups with distinct clinical features. Children develop severe sunburn reactions in childhood and have multiple skin cancers from an early age with a 100 fold increased risk for skin cancers in sun-exposed sites compared to the general population (Figure 2). The average age of onset of NMSCs is aged 7-8. The patients also have irregular freckled pigmentation and photophobia. Patients are also at increased risk of internal malignancy: lung, breast, pancreas, gastric and brain cancers. Some subgroups have ophthalmic and neurological abnormalities in addition.

Clinical Picture of Skin Cancer in Pigmented Skin

The site of cSCC is in the head and neck region in Albinos (Asuquo et al, 2010) but although cSCC is the commonest form of skin cancer in non-Albino Africans, the commonest site is not the head and neck but mainly on the legs (as well as anogenital area). Thus it seems less associated with UV exposure and the main risk factors are chronic scarring or inflammation such as burn scars and chronic non-healing ulcers. Chronic inflammation such as lupus erythematosus or leprosy can also be predisposing factors. These cSCCs can be aggressive with a high tendency to metastasis (up to 30%). In contrast BCCs are mainly found in sun-exposed sites. The clinical presentation of melanoma is also distinctive in Africans with a high proportion of acral lentiginous melanomas on the palms, soles or under the nails. They also occur in the lining of the mouth.

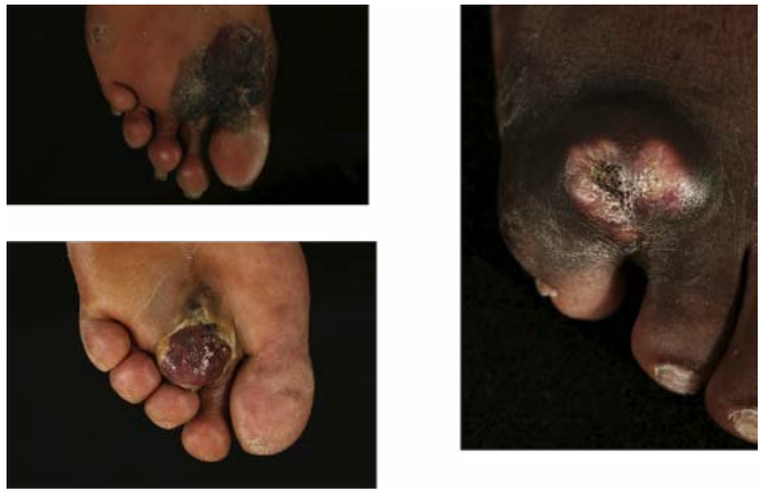

Figure 3: Typical presentations in Africa of melanoma and cutaneous squamous cell carcinoma: acral lentiginous malignant melanoma, invasive melanoma and cutaneous SCC on foot in Black skin.

Emerging Problems with Skin Cancer in Africa: Melanoma and Non-Melanoma Skin Cancer

HIV infection has been associated with malignancies, in particular Kaposi's Sarcoma, non-Hodgkin's lymphoma and invasive cervical cancer, which are termed AIDS defining cancers. However other non-AIDS defining cancers in HIV infected persons have been identified (Shiels et al, 2009). OTRs have been documented to have a greatly increased risk of skin cancer, particularly 100 fold increased risk of cSCC and oncogenic HPV driven anogenital cancer is also a clinical problem (Harwood et al, 2016). It might be surmised that HIV-seropositive patients might have an increased risk of skin cancer compared to HIV seronegative populations. cSCC has been found to be higher in HIV patients in the United States (aOR 2.695%CI 2.1-3.20) with a trend to association with lower CD4 counts (Silverberg et al, 2013). A recent study from West Africa systematically screened the prevalence of HIV defining and non-defining cancers in 184 HIV infected cancer patients. In addition to the well-established AIDS defining cancers, a strong association was found with anogenital cancer (aOR 17.7(CI: 17.3-69.0)) and cSCC (aOR 5.2 (CI2-14.4)). This supported a strong association between HIV and HPV associated cancers (De Vuyst et al, 2009; Jaquet et al, 2015). SCC of the lip is also increased in HIV-positive immunosuppressed patients compared to HIV sero-negative individuals (Frisch et al, 2001; Grulich et al, 2007) which could also implicate HPV.

Anogenital Cancer

The identification of high risk human papillomavirus (HPV) types as causative in anogenital (and oropharyngeal cancers) led to development of preventive vaccines against HPV16 and 18, but global availability of such vaccines would require a major lowering of costs. Anogenital cancer has

previously been reported as 20-80 fold increased risk in association with HIV infection in high resource countries (Silverberg et al, 2012). Although HPV16 and 18 and related HPVs are responsible for anogenital skin cancers they rarely occur in cancers of the rest of the skin, where carriage of beta and gamma papilloma viruses in widespread. Certain oncogenic genotypes (such as HPV8 and 38) are increased in skin cancers in OTR (Bouwes Bavinck et al, 2010).

Much of the literature concerning anogenital cancer (and HPV) in SSA rightly focuses on cervical cancer as being the most common cancer in women (De Vuyst et al, 2013), and there is a dearth of data on anal, penile or vulvar cancers, which are strongly linked with high risk HPV in the rest of the world. Penile cancer is uncommon in developed countries but is commoner in East Africa (Curado et al, 2007). Multiple HPV genotypes are common in precancerous lesions in HIV infected populations, both carcinogenic and non-carcinogenic (Clifford et al, 2006). Genital warts caused by HPV6 and 11 are also commonly found in Africa (Banura et al, 2013) with aetiological association with anogenital cancers. Genital warts are also found more commonly in HIV positive women than HIV negative. The prevalence of anogenital warts in SSA was subject to a systematic review (Banura et al, 2013) in high risk individuals and ranged from 3.3% to14% across African Regions in women and 3.5%-7% in men. The prevalence rates were therefore significantly higher in HIV+ women and the incidence rate was higher in uncircumcised than circumcised men.

Sun Protection and Skin Cancer Prevention in Africa

Public health initiatives aim to reduce the incidence of skin cancer and to detect and treat lesions early before invasion and metastasis can occur, as effective treatment options are then very limited. The main thrust is to avoid sun exposure from early childhood (Table 2). These measures include:

- Shade and reduction of outdoor activities at times of peak UVR. Direct sunlight between 10:00 and 15:00 should be avoided by staying in the shade (trees or buildings) or under an umbrella. This is just as important on overcast days.
- Protective clothing including hats. Wide brimmed hats and loose fitting tight weave clothing are the best protection. In some African countries traditional dress involves full body coverage and headgear varies regionally but may provide good protection
- Sunscreens. A sun protection factor (SPF) is the amount of protection obtained by applying a specific sunscreen (or other intervention) and reflects the number of times the intervention extends the time taken for the skin to burn (minimal erythema dose: MED). If the skin turns red with 10 minutes exposure, then an SPF of 10 extends this to 100 minutes. However these figures generated in testing sunscreens don't translate to real life where sunscreen is often applied in a much thinner layer. Topical sunscreens are widely used in high resource countries when a sunscreen with a Sun Protection Factor (SPF) of a minimum of 20 and not higher than 50, should be applied to all exposed skin areas. However these preparations are very expensive and therefore unrealistic for low and medium resource countries. In some countries, such as South Africa, sunscreen is available for albinos from government or charitable resources. The RDTS programme in Moshi manufactures its own low cost sunscreen. Traditional African skin clays may provide some sun protection in some communities (Dlova et al, 2013)
- Sunglasses. To prevent the eye complications of excessive UVR, eyes should be protected by wearing sunglasses with a UV protection rating of UV400. This is also not economically feasible for the majority of people living in Africa but sunglass usage, largely seen as a fashion item, has not been systematically assessed in Africa (<20% in Morocco)
- Sunlamps and tanning parlours should be totally avoided
- Children need special protections - babies younger than one year should never be exposed to direct sunlight.

Table 2. Sun avoidance and skin cancer prevention: key messages

Seek shade from 11am-3pm
Cover up with a hat, T shirt and sunglasses
Use a sunscreen liberally and apply often
Protect Children from sun exposure
Seek early advice for suspicious lesions

School Based Teaching About Sun Safety and the Risks of UVR

The WHO recommends implementation of sun-protection practices in schools, such as the Sunsmart School Accreditation Programme (SSAP) operating in Australia (Dobbinson et al, 1998) which has increased availability of physical sun protection at school and improved the use of hats, clothing and shade. An exploratory study in South Africa by the Cancer Association of South Africa (CANSA) showed that despite urban government schools doing little in this area, some primary school students were aware of the need for sun protection. However the reported occurrence of sunburn was relatively high (Wright et al, 2016).

Wider public health measures to reduce sun damage in Africa are not very successful due to difficulties in understanding, compliance and the necessary drugs.

Early Diagnosis and Skin Screening

A good outcome from all skin cancers depends on early diagnosis, which has led to many public campaigns and also to the suggestion that skin screening should be considered. Skin cancer screening has been proposed to recruit healthy individuals to examine their whole skin. European opinion has been influenced by a population based skin screening project (SCREEN) which was undertaken in Schleswig Holstein by trained non dermatologist observers. Although a 50% reduction of mortality was claimed after 5 years, there were significant methodological concerns regarding historic non-screened controls and an apparent short term benefit which was not sustained (Breitbart et al, 2012). There is currently no support for the effectiveness of population-based measures for early detection of skin cancer although patients are at increased risk of skin cancer for hereditary (familial cancer) or acquired reasons (immunosuppression, age) need increased surveillance. False positives lead to unnecessary surgery and scarring as well as being a cause of anxiety and stress. Skin cancer education campaigns such as Euromelanoma and "melanoma days" raise the awareness of skin cancer and may increase case numbers but the ratio of interventions to accurate diagnosis can be high (Waldmann et al, 2012) and adequate resources need to be available to deal with the aftermath of such campaigns. There is no role for skin screening in Africa but there is a need for education to enhance early detection.

Early Diagnosis and Chemoprevention

In the early stages, both melanoma and NMSC are confined within the epidermis, called the melanoma in situ and the carcinoma in situ, respectively. But once the basement membrane is crossed the tumours invade and can metastasise. It is best therefore to treat these cancers when localised and minor surgery can be curative. However large areas of the skin are exposed to UVR and the whole field can bear mutations in cancer genes, which has now been shown by multiple studies (Harwood et al, 2016). The field can be treated by topical reagents effective in treating actinic keratosis such as 5-Fluorouracil cream, Imiquimod, Solaraze and Ingenol. As vitamin B3 (nicotinamide) has been shown to protect

against UV damage a phase 3 double blind randomised controlled trial of nicotinamide (500 mg bd) (ONTRAC trial) was performed to evaluate the number of new NMSCs after 12 months in "high risk" patients with more than to NMSC in 5 years. They found a reduced number of actinic keratosis (13% at 1 year) in the treatment group (Chen et al, 2015). This was supported in correspondence from a small study in OTR in immunocompetent patients but needs much more extensive testing.

Treating Skin Cancer in Africa

The most important method of treatment for skin cancer is excisional surgery, preferably following early diagnosis. In many cases, this can be performed by medical assistants and other trained health personnel, except where reconstructive surgery or lymph node clearance is needed. Therefore the availability of effective treatment depends entirely on the local availability of suitable surgical facilities. Radiotherapy may be helpful in advanced localized BCC and cSCC, but once metastasis of cSCC has occurred there are few effective treatments or chemotherapy regimes. Metastatic melanoma also has a very poor prognosis and until recently this was also the case in high resource countries. However understanding the high rate of B-Raf mutation in melanoma led to the development initially of BRaf inhibitors and subsequently to other targeted therapies inhibiting other signalling pathways (such as MEK). Melanoma has also been long known to have significant potential for immunotherapy although vaccination with melanoma antigens has been disappointing. New drugs, which are immune checkpoint inhibitors, are promising for metastatic melanoma. Unfortunately these drugs are currently limited in availability and very expensive, so are unlikely to be applicable in low and medium resource countries. The annual cost of treating skin cancers in the United States is estimated at US$ 8.1 billion (Guy et al, 2015). The health costs of treating skin cancer are difficult to assess in Africa and there is little published data. A recent study in South Africa recognized that skin cancer is a growing public health problem in South Africa with a yearly incidence of melanoma being 4.76 /100,000 overall and 19.2/100,000 in whites (Norval et al, 2014). The total annual cost was estimated to be US$15.7 combining the costs of excisions, radiotherapy, cryotherapy, lymph node dissection and follow up.

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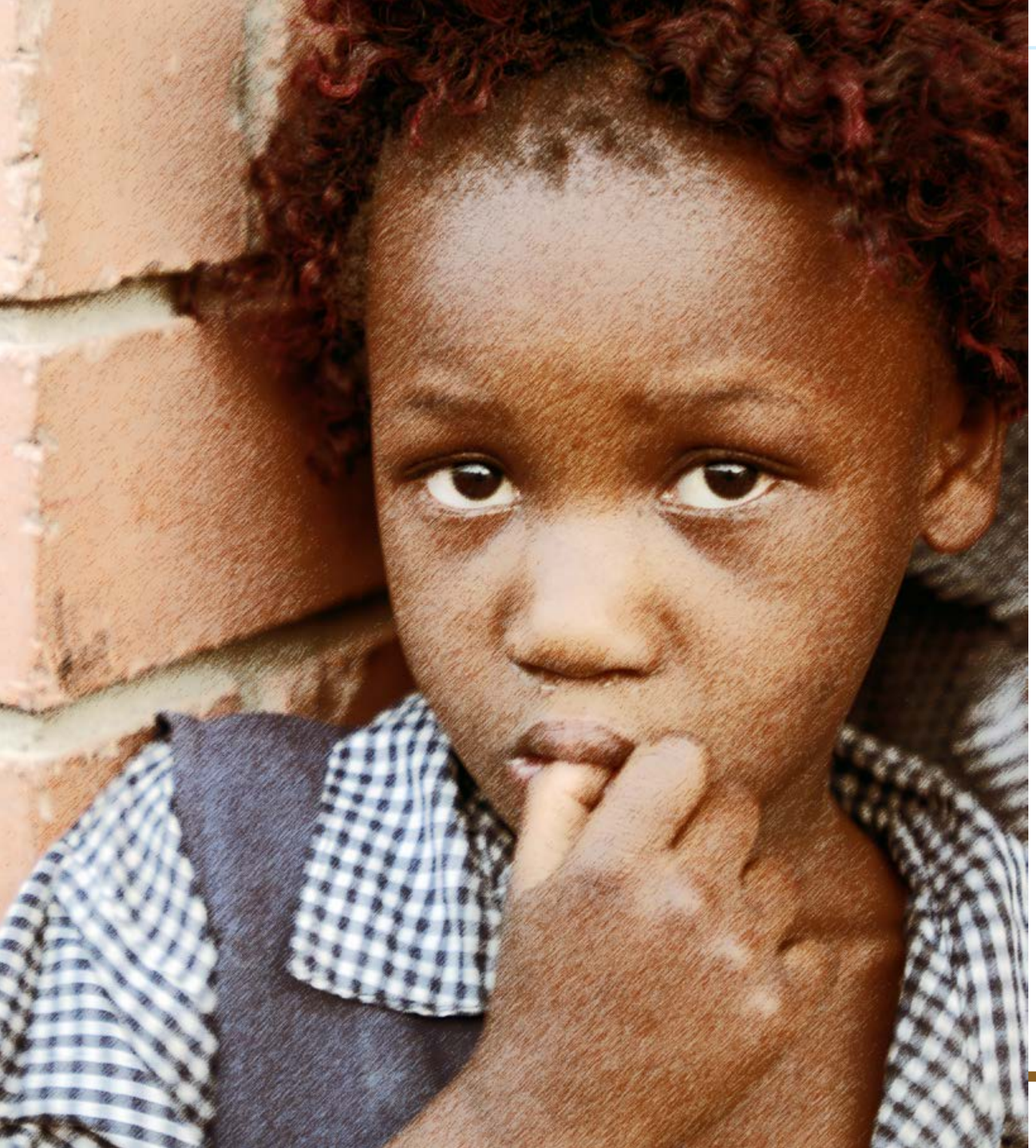

Chapter 15

Africa: Biobanking

Biobanking in Africa: Opportunities and Challenges

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Biobanking and its associated policies and procedures for managing biological specimen collections are critical to the success of a variety of research endeavours. Several international organizations have produced best practices which cover the important technical and ethical-regulatory issues that are important for the collection and management of biospecimens and associated data. The expanding and global nature of biomedical research has resulted in disparities in biobanking practices among high-income countries (HIC) and low- and middle-income countries (LMIC). In Africa, projects such as H3Africa and B3Africa have resulted in new and promising advances in biobanking infrastructure and the creation of biobanking networks. However, the initiation of such projects has highlighted some of the challenges faced by biobanks in Africa, from both the technical and ethical-regulatory perspectives.

Introduction to Biobanking

Biobanking involves the collection, processing, storage and use of biological specimens for research purposes. For the purpose of this chapter we will generally concentrate on biospecimens collected for research into the aetiology, diagnosis and treatment of cancer, although most of the issues discussed apply to infectious disease biobanking efforts as well. Historically, early biobanks emerged from the collection of samples by surgeons and pathologists for diagnostic purposes. Thus, the earliest biobanks evolved from collections housed in pathology departments. In the United States, the Armed Forces Institute of Pathology (AFIP) collection was initiated during the American Civil War (Armed Forces Institute of Pathology, 2016). A similar example in Africa is the Kampala Cancer Registry (KCR), which is situated in the Department of Pathology, School of Biomedical Sciences, Makerere University College of Health Sciences and has maintained tissue samples collected for diagnosis dating back to 1954 (Doll et al, 1982).

Biobanks may be small collections within a pathology laboratory, a few freezers in a basic or clinical research department, or a large government or commercial operation with hundreds of freezers and millions of biospecimens (Vaught, 2016). Biobanks may house tissues in the form of formalin-fixed, paraffin-embedded blocks or in the frozen state. Fluids such as blood and blood fractions (serum, plasma, and buffy coat), urine and saliva are also collected. The type of biospecimens collected and the processing and storage conditions chosen by researchers depend on

the intended analyses, e.g. for cancer biomarker development (Hewitt et al, 2012). Pre-analytical variables such as ischemic time, freeze-thaw cycles and other factors may affect the quality of the samples and result in misleading laboratory data (Vaught, 2015). The field of "biospecimen research" has emerged to study and mitigate such pre-analytical factors (Moore et al, 2011).

As biobanking has grown and expanded globally, a general trend toward "professionalization" has emerged. Organizations such as the International Society for Biological and Environmental Repositories (ISBER, 2016), the European, Middle-Eastern and African Society for Biopreservation and Biobanking (ESBB, 2016), the Biobanking and BioMolecular Research Infrastructure (BBMRI-ERIC, 2016) and Biobank Cohort Building Network (BCNet, 2016) initiatives are all promoting biobanking education, standards development and research. Graduate level biobanking degree programs will result in a new generation of biobankers (Catholic University Lyon, 2016). Before these developments over the past 20 years, biobanking was a secondary career for pathologists and other research professionals who created and operated biobanks, and developed practices on an empirical basis to fit their needs.

The trends toward more organized and professionally-managed biobanks have created new opportunities for international cooperation and collaboration (Vaught et al, 2014a). However, such international collaboration requires standard practices for collecting and exchanging biospecimens and data (see next section, Biobanking Best Practices). In addition, the larger biobanks now usually will benefit from developing a business plan and a strategy for long-term sustainability, i.e. in the event of funding limitations (Vaught et al, 2011). In terms of the technical aspects of biobanking, emerging technologies for collecting, processing and storing sample need to be followed closely, as the success of a research project may depend on developing new evidence-based practices (Engel et al, 2014; Vaught, 2016). Even more difficult to manage are the ever-changing ethical and regulatory aspects of biobanking, including informed consent, privacy, intellectual property and sample and data access policies (Forsberg et al, 2009; Office of Human Research Protections, 2016; Vaught et al, 2007).

A reform of the European General Data Protection regulation (GDPR) has been proposed and discussions at the European Trilogy (Parliament, Council and Commission) are ongoing. The reforms aim to strengthen and unify data protection for individuals within the European Union (European Data Protection Reform, 2016). The GDPR also addresses export of personal data outside the EU which poses more challenges that will need to be managed by biobanks.

A "Q & A" article in Clinical Chemistry in 2014 (Vaught et al, 2014b) outlined "Critical Issues in International Biobanking," including: quality management; sustainability; centralized versus distributed biobanks; communicating the value of biobanks; data sharing; and the management of return of research results and incidental findings (see Challenges to Biobanking in Africa). As discussed in the following sections, such issues are not unique to biobanking in Africa, but are among the challenges that must be managed for the long-term success of biospecimens-based research on the continent.

Biobanking Best Practices

As mentioned in the last section, as biobanking has grown into a global enterprise, it has become necessary to develop best practices to control the technical and ethical-regulatory aspects of biospecimen management. Prior to the publication of such best practice documents, it was customary in biobanks as well as, for example, pathology laboratories, to develop biospecimen collection, processing and storage protocols to fit local needs. However, as problems emerged with sample and data exchange among collaborators, a number of international organizations published best practices, which have been widely adopted over the past 15 years. Among the organizations which have led in developing such documents are IARC (International Agency for Research on Cancer, 2016, wesite undergoing revision in 2016), ISBER, OECD and others. Several comprehensive reviews have outlined the evolution of such guidance documents (Vaught et al, 2012; Vaught et al, 2010).

Biobanking best practices are generally divided into technical and ethical-regulatory (also referred to as ELSI or ethical, legal and social issues) recommendations. The list below shows the table of contents from the U.S. National Cancer Institute Best Practices for Biological Resources (U.S. National Cancer Institute Best Practices for Biological Resources, 2016):

The following shows the major contents headings from the U.S. National Cancer Institute Best Practices for Biospecimen Resources

- A. Scope, applicability, and implementation
- B. Technical and operational best practices
  - B.1. Biospecimen resource management and operations
  - B.2. Biospecimen collection, processing, storage, retrieval, and dissemination
  - B.3. Quality management
  - B.4. Biosafety
  - B.5. Collecting and managing clinical data
  - B.6. Biospecimen resource informatics: data management and inventory control and tracking
- C. Ethical, legal, and policy best practices
  - C.1. Principles for responsible custodianship
  - C.2. Informed consent
  - C.3. Privacy and confidentiality protections
  - C.4. Access to biospecimens and data
  - C.5. Intellectual property and resource sharing
  - C.6. Conflicts of interest

The technical and operational recommendations from IARC, ISBER, OECD and NCI provide varying levels of details concerning collection, processing, storage and shipping practices, as well as the necessary supporting informatics systems. (See below)

Informatics: The Electronic Glue of the Biobank

(Reprinted from Vaught, 2016)

Biobanks are dependent on information systems for a number of critical functions. At every step of the processes of receiving, shipping, collecting, processing, storing and retrieving specimens from storage, the samples must be accurately tracked, with every movement and process recorded. Chain of custody is an important concept in biobanking. Bar coding or RFID tracking are necessities. Freezer inventory systems are necessary to maintain up to date information on all steps of storage and retrieval. Laboratory information management systems (LIMs) have been adapted to biobanking applications and have been widely adopted.

The annotation of specimens with clinical, demographic and analytical, as well as sample handling data, contribute to their long-term value. Standards for collecting and transmitting specimen data are critical to the biobank's success. Developing a minimal set of data elements for each biospecimen research project should be an early step in project planning. There are some issues which must be resolved in order for biospecimen research collaborations to be successful. Often informatics systems developed for one institution cannot communicate with other institutions without the development of an interface to allow the systems to be interoperable. Biobanking best practices provide general guidance on overcoming such obstacles.

For a review of biobanking practices specific to projects being conducted in Africa, see the chapter by Mendy et al. "Biosampling and Biobanking," in the Handbook for Cancer Research in Africa (Rebbeck, 2013). The IARC, U.S. NCI and ISBER best practices documents also provide specific technical recommendations which may be helpful depending on the biobank and researchers' goals. As indicated above, technical best practices must evolve over time as new technologies emerge and biospecimens methods research result in the adoption of evidence-based practices (Engel et al, 2014). Note however that with multiple best practices documents available, and often-conflicting research results, it has been difficult to harmonize such recommendations on an international basis (Vaught et al, 2014b).

Even more challenging than developing and staying up to date with biobanking technical practices are the issues faced with ELSI practices (Forsberg et al, 2009; Vaught et al, 2007 and various biobanking best practices). As indicated by the NCI Best Practices list on the previous page, the issues cover a broad range of ethical and regulatory recommendations. However, the policies are continually changing and are often controversial. For example, the rules concerning informed consent and privacy differ among countries. And such rules and regulations can change in ways that affect the ability of researchers to collect the biospecimens they need. Other related ELSI practices include: planning for long-term custodianship; policies for access to specimens and data; controlling conflicts of interest; and managing data and sample sharing and intellectual property through, for example, material transfer agreements (U.S. National Cancer Institute Best Practices for Biological Resources, 2016).

A special aspect of biobanking that has emerged over the past few years is the importance of developing strategic and business plans, and planning for the long-term sustainability of the operation (Henderson et al, 2015; Vaught, 2013). During economic downturns and in particular for biobanks in low resource countries it is important to develop such plans. Recommendations related to business plans and sustainability have appeared in a number of editorials and review articles (Vaught, 2013; Vaught et al, 2011).

Biobanking in Africa: Examples of Projects

The chapter by Mendy et al. in the Handbook for Cancer Research in Africa (Rebbeck, 2013) noted the following:

"The global total of new cancer cases is projected to increase by 60% to 21 million annually by 2030, with an estimated 13.1 million deaths from cancer yearly. About half of these cancer deaths will occur in low-income countries and more than 80% of these in African countries."

Given biobanking's central and critical role in basic, translational and clinical cancer research, developing workable standards for biospecimen management in African countries is necessary. Early biobanks in Africa were developed due to the need to collect samples during the AIDS epidemic (Mendy et al, 2014). More recently the Ebola epidemic in western Africa led to additional biobanking needs. Thus much of the early and current biobanking activities in Africa have resulted from the spread of emerging infectious diseases, as well as more long-term issues concerning tuberculosis and malaria (Mendy et al, 2014).

An example of an institution in Africa that had adopted biobanking as a research platform since the early 1970s is the Medical Research Council Unit in The Gambia West Africa (The Gambia West Africa Medical Research Council Unit, 2016). The MRC biobanks have biospecimens collected for research on infectious and chronic diseases since the early 1970's and has provided the facilities for one of the first national DNA bank in Africa (Sirugo et al, 2004).

Recently two projects have been funded which will result in additional progress in biobanking and research infrastructure in Africa: H3Africa (Human Health and Heredity in Africa, 2016) and B3Africa (Bridging Biobanking and Biomedical Research across Europe and Africa, 2016). The H3Africa program, jointly funded by the Wellcome Trust and the U.S. National Institutes of Health (NIH), will study the genomic and environmental

determinants of a variety of diseases (Human Health and Heredity in Africa, 2016). The program required the development of a biobanking network among several African countries. A review by Abayomi et al. noted that developing harmonized technical and ethical standards among the project's network partners was a challenge. In general, the lack of biobanking standards and infrastructure in Africa slowed the initial progress in developing the H3Africa network (Abayomi et al, 2013).

B3Africa, the Bridging Biobanking and Biomedical Research across Europe and Africa project, funded by BBMRI-ERIC (Bridging Biobanking and Biomedical Research across Europe and Africa, 2016), aims to "implement a cooperation platform and technical informatics framework for biobank integration between Africa and Europe. The collaboration harmonises the ethical and legal framework, biobank data representation and bioinformatics pipelines for sharing data and knowledge among biobanks and allowing access for researchers from both continents."

Challenges to Biobanking in Africa

Projects such as H3Africa and B3Africa will result in improved conditions for biobanking and biospecimen research in Africa. However, currently the situation in Africa and among LMICs elsewhere is indicative of the challenges faced in such countries. In a survey conducted by IARC among LMICs in Africa, Asia and Europe (Mendy et al, 2014) it was determined that although there were some exceptions, in general biobanking in LMICs were lacking in the technical and ethical-regulatory standards and infrastructure practiced in HICs.

In terms of technical issues, many of the challenges to successful biobanking among LMICs in Africa relate to infrastructure. The availability of up to date processing and storage equipment is sometimes lacking. If the equipment is available then other issues may interfere with its proper use, such as intermittent power outages (Abayomi et al, 2013). As noted by Fleming (2013) in "State of Oncology 2013" (Boyle et al, 2013), there is also a shortage of trained pathologists in LMICs, which presents a major obstacle to collecting high-quality samples and otherwise developing well-managed biobanks. The problem is particularly acute in sub-Saharan Africa. The shortage of pathology services not only affects the ability to collect samples for biobanking. The quality of patient care is also affected in that tissues are often not collected for diagnostic purposes.

Biobank sustainability is also an issue among African biobanks, as it is among all LMICs. Even among more well-developed biobanks in developed countries, biobanks are generally not self-sustainable without significant contributions from government and/or institutional sources (Henderson et al, 2015; Vaught, 2013).

As noted by Abayomi et al. (2013), ethical, legal and social issues have been difficult to coordinate and harmonize for biobanking initiatives in South Africa, which has a relatively well-developed research infrastructure. For LMICs in Africa the situation is even more complicated. As noted by Mendy et al. (2014) in an assessment of biobanking practices in 26 LMIC centres:

"ELSIs are dealt with by various mechanisms in the different ethics and scientific committees in more than 90% (24/26) of the centres. These committees are responsible for reviewing and approving research activities. However, ELSIs specific to biobanking or biobank projects are usually not included in the committees' review processes, and this is an important challenge in biobank governance in LMICs. For example, most centres do not have patient-consent procedures for the systematic storage of post analysis clinical samples for future research. Informed consent is project-specific, and broad consent, which would enable efficient use of biobanking resources, is not usually obtained from participants."

Going forward, African biobanking practice is expected to improve as the public and researchers become more educated in best practices (see next section, Biobanking Educational Efforts in Africa), and biobanking networks are further developed to support multi-country projects.

Biobanking Educational Efforts in Africa

In addition to biobanking infrastructure issues which are inhibiting research progress in LMICs, there is a general lack of biobanking knowledge among the public and researchers. A number of international organizations have increased their efforts to identify issues and conduct workshops to increase awareness and provide training opportunities.

- IPRI: As noted in its mission statement IPRI has "the broad goal of contributing to the improvement of health in populations worldwide".. and "aims to increase prospects for prevention through training, education, prevention research and research into causes worldwide with a focus on low and lower-middle income countries." For a discussion of biobanking in Africa, two chapters from the iPRI book "State of Oncology 2013" (Boyle et al, 2013) are instructive: "Lack of Pathology in Low Income Countries" (Fleming, 2013), and "Biobanks: Central Importance and Standards" (Pasterk et al, 2013). In addition, IPRI hosts an annual National Cancer Institute Directors conference, where participants from multiple LMICs, including Africa, meet to discuss their research initiatives and challenges.

- IARC: IARC has supported biobanking activities for many years, including the European Prospective Investigation into Cancer (EPIC) (EPIC, 2016), which involved creating a biobanking network centred in Lyon and involving multiple sites in Europe. As noted above IARC investigators have published a number of articles concerning biobanking operations and challenges in LMICs, including Africa (Mendy et al, 2014; Rebbeck, 2013).

- BCNet: BCNet is the LMIC Biobank and Cohort Network, and is a cooperative effort among IARC, the U.S. NCI Centre for Global Health and other international partners. BCNet has engaged in a number of training effort in LMICs and has recently partnered with ISBER to provide online training for ISBER's Best Practices (ISBER, 2016).

- BBMRI-ERIC: BBMRI-ERIC supports biobanking educational activities through its annual Hands On Biobanking conference (BBMRI-ESBB HandsOnBiobank, 2016), and has recently partnered with ESBB to host annual biobanking meetings.

- ISBER: ISBER's Best Practices are available on the Society's web site, and ISBER has developed a Regions program, which includes organizing biobanking efforts in the Europe, Middle East and Africa (EMEA) Region (ISBER Strategic Plan 2014-2017). ISBER's annual meetings attract members from Africa as well as participants from multiple countries.

Conclusions and Future Directions

With the recognition that standardized biobanking infrastructure and practices are critical to the success of basic, translational and clinical research, and that international collaboration is now the norm, biobanking in LMICs in Africa and elsewhere will begin to become more in line with practices in HICs. However, there are a number of challenges that LMIC biobanks will need to overcome.

The following are some of the current trends and ongoing biobanking challenges in Africa:

- Other than large projects such as H3Africa and B3Africa, government and institutional support for biobanking will be necessary for long-term sustainability.

- Biobanking infrastructure upgrades will be necessary, including buildings and equipment, as well as measures to control the effects of power outages.

- Important initiatives by BCNet, IARC, IPRI and BBMRI-ERIC will be providing important training tools and infrastructure support.

- Biobanking workshops to discuss and resolve regional issues in Africa are becoming more frequent, hosted by recognized international biobanking organizations, such as ESBB and BBMRI-ERIC.

- The development and management of biobanks needs to follow best practices which cover technical and ELSI recommendations as well as the necessity for comprehensive governance policies for access and long-term sustainability.

- The current lack of sufficient numbers of pathologists and other professional biobanking personnel should be improved through training programs and biobanking workshops.

- New and alternate technologies and evidence-based biobanking practices will need to be adopted to meet the special needs of African biobankers.

The above recommendations will require time to yield results. And the challenges discussed in this chapter are not unique to Africa or to LMICs. International standardization and harmonization are issues faced in all biobanking endeavours. The major biobanking organizations such as ISBER, BCNet, IARC and BBMRI-ERIC are working to overcome these obstacles, and all are engaged in initiatives on multiple continents (Vaught et al, 2014a).

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"As with cancers everywhere, African cancers deserve to be prevented, to be treated, to be cured and to be palliated. If we don't do it now, starting immediately, it will be too late and Africa's cancer crisis will continue to grow out of control."

Professor Peter Boyle, 2015

Africa: National Profiles

Invitations were sent to Oncologists in many countries of Africa to describe the current State of Oncolgy in their country. This section presents the responses. Each invitation requested some basic information and they invited the author to attach his or her personal observation following this. The resulting chapters are variable but present a broad picture of the current State of Oncology in Africa, as seen from an **African perspective**.

"How is it acceptable that over half the countries in Africa do not have radiotherapy machines? As intolerable, how can over half the countries in Africa outlaw the use of medical morphine leaving thousands to die in pain?

Where is our sense of humanity?"

Professor Peter Boyle, 2015

Chapter 16a

Angola

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Malignant neoplasms (cancers) are a group of over 100 diseases characterized by rapid cell proliferation of an organ's tissues. The clinical presentation of cancers consists of nodules or tumours affecting adjacent organs and developing local or distal metastases. (Merlo et al., 2006)

According to the World Health Organization (WHO), cancer is a worldwide public health problem. In 2012, cancer incidence and mortality were estimated at 14.1 million new cases and 8.2 million deaths. Approximately 32.6 million people were living with the disease after 5 years of diagnosis. (Ferlay et al., 2013) Projections based on these estimates suggest that there will be about 19.3 million new cases in 2030. (Ferlay et al., 2013)

The most prevalent types of cancer are lung cancer (1.8 million, 13%), breast cancer (1.7 million, 11.9%), and colorectal cancer (1.4 million, 9.7%). (Ferlay et al., 2013) However, the distribution of cancer in the world is heterogeneous.

In developed countries, most cases of cancer affect the following organs: lung, breast, prostate, colon and rectum, and endometrium; in addition, neoplastic diseases are the second leading cause of deaths for disease. (Ferlay et al., 2013)

In developing countries, the most common types of cancer are uterine, stomach, liver, and oral cavity cancers, as well as Kaposi's Sarcoma. In these countries, neoplastic diseases are not among the leading causes of death because infectious diseases are the main health problems. (Boyle et al., 2008)

Whereas in developed countries only 10% of cancers are associated with biological agents and more than 60% of patients are diagnosed at an early stage of the disease; in low-income countries it is the opposite. In these countries, more than 25% of cancers are linked to infectious agents and 80% of patients are diagnosed at an advanced stage of the disease. (Boyle et al., 2008; Ferlay et al., 2013)

In spite of such data, the extent of cancer has not been determined in developing countries such as Angola. Deficit of qualified professionals and shortage of diagnostic resources and Population-Based Cancer Registries are suggested to be the main causes of this lack of knowledge on cancer cases. (Parkin et al., 2003)

Since the 1970s, there has been a growing trend of cancer incidence and mortality; therefore, in the 1980s, the WHO started to recommend that every country in the world, even those showing low incidence and mortality rates, should design and implement Cancer Prevention and Control Programs. (WHO, 2002)

The estimated population growth and the increased number of elderly related to higher exposure to the risks of developing malignant neoplasms contributed to increasing both cancer incidence and mortality. Thus, a well-planned cancer control program will contribute to reducing the negative impact of the disease and improving the rational allocation of scarce resources. (WHO, 2002)

A guide to help countries with the preparation and implementation of Cancer Prevention and Control Programs was published in 2001 and updated in 2002 by the WHO. Additionally, in 2010, the WHO also published a series of six modules on the same topic. (WHO, 2006, 2007a, b, c, 2008a, b)

With the purpose of adapting these guides to the African context, the WHO African Region published a guide for health policy maker in 2012. In 2013, the Union for International Cancer Control (UICC) published a checklist for implementation of a National Cancer Control Program. In 2012, the WHO African Region published a guide for cancer control in Africa. (WHO, 2012)

According to the WHO, a Cancer Prevention and control Program consists of a set of public health measures focused on reducing cancer incidence and mortality and improving patients' quality of life. This can be achieved through the implementation of systematic and equitable evidence-based strategies aimed at primary prevention, early diagnosis, curative and palliative care, and rational use of the available resources (WHO, 2002).

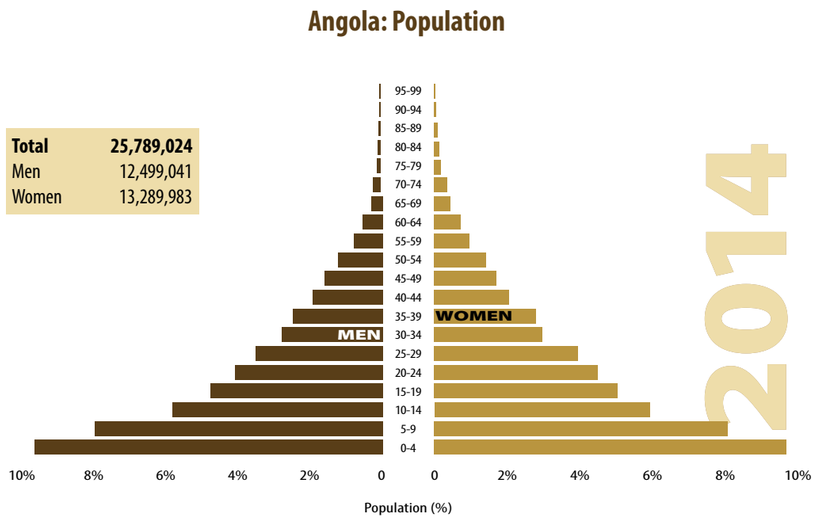

Figure 1: Population in Angola (2014)

Health Care in Angola

Angola is located in Southern Africa. Its surface is 1,246,700 km2 and its estimated population is over 24.3 million inhabitants (INE, 2015) (Figure 1).

After becoming an independent country in 1975, Angola endured a civil war that lasted for 27 years. This conflict resulted in the destruction of a great part of the country's infrastructure and had devastating socioeconomic consequences with a negative impact on the health status of the population.

After peace was established in 2002, the Angolan government drew up an action plan to improve the socioeconomic conditions of the population. Health was a key concern considering that a population with good health status is essential for the country's development (Angola, 2010).

However, it was necessary to design a National Health Policy setting out the strategies to improve the health care provided to Angolans. In order to fulfill this objective, the Angolan Ministry of Health started working on a policy that was approved and published in November 2010.

With the purpose of implementing the National Health Policy, the National Health Development Plan - NHDP was approved in 2012 (Angola, 2012). This plan was prepared by a multisectoral committee established by the Presidential Office by the Order No. 84/11 dated of October 27, 2012.

The NHDP is a strategic and operational tool used to implement the guidelines set out in the Long Term Development Strategy, known as "Angola 2025", and in the National Health Policy. This plan covers all health areas and consists of nine programs, 16 strategies, and 20 projects.

Project 14 addresses the issue of Prevention, Early Diagnosis, and Treatment of malignant tumors. This project sets out the objectives and goals to be achieved to reduce the negative impact of cancer on the population.

The National Oncology Center (CNO, acronym in Portuguese) is responsible for coordinating the activities related to cancer prevention and care in the country. In May 2014, the Presidential Decree No. 229/14 transformed the CNO into the Angolan Institute for Cancer Control (IACC, acronym in Portuguese). The bylaws of the Institute were approved establishing the institute as a center of excellence for cancer. One of the main responsibilities of the IACC is to ensure the implementation of national policies, programs, and plans for cancer prevention and treatment.

In order to achieve this goal, the IACC developed the proposal for the National Program of Cancer Prevention and Control for Angola to be considered and discussed by the Ministry of Health and other partners. This proposal covers six dimensions that comply with the WHO guidelines for cancer prevention and control: prevention, early diagnosis, diagnosis and treatment, palliative care and rehabilitation, education and research, and cancer epidemiological surveillance.

Current Status of Cancer in Angola

According to the WHO STEPwise approach to Surveillance the description of the current status of cancer in a particular region or country is the first step to be considered when developing a program to prevent and control cancer. The objective of this approach is to diagnose the status of the main components of a cancer control program and to plan the goals to be achieved and the strategies to improve the current situation (WHO, 2002).

Current Status of the Cancer Control Program in Angola

Angola still does not have a National Program of Cancer Prevention and Control. In 2007, the IACC, formerly CNO, drafted a proposal for the 2007-2013 Cancer National Policy. The proposal had 14 macro-objectives covering prevention, early detection, treatment, rehabilitation, and palliative care. However, this proposal was never approved.

In 2010, the Angolan National Health Policy was approved. This document does not include any specific descriptions related to the implementation of the cancer prevention and control program. Because there is not a control program, the CNO, as the only institution that specializes in oncology in the country and the advisory body for the Ministry of Health on issues related to cancer, coordinated all cancer prevention and control initiatives in the country.

Cancer prevention and control in Angola has had an official reference plan since the approval of the NHDP in 2012. The 14th project of the NHDP covers the topic of cancer prevention and control.

As mentioned above, in 2014, the Presidential Decree No. 229/14 dated of September 2 transformed the CNO into the IACC. According to this decree, the IACC is a public health facility and a national center of excellence integrated into the National Health Service to provide health care related to prevention, early diagnosis, and specialized and complex treatment of patients with cancer.

The IACC has the following responsibilities:

1. To provide medical care and medications for cancer patients on a permanent basis;
2. To ensure the implementation of national policies, programs, and plans of cancer prevention and treatment;
3. To develop standards of clinical, laboratory, biomedical research, educational, and occupational practice with regard to cancer prevention and treatment;
4. To ensure the rehabilitation of both inpatients and outpatients, as well as the provision of social services;
5. To set out and coordinate the activities related to training, information, education, communication, counseling, treatment, and follow-up in terms of cancer prevention;
6. To promote scientific research in the area of preventive and curative medicine, within the following fields: Clinical Oncology, General Surgical Oncology, Radiotherapy, Anatomic Pathology, etc.;
7. To promote education, training, and technical and professional upgrading of health professionals, and to encourage the establishment of stable social and emotional relations between the personal or family needs of patients and cases of disease;
8. To cooperate with the provinces to support the implementation of Local Cancer Centers;
9. To cooperate with international organizations involved with cancer prevention and treatment.

Nevertheless, it is necessary to develop and approve a National Policy for Cancer Prevention and Control in order to achieve the objectives and goals set out in project 14 of the NHDP, which is the main reason for developing the National Program of Cancer Prevention and Control for Angola.

Extent of Cancer in Angola

The actual number of cancer cases has not been determined in Angola. The Population-Based Cancer Registry has not been implemented in the country so far. Because this tool is not available, the number of cancer cases in the country has been based on estimates from the International

Agency for Research on Cancer (IARC). According to these estimates, cancer incidence and mortality in 2012 in Angola reached 10,305 new cases and 7,213 deaths, respectively (IARC, 2013). However, data from the Hospital-based Cancer Registry of the IACC (the only institution in the country specializing in cancer treatment) indicate that from 2007 to 2013 there were 6,920 new cases, with an annual average of 989 cases.

The most frequent neoplasms in both genders were: breast cancer (22%), cervical cancer (16%), head and neck cancer (9%), Kaposi sarcoma (9%), prostate cancer (6%), skin cancer (4%), stomach cancer (3%), bronchi and lung cancer (2%), and Wilms' tumor (2%) (Table 1). Nevertheless, these data do not reflect the actual amount of cancer cases in Angola because they are limited to the number of hospital-based cases.

Many cancer patients may not seek health care for an array of different contextual reasons. In addition, even those who sought health care may not have received the correct diagnosis due to lack of qualified health professionals and diagnostic resources. Also, even those who received a diagnosis of cancer may not have been referred to the IACC.

Table 1. Distribution of the 10 most frequent types of cancer at the National Oncology Center from 2007 to 2013.

Tumor site	Years							Subtotal	%
	2007	2008	2009	2010	2011	2012	2013		
	n	N	n	n	n	n	n		
Breast	199	164	212	210	196	206	314	1501	22%
Cervix	112	143	200	159	184	144	180	1122	16%
Head and neck	86	124	146	124	67	18	71	636	9%
Lymphomas	48	66	75	68	71	43	62	433	6%
Kaposi sarcoma	55	62	50	63	66	50	65	411	6%
Prostate	14	17	31	55	69	87	101	374	5%
Skin	45	47	58	50	34	7	17	258	4%
Stomach	24	21	31	25	35	22	42	200	3%
Lung and pleura	18	22	23	15	18	13	19	128	2%
Wilms' tumor	8	10	20	22	20	28	43	151	2%
Other	204	286	256	203	160	182	415	1706	25%
Total	813	962	1102	994	920	800	1329	6920	100%

Source: Statistical Division of the Angolan Institute for Cancer Control.

Prevention

Cancer prevention is a public health measure aimed at preventing a specific disease. There is general prevention and specific prevention (WHO, 2002; Boyle, 2008; WHO 2, 2010).

On one hand, general prevention is based on health promotion and detection of risk factors associated with the development of diseases, thus reducing the population's exposure. On the other hand, specific protection consists of vaccination against a particular biological agent (Boyle, 1991).

In Angola, cancer prevention is characterized by the population's low awareness of risk factors and consistent public policies to reduce the population's exposure to these factors. However, there are laudable initiatives, such as education programs to reduce the habit of smoking and alcohol consumption, in addition to the promotion of good habits, such as healthy diet and physical activity (Boyle, 2008).

As for specific protection, it is worth noting that the vaccine against Hepatitis B and C has been included in the immunization schedule for infants in 2006. Some advances have been made regarding the HPV vaccine. In November 2011, the Cervarix® vaccine (GlaxoSmithKline Biologicals SA) was introduced and the first 1,500 doses were donated to a hospital. Each dose cost 29 USD. The implementation of the HPV vaccine is planned for 2015.

Early Detection

Early detection consists of two approaches: screening and early diagnosis.

Screening

It is aimed at detecting precancerous lesions and treat them, thus preventing these lesions from developing into invasive lesions and, as a consequence, reducing cancer incidence and mortality (WHO, 2002; Boyle, 2008; WHO 3, 2010). Currently, this approach is not part of any organized programs in Angola. There are only encouraging initiatives related to breast and cervical cancer.

In terms of cervical cancer, these initiatives have been put in place by the IACC at three hospitals (Maternidade Lucrécia Pain, Maternidade Ngangula, Hospital do Huambo) and some private clinics. Nevertheless, there is still very low coverage. For instance, about 2,300 cervical smear tests were performed at the IACC in 2013. This number is much lower than the recommended considering the size of the population at risk.

As for breast cancer screening, it has been conducted at the IACC. The institute is equipped with five mammography devices; three of them are mobile devices and have been used to carry out campaigns in other regions of the country.

Early Diagnosis

It is focused on educating the population so that people are able to recognize the clinical manifestations of the disease and seek health care when the signs and symptoms are detected. The main objective of this approach is to establish the diagnosis at an initial stage and provide appropriate treatment in order to increase the chance of cure or overall patient survival (WHO, 2002; WHO 3, 2010).

As for this approach, the IACC, in a partnership with the Angolan League of Combat Cancer, has conducted various educational activities through mass media campaigns, lectures, interviews, rallies against cancer, theater, etc. These activities should be encouraged to reach a larger number of people.

Diagnosis and Treatment

Appropriate cancer diagnosis and treatment are key factors to control the disease. They are associated with increased chance of cure and overall survival (WHO, 2010; WHO 4, 2010).

Because of the shortage of diagnostic resources, adequate infrastructure, qualified professionals, in addition to the low educational level of the population and cultural factors, about 80% of cancer cases in developing countries are detected at advanced stages, when the only possible treatment consists of palliative care (Pakin, 2002; WHO, 2008).

Considering the Angolan context, the country has limited infrastructure, poor diagnostic, technological, and human resources, and only one cancer center (the IACC) to meet the demands of its whole population.

The main cancer treatment approaches consist of surgery, radiotherapy, chemotherapy, and hormone therapy. Surgery and hormone therapy have been provided at different health facilities; whereas radiotherapy is available only at the IACC and Clínica Girasol. The IACC has a linear accelerator that is currently being used and other two accelerators are being installed. Clínica Girassol has two radiotherapy devices, however their availability is limited. Chemotherapy is provided at the IACC and Clínica Girassol.

In terms of diagnosis, different public and private hospitals offer imaging studies and pathology tests. However, they do not meet the needs of the country. For instance, the IACC has one CT scanner, one MRI scanner, five mammography devices (three of them are mobile), five ultrasound scanners, and one X-ray machine.

Palliative Care

Palliative care aims to treat cancer patients' pain and provide psychological and spiritual support to patients and their families to ensure a dignified death (WHO, 2002; WHO 5, 2010).

Angola has a health policy on medications for chronic diseases. This policy ensures that opiates are provided free of charge for patients with chronic diseases to relieve their pain. Nevertheless, few patients are able to receive morphine. The IACC provides morphine for inpatients. However, when the patients are discharged they still need to continue being treated with this drug. And this does not happen due to lack of oral morphine. Therefore, patients often go to the Emergency Department of hospitals for treatment. In addition to lack of availability, there is also a small number of specialists in palliative care.

Education and Research

Research is an essential part of a cancer control program. Currently, Angola does not have any training centers for cancer professionals or research centers to conduct epidemiological and clinical studies.

Epidemiological Surveillance

The extent of cancer has not been determined in Angola because the country has not implemented the population-based cancer registry. As mentioned above, the current data on Angola are related to the IARC and IACC, the only center in the country that specializes in the treatment of neoplastic diseases.

Proposal for the National Program of Cancer Prevention and Control for Angola

The implementation of the National Program of Cancer Prevention and Control for Angola was prompted by the need to intensify and coordinate the actions against cancer in the country and reduce the negative impact of this disease on the population. The main objective of the National Program of Cancer Prevention and Control for Angola is to reduce cancer incidence and mortality, improving the quality of life of patients with neoplasms through the systematic implementation of evidence-based interventions for prevention, early detection, diagnosis and treatment, and palliative care.

Structure of the Proposal of the National Program of Cancer Prevention and Control for Angola

The National Program of Cancer Prevention and Control (NPCPC) will be implemented by a coordinator and a National Cancer Council serving as an advisory board. The NPCPC must have a physical facility, receive financial resources, have its own bylaws, and it will be composed of six committees:

- Prevention Committee;
- Early Detection Committee;
- Diagnosis and Treatment Committee;
- Palliative Care Committee;
- Education and Research Committee;
- Cancer Epidemiological Surveillance Committee.

Each committee will have a coordinator and will include a board of experts in various fields of knowledge in order to provide a holistic approach to the issues. The committees will be allowed to invite other experts to discuss specific topics on a temporary basis. The committees will be responsible for preparing and submitting the national recommendations related to their areas. These recommendations must be based on solid and cost-effective scientific evidence; they must be presented at a round table meeting with national and international experts and health managers under the coordination of the NPCPC Coordinator. When no solid scientific evidence is available, the committee may recommend research projects such as surveys, randomized trials, systematic studies, and cost-effectiveness studies. These committees will also be responsible for drafting budget proposals.

NPCPC Vision and Mission

Vision

Being the reference program in cancer prevention, early detection, treatment, rehabilitation, education and research within the 2012-2025 National Health Development Plan.

Mission

Being responsible for promoting and coordinating all integrated actions to decrease cancer incidence and mortality in Angola.

Approaches of the National Program of Cancer Prevention and Control for Angola

According to the WHO, the Cancer Prevention and Control Program is a public health tool designed to reduce cancer incidence and mortality among the population, in addition to improving the quality of life of patients with this disease through the implementation of systematic and equitable evidence-based strategies. A Cancer Prevention and Control Program must include the following dimensions (WHO, 2002):

- Prevention
- Early detection
- Early diagnosis
- Diagnosis and treatment
- Palliative care
- Education and Research
- Cancer epidemiological urveillance

The current proposal defines each dimension as a NPCPC subprogram.

Prevention

Prevention can be defined as the reduction or elimination of the possibility of exposure to risk factors and determinants associated with cancer development. It is the main cost-effective approach to long-term cancer control (WHO, 2002).

Risk factors or health determinants are understood as the conditions whose presence or exposure to increases the likelihood of disease occurrence (Kaufman, 2011; Pontes, 2009) (Andersen, 2007). Thus, these factors must be detected for the development of preventive measures that may reduce the incidence of cancer by 40% (WHO, 2005).

Over the years, various risk factors associated with the development of cancer have been identified. These factors can be grouped into behavioral or lifestyle factors, biological agents, environmental conditions, occupational factors, etc. (Boyle, 2008).

In Africa, the main risk factors that contribute to the increasing incidence of cancer are infectious agents (Hepatitis B Virus, HIV, HPV, Helicobacter Pilory, Schistosoma mansoni), smoking, alcohol consumption, poor diet, physical inactivity, environmental pollution, and, to a lesser extent, genetic factors that represent approximately 5-10% (Boyle, 2008).

Prevention focuses not only on the risk factors, but also on the protective factors. Vaccination against HPV and hepatitis B and C are special protection methods. Therefore, it is essential to implement comprehensive education programs addressing the issues of vaccination against infections that cause cancer, substance abuse, nutritional education, physical activity, and environmental and occupational protection.

NPCPC Prevention Subprogram:

This subprogram will be coordinated by members of the Prevention Committee who will be responsible for drafting and submitting the nation-wide recommendations for cancer prevention. The committee members will be allowed to invite national or international experts in specific issues, as well as to conduct or commission research projects to address specific situations and hold scientific events, and conduct technical visits to other international centers for updating and training purposes.

This proposal suggests the activities to be performed, the agents to be involved, the expected results, and the evaluation indicators to be used.

Early Detection

Early detection includes two different approaches: screening and early diagnosis of the disease. Screening aims to identify pre-invasive lesions and treat them, thus preventing these lesions from developing into invasive lesions and promoting decreased cancer incidence and mortality. Early diagnosis consists of detecting the disease at an initial phase and treating it with the purpose of curing the disease (WHO, 2002; Boyle, 2008; WHO 3, 2010).

The following assumptions should be considered before implementing a screening program:

1. Is the disease a public health problem considering its extent and incidence?
2. Is there a technique allowing the detection of the disease at pre-invasive or malignant stages?
3. Are there resources available to screen at least 70% of the population at risk?
4. Are there diagnostic resources to confirm at least 70% of cases with suspicious results?
5. Are there resources to treat at least 70% of patients with confirmed diagnosis?
6. Are there randomized studies showing the impact on the reduced mortality from the disease?

After considering the assumptions mentioned above, the screenable cancers are breast cancer, cervical cancer, colorectal cancer, lung cancer (in the United States), and oral cavity cancer (in India). In African countries, because of the shortage of human and financial resources, screenable neoplasms are cervical and breast cancers.

Cervical cancer screening - Vaginal cytology, also known as pap test, is the most commonly used test to screen cervical cancer. The countries that implemented this technique, covering 80% of the risk population, reduced cervical cancer incidence and mortality by 75% (Willoughby, 2006). However, because this is a high-cost test for low-income countries, other cost-effective techniques, such as VIA (Visual Inspection with Acetic Acid) and VILA (Visual Inspection with Lugol Acetic), were also developed. A study conducted in India showed that women undergoing screening using VIA had a 30% reduction in their morality rate when compared with women who were not screened (Sankaranarayanan, 2001; IARC, 2005; WHO 3, 2010; WHO, 2012). The WHO recommends this technique for developing countries.

VIA and VILA techniques are simple methods and can be performed by trained nurses. Considering the Angolan context, the best strategy would be to implement both techniques: the pap test in urban areas and VIA in rural areas. The country has experience with both the pap test and VIA.

In terms of raising awareness on the clinical manifestations of the disease, as already mentioned above, the IACC offers a health education program, in cooperation with the Angolan League of Combat Cancer, and several educational activities have been conducted, such as lectures, interviews, rallies against cancer, theater, etc. However, these activities must reach a larger population.

NPCPC Early Detection Subprogram:

This subprogram will be coordinated by members of the Early Detection Committee who will be responsible for drafting and suggesting the nationwide recommendations for early detection. The members of this committee will be allowed to invite national or international experts in specific issues, as well as to conduct or commission research projects to address specific situations, hold scientific events, and conduct technical visits to other international centers for updating and training purposes. It is recommended that the subprogram uses its own financial resources to implement its activities.

Diagnosis and Treatment

Cancer diagnosis involves various techniques and procedures used to detect or confirm the disease. It usually involves evaluating the patient's medical history, laboratory tests, imaging studies, and cytology or histology tests of samples collected by biopsy.

Angola has only one center of excellence for cancer diagnosis (the IACC). Other health facilities also offer these procedures, which include cytology and histology tests, imaging studies (X-ray, ultrasound, CT), and laboratory tests. Molecular tests, such as immunohistochemical analysis, have not been made available. However, some private clinics already offer these tests.

After establishing the diagnosis, a multidisciplinary treatment is required. A large number of skilled professionals is required to provide this type of treatment. Unfortunately, the amount of specialized human resources and equipment does not meet the demand in our country. That is, the only center in the country that specializes in cancer treatment and diagnosis has reduced staff and equipment (Table 2 and 3).

Table 2. List of equipment available for diagnosis at the IACC

Equipment	Amount
Laboratory of anatomic pathology	
Cytology	1
Histology	1
X-Ray machine	1
Ultrasound scanner	2
Computed tomography scanner	2
Magnetic resonance device	1
Mammography device	1
Mobile devices	2
Clinical laboratory	1

Table 3. List of experts working at the IACC

Experts	Amount
Physicians	
Anatomic pathologists	2

Experts	Amount
Clinical oncologists	10
Hematologists	2
Radiotherapists	3
Physicists	3
Surgeons	4
Medical Imaging Specialists	2
Psychologists	4
Pediatricians	2
Nurses	3
Technical Staff	
Dosimetry	2
Anatomic Pathology	4
Imaging Study	3
Radiotherapy	6
Nurses	20

Treatment

Cancer treatment consists of several different types of interventions, including psychosocial support, surgery, radiotherapy, chemotherapy, and hormone therapy, with the purpose of curing the disease or prolonging life (for years), and improving the patients' quality of life.

Currently, complete cancer treatment is only offered at the IACC. Cancer experts from different areas and trained abroad (Brazil, Portugal, Spain, Cuba) provide treatment based on studies published in the literature and adapted to the Angolan context.

Other hospitals only provide surgical treatment, and Clínical Girassol offers chemotherapy. Patients are referred to the IACC for chemotherapy and radiotherapy. Essential chemotherapy agents and supportive drugs for cancer patients are available at the IACC. The institute also has one fully operational radiotherapy device and two devices to be installed. A brachytherapy equipment is also being installed.

Planning Diagnostic and Treatment Services

In spite of the development achieved in terms of scientific research, improvement of prevention measures, diagnosis and treatment techniques, there is an increasing number of new cancer cases, and cancer mortality has not been controlled yet (Boyle, 2008). The worst scenario is expected for developing countries because of the shortage of human and financial resources, poor infrastructure, and absence of cancer control policies. Approximately one third of cancer cases can be cured if detected at an initial stage, such as breast, cervical, and oral cavity cancers. Other types of cancer are very likely to be cured even when detected at an advanced stage, such as metastatic seminoma, acute leukemia, and childhood lymphoma. Therefore, when detected, these cancers can be treated efficiently even in low-income countries (Boyle, 2008).

Such treatment requires a rational planning of resources, combining diagnosis and treatment with early detection strategies and health policies that promote and facilitate the access of all citizens in a timely manner. This strategy avoids diagnosis at an advanced stage, when treatment is

more expensive and ineffective, which leads to the use of palliative care because of the possibility of treating a larger number of patients for the same cost.

The main objectives of cancer diagnosis and treatment are to cure the disease, prolong life, improve the quality of life after a cancer diagnosis that has been appropriately confirmed using the procedures available, and make treatment more effective when associated with early detection programs based on standardized care (WHO, 2002; Boyle, 2008; WHO 4, 2010).

Greater effectiveness is achieved when patients who are more likely to be cured are given priority. The remaining resources should be used to treat patients with treatable but incurable cancers, considering aspects related to cost-effectiveness, purchasing power, ethical and social aspects, therefore promoting equal access for all patients.

Palliative Care

Millions of cancer patients require palliative care worldwide. Based on proper planning, most patients with advanced cancer may have their suffering relieved and their quality of life significantly improved (WHO 5, 2010).

Palliative care promotes the relief of pain and other symptoms, integrates the patient's psychological and spiritual aspects, promotes life in a more active manner as much as possible, and supports the patient's family during the illness. Therefore, palliative care should be started early. Palliative care should be integrated into the existing health system, including proper training of health professionals in this type of care.

Education and Research

The training of professionals to deal with all aspects of cancer prevention and control is critical. Unfortunately, in the African continent and Angola, in particular, high quality training is scarcely available. There is lack of qualified cancer professionals at all levels. Thus, it is necessary to implement a medical specialist training program (for clinical oncologists, radiotherapists, cancer surgeons, pathologists, radiologists, hematologists, pediatricians), radiotherapy technicians, cytopathologists, VIA technicians, cancer nurses, public health specialists, epidemiologists, and statisticians. According to this point of view, it is of utmost importance to implement a training center at the IACC in cooperation with schools of medicine, the Instituto Médio Profissional de Saúde, and other international centers.

In terms of research, it should be noted that this is a process based on the production of new knowledge and the confirmation or refusal of existing knowledge. In this regard, Angola lacks a qualified research center for conducting epidemiological research, clinical research, and collaboration with other international research centers of excellence. Therefore, the implementation of such a research center is essential so that research groups can fulfill this deficiency.

Cancer Epidemiological Surveillance

Cancer epidemiological surveillance is a tool that can provide cancer epidemiological data for the Population-Based Cancer Registries (PBCR). The PBCR is an information system that collects, analyzes, interprets, and disseminates information about cancer in a systematic manner, considering predetermined populations and time periods, with the purpose of measuring the extent of cancer and its future trend. This system provides the basis for the investigation of risk factors and helps plan preventive and care measures for cancer control, monitoring, and evaluation. (Jensen et al., 1991; WHO, 2002) (Shanmugaratnam, 1991).

In addition to the PBCR, there is the Hospital-Based Cancer Registries (HBCR), which collects cancer data from a particular hospital or cancer facility focused on clinical care and hospital administration, serving as the main source of information for the PBCR at the same time (Greenwald, 1986; Shanmugaratnam, 1991).

Despite its usefulness, many developing countries lack or have low coverage of PBCR, which is an important limitation when it comes to determining the extent of this disease. According to the IARC, only 11% of the African population, 8% of the Asian population, and 21% of the Latin American population have cancer registry coverage (Parkin, 2006). The data on cancer incidence and mortality available in the GLOBOCAN are estimates. Within an optimal framework, the data to support the rational design of a National Policy of Cancer Control must be based on confirmed data provided by the PBCR (Estefan et al, 2013).

Angola is an African country where the extent of cancer is unknown (WHO/ICO, 2010). The Cancer Registry that was initiated in 1987, culminating with the publication of a series of four years (1987-1990) in 1991 was interrupted. (Parkin et al., 2003) (Teixeira, 1991). Developing a National Policy of Cancer Control that is able to determine the extent of cancer and its epidemiological profile is essential to achieve rational planning, monitoring, and evaluation. Thus, the implementation of a PBCR is required.

This subprogram will be coordinated by members of the Education Committee who will be responsible for drafting and suggesting the syllabus of the courses to be implemented. The members of the committee will be allowed to invite national or international experts in specific issues, as well as to hold scientific events and conduct technical visits to other international centers for updating and training purposes. It is recommended that the subprogram uses its own financial resources to implement its activities.

Conclusions

The objective of the current proposal of the National Program of Cancer Prevention and Control for Angola is to implement measures aimed at reducing the negative impact of cancer on the Angolan population. This document was prepared based on the WHO recommendations concerning cancer prevention and control adapted to the Angolan context. The document was drafted by the technical group of the IACC under the supervision of the General Director, Dr. Fernando Miguel.

The project was divided into six major dimensions of cancer prevention and control: Prevention, Early Detection, Diagnosis and Treatment, Palliative Care, Education and Research, and Cancer Epidemiological Surveillance.

Each dimension of the program will be coordinated by a committee named after each dimension, which will be responsible for preparing the recommendations, supervision, and evaluation of the planned activities. Each dimension of cancer prevention and control is presented as a NPCPC subprogram with its activities, people in charge, expected results, and evaluation method. Goals have not been established during this first phase because baseline data are missing for most situations.

All those involved in the implementation of this project who have access to this document are expected to give suggestions and recommendations to improve the document.

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Chapter 16b

Burkina Faso

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Burkina Faso has a population, estimated in 2014, of 17,880,386 inhabitants. An important proportion (48%) of inhabitants is aged less than 15 years.

Table 1: Burkina Faso's population by age group as of 2014.

Item	Less than 1 year	1-4 years	5-14 years	15 years and more - men	15 years and more - women	Total
Number	719,287	2,594,915	5,224,431	4,249,581	5,092,172	1,7,880,386

Burden of Cancer

There is no operational cancer registry in Burkina Faso. A cancer registry in the city of Ouagadougou was set up within the pathology service of the "Centre Hospitalier Universitaire Yalgado Ouédraogo" with the help of the International Agency for Research on Cancer (Lyon, France). Unfortunately, this registry is currently not running due to lack of funding.

According to the national annual statistical report, 3,886 cancer cases were notified by health facilities in 2014.

Table 2: Number of cancer cases notified by health facilities to national statistical report in 2013 and 2014

Items	2013	2014
Total number of cancer cases	3,784	3,886
Liver cancer	836	876

Items	2013	2014
Breast cancer	432	387
Cancer of the digestive tract	309	340
Cervical cancer	242	281

There is no registry of number and cause of deaths in Burkina Faso. Of note, many patients are treated by traditional healers and sometimes die without receiving any notification to a health facility. The number of patients is therefore largely underestimated.

Resources in Oncology

There is no specialised cancer centre in Burkina Faso. Cancers remain treated in university hospital centres. The following four centres are the largest hospitals currently treating cancer:

- Centre Hospitalier Universitaire Yalgado OUEDRAOGO Ouagadougou
- Centre Hospitalier Universitaire Souro SANOU Bobo Dioulasso
- Centre Hospitalier Universitaire Pédiatrique Charles de Gaulles Ouagadougou
- Centre Hospitalier National Blaise COMPAORE Ouagadougou

One medical school is located in Ouagadougou, the "Ecole Superieure de Sciences de la Sante", University of Ouagadougou.

Human Resources

Medical Oncology resources in Burkina Faso are limited.

Table 3: Summary of available medical oncology resources in Burkina Faso

Population	18,184,000
Number of pathologists	8
Number of pathologists per million population	0.44
Number of pathologists in training	0
Number of oncologists	3
Number of oncologists per million population	0.16
Number of histotechnologists	3
Number of histotechnologists in training	0
Number of cytotechnologists	0
Number of cytotechnologists in training	0
Histo/cytotechnologists per million	0.16
Are IHC services available?	No
Is chemotherapy available?	Yes
Is radiation therapy available?	No
Number of small biopsies (BX) per year	501-1000
Average turnaround for small biopsies	2 wks

Number of fine needle aspirations (FNA) per year	<100
Average turnaround for FNAs	2 wks
Total diagnostic procedures (BX + FNA) per year	501-1000
Average turnaround time for diagnostic procedures	2 wks

For a population of more than 18 million inhabitants, human resources for treating cancer are limited to only 8 pathologists, 2 medical oncologists, 2 surgical oncologists, one radiotherapist, four medical doctors trained on nuclear medicine, one radio-pharmacist. A few additional specialised medical doctors have a training in oncology: two in paediatrics, two in haematology, one in gynaecology, three in general and digestive surgery.

Radiotherapy Resources

Not a single radiotherapy resource is available in Burkina Faso. Patients requiring radiotherapy can sometimes be referred to Ghana or other countries.

Pathology Resources

All pathologists are located in Ouagadougou. The CHU Yalgado Ouédraogo is the reference centre for anatomopathology and is under equipped for fulfilling its activity. Results of pathological exams can not be obtained within three weeks. Two private clinics are also operating and can provide a result with a two week delay. There is no extemporaneous exam.

Lab Resources

One private molecular biology laboratory is in activity in Burkina Faso but not known by oncologist. This results in as absence of collaboration.

Table 4: Lab responses

Pathologist Training	No
Pathology Services	No
Diagnostic Services	Unknown

Oncology Policy

Cancer is recognised as a public health problem for Burkina Faso. This results in September 2013 in the adoption of a strategic plan to fight against cancer, with an ongoing setting up of a dedicated cancer centre in Ouagadougou.

There is currently no screening policy ongoing. Few non-governmental organisations organise campaigns for the screening of cervical cancer, they embed in these campaign breast self-examination.

While treatments for breast cancer are almost identical between different health facilities, cancer treatment is in general highly heterogeneous across the country. The absence of a cancer centre results in patient's treatment being organised in different services and in private clinics. A service of medical oncology is linked with the department of general surgery.

In term of primary prevention, smoking in public places is officially forbidden.

Several problems can be identified:

Problems for cancer diagnostics and prevention

Clinically

With the absence of organised screening, early detection is done on an individual basis. Only cervical cancer could benefit from NGO's campaigns. Vaccination against HPV exists in some dispensaries (Cervarix). While smoking in public places is forbidden, the law is not enforced and therefore non-operational.

Pathology

Results from pathological examination are reported with sometimes long delays. Some results are incomplete or non-useable. There is an absence of immunohistochemistry with dosage of hormonal receptors, Her2 and CD. There is no immunological typing and no extemporaneous exams.

Haematology

Trocars for bone marrow biopsies are rare and myelograms delayed.

Medical imaging

Reports are sometimes hard or impossible to exploit. Scanners and MRI are available in the country but not always reachable by patients.

Problems for cancer treatment

An important problem is the absence of institutional multidisciplinary meetings.

Medical Treatment

More than 70% of patients receiving chemotherapy were initially diagnosed with advanced stage cancers. No national protocol exists to define chemotherapy plans to be applied throughout the country, and several anti-cancerous drugs are lacking in hospital and national pharmacies although some molecules can be available in private pharmacies. Mostly used molecules are: doxorubicin, cyclophosphamide, fluorouracil, docetaxel for breast cancer, cisplatin for cervical cancer and methotrexate for choriocarcinoma. All other molecules can only be obtained by purchasing them in private pharmacies. Conditions for elaboration of anti-cancerous drugs are inadequate with no centre for preparing them and no trained paramedical personnel to administer drugs, drugs are prepared for administration by external service providers.

Anti-cancerous and adjuvant drugs are expensive and not covered by health insurance. It results that all costs should be handled by the patients. Morphine treatments are rarely available.

Surgical Treatments

With a majority of advanced stage tumours, surgery is often limited to palliative surgery while more and more patients are diagnosed with operable cancers. Surgical skills are concentrated in Ouagadougou only. As mentioned earlier, a limitation of surgical treatment is the absence of extemporaneous exams. Material for surgery is often lacking or absent such as material for oncoplastic surgery and implantable ports.

Radiotherapy Treatment

As mentioned earlier, there is no radiotherapy machine in Burkina Faso.

Other Difficulties

Other difficulties are worth mentioning. There is major insufficient human resources in oncology, paediatric oncology, pathology, onco-haematology, onco-gynaecology, and trained paramedical personnel.

There is an absence of statistics in oncology with the cancer registry of Ouagadougou not operational anymore and no hospital statistics. Overall, no support for patients to cover treatment costs.

Perspectives

Some perspectives of improvements in oncology are ongoing in Burkina Faso. First, a strategic national plan to fight against cancer is in deployment phase. A cancer centre will be established in Ouagadougou. Universal health coverage will be developed and reduce the burden of cancer treatment costs to the patients.

Chapter 16c

Burundi

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* This chapter should be referenced as: Ngendahayo L, Niyongere JO, Ntagirabiri R, Kamwenubusa G. Burundi. In: Boyle P, Ngoma T, Sullivan R, Ndlovu N, Autier P, Stefan S, Fleming K and Brawley OW. The State of Oncology in Africa 2015. iPRI Scientific Publication 4, iPRI, Lyon, France (2016).

Burundi is a landlocked country in East Africa with a total area of 27,834 km^2. The country is divided into 19 provinces. According to the 2008 census Burundi has a total population estimated to 9,863,117 millions in 2010. There is a slight preponderance of women. The population is relatively young with 45.7 percent being below the age of 15 years and 19.3% aged between 15-24 years. This represents 65% of the population under 25 years and only about 2.5% being 65 years and above. The population growth rate is 3.28%. Most of this population (89.1%) lives in is rural areas and about 10.9% urban population. Life expectancy from birth is approximately 59 years.

Cancer Registration and Overview of Cancer

Burundi does not have national cancer registry and therefore the data for the incidence of cancers and cancer mortality in Burundi can only be estimated. A study conducted from 1984 to 2008 discovered 4,305 cancer cases (unpublished data). This survey showed that most frequent cancers in men are stomach (16.99%), soft tissue and Kaposi's Sarcoma (12.09%), skin cancer (9.78%) and lymphoma (7.26%). The most frequent cancers in women are cervical cancer (15.35%), breast (12.78%), stomach (12.58%), skin (7.55%) and lymphoma (7.15%).

Others findings from the 7th Congress of Surgery organised by the Burundian Association of Surgery (ABUC) in October 2013, highlighted that stomach cancer is the commonest form of cancer in men followed by lung and prostate. Cervical cancer, breast and ovary are the most common cancers in women. In children, retinoblastoma and nephroblastoma are the two most frequent solid tumours.

There is lack of data on HIV/AIDS related to cancers.

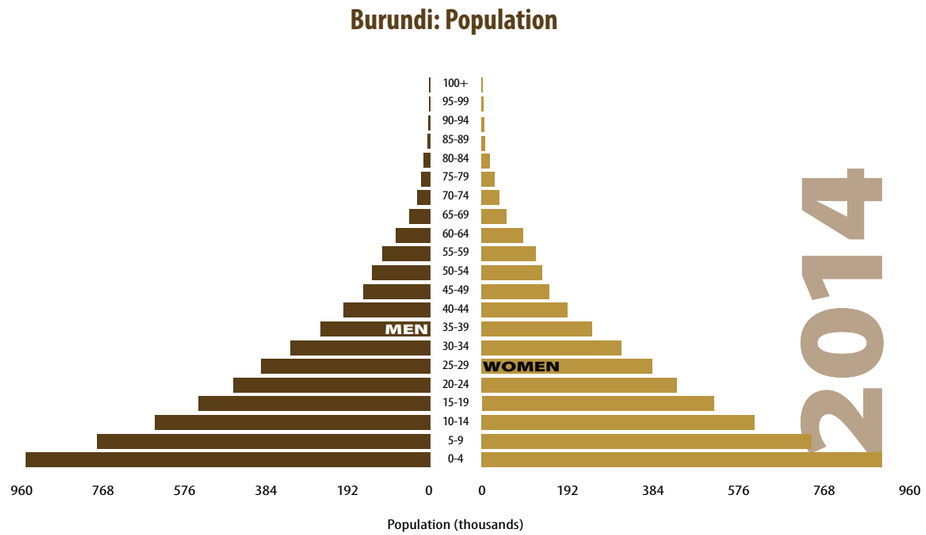

Figure 1: Population Pyramid by Age Group and Gender, 2014 (CIA World Factbook)

Cancer Centres

There is no oncology unit in the country. The four referral hospitals are University Hospital Centre of Kamenge (Centre Hospitalier Universitaire de Kamenge, Bujumbura) called also "King Khaled Hospital", Prince Charles Hospital, Kamenge Military Hospital and Prince Louis Rwagasore Clinic. All are located in Bujumbura and are handling cancer cases based essentially on a surgical approach.

Medical Oncology Resources

There are no radiotherapy resources or chemotherapy drugs available in the country. The policy of supplying chemotherapy drugs is lacking.

Pathology Resources

Histopathology services are centralised in the only laboratory existing at the University Teaching hospital (CHUK) located in the capital city, Bujumbura. It takes between 1 week and 6 weeks to get a histology result. Immunohistochemistry stains and molecular tests are not performed.

A number of reasons govern such time factors, these include distance of the specimen collecting centre to the main hospital, time taken to process the specimens and release results. Shortage of reagents, broken equipment and lack of good maintenance are additional reasons existing

in that laboratory. Services are greatly affected by shortage of skilled staff. There are only 2 pathologists for the whole country. It is estimated that 12 pathologists are needed for the whole population of Burundi if one pathologist is to serve 250 000 people. The three technicians working in the laboratory are trained on the bench and qualified as histotechnologists.

Appropriate preservation of specimen is needed and includes prompt immersion in formalin. Sometimes this can present challenges especially in outlying areas where alternative media may be used which may distort results. Due to a limited number of pathologists and lack of equipment, quick-frozen section diagnosis is not available. Fine needle aspiration is not frequently performed in the teaching hospital and is not available in all hospitals.

There is no residency training in pathology in the country.

Oncologists Available

There is no medical/radiation oncologist or paediatrician, surgeons, gynaecology oncologist working in the country. There is no residency training in radiation oncology/clinical oncology in country.

The National Cancer Control and Prevention Program

The Ministry of Public Health and Aids Control formulated and adopted the National Cancer Control policy and programme and the Cancer Prevention and Control Strategy (2015-2020). The overall goal of the strategy is to reduce cancer morbidity and mortality through implementation of evidence-based, cost-effective prevention and control interventions and providing palliative care to improve quality of life of people living with cancer and their families by 2020. The Goal Areas are Programme Strengthening, Primary Prevention, Early Detection, Diagnosis and Treatment, Palliative Care/Rehabilitation and Surveillance and Research.

Prevention and Early Detection

Currently there is no screening programme for cervical cancer or breast cancer. However at the individual level, the practice of taking Pap smears, making mammography screening and PSA testing are recommended by clinicians for those people who can afford to pay.

The main risk factors contributing to the high incidence of cancer in Burundi, as with most African countries, include infectious agents and lifestyle related factors such as tobacco use, harmful alcohol use, unhealthy diets and physical inactivity. Prevention becomes the most cost-effective intervention; therefore, this approach that has been adopted in Burundi. Many of the cancers are diagnosed at an advanced stage, due to limited resources. A focus on early detection is therefore warranted.

Tobacco

It is important to be noted that the Framework Convention for Tobacco Control has not yet been ratified in Burundi.

Alcohol Consumption

There is no national survey of alcohol consumption and the prevalence is unknown. Some measures have been taken to try to reduce the consumption of alcohol for example restricting the places and times alcohol is available and raising the minimum legal age at which alcohol is purchased.

Diet and Exercise

The prevalence rate of obesity is 2.9% (2008) in Burundi. The life style in urban areas is changing. The message of losing weight and exercising to help reduce the risk of developing cancer is promoted through some media.

Infections

At national level, the prevalence of HBV is 4.6% and 8.1% for HCV (Ntagirabiri R et al, 2014). Infectious risk factors which promote cancer in Burundi include HPV, Hepatitis B and C, HIV, EBV, Helicobacter Pylori. Promotion of interventions such as hepatitis B vaccination is offered in large immunisation programme.

HPV vaccination was approved in 2014 and supported by the Global Alliance on Vaccines and Immunisation (GAVI): this requires sharing ability to vaccinate an adolescent population. In April 2016, the HPV vaccination demonstration project will be implemented in two district hospital: Rumonge and Ngozi have been selected for this project. Vaccination will be conducted in 10 year old girls using the school based strategy. National scale up vaccination will follow.

Cancer Screening Services

National cancer screening programs are not yet running in the country. Initiatives for individual screening are organised in different clinics/ hospital for some conditions and cancers: these include cirrhosis surveillance in HBV and HBC chronic infection, pap smears for cervical cancer and mammography for breast cancer.

Awareness of the importance of breast self-examination still needs to be prioritised together with instruction on the technique of how to perform self-examination of the breasts.

Cervical Cancer

Visual Inspection with Acetic Acid (VIA) was initiated in health centres located in the capital city after training organised by a team of researchers from the Department of Obstetrics and Gynaecology, the pathology laboratory, University of Burundi and in collaboration with the Division of Non communicable disease of MOH under the logistics support from WHO office in Burundi.

PAP smear services are available at the pathology laboratory of the University teaching hospital but not available to the majority population in need for screening.

Palliative Care

Palliative care and rehabilitation are not well organised for cancer patients in Burundi.

Drugs

There is a lack of drug supply and there is no policy for managing their supply and distribution.

Education of Cancer Care Professionals (human resource development)

There is no existing training programme for different categories of cancer care professionals. This is a challenge which requires to be overcome for the success of the implementation of the cancer prevention and strategy adopted recently by MSPLS. It is essential to develop a multidisciplinary approach to cancer management.

The Cancer Community

There are a few numbers of local voluntary organisations that are involved in cancer efforts in Burundi.

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Chapter 16d

Cameroon

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The Republic of Cameroon is a bilingual country (French and English) in the Central Africa region. Its surface area is 475,440 km² and its total population is 19,406,100 inhabitants, according to the 2010 census. The Ministry of Public Health is responsible for Cameroonian population's health issues. This Ministry has developed several plans relating to the main public health issues of the country. One of them is the National Plan to Fight against Cancer. Founded in 2002, this plan is in charge of managing cancers across the country. It mainly aims at reducing cancer incidence, morbidity and mortality. To this end, prevention, diagnosis and treatment activities are carried out in some cities of the country.

Epidemiological Data

In Cameroon, an average of 14,000 new cancer cases is registered each year, with 25,000 prevalent cancers. When patients arrive in cancer centres, about 80% of them are diagnosed at an advanced stage of cancer. According to estimates by the Yaounde Cancer Registry, 8 to 10% of deaths are due to cancer.

Between 2004 and 2011 Yaounde Cancer Registry has registered 6,152 registered cancer cases, approximately one third in men and two-thirds in women. Children represent 10.3% of cases (633 cases). Figure 1 shows the most common cancers.

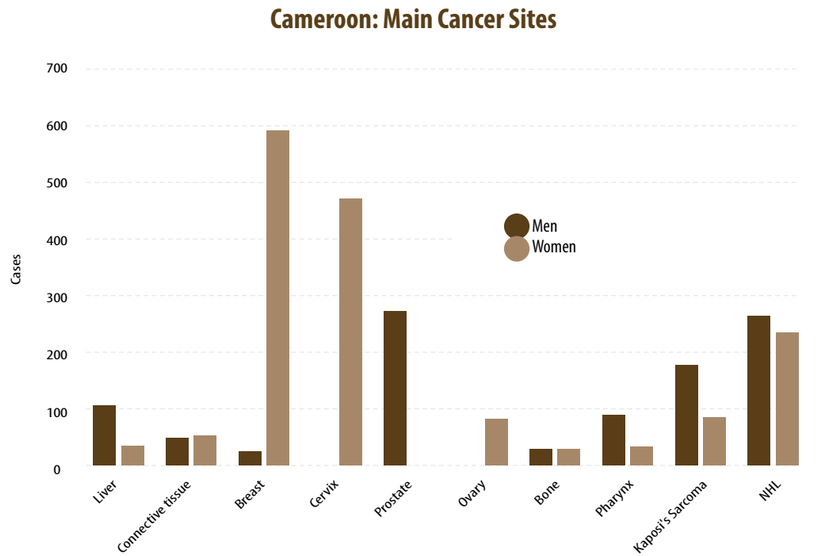

Figure 1: Main cancer sites in men and women, 2004 – 2011

Source: Yaounde Cancer Registry

In 2012 hospital statistics of the most important Department of Medical Oncology of the country, at Yaounde General Hospital (SOMHGY), show that most cancers occur in young people and women (Tables 15.3.1 and 15.3.2). They also present frequently at an advanced stage (Ekortarh and Ndom, 2005).

Table 1: Distribution of cancer cases at SOMGHY by age group in 2012

Age group	Number of cases	%
[0 - 4]	1	0.1
[5 - 10]	2	0.2
[11 - 20]	29	3.1
[21 - 30]	98	10.5
[31 - 40]	188	20.1
[41 - 50]	227	24.2
[51 - 60]	219	23.4
Total	937	100

Age group	Number of cases	%
[61 - 70]	108	11.5
(+70)	57	6.1
undefined	8	1.0
Total	937	100

Table 2: Distribution of cancer cases by gender in 2012

N°	Gender	Number of cases	%
1	Female	606	64.7
2	Male	331	35.2
Total	937	100	

Mass screening is sporadic and mostly focuses on breast, cervical and prostate cancers. Only two to three regions are concerned by this screening, due to lack of logistics and financial resources. A training course for cytologists and midwives took place in 2006 and 2007, in order to increase human resources within screening teams.

Cervical cancer screening in Cameroon is carried out with smear tests and by visual inspection with acetic acid (VIA) or lugol's iodine (VILI). Regarding breast and prostate cancers, medical examination is the preferred screening method, supported by mammography, ultrasound scan techniques and PSA blood test, depending on the case.

Vaccination Campaign

Vaccination against viral hepatitis is part of the Expanded Program on Immunization (EPI) of Cameroon between 0 and five year old. HPV vaccination is not yet systematic, although a preliminary study on Gardasil involving 5,000 young girls has already been carried out in 2009.

Awareness Campaigns

Awareness campaigns are conducted in some communities or through media and usually target the fight against risk factors, especially smoking and environmental factors. NGOs, as for instance SOCHIMIO (Solidarity Chemotherapy) play a major role in education and communication in spite of their lack of financial means.

Diagnosis

Cancers are mostly diagnosed in large hospitals, which have laboratories of anatomical pathology and more radiological equipment (standard x-ray, scanner and MRI). Diagnostic nuclear medicine is only practised at Yaounde General Hospital. The Pasteur Centre in Cameroon is the reference laboratory for the dosage of tumour markers and hormone receptors.

Therapies

The main cancer therapies are surgery, chemotherapy and radiotherapy (Ndom, 2008). Targeted therapies are not yet implemented. These therapies are used in general hospitals in Yaounde and Douala. At this level there is a critical issue of supply of antimitotics and maintenance of radiotherapy equipments. Medical oncologists and radiotherapists are too few and are gathered in both the biggest cities of the country, Yaounde and Douala.

Palliative Care

There is no actual centre for palliative care. Considering the high number of examined patients who have advanced-stage cancer, most treatments are palliative. The main analgesics, especially morphine, are not used at a large scale. SOCHIMIO is conducting a project about palliative care at home, but it struggles to start due to the lack of funding.

Follow-up

The large distances between care centres and places where patients live leads to a high number of lost to follow-up. Therefore follow-up care is problematic. Some district hospitals are not trained for the follow-up of cancer patients.

Research

Research in oncology is mostly carried out in general hospitals and in faculties of medicine during some thesis works. Research is rarely funded.

Training of Human Resources

For about three years, the Faculty of Medicine and Biomedical Sciences of the University of Yaounde has been training medical oncologists, radiotherapists, anatomical pathologists, radiologists and other specialists. The Republic of Cameroon is behind the times in terms of training of nurses and specialised technicians.

Difficulties

There are considerable challenges in providing adequate cancer care in the Republic of Cameroon as well as other developing countries (Price et al, 2011). Difficulties in management of cancers in the Republic of Cameroon are due to the very small grant awarded to the National Plan for Fight against Cancer by the Ministry of Public Health and international organisations. There is no social security in the Republic of Cameroon and cancer patients have to pay themselves their treatments. All antimitotics are imported. One cancer treatment sometimes costs five times as much as the patient's annual income. The delayed arrival of patients to the hospital shows the insufficiency of awareness, as well as financial and logistics difficulties faced by these patients. The northern part of the country is very far from specialised hospital trainings that are concentrated in the central region of the Republic.

Outlook

The fight against cancer in the Republic of Cameroon should extend to the most distant communities, more focusing on education and communication. This action will require more logistics, financial and human resources. An international grant like those awarded to plans for AIDS, tuberculosis and malaria wouldbe of major importance to help solve cancer patients' problems. The same applies for the opening of a cancer institute in Yaounde. Training of human resources (doctors, nurses, technicians, etc.) is essential when we know that, according WHO, "65% of cancers will come from developing countries in 2020 if nothing is done".

Chapter 16e

Congo - Brazzaville

Judith Nsondé Malanda*

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The Republic of Congo, also known as Congo-Brazzaville, is located in Central Africa. There were 4,755,000 inhabitants as of 2015. The population is very young as more than 50% of the population is aged below 25 years of age.

Cancer Burden

The Brazzaville population-based cancer registry (PBCR) collects data on cancer cases occurring in the Brazzaville population. It was created in 1996 with the support of the International Agency for Research on Cancer and has been collecting reliable data since 1998 (Nsondé Malanda et al, 2013). The registry gathers information on new cancer cases from four hospitals and four private clinics. It covers a population of around 1,700,000, i.e. around a third of the total country population (Figure 1). The population structure is similar to the rest of the country, with a very young population.

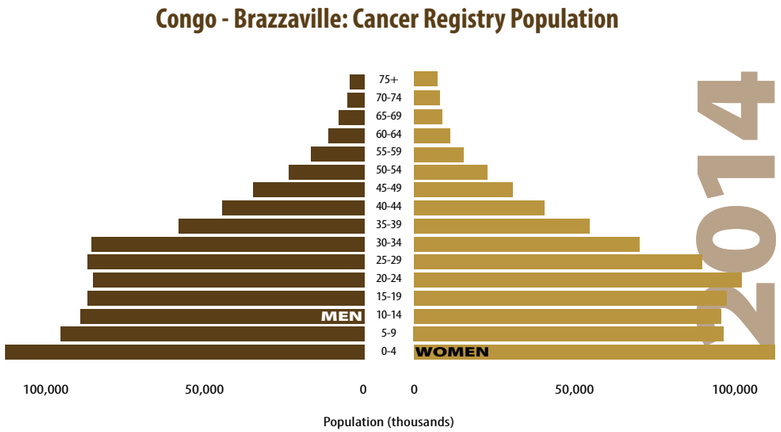

Figure 1: Population pyramid of the population covered by the Brazzaville cancer registry, 2014.

The most common cancers in men are prostate, liver, stomach, skin and lung (Table 1).

Table 1: Frequency of cancer sites by age in men, from the Brazzaville cancer registry.

Site	ICD-O	Age Group																Total	%
		0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-+		
Prostate	C61.9	0	0	0	0	0	0	0	0	0	0	0	2	8	53	26	17	106	37.7
Kidney	C64.9	0	3	0	0	0	0	0	1	0	0	1	0	0	0	1	0	6	2.1
Bladder	C67.9	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0	1	3	1.0
Lip	C00.9	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	0.3
Tongue	C02.9	0	0	0	0	0	2	0	0	0	0	0	0	0	1	0	0	3	1.0
Nasopharynx	C11.9	0	0	0	0	0	0	0	0	0	0	0	0	3	1	0	0	4	1.4
Larynx	C32.9	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	0.3
Salivary Gland	C02.9	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	2	0.7
Lung	C34.9	0	0	0	0	0	0	0	0	0	0	1	0	1	5	1	0	9	3.2
Oesophagus	C15.9	0	0	0	0	0	0	0	0	0	0	1	0	1	2	2	0	7	2.4
Stomach	C16.9	0	0	0	0	0	0	0	1	3	0	5	4	1	1	0	0	16	6.0
Colon	C18.9	0	0	0	0	0	0	0	0	1	0	2	0	1	1	0	0	5	1.7
Rectum	C20.9	0	0	0	0	0	0	0	0	0	1	0	0	0	2	0	0	2	0.7
Anus	C21.0	0	0	0	0	0	0	0	0	0	1	1	0	1	1	0	0	5	1.7

Site	ICD-O	Age Group																Total	%
		0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-+		
Liver	C22.0	0	1	1	1	1	4	2	3	10	4	7	3	3	1	4	3	49	17.4
Pancreas	C25.9	0	0	0	0	0	0	0	0	0	0	0	2	1	1	1	0	5	1.7
Lymph node	C77.9	0	0	0	0	0	0	0	0	0	0	1	2	1	0	0	0	4	1.4
Blood	C42.0	0	0	3	0	0	0	0	1	0	0	1	0	3	0	0	0	8	2.8
Bone marrow	C42.1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	2	0.7
Thyroid	C73.9	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0.3
Bone	C40.9	0	0	5	2	2	0	1	0	0	1	0	0	0	0	0	0	11	3.9
Soft tissue	C49.9	0	0	3	0	0	0	2	0	1	0	1	1	1	1	0	0	10	3.5
Breast	C50.9	0	0	0	0	0	0	0	0	1	0	1	2	1	0	0	1	6	2.1
Skin	C44.9	0	0	0	0	0	0	0	0	1	0	1	2	0	4	2	0	10	3.5
Retina	C69.2	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	3	2.4
Eye	C69.9	0	0	0	0	0	0	0	0	0	0	0	1	0	1	0	0	2	0.7
Total		3	4	12	3	3	6	5	6	17	9	24	19	27	80	39	24	281	100

In women, the most frequent cancers are breast, cervix, liver, ovaries and haematopoeitic system (Table 2). In children, cancers of the kidney, retinoblastoma, bones, liver, blood and soft tissues are the most frequent.

Table 2: Frequency of cancer sites by age in women, from the Brazzaville cancer registry

Site	ICD-O	Age Group																Total	%
		0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-+		
Breast	C50.9	0	0	0	0	1	1	6	9	12	22	16	22	14	3	6	3	115	35.8
Cervix	C53.9	0	0	0	0	1	2	3	4	5	6	21	14	12	15	7	3	93	28.9
Ovary	C56.9	0	0	0	0	2	0	1	0	2	1	0	1	3	0	0	3	13	4.0
Corpus	C54.9	0	0	0	0	0	0	0	0	0	0	0	3	1	1	0	2	7	2.1
Vagina	C52.9	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	0.3
Vulva	C51.9	0	0	0	0	0	0	0	0	0	0	0	2	1	0	0	0	3	0.9
Blood	C42.9	0	0	0	0	0	0	0	0	0	1	2	6	2	0	0	0	11	3.4
Lymph node	C77.9	0	0	0	0	0	0	0	0	0	0	2	0	1	0	0	0	3	0.9
Bone marrow	C42.1	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	2	0.6
Eye	C69.9	0	0	0	0	0	0	0	0	0	0	0	1	0	1	0	0	2	0.6
Conjunctive tissue	C00.1	0	0	0	0	0	0	1	0	1	0	0	0	0	0	0	0	2	0.6
Retina	C69.9	3	1	2	0	0	0	0	0	0	0	0	0	0	0	0	0	6	1.8
Lip	C00.3	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	0.3
Salivary gland	C02.9	0	0	0	0	0	0	0	0	0	0	1	0	0	1	0	0	2	0.6
Nasopharynx	C11.9	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	1	0.3
Lung	C34.9	0	0	0	0	0	0	0	1	0	0	0	1	0	1	0	1	3	0.9
Stomach	C16.9	0	0	0	0	1	0	0	0	0	0	2	1	0	0	0	0	5	1.5

Site	ICD-O	Age Group																Total	%
		0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-+		
Pancreas	C25.9	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	2	0.6
Liver	C22.0	1	1	2	0	0	1	3	0	3	1	4	0	0	1	0	2	18	5.6
Colon	C18.9	0	0	0	0	0	0	0	0	2	0	2	0	0	0	0	0	4	1.2
Rectum	C20.9	0	0	0	0	1	0	0	2	0	1	0	0	0	0	0	0	4	1.2
Kidney	C64.9	2	7	0	0	0	1	0	0	0	0	0	0	0	0	0	0	9	2.8
Bone	C40.9	0	0	2	0	1	0	0	0	0	0	0	0	1	0	0	0	5	1.5
Soft tissue	C49.9	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	0.3
Skin	C44.9	0	0	0	0	0	0	0	0	1	1	0	1	0	4	1	0	8	2.4
Total		6	9	6	0	7	5	14	16	26	34	50	55	37	29	16	14	321	100

In terms of age-standardised incidence rates, a recent study reported 30 cases per 100,000 person-years in men for liver cancer, and 4 per 100,000 in women. Rates of breast and cervical cancers were 14 per 100,000 and 12 per 100,000, respectively (Nsondé Malanda et al, 2013).

Resources in Oncology

Cancer Centres

There are cancer centres in Brazzaville (the capital city) and Pointe Noire (the economical capital). Those hospitals employ medical oncologists. There is a radiotherapy service in the University Hospital of Brazzaville. The radiotherapy unit uses a cobalt machine, and this is the only radiation therapy equipment available in the whole country. There is no brachytherapy unit in Congo. Few secondary centres provide services in oncology and surgery.

Human Resources

Cancer health professionals in the Republic of Congo are scarce. In Brazzaville, there is one radiation therapist, one general surgeon with a diploma of Medical Oncology, three onco-haematologists and eight medical oncologists. In Pointe Noire, there are only two medical oncologists. There are no other oncologists in the rest of the country.

The number of patients who need radiation therapy is much higher than the only radiation therapist can handle, which causes delays. In addition, surgical care of cancer cases is often postponed as there is no surgical oncologist.

Unfortunately, the lack of personnel is expected to worsen in the near future as several medical oncologists are close to retirement.

Pathological Laboratories

There are two pathological anatomy laboratories in the Republic of Congo, in Brazzaville and Pointe Noire. The laboratories are limited to morphological studies in 95% of cases. Immunohistochemistry and molecular studies are rarely done. Because of the lack of human resources, it takes between three and 12 months to get results of a sample examination. This leads to more delays in diagnosis and treatment of patients. There is no specific molecular oncology laboratory.

Oncology Policies

A strategic plan to fight against cancer has been adopted in May 2013, yet has not been enforced to date. So far, anti-cancer policies are often the result of isolated experiments.

A tobacco control law has been voted in 2012 at the National Assembly of the Republic of Congo. This law forbids:

- the advertisement of tobacco products on TV, radio and other media;
- tobacco use in public places and public transports;
- sell of tobacco products to minors and pregnant women;
- free distribution of tobacco products;

In addition, prevention messages must be written on tobacco products.

Concerning cervical cancer, two pilot areas received HPV vaccination in 2013-2014. Moreover, there were some prevention campaigns based on visual inspection methods, but they were concentrated in the city of Brazzaville.

Vaccination against hepatitis B has recently been added to the vaccination programme of infants, which should help reducing the incidence of liver cancer in the future.

Finally, breast cancer awareness campaigns have been organised by local associations fighting against cancer. However, no national initiative exists.

Perspectives

Medical Oncology in the Republic of Congo is still an orphan. Structures and human resources are largely insufficient for a nearly 5,000,000 inhabitant's country. There is only one old Cobalt radiotherapy machine and one radiation therapist and no brachytherapy. The lack of personnel leads to delayed diagnosis and treatment of patients, who mostly present at a late stage of the disease. Because of these delays, combined with the late stage at presentation, many patient die before any investigation is conducted, or die before receiving any treatment.

The absence of immunohistochemistry and molecular studies have implications on the availability of targeted therapies. Finally, the unavailability of anti-cancer drugs, remains a problem which partly explains poor adherence to treatment.

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Chapter 16f

Egypt

Cancer Control in Egypt: Current Status, Challenges and Future Priorities

Karima Elshamy*

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Cancer in the developing world is characterized by far more advanced stages at diagnosis, fewer allocated resources for prevention and treatment, and higher incidence than in countries with more developed health systems. In Egypt, it is already and will become an important health problem not only in terms of rank order, but also in terms of incidence and mortality. The commonest sites were liver among men and breast among women. During the period 2013–2050, the population of Egypt is expected to increase to approximately 1.6 times the 2013 population size. Applying the current age-specific incidence rates to successive populations would lead to a progressive increase in number of incident cases of cancer. The resources for cancer control in Egypt are directed almost exclusively to treatment. Most cancers present at an advanced stage (stage III and IV) when cure is improbable even with the best treatments. Comprehensive cancer care requires the integration of palliative care practices and principles across the trajectory of the cancer experience and may be the sole focus of care for those patients with advanced incurable disease. As the incidence of cancer increases worldwide and the burden of cancer rises, especially in low and middle resource countries, the need for palliative care is greater than ever before and this care is most effectively provided by a multidisciplinary team. So, recognizing palliative care as a new subspecialty for nurses, and expansion of palliative care services to a larger number of patients and illnesses throughout the country, considering home-based palliative care service is urgently and badly needed, strengthening health care systems; focusing on patient centred care, education and training to all levels of health care professionals, and effective cancer prevention programmes customized to the community should be fostered, particularly for prevention of hepatitis B and C infection, and breast cancer awareness, reducing cultural barriers, and detecting cancer as early as possible.

Introduction

Cancer is a global and international problem. It is the second leading cause of death worldwide after heart and vascular disease. It accounted for 8.2 million deaths in the year 2012. Among the most frequent causes of death are liver, stomach, colorectal and breast cancers. Unfortunately,

annual cancer cases are expected to rise from 14 million in 2012 to 22 million within the next two decades (Ferlay et al, 2012). Cancer is an increasing problem in Egypt. The commonest sites were liver (23.8%), breast (15.4%), and bladder (6.9%) (Both sexes): liver (33.6%) and bladder (10.7%) among men, and breast (32.0%) and liver (13.5%) among women. By 2050, a 3-fold increase in incident cancer relative to 2013 was estimated, these results based upon results of National Cancer Registry Program (NCRP) (Ibrahim et al, 2014). Egypt is expected to experience the highest increase in the coming two decades. Cancer is already an important health problem and will become increasingly important not only in terms of rank order, as infections are better controlled, but also in terms of incidence and mortality, which will both increase as populations continue to grow and age, and as risk factors for cancer associated with greater affluence continue to increase. At present, resources for cancer control in Egypt are not only inadequate but directed almost exclusively to treatment. This strategy, although successful to a degree, is suboptimal because the impact of preventive measures on incidence is not taken full advantage of, while the lack of approaches to earlier diagnosis reduces the value of therapy. The curability of cancer is directly related to its stage at the time of diagnosis, and in the majority of cancer is generally diagnosed when at a relatively advanced stage. According to WHO, 40% of cancers could be avoided (prevention), 40% could be cured (if detected early) and the rest should be managed with palliation. Prevention therefore offers the greatest public health potential and the most cost-effective long-term approach for cancer control (World Health Organisation, 2009).

Diagnosis of cancer and its treatment can have a devastating impact on the quality of a patient's life, as well as on the lives of families and other care givers. Patients face new fears, uncertainties and may have to undergo unpleasant and debilitating treatments. Therefore, patients and their families need access to support from the time that cancer is first suspected, through all stages of treatment to recovery or, in some cases, to death and into bereavement (Ellershaw et al, 2003). Patients with advanced cancer experience a range of complex problems that cannot always be dealt with effectively by generalist services. Therefore, they require a range of services to ensure that their physical, psychological, social and spiritual needs are met effectively and to enable them to live and die in the place of their choice. Thus, hospices and specialist palliative care services should be accessible and available (NHS CYMRU Wales, 2001).

Palliative care is the active holistic care of patients with advanced, progressive illness. Management of pain and other symptoms and provision of psychological, social and spiritual support is paramount. The goal of palliative care is achievement of the best quality of life for patients and their families. Many aspects of palliative care are also applicable earlier in the course of the illness in conjunction with other treatments (World Health Organisation, 2002). Palliative care goes beyond the traditional medical model to focus on psychosocial issues, spiritual matters, medical decision-making, and on the relief of suffering in all its dimensions throughout a person's illness (Smith et al, 2012). Because of its focus on the whole person, more experts are advocating that a palliative approach to care could and should be integrated into care for all people with chronic, life-limiting conditions (including cancer). The rationale for integrating palliative care into chronic disease management is the recognition that people with chronic diseases often have a long illness trajectory and, during that time, may have different palliative care needs. As their disease progresses, they may experience a complex range of social and emotional needs including isolation, decreased independence and burden on family members. Most people with chronic illnesses other than cancer often reach the terminal phase of their life without having been offered many of the physical and social resources available through palliative care (Fitzsimons et al, 2007).

Egypt: Background Information

Egypt is located in the north-eastern corner of Africa. Rectangular in shape, it covers an area of 386,000 square miles. To the West lie the Western Desert and Libya, and the East is bordered by a desert plateau, Red Sea, Sinai and Israel. The Sudan is on Egypt's southern border and to the North lies the Mediterranean. Egypt can be divided into: The Eastern Desert, The Western Desert, and The Nile Valley. 90% of Egypt is desert; the majority of the people live near the banks of the Nile River where suitable land for cultivation can be found. The majority of the 80 million Egyptians reside in 3% of the total geographic area. Cairo, the capital city and Alexandria are the major inhabited centres.

The people: Population (2012 est.): 83,688,164 (growth rate: 1.92%.Cairo, 10,902,000, Alexandria, 4,387,000; Giza, 2,597,600 and the country is divided into 26 governorates. Poverty has declined over the past few decades; however, there is disparity - poverty in Upper Egypt increased from 29 to 34% in rural areas and from 11 to 19% in urban areas. Although Egypt has experienced a rapid transition to lower fertility, Egypt is the second most populous country in the WHO Eastern Mediterranean Region, with 43% of the population living in urban areas and overcrowded conditions. The Egyptians are outgoing, warm and have a distinct sense of humour. They have respect and a liking for foreigners, and a deep sense of tolerance for other races, religions and nationalities (CIA World Factbook, 2011).

Language: Arabic is Egypt's official language. However, most Egyptians understand and speak English and French. In larger towns, the foreign visitor will encounter no difficulty in communicating with the people (World Health Organisation, 2013a).

Religion: Approximately 85 percent of the populations of Egypt are Moslems. Most of the balance, about 9 million, is Christian Orthodox who belongs to the Coptic Church. In most cities in Egypt, mosques and churches can be found next to each other. There are also some synagogues since a small Jewish community still lives in Egypt (World Health Organisation, 2013a).

Economy: Egypt is classified as a lower-middle-income country; however, characteristics of high-income, middle-income, and low-income countries coexist. Poverty has declined over the past few decades; however, there is disparity - poverty in Upper Egypt increased from 29 to 34% in rural areas and from 11 to 19% in urban areas (World Health Organisation, 2013a).

The structure of the Egyptian Government is a democracy in transition, having recently elected a president; with all political authority is vested in the Government in Cairo (World Health Organisation, 2013a).

The Egyptian health system: The health care system in Egypt is quite complex with a large number of public entities involved in the management, financing and provision of care. Egypt's wide network of public (several Ministries beside the military and police), NGO, faith based charity organizations and private health facilities allow good geographic accessibility and coverage. The Ministry of Health and Population is responsible for overall health and population policy as well as the provision of public health services, and is responsible for health insurance organization that provides services too. The Ministry of higher education is however responsible for health profession education (medical, nursing, dentistry and pharmacy etc.) and also runs university teaching hospitals. Public health expenditure is low and has pluralistic and complex financing mechanisms: tax-based financing; health insurance and fee for service through out-of-pocket expenditures. To achieve universal coverage, Egypt is rolling out a new insurance scheme, currently being piloted in Suez Governorate, based on a 'family physician model' which will separate financing from service provision. Despite Government's efforts for universal coverage, about half of total health expenditure comes from out-of-pocket (50%) at the point of service in public and private facilities. Egypt produces over 90% of the pharmaceuticals it consumes. Pharmaceuticals account for just over one-third of all health spending, of which approximately 85% is private expenditure. Publicly produced medicines are heavily subsidized, which to a considerable extent accounts for their overuse (World Health Organisation, 2013a) (Ministry of Health and population, 2008).

The Egyptian constitution enshrines free medical care as a basic right for all citizens, and though access to primary health care is fairly widespread, this ideal has yet to be fully realized. Vaccination rates, a good indicator of the access to basic health services, are high, and Egypt has also achieved some success in controlling communicable diseases. However, access to even basic services varies widely according to gender, region of residence, and socio-economic status (World Health Organisation, 2013a) (Ministry of Health and population, 2008).

The organization of the Egyptian health system is fairly complex. Public health care is highly centralized within the Ministry of Health and Population (MOHP), though a number of other public entities are involved in managing and financing health care services. The most important of these are the Health Insurance Organization (HIO), which finances and provides services to almost half the population, and the Ministry of Higher Education (MOHE), which is responsible for medical education and some service delivery (i.e. in University Hospitals). There is no overarching institutional oversight of all public entities involved in providing health services, limiting coordination between the various branches (World Health Organisation, 2013a), (Ministry of Health and population, 2008).

Organization of the Health System in Egypt

Figure 1: Organisation of the Health System in Egypt

Expenditure on health: is divided in the following manner: 36% goes to pharmaceuticals, 19% to services provided by the MOHP, 18% to the private sector, 10% to university hospitals, 8% to services provided by the insurance system, 6% to NGOs, and 3% to other public institutions. Private insurance is fairly limited in Egypt, as premiums are low and companies find it hard to turn a profit. Recent reforms have de-regulated premiums, making the regulatory environment somewhat less restrictive, but still difficult to operate in (World Health Organisation, 2013a) (Ministry of Health and population, 2008) .

Medicine and Health Care:

- Naturalistic and social causes of sickness include bad luck, stress and bereavement; for children loss of love, germs, wind and drafts, hot/cold, imbalance and fear. Supernatural causes are Evil Eye (most Arabs believe in Evil Eye and keep special amulets during illness), God's punishment for sins and the curse of the devil.
- Illness and suffering are believed to be God's will.
- Mental illness is highly stigmatized and help is sought in advanced stage. The Zar, a 'trance religious ceremony', using drumming and dancing is thought to cure mental illness caused by a demon.
- Disabled are treated with compassion and indulgence, and kept from the public as those with genetic defects; genetic counselling is generally refused.
- Institutional care is shunned. Egyptians will likely combine the present health system with traditional beliefs and customs for the purpose of healing.
- Camphor ointment, herbs as teas and poultices are used to treat cold, abdominal discomfort, musculoskeletal aches and pains.
- In Egypt, there are the traditional health practitioners such as seers and spirit healers. When the Arabs came to Egypt, Arabic medicine was practiced. These traditional herbal medications are available in Attar shops and an increasing number of Egyptians are seeking herbal remedies because they are cheap and viewed as safer.
- Medical professionals should avoid frank discussions of diagnosis and poor prognosis.
- Families may prefer to tell the information to the patient, but may ask a healthcare provider to be in attendance.
- The information should be given gradually and in a prolonged manner. Arab patients express their pain comparing it to fire, knives, rocks and iron.
- The patient's concentration is on the present pain experience. The pain scale response may not indicate the actual acuity, for example, minor pain may be reported as a 10. Pain injections are thought to be more effective than pills.
- Most patients and families may avoid activities after surgery such as ambulation, coughing, and physical therapy for fear of pain and prolonging the disease.
- Admittance of depression and symptoms of depression are never disclosed. Verbal permission based on trust is more acceptable than written consent.
- Patients and their families do not like knowing about the potential complications before a medical procedure because it is thought to be bad luck (Lamar Soutter Library, 2016).

Death and the Afterlife: Death is feared, accepted as "God's will", but believe death should be delayed by biomedical interventions. Critically ill patients may prefer to die in the hospital. Families will not openly grieve before death of family member; they will however grieve openly and loudly and a private room may be beneficial. After death Christians and Muslims try to bury the body the same day. Koran reading may be an indicator of the Islamic condolence sessions. Condolences are expressed without delay, and again after 40 days and after a year. Christian Families may ask for a minister or priest to visit. Egyptian Muslims do not need an Imam present. Egyptian Muslims handle the body by same gender Muslim with modesty; oropharyngeal orifices are sealed with cotton, the body is covered with a sheet and turned towards Mecca (Lamar Soutter Library, 2016).

Magnitude of Cancer Care in Egypt

The Demographic Profile of Egypt

1. Population Trends

   A. The Population Size of Egypt: Currently, Egypt is experiencing significant size, age structure changes that will have major implications for its socioeconomic development. The population size of Egypt increased from 44.9 million in 1980 to approximately 78.1 million in 2010. It is projected that in 2050, the population size of Egypt will reach approximately 121.8 million as shown in Table 1, (United Nations, 2012).

Table 1: Egypt's population, both genders (thousands)

Year	Men	Women	Total
1980	22,516	22,416	44,932
1985	25,257	25,089	50,347
1990	28,301	28,035	56,337
1995	30,731	30,437	61,168
2000	33,269	32,867	66,137
2005	36,081	35,696	71,778
2010	39,206	38,869	78,076
2015*	42,536	42,170	84,706
2020*	45,690	45,372	91,062
2025*	48,609	48,380	96,989
2030*	51,330	51,223	102,553
2035*	53,933	53,967	107,900
2040*	56,410	56,590	113,001
2045*	58,688	59,000	117,689
2050*	60,686	61,111	121,798

* United Nations. Word Population Prospects: The 2012 Revision. Available from: http://esa.un.org/wpp/unpp/panel_indicators.htm.

B. Population Growth in Egypt: The growth rate of the population of Egypt has been decreasing since the period 1980-1985, where it stood at 2.28 per cent. It reached 1.56 per cent in the period 1995-2000 and slightly increased afterwards to 1.68 per cent in the period 2005-2010. The population growth rate is expected to continue declining and will reach 0.69 per cent in the period 2045-2050.

2. Indicators of Demographic Transition

A. Mortality Transition in Egypt – Life Expectancy at birth in Egypt gained 10 years from the period 1980-1985 to the period 2005-2010, increasing from 59.9 years to 69.9 years. It is expected to reach 77.3 years in 2045-2050.

3. The Population Structure

A. Egypt's Population Age composition — The proportion of the population under 15 years of age has been decreasing since 1980 and is estimated to continue declining to 2050. At the same time, the proportion of the working-age population (15-64) has been increasing since 1980. It is projected to reach 66.9 per cent in 2040 then it will decline to 65.9 per cent in 2050. The proportion of the elderly population (65+) has also been increasing and is expected to reach 12.3 per cent in 2050. The age distributions in Egypt vary widely with major differences in the percentage of young and old as seen in Table 2. Hence, currently there is less cancer, but the expected change in demographics over the next 20–30 years is likely to result in an explosive increase in non-communicable diseases such as cancer and heart disease as shown in Table 2, (United Nations, 2012).

B. Changing Age Structure — In 1950, the pyramid had a wide base signalling the structure of a young population. In 2050, the pyramid is expected to narrow down (United Nations, 2012).

Table 2: Egypt's Population Age composition

	Population by age group (%)			
Year	0-4	5-14	15-64	65+
1980	15.3	25.0	55.2	4.5
1985	15.2	24.5	55.6	4.6
1990	14.7	24.8	55.7	4.8
1995	12.6	25.3	57.1	5.1
2000	11.8	23.6	59.2	5.3
2005	11.2	21.3	62.0	5.5
2010	11.4	20.1	63.0	5.5
2015*	11.0	19.9	63.2	5.9
2020*	10.1	19.9	63.7	6.3
2025*	9.3	19.0	64.7	7.1
2030*	8.7	17.7	65.7	7.9
2035*	8.3	16.5	66.5	8.7
2040*	8.0	15.7	66.9	9.3
2045*	7.6	15.2	66.7	10.5
2050*	7.1	14.7	65.9	12.3

* United Nations. Word Population Prospects: The 2012 Revision. Available from: http://esa.un.org/wpp/unpp/panel_indicators.htm.

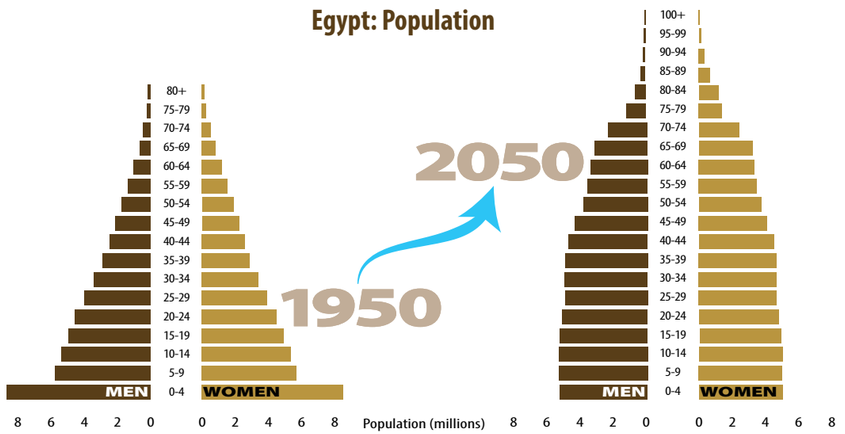

Figure 2: Egypt's Changing Age Structure

C. Egypt's Youth Population — In 1980, youth aged 15 to 24 years constituted 19.4 per cent of the total population and 35.16 per cent of the working-age population. In 2005, the percentage of youth increased to reach 21.1 per cent of the total population then started decreasing and is projected to reach 14.5 percent in 2050 (United Nations, 2012).

D. Egypt's Elderly Population — The percentage of the Elderly population (65+) in Egypt increased from 3.0 per cent in 1950 to 5.5 per cent in 2005 and remained as such in 2010. It is projected to continue increasing to reach 12.3 per cent in 2050 (United Nations, 2012).

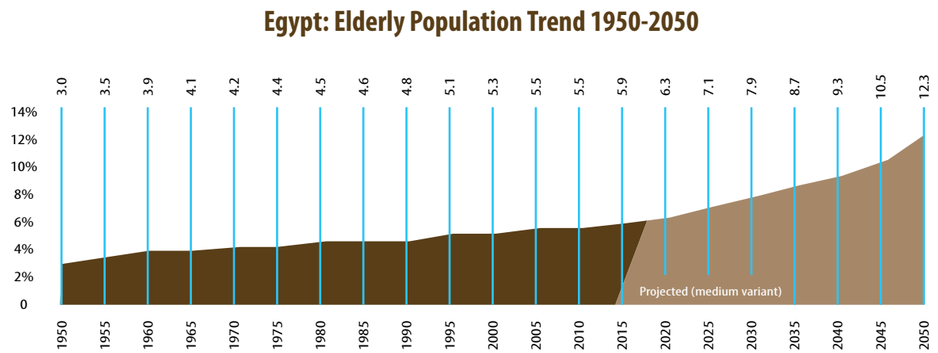

Figure 3: Egypt's Elderly Population

Source: UN World Population Prospects 2012 revision

Current status of cancer care in Egypt

An Overview and Profile of Frequent Cancers in Egypt

Table 4: The most frequent cancers in Egypt estimated using the results of the National Population-Based Registry Program of Egypt 2008–2011. (Ibrahim et al, 2014)

Site	Percentage	Crude Rate	ASR
Men			
Liver	33.63	39.5	61.8
Bladder	10.71	12.6	21.1
Lung#	5.69	6.7	10.4
Non-Hodgkin lymphoma	5.48	6.4	8.8
Brain##	5.48	6.4	8.8
Prostate	4.27	5.0	9.3
Women			
Breast	32.04	35.8	48.8
Liver	13.54	15.1	24.4
Brain##	5.18	5.8	8.0
Ovary	4.12	4.6	6.3
Non-Hodgkin lymphoma	3.80	4.2	6.1
Thyroid	3.28	3.7	4.3

Site	Percentage	Crude Rate	ASR
Both Sexes			
Liver	23.81	27.5	43.6
Breast	15.41	17.8	24.3
Bladder	6.94	8.0	13.5
Brain##	5.29	6.1	8.5
Non-Hodgkin lymphoma	4.64	5.4	7.5
Lung#	4.22	4.9	7.5

Includes trachea, bronchus, and lung tumours.

Includes brain and nervous system tumours

In men, liver and bladder cancers represented approximately 44% of cancer.

In women, breast cancer occupied the top rank accounting for 32.4% of all cancers, followed by liver which accounted for 13.54%.

In both sexes, the proportions and rates of the most frequent cancer sites by gender, there was predominance of liver, breast, and bladder cancer that represented approximately 46% of all cancers (Table 4).

Cancer Mortality Profile: According to World Health Organization - Cancer Country Profiles, 2014, 39,300 deaths were among men, and 33,000 deaths were among women as illustrated in Figure 4.

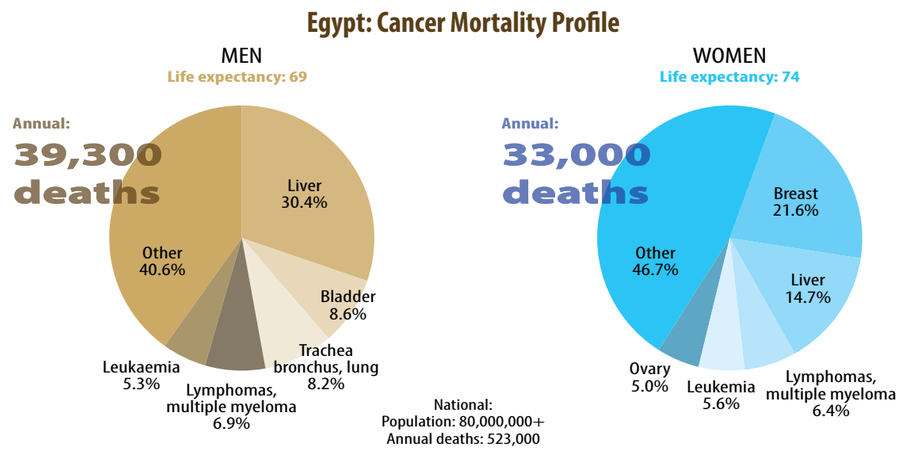

Figure 4: Cancer mortality profile (World Health Organisation, 2014)

Source: Age-Standardized Cancer Mortality Trends: According to World Health Organization - Cancer Country Profiles, 2014.

Figure 5 illustrates Age-Standardized Cancer Mortality Trends among men and women.

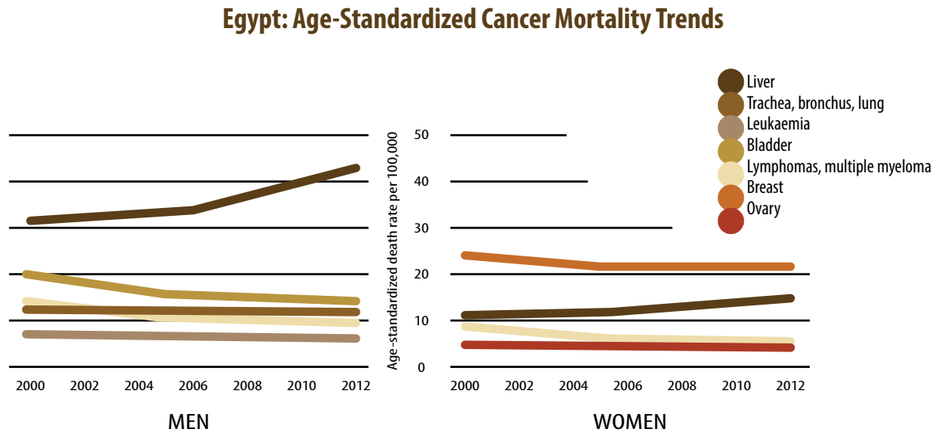

Figure 5: Age-standardized cancer mortality trends

Source: Cancer Incidence: According to World Health Organization - Cancer Country Profiles, 2014

Figure 6 illustrates cancer incidence among men and women, breast was the highest among women, and liver among men.

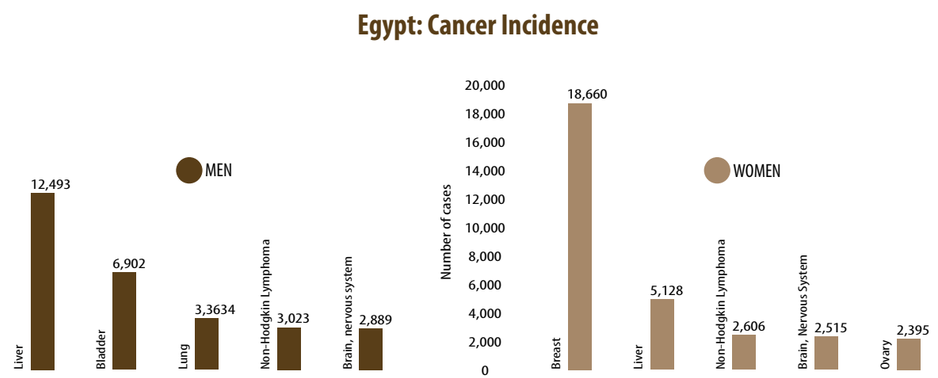

Figure 6: Cancer Incidence

Source: World Health Organisation, 2014

Table 5: Cancer treatment and palliative care

Source: World Health Organization, Cancer Country Profiles, 2014

Radiotherapy	Not generally available in the public health system
Total high energy teletherapy units	0.8 / million inhabitants
Number of radiotherapy centers	34
Number of radiation oncologists	237
Chemotherapy (medicines not specified)	Not generally available in the public health system
Oral morphine (formulation not specified)	Generally available in the public health system
Non-methadone morphine equivalent consumption per cancer death (mg)	No data available
Community / home care for people with advanced stage cancer and other NCDs	Not generally available

Table 6: Incidence rates of Cancer in Egypt (/100,000 populations) classified by region and gender for all cancer sites with and without non melanoma skin cancer (C44)

Source: Ibrahim et al, 2014

	Man		Women		All		Male : Female Ratio	
	Crude rate (95% CI)	ASR (95% CI)	Crude rate (95% CI)	ASR (95% CI)	Crude rate (95% CI)	ASR (95% CI)	Crude rate	ASR
All sites								
(i) Upper Egypt	97.1 (89.1–105.8)	142.8 (133.1–153.2)	116.9 (108.1–126.5)	167.1 (156.5–178.4)	107.0 (101.0–113.3)	155.0 (147.7–162.6)	0,8:1	0,9:1
(ii) Middle Egypt	109.7 (105.4–114.1)	170.0 (164.7–175.5)	95.9 (91.1–100.2)	132.1 (127.4–137.0)	102.9 (100.0–106.0)	151.1 (147.5–154.8)	11:1	13:1
(iii) Lower Egypt	138.5 (133.2–144.0)	191.8 (185.6–198.2)	131.7 (126.5–137.2)	173.3 (167.3–179.6)	135.2 (131.4–139.1)	182.6 (178.2–187.1)	11:1	11:1
(iv) Calculated rates of Egypt	117.3 (116.0–118.6)	178.5 (176.9–180.2)	111.7 (110.4–113.0)	159.1 (157.6–160.7)	114.5 (113.6–115.5)	169.0 (167.9–170.2)	11:1	11:1
All sites (excluding nonmelanoma skin cancer C44)								
(i) Upper Egypt	96.0 (88.1–1104.6)	141.0 (131.4–151.4)	115.1 (106.3–124.5)	163.9 (153.4–175.1)	105.5 (99.5–111.8)	152.5 (145.5–160.1)	0,8:1	0,9:1
(ii) Middle Egypt	108.0 (103.8–112.3)	167.2 (162.0–172.6)	94.9 (90.9–99.1)	130.7 (126.0–135.6)	101.6 98.7–104.6)	149.0 (145.5–152.6)	11:1	13:1
(iii) Lower Egypt	136.7 (131.5–142.2)	189.1 (182.9–195.5)	130.1 (124.8–135.5)	170.9 (164.9–177.1)	133.5 (129.7–137.3)	180.0 (175.7–184.4)	11:1	11:1
(iv) Calculated rates of Egypt	115.7 (114.4–117.0)	175.9 (174.3–177.5)	110.3 (109.0–111.6)	157.0 (155.4–158.5)	113.1 (112.2–114.0)	166.6 (165.5–167.8)	11:1	11:1

Egypt: Calculated age specific incidence rates for liver cancer

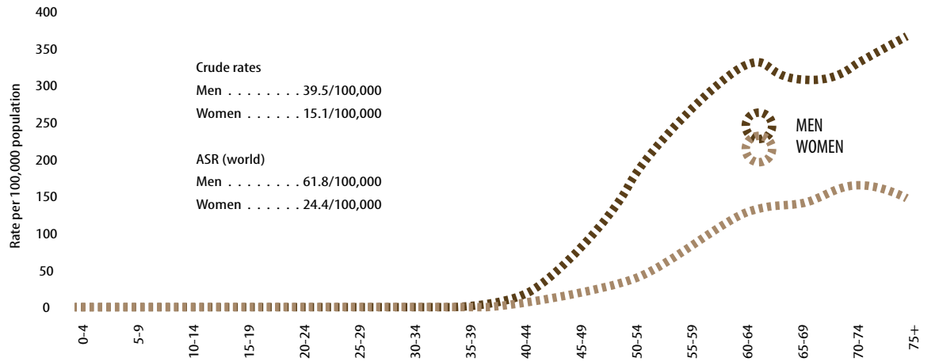

Figure 7: Calculated age specific incidence rates for liver cancer in Egypt 2008–2011

Egypt: Calculated age specific incidence rates for breast cancer

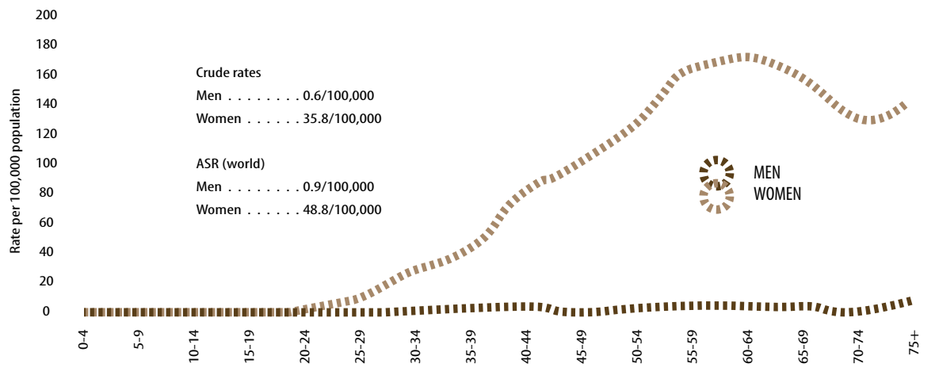

Figure 8. Calculated age specific incidence rates for breast cancer in Egypt 2008–2011

Egypt: Estimated Number of Incident Cancer Cases

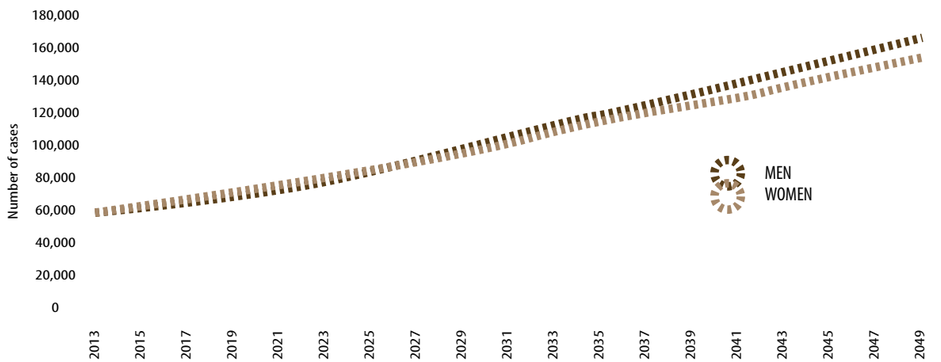

Figure 9: Estimated number of cases in Egypt (2013–2050)

Egypt: Cancer Cases and Causes for Increases

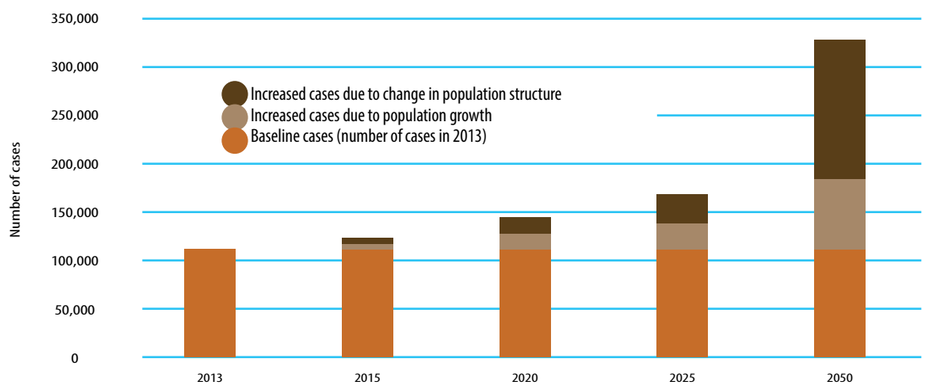

Figure 10: Estimated number of cases in Egypt (2013–2050) and causes of the increase in cases

During the period 2013–2050, the population of Egypt is expected to increase to approximately 1.6 times the 2013 population size. Applying the current age-specific incidence rates to successive populations would lead to a progressive increase in number of incident cases from 114,985 in 2013 to 331,169 in 2050, nearly three times the burden in 2013. This increase reflects both population growth and demographic change mainly due to the ageing of population. Population growth alone would increase the number of incident cases by 55.2% in 2015. This fraction progressively decreased to become 32.8% in 2050. The fraction due to ageing gradually increased to reach 67.2% in 2050.

Table 7: Estimated cancer incidence in the period 2013–2050 and causes of increase

Source: Amal S. Ibrahim et al. 2014

	2013	2015	2020	2025	2050
Estimated population	85,294,388 (100%)	88,487,396 (103.7%)	96,260,017 (112.9%)	103,742,157 (121.6%)	137,872,522 (161.6%)
Number of cases [1]	114,985	122,783 (106.8%)	144,255 (125.5%)	168,723 (146.7%)	331,169 (288.0%)
Increased cases from 2013 [2]		7,798 (6.8%)	29,270 (25.5%)	53,738 (46.7%)	216,184 (188.0%)
Increased cases due to population growth [3]		4,303	14,783	24,869	70,880
Increased cases due to population structure change [4]		3,494	14,487	28,869	145,304
% Increase due to population growth [5]		55.20%	50.50%	46.28%	32.79%

[1] Number of expected cases extrapolated from the 2013 incidence rates

[2] Number of increased cases from 2013 number of cases

[3] Number of increased cases (from 2013) that is attributed to increase in population number (population growth)

[4] Number of increased cases (from 2013) that is attributed to change in population structure (aging of population) and not to population growth

[5] Percent of increased number of cases (from 2013) that can be attributed to population growth only (not due to change in population structure)

Cancer Care Facilities in Egypt

Egypt has more facilities for cancer treatment than any other country in Africa; however, many elements of cancer control strategy still need to be implemented or improved. There are 32 Cancer management facilities including the biggest and the most specialized centre in the Middle East is the National Cancer Institute (NCI) which is affiliated to Cairo University. NCI is carrying research, education and clinical responsibilities and is considered the main reference in Egypt regarding cancer. Also,; South Egypt Cancer Institute, Assiut University, Assiut, Egypt, 14 clinical oncology departments in the other public universities; ten cancer centres affiliated to the Ministry of Health in 12 governorates; 11 military cancer units that treat both civilian and military patients; oncology clinics at the hospitals run by the Egyptian Health Insurance Organization in most major cities; semi-private, NGO-operated cancer facilities; a charity-run Centre of Excellence of Paediatric Oncology in Cairo; and private-sector clinics and centres. In addition to surgery, most of these facilities have chemotherapy and radiotherapy capabilities (either linear accelerators or cobalt-60 units). Most centres have CT scanners and MRI machines, and the country has five PET-CT scanners (Stefan et al, 2013).

According to the WHO survey, Egypt had an operational policy, strategy, or action plan for cancer in 2010. However, no structured national cancer control programme as recommended by WHO is in place. Practical measures are needed for the optimum allocation of available resources to reduce the numbers of cancer cases and deaths and to improve quality of life for patients with cancer, through adoption of WHO recommendations (World Health Organisation, 2013b).

Approaches to Cancer Control

Prevention and Early Detection of Cancer

Although screening by mammography has been accepted as the gold-standard to ensure early detection of Breast Cancer, its cost-benefit ratio is still debated in the scientific community. It is important to keep in mind that even in the best screening settings, most deaths from breast cancer are not currently prevented by mammography screening. The latest reviews indicate a reduction of no more than 15% in BC mortality rate after introduction of mammography screening in western countries. Recent studies suggest that screening by Clinical Breast Exam could achieve a reduction of 52% to 88% of this magnitude with a better cost effectiveness ratio.

Whatever screening tool is used, screening programs are resource-demanding and heavy-to-implement health interventions. Down staging programmes are an appealing alternative when resources are scarce, and should be considered as the first option in regions where a majority of Breast Cancer is diagnosed at late stage.

In Egypt, most cancers present at an advanced stage when cure is improbable even with the best treatments. Where still a vast majority of tumours diagnosed are above 2 cm, there is room for improvement by a down staging approach. Screening by CBE would be relevant to regions/groups where stage distribution is good enough that down staging has no potential for major improvement. Reductions in mortality can result from both down staging in some part of the country and screening in other parts. However, Egypt should follow the WHO and BHGI guidelines which call for countries to conduct research and pilot projects prior to establishment of national programs, as neither benefit of screening, nor benefit of down staging programs have been formally demonstrated to date in any developing country. A major element in improving survival rates in many cancer has to be the much earlier stage of disease at diagnosis and this could brought about by public education and, in some cases, screening for pre-malignant lesions or early cancer (World Health Organisation, 2002).

In Egypt, primary health care workers are rarely provided with sufficient education about the early signs of cancer or where to refer suspected cases. This could be remedied by short training courses (ideally coupled to continuing education programmes), brochures or posters, and by establishing links between those who deliver primary health care and referral centres. Population based registries disease data are recorded. These data for breast cancers show that 25.5% of cases present at an early stage. However, it is clear that a large proportion of patients reaching these centres predominantly have advanced stage (stage III and IV) (Anwaar A, 2011).

The Ministry of Health and Population Pilot Screening Program

The Ministry of Health and Population (MOHP) of Egypt has launched a pilot screening program in October 2007. This program is coordinated by Dr. Dorria Salem, Prof. of Radiology Cairo University and Head of Women's imaging unit. The purpose of this program is to screen women from 45 years of age for:

1. Breast cancer (digital mammography exam)
2. Diabetes (Blood sugar test)
3. Hypertension (Blood pressure test)
4. Obesity (weight and height measurement)

The recruitment process is based on the presence of mobile vans where all of the above exams take place. A few weeks before a van is moved to a district, the population is informed about the importance of screening, thanks to posters and pamphlets distributed in mosques, churches and streets. Women eligible for screening (i.e. 45 years old or more) are contacted by phone or visited by health workers of the Red Crescent to encourage them to come to the vans. Only women without breast complains are admitted for breast cancer screening. The symptomatic patients can go to the Women's Imaging Unit at Al-Kasr Al-Ainy teaching hospital.

The pilot phase of the project has begun in October 2007. By February 2009, 25 different locations in Cairo, Giza and Alexandria governorates were visited; up to 22,000 women had been screened, 406 were referred for further diagnosis, 75 (18%) turned out to be false positive. Out of the real positive, 59 (18%) were operated, 73 (22%) refused diagnosis or treatment, 35 (11%) were not reachable and the remaining were into the diagnosis or treatment process.

One of the main problems encountered is to convince women who have a suspicious mammogram, to go for diagnosis and treatment as some refuse or disappear. Health workers from the NGO "Hope" are dedicated to this task. This kind of problem is frequently observed in developing countries when screening for breast cancer

A TV media campaign about screening has taken place during the autumn 2008 to raise awareness about breast cancer and facilitate acceptance of screening, as well as a campaign on the local radio station Nogoom FM; a new TV campaign should start soon (Salem D).

The Breast Cancer Cairo Trial

The Breast Cancer Cairo Trial is a research project designed to evaluate the efficiency of screening by clinical breast examination (CBE) in the context of primary health care (PHC). The project has been designed by Professor Anthony Miller, Epidemiologist at the Public Health Sciences Department of Toronto University (Canada) and is headed in Cairo by Dr Salwa Boulos, radiologist in charge of the mammography unit at the Italian hospital until recently and now at El-Gallaa Hospital. The project has been financially supported by the Italian embassy in Cairo and the European School of Oncology (Milan).

The study has been launched in other countries of the region (Yemen, Iran, Sudan) but Cairo was the first and is thus the more advanced centre of the study. The study was launched in May 2000 and has begun by a pilot phase (phase I) followed by a classical randomized trial (phase II and III).

Phase I (pilot study)

The initial target group was women 35-64 living in a geographically defined area (8 blocks) around the Italian Hospital (Abasseya district). In this pilot phase, 4116 women were contacted by social health worker (door to door visit) to attend designated PHC centres for Clinical Breast Exam at pre-determined date and time.

Of the women targeted, 60% (N=2481) attended, of those who attended 12% (N=291) were found to have abnormalities, of these 82% (N=236) attended the Italian hospital for diagnosis, and of these 3.4% (20 women) were diagnosed with Breast Cancer. This latest number corresponds to a quite high prevalence of Breast Cancer: 8/1000. Only one Breast Cancer patient was less than 40.

Phase II and III

The target group was restricted to women 40-64 and divided in 2 groups based on residential blocks (4 blocks each). Group A was offered active screening as in the pilot phase, the group B received only health education. Two additional areas were identified each with 5000 women aged 50-65 who were cluster randomized. The reputation of the trial preceded subject recruitment and there was higher acceptance than in the pilot phase, with 85-91% of women accepting to go for screening.

Although follow up of all groups is yet to be completed, preliminary results are encouraging. Stage distribution in both screened and control groups are given in table 8.

Table 8: Preliminary comparison of the stage distribution in the Cairo Trial

	Screened Group	Control Groups
Stage I	30%	8%
Stage II	43%	18%
Stage III	20%	44%
Stage IV	7%	30%

This trial is testing an approach to early detection which is promising for Egypt; it would be beneficial to extend this trial to other centres/towns of Egypt. However this requires important resources, especially human resources i.e. dynamic and dedicated local PIs, not mentioning international specialists.

It has to be mentioned that the idea of screening by clinical breast exam usually receives very little support from the medical community in low and middle income countries; Clinical Breast Exam is erroneously perceived as inefficient because of its low-tech nature. This is a misconception that could be tackled in Egypt by an increased publicity about the Cairo Trial (Miller et al, 2008).

Remarks on the Two Screening Experiments Taking Place in Egypt

The populations at risk of Breast Cancer in Egypt, i.e. the women above 45 year of age are approximately 8.5millions. The 22,000 women screened by the MOH mammography program in 1.3 years and the 15,000 women screened by the Cairo trial screened women in 8 years represent

respectively 0.26% and 0.17% of this target population. Such percentages are a little demoralizing in view of the dedication, effort and resources which were put in these two screening programs. However these programs are pilot studies and they are not aiming at a rapid national expansion, especially the Cairo Trial which should be viewed as a research project, but their results raise some concerns about the feasibility of a national screening program in a country like Egypt in a foreseeable future (Miller et al, 2008).

Fakous and Port Said program

A programme in the rural region of Fakous and the urban region of Port Said to use local resources to increase awareness of breast cancer and its treatment by organizing home visits from primary care workers and meetings with local women resulted in a substantial reduction in cases of advanced breast cancer. About 20% of breast cancer cases in Port Said were amenable to conservative breast cancer surgery in 2008, and the number of stage III and IV cases had halved by 2004—08 compared with 1992—2003. Conversely, early detection programmes without access to treatments would be fruitless and frustrating for both patients and health professionals.

The Breast Cancer Foundation of Egypt (BCFE)

The Breast Cancer Foundation of Egypt was established in 2003 by a small group of health care professionals, survivors and public spirited citizens as a non-governmental, non-profit organization under the Ministry of Social Solidarity. At that time, there was no established Breast Cancer awareness governmental program and no other NGO was working in this area. The public in general was not receptive to information about cancer. The topic was considered taboo in Egypt.

The BCFE philosophy is to advocate for BC awareness and services by serving the public in a manner that generates happy clients and positive recognition. BCFE partners with the National Cancer Institute (NCI) for teaching health care professionals. It is a mutually beneficial arrangement that does not involve the exchange of money.

In the past few years BCFE has undertaken educational presentations and opportunistic screening programmes wherever asked for, i.e. private companies and ministries. The BCFE staff designed the screening program, all the tools for implementing it, the training program for doctors and nurses to provide screening services. BCFE surveyed the facilities of hospitals that wanted to establish an early detection clinic and recommended changes to support a good patient flow, privacy and efficiency. These services were provided free of charge to any facility requesting this assistance. The cost was supported by the sponsored screening program.

BCFE deals directly with many patients. Quick referral mechanisms and the link to treatment services are ensured. Poor patients are referred to free clinics of NCI. If they are covered by insurance they are advised WHERE and WHO to go to. If they do not want to go to NCI and are not covered by insurance, BCFE arranges for treatment for them at a low cost facility, or through a doctor that will charge reasonably.

Egyptian Society for Promotion of Women's Health (ESPWH)

The Egyptian Society for Promotion of Women's Health (ESPWH) is a non-profit organization, non-governmental organization under the Ministry of Social Solidarity, was established in June, 2009, Dr. Karima Elshamy is the founder and executive director. The aim of establishing ESPWH is to improve and promote the health of women, increase women' awareness regarding many diseases, especially cancer awareness, control and prevention, reducing cultural barriers and detecting cancer as early as possible, also for education of people, healthcare personnel, and research.. ESPWH is a member of Alliance of African & Mediterranean French Speaking Leagues Against Cancer.

Liver Cancer Prevention

Many countries, including the United States, are experiencing a decades-long trend of increasing rates of liver cancer. The most common type of liver cancer, hepatocellular carcinoma (HCC), has a high mortality rate and limited therapeutic options, to which most populations have limited access.

The prevention of this type of cancer is especially urgent in developing countries. Among the major contributing factors to the development of HCC are chronic infections with hepatitis B (HBV) or hepatitis C (HCV) virus, and food contaminated with aflatoxins (toxins secreted by moulds that infect improperly stored grains and nuts).

Fortunately, these factors are amenable to prevention, including protection against blood-borne viral infections, vaccination against HBV and improved food safety.

But would such strategies work in a developing country, such as Egypt, and why would Egypt be an appropriate place to test the effectiveness of liver cancer prevention programs?

The research group began studying HCC in Egypt more than 10 years ago, following ground-breaking work on HCV led by Dr. G.T. Strickland of the University of Maryland, Baltimore. Dr. Strickland's studies of HCV in communities in Egypt revealed that the country has the highest rates of HCV in the world, the unintended consequence of a massive public health campaign that used injected drugs to halt the suffering from a type of parasitic infection (Schistosoma species) native to the Nile River valley.

The evidence suggests that improper sterilization techniques applied to the needles in that campaign resulted —over a span of 50 years — in the spread of HCV and other viruses to a large segment of the population. The situation resulted in massive epidemics of chronic liver disease, cirrhosis and HCC that have not yet reached their peak. The rate of HCC is about four times higher in Egypt than in the United States, and rising at a faster rate. Each year, over 15,000 Egyptians die from liver cancer.

Dr. Karima Elshamy mentioned that the major risk factors for HCC in Egypt, in addition to chronic infections with HCV and HBV, are occupational exposures to chemicals, pesticides and contamination of the diet with aflatoxins (alcohol abuse is uncommon due to religious customs that forbid drinking).

Each of these factors is preventable; yet beyond HBV vaccination, scant attention is being paid to preventive research or effective interventions, even in the more developed countries. In fact, a recent report by the U.S. Institute of Medicine concluded that the lack of knowledge and awareness of viral hepatitis among members of the public and policy-makers were major barriers to prevention.

Added to the burden of viral hepatitis in Egypt is the unsafe handling of pesticides in agriculture — its predominant industry — and the lack of awareness of safe food handling practices regarding aflatoxins. A program of health education focused on these and other risk factors for HCC could deliver appropriate information at low cost, aimed at empowering households to interrupt the current cycle of viral hepatitis transmission and carcinogenic exposures.

Over the long-term, this approach could be used by many countries to reduce the human, economic, and societal costs of this fatal and increasingly common type of cancer.

To fit the specific needs of Egyptians in the context of their society and culture, a community-based health education approach tailored to the population at risk for cancer would offer many advantages. Community-based participatory research involves members of local communities in all aspects of a study-from design to dissemination-to ensure that the proposed intervention reflects the specific needs of the communities, and to strengthen the capacity of the community to implement public health activities.

Moreover, the engagement of peer educators to deliver the health education program, which has been shown by Sarah Dalglish and others to be highly effective in such issues as tobacco prevention and reproductive health interventions, would be highly innovative in the context of HCC, where little or no such work has been previously reported (Shaalan M).

Egypt's Infection Control Program (ICP) was designed in collaboration with the WHO and is considered the reference for the Eastern Mediterranean region. In 2001, MOHP began by assessing infection control policies, indicating a need for action. For example, only 16% of HCW were vaccinated against HBV, hand washing rates were extremely low and needle stick injuries occurred at a rate of 4.9% per worker per year.

The resulting program includes training of HCW; the establishment of infection control committees at the levels of the governorate, the directorate, and the hospital; and regular monitoring by local and national teams. As of January 2008, the plan has been implemented in 283 hospitals, representing all MOHP hospitals with more than 50 beds in 21 governorates. Further, all HCW in all MOHP facilities, including primary health care units, have been vaccinated against HBV in six governorates (Cairo, Alexandria, Sharkia, Monofiya, Menia, and Qena). In 2009, MOHP will add the remaining 70 hospitals with more than 50 beds, to cover all 27 governorates, and vaccinate all healthcare workers in these facilities nationwide.

The National Committee on Viral Hepatitis, under MOHP, mandated the development of the *Control Strategy 2008-2012* to ensure the strengthening and expansion of the national, multicultural response to viral hepatitis. This plan builds on what has already been achieved and is based on the best epidemiological estimations of viral hepatitis in Egypt and the latest scientific knowledge (Shaalan M, personal communication).

Egyptian National Control Strategy for Viral Hepatitis 2008-2012

The National Control Strategy for Viral Hepatitis is the first comprehensive approach to reducing the prevalence, incidence, and burden of disease associated with hepatitis B and C in Egypt. It represents a comprehensive, multisectoral response to the challenge of this major public health issue and is informed by the latest medical and scientific research on viral hepatitis in Egypt. The Strategy seeks to provide guidance to various government ministries and agencies, as well as to non-governmental partners, in order to ensure coordination and cooperation among them. The plan has been elaborated in concert with the Egyptian National Committee on Viral Hepatitis and in consultation with officials from the Ministry of Health and Population, the Ministry of Higher Education, various United Nations' agencies and the WHO (Geneva and Cairo), as well as researchers at Egyptian universities and other local and international stakeholders involved in the fight against viral hepatitis (Ministry of Health and Population, 2008).

Research

One of the most successful elements of the fight against viral hepatitis in Egypt has been the creation of an international research network called the Liver Disease Research Unit. The network brings together Egyptian, French, American, Swedish and Finnish universities and research institutes. External funding has been provided by USAID, the National Institutes of Health (USA), the European Commission, the French ANRS and Ministry of Foreign Affairs, and the Welcome Trust, among others.

Diagnosis and Treatment of Cancer

Viral hepatitis cannot be treated at the periphery of the health care system (e.g. in primary health care units), since its management requires special training for physicians and special equipment for diagnosis, follow-up, and drug storage. Some 100 hospitals in Egypt are currently equipped to treat patients with advanced liver disease, and there are approximately 400 specialists in advanced liver disease working mostly out of major cities. However, the quality of care and degree of access to drugs may be heterogeneous throughout these facilities.

Recently, 10 National Treatment Reference Centres were opened under the supervision of the National Committee on Viral Hepatitis, providing care for patients with HBV and HCV according to standardized guidelines and at subsidized costs. The Egyptian government provides 20,000 LE for the treatment of each HCV patient treated under HIO and or at government expense, categories which include 94.1% of the 12,089 patients having started treatment as of February 2008. These outlays do not include financial expenditures required for monitoring, testing, facilities and related costs. The total cost to the government is thus a not insignificant percentage of the annual MOHP budget.

Transplants are currently available at approximately 10 public and private facilities, though donors can be difficult to come by and cadaveric livers are not yet available in Egypt. As of 2008, the cost is high (220,000-400,000 LE), though some government assistance is available (World Health Organisation, 2012).

Surveillance and Monitoring

The most recent population-level surveillance study is the 1996 /7 Egyptian household and workers national survey. It is impossible to say with any confidence how prevalence rates have changed in the years since the completion of this study.

There is currently no ongoing sentinel surveillance of chronic HBV and HCV, with the exception of monitoring of infection rates in Haemodialysis units as part of the national Infection Control Program. Additionally, the MOHP's Epidemiological Surveillance Unit, established in 1999 with the cooperation of WHO, EMRO and the CDC, coordinates surveillance of 26 communicable and non-communicable diseases.42 Cases of acute hepatitis A, B, and C are reported monthly from the network of 256 district surveillance units.

However, surveillance figures do not accurately reflect the number of cases for several reasons: under-reporting due to time constraints on health care workers (HCW); the lack of a reliable IgM assay for acute HCV, making it more difficult to diagnose than HAV or HBV; and the fact that surveillance only covers MOHP facilities. Participation by private facilities is voluntary, and thus difficult to enforce. The laboratory support for surveillance also needs strengthening, as labs are not always fully equipped (World Health Organisation, 2012).

The National Cancer Registry Program of Egypt (NCRPE)

The National Cancer Registry Program of Egypt (NCRPE): Population-based cancer registry, it was initiated through a protocol of cooperation between the Ministries of Communication and Information Technology, Health, and Higher Education. The Supreme Committee of the Program decided to start by population-based registration of incident cancer cases and to explore the possibility of establishing a national cancer database through eventual inclusion of hospital based cancer registries in due time. The registry program started in 2008 and covered Aswan Governorate followed by El Minia, Beheira and Damietta. Governorate of Gharbiah already has a registry that was established 10 years ago and will be included in the national registry program in a subsequent phase. Egypt will thus be covered by a network of population based registries geographically spread all over the country. The Metropolitan Cairo is not covered by population-based registration due to logistic difficulties. Nonetheless,

comparison of program results with those of the National Cancer Institute in Cairo would give a clue to the profile of cancer in the Metropolitan Cairo Area and complete the picture for Egypt (Al-Jibaly, 1998).

Government Involvement in the Care for Cancer Patients

The Ministry of Health and Population is responsible for overall health and population policy as well as the provision of public health services, and is responsible for health insurance organization that provides services too, cancer registration, access to public health awareness through working as change agents, increase health awareness and literacy, educating patients on patients' rights, encouraging volunteerism, and public campaigns & community outreach, access to early detection through: leading the Egyptian breast cancer program, increasing accessibility of early detection services, and improving the quality of services across the country. Also, the accreditation program through capacity building of healthcare providers from all sectors, access to quality cancer treatment, and prioritizing quality cancer care

The Ministry of Higher Education

The Ministry of Higher Education is responsible for health profession education (medical, nursing, dentistry and pharmacy etc.) and also runs University Teaching Hospital, access to research through creating an enabling environment for research and academics, moving toward evidence based decisions at the national level and pushing boundaries of clinical research, in addition to community services

Non-Governmental Organization Responsibilities

Non-governmental organizations focus on the prevention and early detection of cancer. The non-governmental sector is an important source of technical knowledge, skills and resources relevant for cancer care and research, this involvement implies either direct provision of the services or acting as funding institutions Furthermore, non-governmental organizations provide an important ability to reach out to the professional and public communities, advocate for cancer prevention and control, offer cancer education and screening services in our community, support cancer patients and survivors. Access to patient support and survivorship, patients support groups, financial support, treatment cost, transportation, accommodation, food coupons, and sharing survivors' stories sessions Nongovernmental and voluntary organizations can, therefore, play a significant role in assisting the efforts of the government health system in reducing disparities in coverage regarding cancer care services.

Prof. Dr. Karima Elshamy (Head of Gerontological Nursing Department, Faculty of Nursing, Mansoura University, Egypt and AORTIC Vice President of North Africa) reported that, it is very important for all organizations to be aware of the complexity of cancer control, and of the role they should play in achieving the goals of the cancer control programme or strategy, through a unified effort with other sectors. Improved cancer control will, to a substantial degree, relate to prevention strategies and early detection programmes, including information campaigns and population-based screening programmes. Success of the early detection programmes will rely on effective and optimal use of treatment possibilities.

Cancer Education in Medical, Nursing, and Pharmacy Schools in Egypt

More than 1500 Egyptians have postgraduate qualifications in clinical and medical oncology. The medical and health-related educational system in Egypt has advantages and limitations. Medical education includes a unique system of three-year community-based public health training, but better planning and collaboration among schools could notably increase new physicians' knowledge of cancer detection and prevention. Nurses and pharmacists exert great influence in the provision of health care. Yet, their training includes neither cancer education nor information about prevention. The medical and health-related educational system in Egypt has many limitations, but it has the structure and inherent ability to

achieve cancer education goals (Ibrahim A.S). Prof. Dr. Karima Elshamy added that many nursing researches, master and doctoral thesis in faculty of nursing, Mansoura University focus on cancer and palliative care.

Interrelationship Between Cancer Care and Local Culture

Culture refers to a set of shared attitudes, values, goals and practices that characterize a group. Cancers are known to be a result of both genetics and lifestyle factors. Lifestyles emanate from cultural beliefs, values and practices. Thus culture affects both the risk factors for cancers and the meaning of the disease by influencing the behaviour responding emotionally, cognitively and socially to this disease. Culture will determine approaches to prevention, early detection, treatment choices, and management of side effects such as pain, appropriate psychosocial support, rehabilitation efforts, survivorship issues, hospice use and effective end of life care.

Cultural values, beliefs, and assumptions influence healthcare. In every clinical encounter, providers decide what to say and what not to say, who to include in important discussions, how to provide patient teaching, and when to schedule follow-up care. When providers are working with someone from another culture, these decisions may be influenced by assumptions and stereotypes about what people from that culture are like. If the assumptions are wrong, a person's health can be seriously jeopardized.

Cultural influence in Cancer Screening

There has been much debate regarding cultural influence on cancer screening, especially regarding culturally sensitive regions of the body such as the breasts, cervix and colon. Cultural factors have been shown to play a vital role in women's attitudes to breast cancer screening. Cervical cancer screening has been widely implemented and has been subject to much study (Soliman et al, 2003).

Cultural Influence in Cancer Diagnosis and Disclosure

Confucius teaches that in a society, every person has a role and obligations to fulfil. In the context of cancer diagnosis, this phenomenon is particularly acute. To a parent of a young family, a diagnosis of cancer immediately brings the burden of the possibility of being unable to fulfil his or her duties to raise the young and provide for the family. This may produce intense feelings of guilt, shame and anger. These reactions must be taken into consideration by the healthcare provider in relating to the patient.

Another factor relates to the phenomenon of reciprocity and filial piety (righteousness). As the parents grow old and the children come to maturity, the role of the provider is gradually passed to the children and in the twilight years, it often comes to pass that the family will make most of the decisions for the elderly ones. It is widely observed in local medical practice that in Egyptian families, the children often wish to conceal the diagnosis of cancer from the patient. At times, the diagnosis is explained to the children who stay behind in the consultation room after the patient leaves. This is entirely opposite to the grain of Western bioethics of medical confidentiality and patient disclosure. Indeed, this practice is not usually seen in clinics in the West where the very opposite occurs: the patient attends the consultation alone and certainly would hold the confidentiality of his medical information dear.

Amongst Muslims, again the concept of God's will influence the willingness to accept bad news and even mishaps and regard it as fate and thus may be more forgiving to the carers. Research has shown that distribution of Breast Cancer is within the younger age group of Egyptian patients, the majority of cases occurring between 30-60 years of age. The median age at diagnosis is 49 years, one decade younger than the corresponding age in Europe and North America (IARC, 2005).

Reduction in mortality from BC depends to a large extent on interventions aimed at early detection and treatment; including breast self examination, clinical breast examination, and mammography (Holroyd et al, 2004). Lack of early detection programs is the primary reason for the escalation of the mortality rate from BC in developing countries (Shi et al, 2008).

Not seeking medical advice unless one is ill, followed by the women's beliefs that physical checkups were not worthwhile were the most common personal barriers revealed by the present participants. In their study among women from rural Egypt (Younis et al, 1993), it was stated that many Egyptian women suffered in silence, endured much pain and discomfort before they would admit to being ill, and would mostly only seek treatment when their symptoms became severe (Solomon et al, 2007).

Unsurprisingly, a significant proportion of the women in the present study reported they were afraid of discovering that they had cancer, and embarrassment by the screening was a personal barrier. Generally, there are many personal obstacles for women to access prevention services. The fear of discovering cancer, embarrassment, and fear of the screening procedure were among the most commonly reported personal/cultural barriers to using the screening services (Younis et al, 1993) (Thompson et al, 2006). Spirituality and religion have been identified as major determinants of fear and fatalism with regard to BC in previous research (Thompson et al, 2006). Personal barriers can be overcome by promoting health seeking behaviour and educating the public on the importance of early detection of cancer with a message that empowers women to take charge of their own health.

The Impact of Culture and Religion on Truth Telling At the End of Life

In Islamic ethics, family and community are intrinsically linked with each individual's well-being (Flynn et al, 2007). Similarly, in many Asian cultures, illness is a shared family event rather than an individual occurrence (Beyene, 1992). The family provides a source of strength, hope and connectedness to others. Accordingly, the principle of autonomy does not bear the same weight as it does in many Western cultures and thus the family is the locus of the decision-making process (Sachedina, 2005). A Japanese study (Searight et al, 2005) found that 46% of the population felt it was the family's duty to provide 'a protective role in shielding the patient from a painful diagnosis' (Chattopadhyay et al, 2008). Equally, in Ethiopia and Saudi Arabia, information regarding a patient's illness belongs to the family, who then use the information in the best interests of the patient (Seo et al, 2000) (Surbone, 2008). Physicians, consequently, respect the 'autonomy of the family as a unit' (Sachedina, 2005).

Society Reaction towards Cancer Patients

Cancer is one of the oldest diseases of human beings. Diagnostic and therapeutic aspects have advanced significantly. The life span of a cancer patient of today is increased considerably, because of multifarious approach by scientists and medical personnel. However nothing much is done regarding the status of the patient in relation to the society and the mental, behavioural and physical aspects.

Social reaction towards the cancer patient ranges from total nonnormalcy to almost normalcy. Most of the families believed in 'God's Way', the others were showed no significant reaction. Children of the patient were more concerned, affectionate and sympathetic to their mother that the others. The husbands were either badly affected psychologically or kept up calm to face the situation. This was more so in educated ones. Some families encouraged the patients to gain strength and to face the disease which in turn has helped the patient to lead an almost normal life. The non-acceptance in the society, based on no firm grounds, is leading the patient to despair. However, avoidance of the patient in one pretext or the other is prevailing in significant number of cases.

Anger, irritation, sense of inferiority, insecure feeling, emotional stress and total lack of hope of survival were the main feelings. Given a proper atmosphere of normalcy and affection, the quality of the life and survival time would be enhanced significantly. Philosophy has come as important source of solace to many affected families (Younge et al, 1997).

Current Status of Palliative Care Nursing In Egypt

Clinical Implementation

In most of the world, the majority of the cancer patients present with advanced disease. For them, the only realistic treatment option is pain relief and palliative care. Effective approaches to palliative care are available to improve the quality of life for cancer patients. Lack of access to basic pain relief continues to make living and dying with cancer in Egypt a very different experience from that in developed countries.

The National Cancer Institute (NCI) in Cairo was established in 1969 as a specialized institute, affiliated with Cairo University. In 2004, palliative care was included in the oncology medical training programme at the National Cancer Institute at the University of Cairo. In 2006, there were two organizations providing hospice palliative care in Egypt: the Cairo Evangelical Medical Society (which has hospice facilities in Cairo and Alexandria) and the National Cancer Institute (which puts an emphasis on cancer pain relief).

In 2010, the NCI, Cairo has cared for 18 156 new patients which comprised 70%–80% of all cancer patients in Egypt. A total of 70% of all new cancer patients were diagnosed with an advanced stage of the disease. NCI's first initiative towards the development of palliative care services was in 1981 when the first pain clinic was established as part of the Department of Anaesthesiology. This clinic handles 120–150 patients daily, while slow release morphine tablets are the only available pain medicine (Ministry of Health and Population, 2008). At the present, NCI is running a pain care clinic at its outpatient pain department. This clinic operates on a the capacity of a 24 hours/7 days basis, and its staff (multidisciplinary team) comprises pain management physicians, specialized nurses, clinical social workers, pharmacists, psychiatrists, dieticians and administrative manpower. In addition, a hotline service was established, thus enabling easier access to the experts on the team. In addition to the NCI, Cairo, the Kasr Elaini Cancer Centre in Cairo also runs a pain clinic and a palliative care service started in 2007. The new Children's Cancer Hospital 57357 in Cairo runs paediatric palliative care services including psychological support. The Cairo Evangelical Medical Society provides in-patient and day care hospice services (opened in 2001), while similar services are provided by the Elhadra Elromany hospice in Alexandria (Ministry of Health and population, 2008).

Palliative care in Egypt is in an early stage of development with very few palliative care activities available even in all of the above specialized Centres. At this stage, research is crucial to develop suitable palliative care models with respect to the needs, culture, and resources in Egypt. In addition, a range of health professionals, other workers, carers and volunteers provide palliative care services: nurses, including registered and non-registered nurses with and without specialized palliative care qualifications, medical practitioners, including specialist palliative care physicians, hospital-based specialist palliative care trainees, hospital-based non-specialists and general practitioners (GPs), health professionals, including psychologists, physiotherapists, occupational therapists and pharmacists, volunteers, carers, including both formal and informal carers. While palliative care can be provided to patients in a variety of settings, a distinction is commonly made between care provided in hospitals (which includes hospices or dedicated palliative care wards) and the community (such as in the patient's home or in residential aged care facilities).

Opioid consumption figures in Egypt are among the lowest worldwide indicating largely inadequate cancer pain control. Based on the data published in the most recent annual report of the International Narcotics Control Board, the average opioid consumption in Egypt during 2008-2010

was 62 defined daily dosed for statistical purposes (S-DDD) per million inhabitants per day. With this Figure, Egypt was ranked 115th among 184 countries (Lamar Soutter Library, 2016).

In Egypt, palliative care and cancer pain control are at an early stage of development. Very few services are available, and there are many barriers to be faced, such as limited opioid accessibility and availability for medical use. Palliative care is still misunderstood among health professionals, cancer patients and the public at large. One reason to that is because the term does not obviously communicate the intent of this clinical discipline, which is lending better quality of life while combating cancer.

The Society for the Management of Pain was founded in Egypt in 1980. A postgraduate training program was subsequently established to equip physicians with advanced knowledge and skills in pain management. Parenteral morphine is locally manufactured whereas oral preparations are imported. One Egyptian experience that could have possible implications for other Muslim communities is the success that Egypt has had in training patients' relatives to care for patients in their homes. A patient's relative is selected as the principal caregiver and is then given basic teaching on the disease and some tips on patient care at home. The home caregiver is provided with a booklet that contains a daily observation sheet, which is completed by the caregiver and reviewed by the health professionals weekly (United Nations, 2012).

Practice: Only a few healthcare providers have adequate knowledge of pain assessment and management and palliative care, so, it is important to integrate pain and palliative care into the health unites.

Egypt has National Guidelines for the management of acute and chronic pain, management of other physical symptoms. New guidelines are currently worked out for End-of-Life Care and for home-based hospice services. National guidelines for palliative care were not initiated till now. The NCI, Cairo offers MD and Master degrees in pain management and palliative care has been incorporated in the curriculum of the oncology nursing program in the same institute.

Ethical, Religious and Cultural Issues

All patients probably undergo the stages of acceptance of terminal cancer in the same fashion. The difference between Egyptian and Western cultural practices would likely be in the culturally specific coping strategies. Ultimately, the physician and other healthcare providers have to assess the patient in his cultural context and find out what would help the patient the most to go through the terminal phase of the disease. The community bond amongst Muslims is very strong, most end of life issues are preferably taken care at home amongst family members rather than in hospice facilities.

In dealing with a patient, a physician must take into account the degree of his cultural inclinations as well as that of his family in order to communicate and provide best medical treatment effectively. Invariably, communication and empathy are indispensable in achieving this. In an increasingly westernizing society, a physician should be wary of imposing generalized belief models on patients without first understanding their background and preferences.

Islam is the dominant religion in Egypt, and observant Muslims believe that having an illness represents an opportunity to enhance the Muslim's degree or expiating personal sins. Yet, Islamic teaching encourages Muslims to seek treatment when they fall sick, as it is believed that Allah did not send down a sickness but rather a medication for it (Stefan et al, 2013). Muslim's beliefs attribute to occurrence of pleasure and suffering to the will of Allah, and that every effort should be made to relieve suffering. Moreover, Islamic teaching considers the relief of suffering to be highly virtuous (World Health Organisation, 2013b). According to Islam, adults of both genders are granted the full right to accept or decline medical

intervention. In reality, close family members are more often directly involved with the decision-making process. Generally, parents, spouses and older children, in descending order, have greater decision-making power than the other members of the family (World Health Organisation, 2002).

Islamic teaching encourages the community members to visit the sick and the sick to welcome their guests. Patients, therefore, may entertain a larger number of visitors during their hospitalization (Stefan et al, 2013). The use of drugs that might affect consciousness is strictly prohibited in Islam. However, medically prescribed opioids are generally permissible because of their necessity. Usually, patients and families accept the use of opioids for symptom management, provided the rationale for their use is clearly explained to them. Of great importance is to explain patients and their relatives the possible side effects, as there are great concerns about an imposed drowsiness (Anwaar, 2011).

Issues that relate to end-of-life are compounded spiritually and ethically, and are open for interpretations. While discussing the prognosis of the loved one, Muslim families are often sceptical about receiving clear cut massages from the treating physician. The former are for the most part more comfortable receiving less concrete information and quite often would respond with: 'This is in Allah's (God's) hands, and we are not to predict the fate of the patient'. Such a response is largely due to the Islamic belief that the life expectancy of every person is only up to Allah, who is the one to determine the timing of death. Families, however, are very appreciative being updated as to the patient's condition, in order to enable them to carry out the traditional funeral rites. Taking all of the above into consideration, caregivers in Egypt exercise all the precautions and sensitivity while talking to terminally ill patients and their families (Ministry of Health and population, 2008).

Culture and Religion on and Commutating Bad News at the End of Life

In Islamic ethics, family and community are intrinsically linked with each individual's well-being (Salem D, personal communication). Similarly, in many Asian cultures, illness is a shared family event rather than an individual occurrence (Miller et al, 2008). The family provides a source of strength, hope and connectedness to others. Accordingly, the principle of autonomy does not bear the same weight as it does in many Western cultures and thus the family is the locus of the decision-making process (Miller, 2008). A Japanese study found that 46% of the population felt it was the family's duty to provide 'a protective role in shielding the patient from a painful diagnosis. Equally, in Ethiopia and Saudi Arabia, information regarding a patient's illness belongs to the family, who then use the information in the best interests of the patient. Physicians, consequently, respect the 'autonomy of the family as a unit (Miller et al, 2008).

Methods to Improve Application of Palliative Care Principles

Palliative care guidelines provide a framework for the care needed for patients with serious and life-threatening cancers. Approaches to improving the application of this care include education, training, and research endeavours.

Palliative Care Education and Training

Undergraduate education: The concepts of pain have been integrated into the education of nurses at some faculties and schools of nursing. . Little attention has been paid to the education and training of health professionals on palliative care. Little information has received in undergraduate palliative Care education. Most have acquired knowledge and skills after graduation.

Postgraduate Education: The concepts of pain, palliative care and end-of-life content are integrated throughout most of contents in Egyptian nursing faculties for postgraduate nursing curricula. In addition, assessment and management of palliative nursing is accomplished through

palliative Care clinical education, bedside teaching, and working in a variety of clinical areas, conferences and workshops. Some of Egyptian nursing faculties offer a hospice and palliative care courses. Students have the opportunity to chose and interact with palliative care team in hospitals, attend palliative care training program, and investigate palliative care and hospice care as delivered at hospital settings. The faculty of nursing palliative care training program and end-of-life (EOL) care focuses on the following contents:

- Pain Management that include: definitions of pain, current status of and barriers to pain relief, components of pain assessment, specific pharmacological and non-pharmacological therapies including concerns for different patients
- Symptom Management: Detailed overview of symptoms commonly experienced at the EOL, and for each, the cause, impact on quality of life, assessment, and pharmacological/non-pharmacological management.
- Ethical/Legal Issues: Recognizing and responding to ethical dilemmas in EOL care including issues of comfort, consent, prolonging life, withholding treatment; euthanasia, and allocation of resources; and legal issues including advance care planning; advance directives, and decision making at EOL.
- Cultural Considerations: End-of-life care, multiple aspects of culture and belief systems, components of cultural assessment with emphasis on patient/family beliefs about roles, death and dying, afterlife, and bereavement.
- Communication Essentials: Communication at EOL, attentive listening, barriers to communication, breaking bad news, and interdisciplinary collaboration.
- Nursing Care at the End of Life: Overview of death and dying in Egypt, principles and goals of hospice and palliative care, dimensions of and barriers to quality care at EOL, concepts of suffering and healing, role of the nurse in EOL care.
- Grief, Loss, Bereavement: Stages and types of grief, grief assessment and intervention, and the nurse's experience with loss/grief and need for support.
- Achieving Quality Care: End-of-life challenge for nursing in EOL care, availability and cost of EOL care, the nurses' role in improving care systems, opportunities for growth at EOL, concepts of peaceful or "good death," "dying well," and dignity.
- Preparation and Care: Time of death nursing care at the time of death including physical, psychological, and spiritual care of the patient, support of family members, the death vigil, recognizing death, and care after death.

Currently there is no postgraduate training in pain management or palliative care in Egypt. To effectively manage the large number of patients in need of palliative care services, Egypt should have adequate numbers of specialists in pain management and palliative care who in turn can support the primary care providers in the management of difficult and complex pain patients across Egypt. It is suggested that postgraduate training programs be developed for both doctors and nurses who wish to acquire special expertise in pain management and palliative care. Certification of healthcare workers in pain management and palliative care should be instituted. It is recommended that palliative care should be integrated into the undergraduate training provided by all medical and nursing schools in Egypt, and to be integrated into all examinations of doctors and nurses.

Research

Current Status

Egypt has significant quantitative and qualitative palliative care researches that were done by nursing, medical, psychological professionals these researches are directed at improving the care of seriously ill patients and their families, improving the clinical practice, symptom control in advanced cancer, and interventions for ICU patients and families. These researches provide evidence-based practices geared toward the specific needs of patients, and to increase awareness of palliative care programs and the special needs of nurses who care for dying.

Need for Additional Research in Palliative Care

Further research studies are needed to explore strategies to decrease work-related stress in nurses caring for dying patients. Another beneficial study could involve clearly identifying the role of the nurse in paediatric palliative care programs and establishing protocols for staff development. These studies may also discover other innovative ways to increase satisfaction of patients, family members, and nurses overall.

There is much need to increase a robust research agenda, targeting resource-poor areas, where disease burden and poverty are high and where health care is limited. Nurses are in a key position to do this, as they are globally advocating for increased awareness of palliative care as a public health issue and a human right, educating citizens about vaccinations and other preventive measures, and consulting in the development of competencies for this care. Targeted areas may include: Exploring the relationship of pain and other distressing symptoms on quality and quantity of life, independence, function and disability, and developing interventions directed at their treatment in patients with advanced and chronic illnesses; Studying methods of improving communication between adults living with serious illness, their families and their healthcare providers; Evaluating models and systems of care for patients living with advanced illness and their families. Future research questions include the following: What are the barriers to pain and other symptom management related to palliative care? Why do some resource-poor countries have excellent availability of opioids for medical purposes and other countries do not? What role do nurses play in advocacy in promoting palliative care? What are the needs of dying patients and their families in Egypt? What interventions need to be developed/made available to meet these needs?

Challenges for Implementing Palliative Care

Healthcare systems and policies: the big challenge to Egyptian palliative care professionals is the development of hospice systems along with well-organized home-based services, lack of national health policies in support of palliative care development, focus on acute care, poor understanding and awareness of the role of palliative care in community, lack of legislation and accreditation of this new specialty discipline, lack of facilities and resources for palliative care, lack of communication with concerned departments, palliative and end-of-life care not prioritized in healthcare strategies, lack of long-term care and community services, no statistical data about how and where patients die, how many receive palliative care, and the characteristics of the caring process, and insufficient supplies and equipment. Raising the awareness and knowledge of palliative care among health care professionals and providers; monitoring and surveillance of the implementation of the national palliative care policy; introducing more core palliative care curricula at all levels of all health professional training; and educating the public

Healthcare professionals: inadequate training for both health care professionals and general public about the necessity and importance of palliative care as integral part of cancer care, palliative care as a discipline is being seen as less prestigious, lack of interdisciplinary concepts and

teams, negative attitude towards caring for dying patients fear of opioid use (fear of side effects and/or fear of prosecution), resources focused on curative treatments and acute care, and perceived sense of failure

Patients and families: fear of addiction to opioids, fear of abandoning family members unrealistic hopes of cure, families also refuse admission to hospice which is considered as a place of death, isolated and unfriendly, diversity in religious interpretation of death and dying

Poor accessibility of essential palliative care drugs: general lack of opioids and unavailability of opioids in remote areas, very strict opioid prescription and dispensing policies, lack of other essential medications lists, and poor accessibility of essential palliative care drugs. Other challenges include changing the current opioid dispensing regulation to enable emergency opioid prescription by phone or fax, and the expansion of palliative care services to a larger number of patients and illnesses throughout the country.

Lack of relevant training to healthcare workers: lack of palliative care education programmes at all levels, Lack of updated education and clinical training to both physicians and nurses.

Summary and Recommendations

In Egypt, cancer is already an important health problem and will become increasingly important not only in terms of rank order, as infections are better controlled, but also in terms of incidence and mortality. The commonest sites were liver and breast among men and women respectively. Based upon the results of National Cancer Registry Program, Egypt is expected to experience a very large increase by 2050. The following recommendations could enhance the effectiveness of cancer care in Egypt.

1. The Ministry of Health and Population should recognize palliative care as a new subspecialty for nurses, and expansion of palliative care services to a larger number of patients and illnesses throughout the country, considering home-based palliative care service is urgently and badly needed

2. National Committee for Pain Relief and Palliative Care should be developed, and the latter committee should develop a national plan that involves: education, clinical practice including opioids availability, accessibility and disposal, research, public policy, and evaluating and monitoring care plans and activities.

3. Strengthening health care systems; focusing on patient centred care that optimizes outcomes for patients that are patient focused and are based on the patients need as opposed to prognosis, optimal care to optimizes systems and access to services within available resources to provide the best care for the patient that is high quality and safe, also, management, monitoring and evaluation of interventions to ensure they are effective and remain effective. Making real improvements in management will require the proactive efforts of many organizations, and we believe that education as well as discipline should be the cornerstone of efforts to improve cancer care in general and pain relief and palliative care specifically.

4. Education at all levels to be undertaken to all staff members in the oncology units throughout Egypt would gain basic practical training in dealing with cancer patients suffering from pain and other physical, psychological and spiritual symptoms. In order for such a plan to come about a ministerial-driven program is needed, whereby trained oncologists and oncology specialized clinical nurses be educated and trained in the following topics: communication skills between the clinical caregivers, the patients and their families, basic concepts of pain pathophysiology, pain assessment, choosing of analgesics and their dosing, management of visceral, somatic and neuropathic pain, management of other symptoms such as nausea, vomiting, constipation and delirium ,wound care, management of last hours of life including dyspnoea, and how to overcoming cultural barriers. Also, to focus on subspecialties on the psychological, behavioural, physical, and spiritual

5. Effective cancer prevention programmes customized to the community should be fostered, particularly for prevention of hepatitis B and C infection, and breast cancer awareness and early detection, and encourage community share in the program by money donations, hospice places, volunteers and training.

6. Pain and palliative care education and training should be incorporated in the training curricula of all medical schools, family residents training program and all postgraduate oncology and other chronic disease nursing training program, also palliative-care certified physicians are going to be central in coordinating this kind of care, clinical nurse specialists in palliative care, who provide palliative care at both institutional and community settings throughout the country are also needed.

7. Setting up hospital-based palliative care support teams would be the biggest foreseeable challenge; as currently there are neither nurses nor physicians trained in palliative care within the public hospitals. These teams working within hospitals will offer an in-house consultant service, and facilitate their transfer to the community. The hospital-based teams will continually liaise with other services within the hospital as well as the home care teams to improve continuity of care, as well as provide education for both hospital and community health care professionals.

8. Many important breast cancer screening barriers have been identified among this group of Egyptian women. Women's perception of these barriers was associated with some sociodemographic characteristics. Identifying barriers to breast screening in the local community will help to remove those obstacles and design more culturally relevant strategies to increase the utilization of breast screening service and to ensure adequate breast care of these women.

9. Changing the current opioid dispensing regulation and ensuring the availability of this and other essential drugs,

10. Training and workforce capacity building are needed to improve research into cost-effective cancer-control interventions and clinical trials.

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Chapter 16g

Ghana

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The Republic of Ghana is a country located in West Africa. It is bordered by Cote d'Ivoire on the west, Burkina Faso in the north, Togo in the east, and the Gulf of Guinea to the south. Initially colonised by the British under the name Gold Coast, it was changed to Ghana which means "warrior king" after attaining independence in 1957. The Country spans an area of 238,500 square kilometres and has a population of approximately 25 million. Ghana is divided into 10 administrative regions and English is the country's official language which predominates in government and business affairs. Life expectancy is 65 years for men and 67 years for women. The country's economy is considered to be low middle income and is dominated by agriculture, which employs about 40 percent of the working population. The literacy rate is 71.5% and government spends 5.4 % of GDP on health.

Table 1: Facts from Ghana

Capital	Accra
Population	25,758.003
Country code	233
Internet country code	.gh
Bordering countries	Burkina Faso, Togo, Cote d'Ivoire
Date of founding	March 6, 1957
Type of government	Constitutional presidential republic
Religions practiced	Christianity, Islam, Traditional
GDP per capita	$3,500 (2013)
Top exports	Gold, Cocoa

General Health System

In the 16th century, traditionally, village healers and clerics were the primary care givers, offering herbal remedies. Western medicine was introduced by Christian missionaries to the Gold Coast in the 19th century.

Health care is provided by the government and largely administered by the Ministry of Health and Ghana Health Services. The healthcare system has five broad levels of providers: health posts which are first level primary care for rural areas, health centres and clinics, district hospitals, regional hospitals and tertiary hospitals.

Patterns of Patient Referral

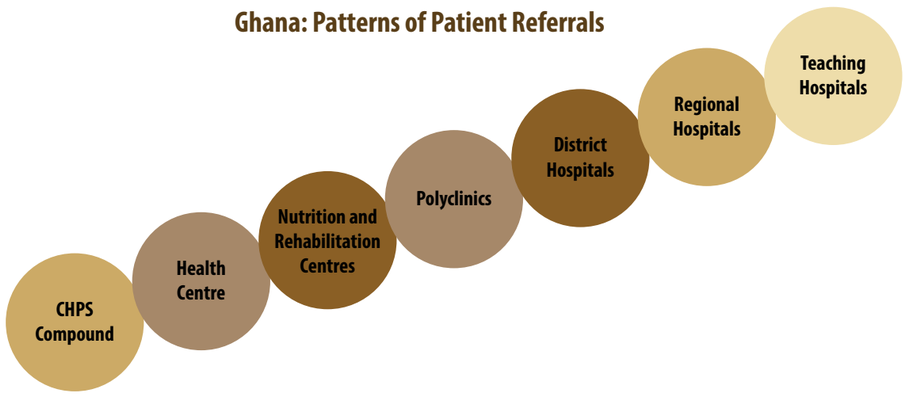

Figure 1: Patterns of patient referral in Ghana

*CHPS - Community-Based Health Planning Services

Hospitals and clinics run by Christian Health Association of Ghana also provide healthcare services. In 2005, Ghana spent 6.2% of GDP on health care, or US$30 per capita. Of that, approximately 34% was government expenditure.

The country's doctor and nurse population ratio is 1: 10,452 and 1: 1,251 respectively (Government of Ghana, 2012). There are about 1,294 private hospitals, 1,818 public hospitals and 204 religious health institutions. Both public and private institutions are generally located in urban areas whilst religious institutions are found predominantly in rural areas.

Urban centres are well served and contain most hospitals, clinics, and pharmacies whereas rural areas often have no modern health care. Patients in these areas either rely on traditional medicine or travel great distances at substantial cost for health care.

About a decade ago, the health need of an individual was only attended to after initial payment for the service was made even in cases of emergency, known as the *cash and carry system*. In order to promote universal coverage and equity in healthcare delivery services, the government of Ghana adopted the National Health Insurance Scheme (NHIS) in 2003, which was fully implemented in 2005. This was to assure equitable and universal access for all citizens to an acceptable quality package of essential healthcare services and to abolish "out-of-pocket" payment. As of June 2009, about 67% of the population had subscribed to the NHIS and this figure is improving over time and currently officially stands at 75%.

The burden of non- communicable diseases is increasing rapidly whilst infectious diseases continue to pose major challenges. We still have high birth rates, decreasing death rates and by consequence an increase of the older population leading to increases in chronic and non- communicable diseases. The most significant of these are cardiovascular related diseases, diabetes and cancers. GLOBOCAN 2012 data estimates that 16,600 cases of cancer occur annually in Ghana, yielding an age-standardized rate of 109.5 cases per 100,000 persons. There is low awareness of cancer in Ghana and as a result most cases present at late stages. Early diagnosis and treatment efforts are frequently hampered by sociocultural influences including seeking traditional or spiritual resolve. Diagram below depicts the top reasons why patients with breast cancer diagnosed in Ghana absconded or presented with late disease.

Table 2: Reasons for Late Reporting

Reason	N	%
Medical consultation	26	39.4%
Ignorance	19	28.8%
Fear of mastectomy	16	24.2%
Herbal treatment	13	19.7%
Prayers and prayer camps	13	19.7%
Financial Incapability	12	19.7%
Fear of diagnosis	7	10.6%

Table 3: Reasons for Absconding

Reason	N	%
Fear of mastectomy	20	57.1%
Herbal treatment	13	37.1%
Financial incapability	11	31.4&
Prayers and prayer camps	10	28.6%
Chinese medication	5	14.3%

The fear of mastectomy, use of herbal treatment, prayers and Chinese medicines accounted for more than 75% of reasons for either presenting late or absconding treatment.

According to GLOBOCAN 2012 data (Globocan, 2012), cervical cancer is the top most frequent cancer in Ghana, however recent data from registries in Kumasi and Accra indicate that breast cancer ranks first.

GLOBOCAN 2012 Country Data

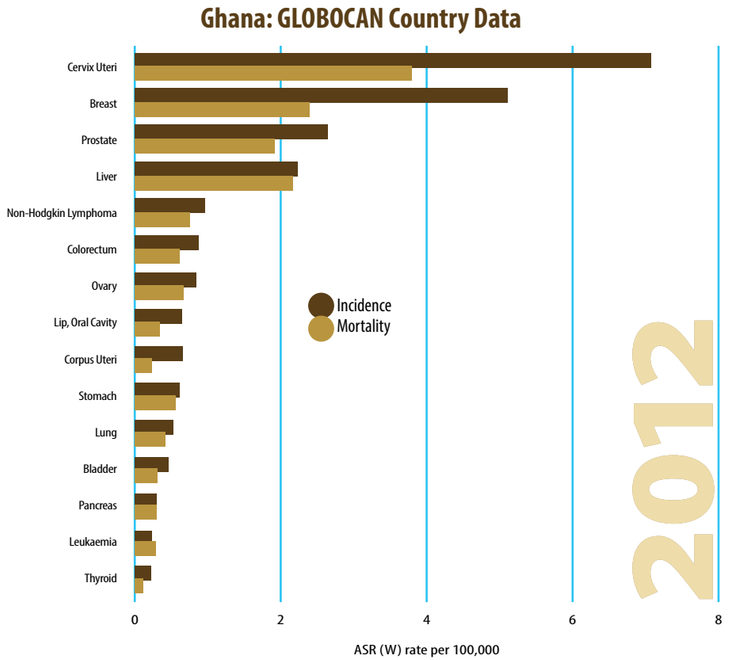

Figure 2: GLOBOCAN Country Data for Ghana, 2012

Source: Ferlay J, Soerjomataram I, Ervik M, et al. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Available from: http://globocan.iarc.fr, accessed July 7, 2014.

Cancer Registry

Until recently, cancer statistics in Ghana were extrapolated from small studies and estimates replaced absent factual data. To circumvent this and also realising the need for accurate data to help formulate effective cancer control strategies, the teaching hospitals in Kumasi and Accra now have hospital based cancer registries, both of which in the very near future will be certified as population based registries. Preliminary data from the two registries are available as open access publications. Below is a diagram depicting initial data from the Kumasi cancer registry (Laryea et al, 2014).

Top Ten Cancer Cases Seen at KBTH By Sexes in 2012

Table 4: Cancer registry Korle-Bu Teaching Hospital, Accra. (Calys-Tagoe et al, 2014)

OVERALL		MEN		WOMEN	
Site	N (%)	Site	N (%)	Site	N (%)
Breast	333 (29.3)	Prostate	90 (26.5)	Breast	325 (40.8)
Cervix	194 (17.1)	Pharynx	25 (7.4)	Cervix	194 (24.3)
Prostate	90 (7.9)	Colorectal	22 (6.5)	Uterus	36 (4.5)
Colorectal	57 (5.0)	Stomach	19 (5.6)	Colorectal	35 (4.4)
Uterus	36 (3.2)	Bones	17 (5.0)	Ovary	34 (4.3)
Ovary	34 (3.0)	Skin	17 (5.0)	Thyroid	17 (2.1)
Pharynx	33 (2.9)	Larynx	12 (3.5)	Bone	15 (1.9)
Bones	32 (2.8)	Lung	9 (2.7)	Lung	10 (1.3)
Skin	26 (2.3)	Liver	9 (2.7)	Skin	9 (1.1)
Stomach	25 (2.2)	Bone marrow	8 (2.4)	Brain	9 (1.1)

Top Five Paediatric Cancers (and sub-types)

Table 5: Paediatric tumour; Korle-Bu teaching hospital, Accra

DIAGNOSIS	2008-20011	
	No.	%
Lymphoma	152	30.7%
BurkittS'lymphoma	109	
Non- Hodgkin's lymphoma	31	
Hodgkin's lymphoma	12	
Leukaemia	93	18.8%
Acute lymphocytic leukemia	65	
Acute myeloid leukemia	24	
Chronic leukemia	4	
Retinoblastoma	78	15.8%
Wilms tumor	61	12.3%
Soft tissue sarcoma	32	6.5%

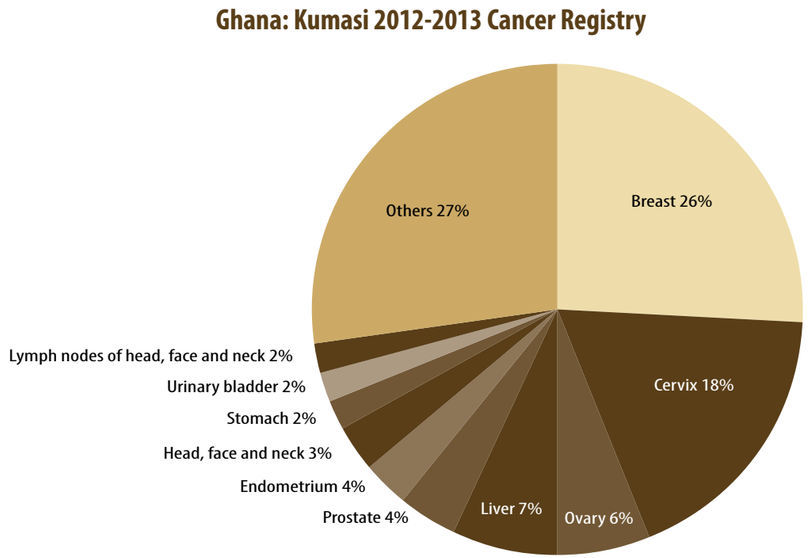

Figure 3: Pie chart depicting total cancer cases seen in 2012

National Cancer Control Plan

In partnership with various international organisations, Ghana rolled out a cancer control plan which was launched in 2015. The plan aimed at reducing cancer mortality by 30% through primary prevention, effective screening and early detection; improve effective diagnosis and treatment of cancer. The strategies outlined can only be fully achieved when cancer is recognised as a human resource menace by policy makers. Maternal and child health, HIV, TB and malaria are still considered priority and are comparatively allotted a big chunk of the limited health budget. Health education and screening starting from the grass roots i.e. community health workers will go a long way to achieve the goals of the plan. Referral patterns for cancer treatment need to be simplified to improve accessibility. Other important but overlooked aspects are the financial burden of cancer care as well as the inadequate numbers of skilled health personnel across the cancer continuum of care.

Prevention And Early Detection

Although the knowledge on cancer is generally low among the general population, it has considerably improved over the last few years especially in the area of breast, cervical and prostate cancers. Several health facilities in urban areas have equipment for mammograms, pap- smear and PSA testing but are lacking or limited in the rural areas. Individuals who want screening have to pay out of pocket for the service because these tests are not covered under the national health insurance scheme. There are ongoing governmental and non-governmental sponsored pilot studies in some rural areas for cervical cancer screening using Visual Inspection with Acetic acid, HPV DNA testing and vaccination of young girls against HPV infection. These pilot projects include home screening methods driven by community health nurses. The cost of vaccination is a limiting factor preventing full scale adoption as part of the national immunisation schedule. Ghana can proudly boast of 100% vaccination coverage for hepatitis B as a measure to reduce the incidence hepatocellular cancer. Most cancer cases seen in health facilities present with advanced stage and several reasons may account for this occurrence including the poor knowledge and attitude of people towards cancer. Most people attribute the symptoms of cancer to spiritual forces and other superstitious reasons and as such will seek help from a spiritual healer or herbalist first before reporting to the hospital when symptoms persist. Another reason is the poor access to healthcare especially in the rural areas causing people to self- medicate for several months to years before seeing a doctor. Delay due to misdiagnosis at the health facility is another major cause of late presentation which could be averted with inclusion of oncology in curricula of medical and nursing schools. In the past, delay in obtaining a histopathological report was a major cause of advanced stage presentation since pathological report could take up to several months. However, the establishment of many private pathology services coupled with the training and posting of pathologists to various regions in the country has led to marked improvement in the service.

Training of Health Care Personnel

There is paucity of skilled health personnel in the oncology spectrum across most of sub-Saharan Africa. The deficiency spans across medical physicists, nursing care, palliative care, surgical and radiation oncologists. With the help of the International Atomic Energy Agency, a branch of the United Nations, millions of dollars were spent on training required staff for setting up mainly radiation oncology facilities in some countries. Unfortunately due to poor remuneration and lack of facilities in their home countries, most preferred to seek greener pastures. With this experience, Ghana developed accredited undergraduate and post graduate programs for medical physicists, radiation therapists, radiation, clinical and paediatric oncology and most recently oncology nursing. Some of these programs involving radiation therapy are supported by the IAEA through regular externships. The West African College of Surgeons and Physicians and the Ghana College of Physicians and Surgeons are in the process of developing fellowship training programs for gynaecology oncology and surgical oncology. Under the PACT mission of the IAEA, the virtual cancer control university (VCCUNET) online programs are being developed to improve and standardise health care training in cancer care of which Ghana is a pilot site. The tables below summarise training for clinical oncologist in Ghana.

Medical Training in Ghana

Table 6: Medical schools in Ghana

Medical school	Location
University of Ghana Medical School	Accra
KNUST School of Medical Sciences	Kumasi
University of Development Studies, School of Medicine	Tamale
University of Cape Coast Medical School	Cape Coast
University of Allied Health Sciences	Ho

Post Graduate Training institutions

- West African College of Physicians and Surgeons established 1975
- Ghana College of Physicians and Surgeons established in 2003

Duration of training

- Membership training in radiotherapy and oncology – 4 years
- Fellowship training in radiotherapy and oncology - additional 2 years

With the advancement in cancer care over the past few decades, developed countries have separate specialties for medical and radiation oncologist. In most of sub-Saharan Africa, physicians trained in both the delivery of systemic therapies and radiation therapies are necessary to bridge the human resource gap and reduce the ambiguity of the referral system. With the increasing complexity of managing individual cancers using radiation and systemic therapies, separate medical oncology specialisation will be necessary in the very near future. This is only achievable with the adequate development of human resource and facilities for training. Haematology is considered a separate specialty from medical oncology.

Facilities for the Treatment of Cancer

There are three radiation therapy facilities available for the treatment of cancers.

- National Centre for Radiotherapy and Nuclear Medicine, Korle-Bu Teaching Hospital, Accra (Fig. 4).
- National Centre for Radiotherapy and Nuclear Medicine, Komfo Anokye Teaching Hospital, Kumasi.
- Swedish Ghana Medical Centre, Accra (Fig.4).

The establishment of the first radiotherapy centre in Accra was in fulfilment of a cherished dream dated as far back as 1960. During that period a cobalt machine was donated by the Canadian Government to be used for medical purposes. However, because of lack of funds to house it, the machine was donated to the Lagos University Hospital in Nigeria. Further attempts at establishing the facility in Accra began in 1975. In 1993, population based figures calculated with the help of the WHO and the International Agency for Research on Cancer estimated that Ghana had over 10 000 cases of cancer occurring annually, and that this could be expected to rise to 20, 000. The regional need for cancer care was further exacerbated by the fact that the neighbouring countries of Côte d'Ivoire, Burkina Faso, Togo, Benin and Sierra Leone had no treatment facilities of their own. The Korle-Bu Teaching Hospital was selected as the site of the first IAEA supported radiotherapy project in Ghana. This facility treated its first patients in November 1997. The number of patients treated annually increased from 486 in 1998 to 1167 in 2014. Patients are referred from various parts of the country as well as other African countries. The waiting time to commence treatment ranges from 2-4 weeks due to the high patient load and sometimes the inability of patients to complete the necessary investigations prior to commencing treatment. The top five cancers are breast, cervical, head and neck, prostate and sarcomas in descending order. It houses a cobalt-60 teletherapy machine, a 3-D planning system, conventional simulator, a high-dose-rate Co 60 brachytherapy machine and a SPECT camera. Preparations are underway to install a newly acquired linear accelerator.

A second facility at the Komfo Anokye Hospital in Kumasi began treating patients in early 2004 and sees averagely seven hundred new cases yearly. It houses a cobalt-60 machine, 3-D planning system, simulator and a low-dose-rate brachytherapy. A linear accelerator and high dose rate brachytherapy unit are yet to be installed.

The third facility, the Sweden Ghana Medical Centre is a private cancer centre established in 2012 and houses a dual energy linear accelerator and CT simulator. It treats an average of 500 hundred new cases per year of which one third are from neighbouring countries.

All these facilities have the expertise for systemic therapy administration with experienced clinical oncologists and oncology nurses. Some regional hospitals have the experience of delivering basic first line chemotherapy especially for breast cancer. Surgery for cancer patients is currently executed by general surgeons and gynaecologists with interest in oncology. As a result some regional hospitals have capabilities to do

simple oncology surgery such as mastectomy and lumpectomy with axillary dissection, total abdominal hysterectomy, and colorectal surgery. Complex surgeries are however referred to the teaching hospitals who have managed a high volume of cases. The lack of pathology services in regions results in poor handling of specimens, delays in reporting and subsequently late referrals for radiation and systemic therapies. There is a current drive to encourage young specialist surgeons and gynaecologists to sub-specialise in oncology.

Multidisciplinary Tumour Boards

The order of sequencing of cancer therapies can have an impact on outcome. Therefore all cancer cases should ideally be discussed by a multidisciplinary team prior to any form of intervention. This is a major drawback for patients treated in private facilities with limited or absence of oncology specialists. Tumour boards for managing breast cancer were established in the teaching hospitals as far back as 2001. At the Korle-Bu teaching hospital in Accra, tumour boards for head and neck cancer, paediatric and gastrointestinal tumours are also active. The limited number of oncologists hampers the ability to discuss all cancer cancers prior to any interventions even though desirable.

Palliative Care

Even though palliative care is readily available to HIV patients in Ghana, other medical conditions were not considered to require palliative care. With the help of institutions like the American Society of Clinical Oncology, Afrox (an NGO registered in the United Kingdom), Hospice Uganda and the Cross Roads Cancer Centre from Canada, palliative care services have improved substantially over the past couple of years. The team comprises a multidisciplinary group who see patients and their families in the clinics, wards and include home visits. Starting originally from the teaching hospitals, the service currently has expanded to some regional hospitals. Frequent training workshops are conducted with the aim of expanding services further across the country. With the expansion of palliative care services, procurement, supply and utilisation of pain medications including narcotics have improved in urban areas but are still restricted by old myths of addiction, poor regulatory and prescription practices and sociocultural beliefs. Narcotics are almost nonexistent in the rural communities. This handicap can be overcome with the incorporation of palliative care and pain management in medical and allied health school curriculum.

Oncology Resources

Table 7: Summary of oncology resources (2015)

National control plan 2012-2016	
Radiotherapy Centers	3
Linear accelerators	3 (two yet to be installed)
Cobalt-60 tele therapy machine	2
Imaging equipment	
SPECT	1
MRI, CT Scan, Ultrasound, mammogram	Regional / Teaching facilities
High dose rate brachytherapy	2 (one yet to be installed)
Image guided radiotherapy	1
Conformal 3-D planning facilities	3
Clinical oncologist	7

National control plan 2012-2016	
Trained oncology nurses	10
Walk in breast and cervical clinics	Regional / Teaching facilities
Palliative care clinics	Regional / Teaching facilities
Generic and patented drugs	Available

Challenges and Way Forward

In a country burdened by communicable diseases: malaria, HIV and TB; the rising incidence of non-communicable diseases, such as cancers, is an additional burden that cannot be ignored. Unlike non-communicable diseases, the awareness of cancers is extremely low even amongst policy makers. Although a five year cancer control program was developed in 2011, many of the strategies are yet to be implemented. Civil groups have a strong role to play in cancer advocacy, which will sensitise policy makers and ensure prompt implementation of the strategy.

The cost of cancer care is not entirely covered by the national health insurance scheme. In a country where the minimum daily wage is approximately $2, the out of pocket cost of cancer care is borne with much difficulty and has led to many presenting late or defaulting treatment. There is a need for cost sharing cancer treatments, removal of high taxes on products, encourage local manufacturing of anticancer drugs and government lobbying of pharmaceuticals to reduce pricing.

There are inadequate number cancer treatment facilities and travelling long distances and renting accommodation, further leading to financial strain.

There are inadequate human resources to tackle the current burden. Investment into oncology health care personnel training is essential for a successful cancer plan.

In the absence of national data, it is difficult to convince policy makers, private and international organisation about the burden of cancer and the need for resource allocation as well as the proper roadmap to cancer control policy implementation.

Summary

Ghana has made positive strides in improving cancer care over the past 15 years. These achievements could translate into controlling the cancer burden with further improvements in accessibility to appropriate cancer treatment facilities, skilled human resource, cancer education, early detection and screening for preventable cancers at the basic health care facilities and strengthening palliative care facilities at all levels of health care. Costs of cancer care should to be shared through effective and realistic national insurance schemes. The negative impact of strong sociocultural beliefs can only be overcome through education of the citizens at all levels.

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Chapter 16h

Guinea

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Guinea, officially the Republic of Guinea, is a country in West Africa with a total area of 245,857 km^2, bordered by the Atlantic Ocean with 320 km of coast. The country is comprised of 4 different geographical areas: (1) a coastal area, Lower Guinea or Guinea Maritime, (2) a mountainous area, Middle Guinea which includes the massive of Fouta Djallon, (3) a savannah area in the north, the Upper - Guinea, (4) an area of forest in Southeast, Forest Guinea that is also mountainous with the maximum altitude of the country, 1,752m (Mont Nimba) rich in iron ore.

These four areas, called "natural areas" do not correspond to administrative areas, which are to the number from 7 they same constituted of 33 prefectures + the special zone of Conakry the capital city.

In 2015, the total population was 11,780,162 with a density of 47.9h /km^2. The population is relatively young with 42. 0 % being below the age of 15 years and only about 3.62 % being 65 years and above. Most of this population (64%) lives in rural area and only 41% of the population is over 15 years (2010).

The schooling rate (primary school) (2006) was estimated at 51% and the adult literacy rate in Guinea is 41% according to the 2010 statistical report. 71% of households have access to safe water that is either piped or from boreholes and protected wells. Life expectancy from birth is 60.08 years. The number of physicians per 1,000 population was 0.1 in 2010. The number of hospital beds per inhabitant is 0.3 beds/1,000 inhabitants (2011) and health expenditure per capita (2012) is estimated at $32.

Guinea is a predominantly Islamic country with Muslims representing 85 % of the population. Guinea's people belong to twenty-four African ethnic groups.

Guinea's economy is largely dependent on agriculture and mineral production. It is the world's second largest producer of bauxite, and has rich deposits of diamonds and gold.

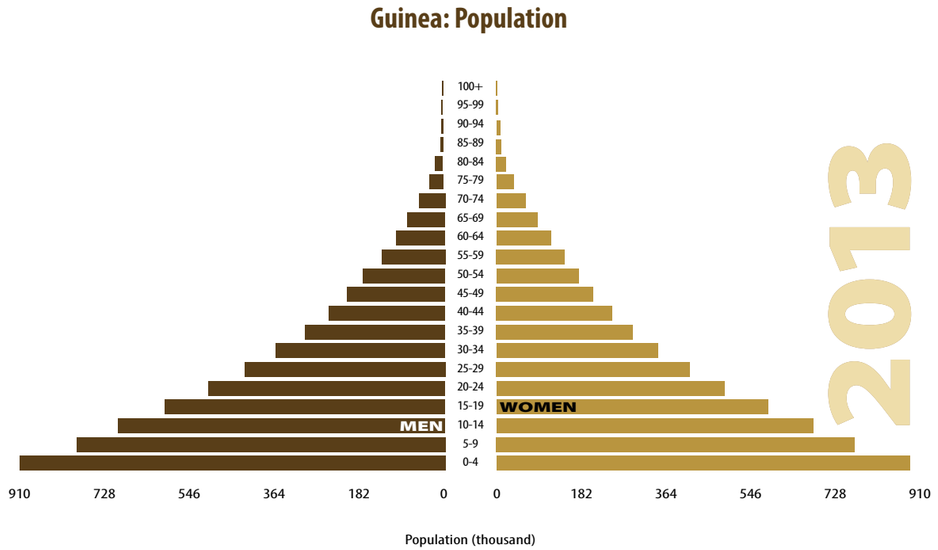


Figure 1: Population Pyramid by Age Group and Gender, 2013

Cancer Registration

The cancer registry of Guinea is population-based, covering the capital city of Conakry. It was established in 1990 and is located in the Department of Pathology at the University Hospital of Donka, Conakry. There are approximately 1,66,864 inhabitants in the city according to the General Population and Health Census of 2014. The Guinean cancer registry has contributed significantly to the improvement of cancer registration and surveillance in Conakry through the improvement of data collection in spite of few means. It is the only registry in the country.

As in most developing countries, the burden of cancer is increasing in Guinea. During the years 1992-1994 the Guinean cancer registry reported 2,064 cases of cancer, corresponding to age-standardized incidence rates (ASRs) of 83.3 per 100,000 in men and 110.5 per 100,000 in women. 2,647 cases in 1996-1999, 1,161 in men and 1,486 in women corresponding to age-standardized incidence rates (ASRs) of 99.8 per 100,000 in men and 121.0 per 100,000 in women. For the period 2006-2010 a total of 3,146 cases were registered, including 1,949 cases among the residents of Conakry with for all three periods, a preponderance in women.

The trends in the analysis of these three periods reported show a steady increase in the incidence of cancer in general. This can be mainly attributed to the high frequency of infections and consequently to the steady increase of infections-related cancer (cervix, liver, prostate cancers…) for both men and women.

Indeed, a study published in 2009 on HPV infection among women in Conakry (Guinea), found an HPV prevalence of 50.8%. This rate was considerably higher than the one observed in areas at high risk of cervical cancer (such as South America, India and some parts of sub-Saharan Africa), with the exception of places where many women are infected with HIV.

Whereas HIV prevalence has steadily declined since 2001, it remains around 1.7% in the general population in Guinea. The high prevalence of HPV and probably hepatitis B may be at the basis of the increase in cancer incidence since both cancers cervix and liver are the most frequent in the country.

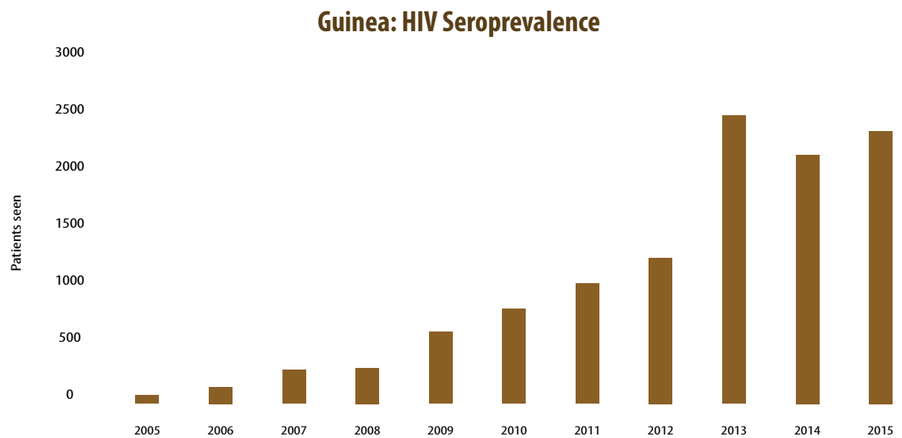


Figure 2: Evolution of HIV seroprevalence in Guinea

Cancer Incidence

As elsewhere in West Africa, the most frequently occurring cancers among women in Guinea is cervix (40%), followed by breast (18%), liver (15%), ovary (4%), skin (3%) and stomach (2%). In men, the top six cancers are the following: liver (33%), prostate (26%), non-Hodgkin lymphoma (5%), non-melanoma skin cancer (5%), large bowel (4%) and stomach (3%). Liver cancer has been the most frequent cancer of either gender. In contrast to East and Central Africa, Kaposi's Sarcoma is exceptional.

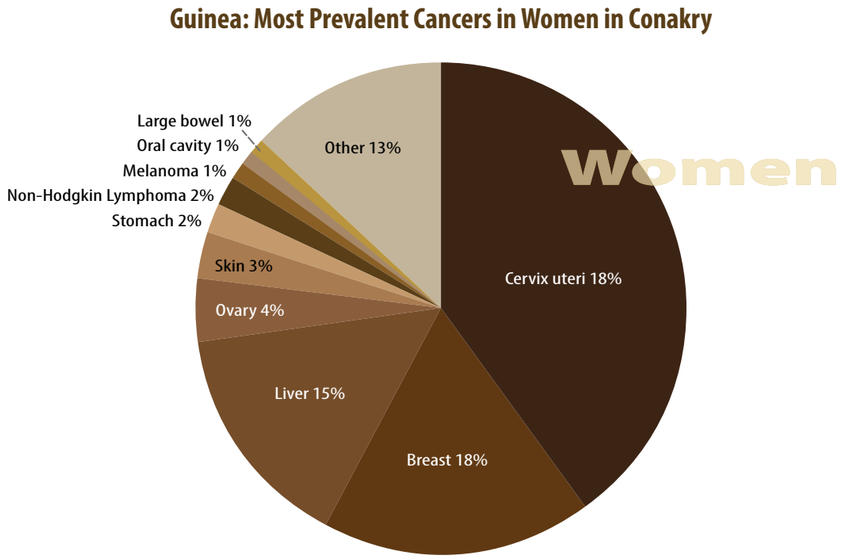
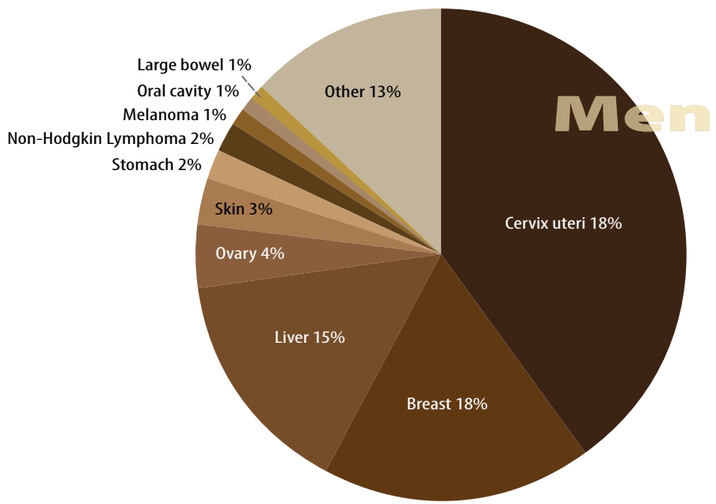


Figure 3a: Most prevalent cancers in women in Conakry 2010

Guinea: Most Prevalent Cancers in Men in Conakry



Figures 3b: Most prevalent cancers in men in Conakry 2010

Source: Cancer Registry

The study of markers of aflatoxins exposure and hepatitis B infections in rural areas conducted by the Institute for Research and Applied Biology of Guinea (IRBAG) showed that more than 95% of people surveyed have markers of exposure to aflatoxins with varying levels according to the natural areas. Percentage of AgHBS positive patients was estimated to be approximately 16.7% in the same areas.

Also, the incidence of prostate cancer in men is high and represents the second most frequent cancer in Guinea. Furthermore, the management service of disease in the country reported a steadily growing incidence.

Guinea: Prostate Cancer Trends

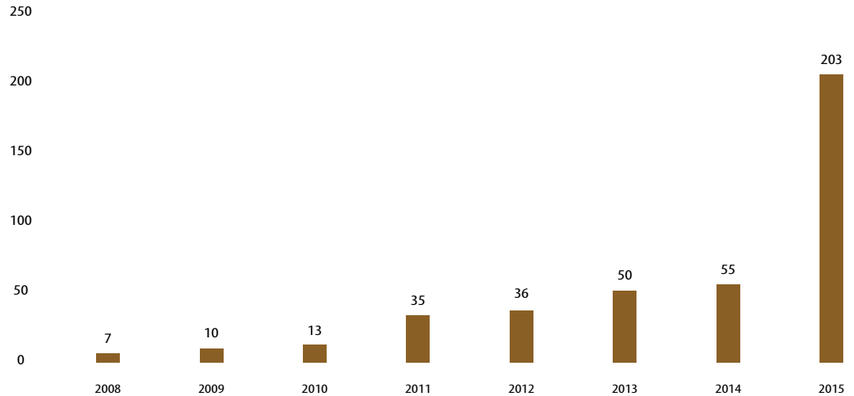


Figure 4: Prostate Cancer Trends in Guinea (CHU ID)

Childhood Cancer

The Guinea cancer registry has not published data on childhood cancers recently. The latest data available for the period 1996 to 1999 was published in 2003. During this period, childhood cancers represented 6.7% of all cancers recorded. A total of 193 childhood cancers (age 0-14) were registered, 60.6% of them having a histological diagnosis. The most frequent childhood cancer was lymphoma (64 cases representing 33.2% of the total), of which 34 cases (17.6%) were Burkitt's lymphoma, with an age standardized incidence of 11.9 per million. Retinoblastoma represents 16.1% of all cancers (ASR 8.6 per million). In view of the low recorded rates and the few cases of leukaemia and brain tumours, it is likely that childhood cancers are under-diagnosed.

Cancer Mortality

In Guinea, the civil registration of deaths, involving certification of death causes, is almost non-existent. By consequence, the published figures are often of estimates which are, in most cases, underestimated. A process of improving the registration of births and deaths is ongoing in the country. According to WHO estimates, cancer mortality is very high and may result from a diagnosis at late stage. A delayed diagnosis may be due to the lack of organised screening or early detection programs. The deadliest cancers of either gender, could have a lower incidence with vaccination and/or screening. Cervix and breast cancers are the deadliest for women while it is prostate cancer for men and liver cancer for both sexes.

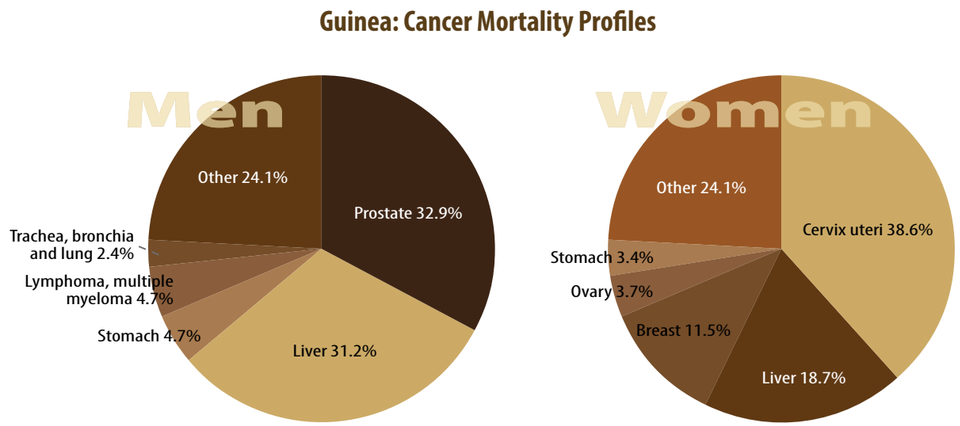


Figure 5: Profile of Cancer Mortality by Gender

Cancer Centres

There is no actual cancer centre in Guinea. The main structures for cancer management are localised in two national university hospitals. Even though staff has not always been specifically trained, surgical therapies can be performed in surgical services (gynaecology, general and visceral surgery, urology, maxillofacial, otorhinolaryngology, thoracic, paediatric surgery and surgical oncology unit).

Medical Oncology Resources

Treatment with chemotherapy is organised in the two university hospitals by the following services: gynaecology, paediatrics, internal medicine, and dermatology. In 1998 a haematology-oncology service has been created and administers chemotherapy for haematologic malignancies. In addition, there is also a unit of surgical oncology led by a surgical oncologist within the general surgery department of the larger of the two university hospitals (National Hospital of Donka) since 2004.

Anti cancer drugs are not included in the National List of Essential Medicines. The availability of chemotherapy drugs is very limited in the public sector, as well as in the private sector. These drugs are imported only by private pharmacists, wholesalers, distributors and sometimes even by non-pharmacists, and are sold at prohibitive prices. Most of all cancer patients must buy their medicines themselves, and/or with the help of their families. Indeed, very few patients have insurance to cover these very high costs.

Patients often give up chemotherapy after a few courses due to lack of funds and also because the start time and/or the interval between the cures are not respected. Another important reason is the continual shortages. Besides, there is no processing unit for chemotherapy in the private sector.

Radiotherapy Resources

Currently, there is no radiotherapy equipment in Guinea. Patients, who can afford it, take in charge their trip out of the country (on the continent or in Europe) to access specialised health care. Since 2006, efforts are underway to establish a National Centre of Oncology and to implement a holistic management of cancers including radiotherapy facilities. Although, one radiotherapist is being trained, there is currently no trained physicist.

Diagnostic Resources

There are only two histopathology services in the country. The first one is the National Centre of Pathology, established in 1990. It is staffed by two pathologists and is located inside the National Hospital of Donka, which is the largest of the two university hospitals. The second histopathology service, newly established in the China-Guinea friendship Hospital, is a general state-owned hospital with a semi private management. It is also staffed by two pathologists. These are the only two cancer diagnostic structures for the country. These laboratories use conventional cytologic methods and basic pathological anatomy. Fine needle aspiration is readily available in the specialised services of the two major teaching hospitals and Friendship Hospital. Interventional radiology is still a common practice. The techniques of immunohistochemistry, cytogenetic and molecular biology are not used. In the absence of suitable equipment, there is no possibility to carry out extemporaneous examinations.

As the brain drain is particularly important in this field, these services are affected by a severe lack of qualified staff. Indeed a number of pathologists sent abroad for further training never returned. Even those willing to come back to Guinea, end up returning to their host country when faced with work difficulties and salary proposed. Another great difficulty is the insufficient availability of formol in private clinics and hospitals inside the country. The improper storage of samples often leads to misdiagnosis. In these circumstances, the delivery time of cytology results ranged from 48 hours to 7 days, and pathological examinations from three to six weeks. Currently, no private histopathology laboratory exists.

However, many biomedical analysis laboratories exist in the private sector and some of them are able to identify tumour markers: PSA, Beta HCG, CA-125, CA 19-9, CA 15-3, carcinoembryonic antigen (CEA). National hospitals' medical imaging services contribute to tumour diagnosis by conventional radiography or ultrasound. All mammography services, as well as the MRI unit, are in the private sector in the capital city. Out of three scanners, only one is in the public sector (Centre for the Diagnosis of National Social Security Fund). Above all, the main problem remains the lack of radiologists and radiology technicians trained in these new technologies.

Figure 6: Scanner unit in the public system

Figure 7: Scanner unit Toshiba

Figure 8: MRI unit in the private sector

Figure 9: Mammography unit in the Public Sector

Availability of Oncologists

There are approximately ten organ specialists and one oncologist surgeon in the country. All are working in the two university hospitals. Two haemato-oncologists treat haematologic malignancies: one at the University Hospital Donka and the second in the private sector. A medical oncologist and a radiation oncologist are currently being trained. Some residents in training in surgical specialty services perform surgical treatments for cancer pathologies without receiving formal education.

The National Cancer Control and Prevention Program (NCCP)

In view of the high level of morbidity and mortality related to certain types of cancer (cervix, liver, breast and prostate), cancer has been recognised as a public health problem in Guinea. Thus, the Ministry of Public Health of the Republic of Guinea has referred to cancer as a chronic disease and included its fight in both the National Health Development Plan (NHDP) from 2003 to 2012 and in the National Reproductive health Program (NRHP) for gynaecological cancers.

A national plan against cancer (2004-2008) was written in 2004 in order to prevent cancers that can be prevented, treat cancers that can be treated and provide supportive care to people in need. This first document was developed through an extensive consultation process involving national and international stakeholders and coordinated by the national coordination of the fight against cancer. The PNLCC was formally adopted in April 2004.

The overall objective of the plan was to reduce the burden of morbidity and mortality from cancer through the implementation of cost-effective prevention and control interventions based on evidence, and to provide palliative care to improve quality of life of people living with cancer and their families. The specific objectives were to strengthen primary prevention, early detection, diagnosis and treatment, palliative / rehabilitation and monitoring and research. Although in recent years, significant progress has been made in the prevention of cervical cancer, the operationalisation of this plan in these different components was not realised for lack of satisfactory financing.

In August 2010, a larger plan to fight chronic and non-communicable diseases (2011-2015) was written with an important component in the fight against cancer. This component has been delayed in its preparation and implementation. It was supposed to give priority to gynaecological cancers, liver cancer, prostate cancer in men and childhood cancer: in the case of the latter, little has been undertaken due to the lack of specialist

in paediatric oncology. This plan will include sections on the revitalization of Cancer Registries, prevention, diagnosis, early detection, treatment, palliative care, quality assurance, training, assessment, monitoring, security and research. To accompany this plan, a strategy document for the fight against cervical cancer is being developed simultaneously.

Cancer Risk Factors and Prevention

Infection

In terms of risk factors, on the African continent including Guinea, it is estimated that 40% of cancers in men and 29% of cancers in women are related to infectious factors. In Guinea, cancer related infectious risk factors include hepatitis B virus, Human Papilloma Virus (HPV) and urinary schistosomiasis. In this context, the study of markers of aflatoxins exposure and hepatitis B infection in rural areas, conducted by the Institute for Research and Applied Biology of Guinea (IRBAG), showed that more than 95% of people surveyed have markers of aflatoxins exposure with varying levels according to the Natural Areas. Chronic carriage of AgHBS was estimated to approximately 16.7% in the same areas. Hepatitis B and C chronic infection are responsible for the occurrence of long-term hepatocellular carcinoma, itself responsible for 18, 7 % of all death related cancer in women and 31.2% in men in 2014.

In the context of primary prevention, some farmers have been trained in seed storage to fight against aflatoxins and; since 2006, vaccination against hepatitis B has been incorporated in the Expanded Programme on Immunization. In 2014 the coverage of hepatitis B vaccination among children was 63%.

Moreover, since cervical cancer incidence in Guinea is among the highest in Africa Region (51/100,000), HPV infection was investigated in women with and without cervical cancer in Conakry, Guinea.

HPV prevalence was 50.8% (32.1% for high-risk types) and relatively constant across all age groups (fig.6). HPV16 was the most common type, both among the general population (7.3%) and, notably in Invasive Cervical Cancer (ICC) (48.6%). The others most common types in ICC were HPV45 (18.6%) and HPV18 (14.3%).

The heavy burden of HPV infection and severe cervical lesions in Guinean women calls for new effective interventions. Sixty-three per cent of cervical cancers are theoretically preventable by HPV16/18 vaccines in Guinea; perhaps more if some cross-protection exists with HPV45. However, for the moment, no vaccination program against HPV has been implemented in Guinea, not even the demonstration project supporting by the Global Alliance for Vaccines and Immunization (GAVI) due to insufficiency of general immunisation coverage. The country is on the list of eligible countries in 2017.

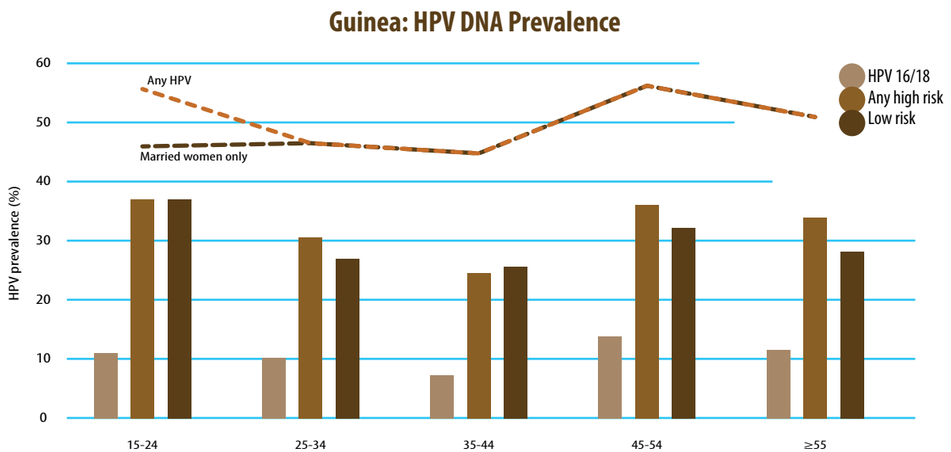


Figure 10: Age-specific Prevalence of HPVDNA by HPV type(s) overall (831women) and among married women only (674 women)

About other risk factors, the steps survey carried out in 2009 in the capital Conakry and Lower Guinea representing 22% of the country in terms of area, examined a number of risk factors for non-transmissible diseases including cancer.

Tobacco

The survey showed that smoking affects nearly 18% of the study population without significant difference between the urban and rural population. The age of onset of smoking is relatively young, 20 years on average for Conakry and urban area and 18 years in rural area.

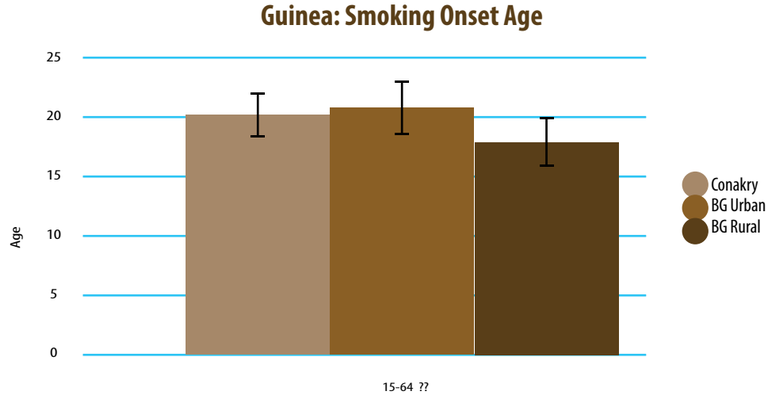


Figure 11: Average age of Smoking Onset (WHO. Country Factsheet, 2010)

In general, tobacco use is much more common in men than in women. Exposure to passive smoking, as in many other countries is not unusual because the restrictive laws on smoking in public areas and even in schools are poorly applied or not applied at all. Various surveys on smoking have been conducted in schools in Guinea in 2001 and 2008 by the Ministry of Health and Public Hygiene in collaboration with WHO Guinea and CDC Atlanta USA. These studies showed that among 17% of smoking students, 4% are women. Young people start smoking between 12 and 13 years, and 78% are in the age group of 16-20 years with an average number of 11 to 20 cigarettes a day. Similarly, these studies demonstrated ignorance among students of the real danger of tobacco. Despite everything, the incidence of cancers of the respiratory tract and oral cavity is low in the Guinean general population.

Regarding the interference of the industry, attention should be drawn to the different strategies used to promote the consumption of this harmful product. This is among other tobacco advertising, sponsorship of major events, pressure on public authorities including corruption.

For all these reasons, a number of achievements have been obtained: the development of many activities to improve access to information (Development of IEC campaigns, education for behaviour change). An anti-smoking law was promulgated by the President of the Republic of Guinea on the 10 December 2012 concerning marketing, consumption, advertising and sponsorship of tobacco and its derivatives. (Law L / 2012/039 / CNT of November 15, 2012). This law comes within the implementation framework of the UN Framework Convention for the fight against tobacco negotiated under the auspices of the World health organisation (WHO). It must be recalled that the anti smoking law banned smoking in public places and in public transport and advertising of cigarettes on all forms. Smuggling is harshly punished. Sellers are required, under pain of penalty, to inform the consumers about the risks. The offenses prescribed by that act, range from simple breach of crime to the misdemeanour. It remains to see the level of enforcement of this law that is far from perfect.

Alcohol Consumption

Alcohol consumption is considered worldwide as an important risk factor for several forms of cancer. In 2010, total alcohol consumption per capita in litres of pure alcohol in Guinea was 0.7%. 1.4% for men and 0.1% among women. For cultural and religious reasons, it is likely that these figures are underestimated because many drinkers deny the use of this product considered illegal by the Muslim religion practiced by 85% of the population. The country has a National Strategy and an operational action plan to fight against the harmful use of alcohol, in the integrated multi-sectoral policy, national NCD encompassing several NCDs and their common risk factors.

Diet and Exercise

Concerning nutritional health, obesity is an increasingly concern in Guinea, particularly in women since being coated is considered a criterion of beauty. In 2014, 5.9% of the population was considered obese; 8.9% among women and 2.8% among men. It is well established now that "junk food" has reached all countries of the world. The Republic of Guinea as most of the African countries is in transition in this field. Eating habits have changed. Traditional food is being replaced by diets too rich in fat and poor in fibre. The same Guinea STEP wise survey in 2009 had already shown that the consumption of fruit and vegetables is low in the studied population and almost 70 to 90% of those surveyed consumed less than 5 fruits or vegetables per day. In addition, the level of physical activity was found low. Between 60 and 65% of people in the 15-64 age range living in Conakry and in urban areas do not practice any physical activity. The combination of these three risk factors associated with other such as overweight, hypertension, and hyperglycaemia showed that among surveyed subjects aged 25-64, 30% of the urban population, 25% the population of Conakry and 17% of the rural population accumulates more than three risk factors for non-communicable diseases. By consequence, risk factors for non-communicable diseases are frequent in the Guinean population.

The nutrition Division of the Ministry of Health and sanitation organises nutrition education and awareness sessions on the consumption of fruits and vegetables via public and private audio-visual media.

The promotion of physical activity is another component of prevention supported by the Ministry of Health and Sanitation through the national program against non-communicable diseases. In this context a marathon is organised once a year. It is a great opportunity to perform greater awareness activities and for media to advertise on the value of physical activity during the week preceding the event.

Cancer Screening Services

In Guinea, as in most of the countries of the continent, cancers are most often seen in advanced stages and involve therefore an important management, costly and often ineffective. Coverage in this type of specialised and high-level care remains very inadequate in the country. Accessibility for patients, who require the services, is not always assured and remains uncertain with regard to needs; because of insufficient technical and financial resources and qualified personnel. All this justifies the introduction of screening programs that are of major interest in the context of public health action. This screening can and should be easy to perform, simple, effective, inexpensive, enabling effective prevention of cancer.

Breast Cancer

Conakry, the capital city, is the only city in the country that has the mammography equipment. Of the five available; one is in the public, in the centre of Diagnosis of the National Social Security Fund. Neither of the two university hospitals, where the management of this disease is carried

out, has mammography equipment. Also very few women benefit from a clinical breast exam even in basic gynaecological services unless they are presenting symptoms. The self-examination also is not yet widely practised except in some intellectual women who are regularly informed by the media and/or internet. This situation is the result of ignorance of most of the women. It explains the huge delay in diagnosis as seen in these photos while the breast is an organ easy to reach.

Figure 12. Breast carcinoma with extensive necrosis

Cervical Cancer

Conventional cytology is available in both pathological anatomy laboratories existing in the public sector in Conakry. However, due to a series of organisational problems, high cost, and lack of sufficient training and equipment to perform this type of procedure, there is very little demand from the population who is itself not sufficiently informed of the existence of this procedure for cervical cancer screening. In the medical population in general, the smear is often considered a diagnostic test. Therefore, since the late 1990s and early 2000s, as part of the fight against cervical cancer, alternative screening methods by visual inspection with acetic acid (VIA) and iodine (VILI) have been tested and implemented with the assistance of the International Agency for Research on Cancer (IARC) under the ACCP. The results in terms of accuracy have been very encouraging and the results of many studies in the literature have finally convinced us to offer this method as a means of screening and trying different approaches favouring the development stage. This approach is currently being implemented with the assistance of other agencies such as USAID, WHO Afro through its non-communicable disease division and UNFPA, in order to obtain at least 50% coverage of the target population (25 to 65) within 5 years. In this context, peripheral screening units for cervical precancerous lesions are being integrated in the health sectors and referral hospitals associated with simple and safe treatment methods validated by the same studies. This refers to cryotherapy, the loop electrosurgical excision (LEEP) and cold conisation. Another method of treatment the "Cold coagulation" is being evaluated.

For the organization of the screening programme, the reference network integrates gynaecology and obstetrics services. These services will be made gradually contribution for clinical diagnosis and for therapeutic management.

For all this to happen, a number of major activities are to be undertaken at each stage:

- Establishment of a training process
- Increase of public awareness
- Invitation to screening and screening clinic available every day in urban health centres (CSUs) and the public hospital of the city or municipality concerned.
- Implementation of the system of diagnosis and treatment for positive cases.
- Establishment of a referral system for both precancerous lesions and invasive cancers
- Establishment of an information, monitoring and evaluation system

It is for these reasons that the Francophone Regional Training Centre for Gynaecological Cancers Prevention has been taking place since 2001 in Conakry. Physical headquarters were built and opened in November 2006.

The main mission of the centre is to support the implementation of national and sub-regional strategies for the prevention of major gynaecological cancers specifically cervical and breast cancer. It supports programmes in education and awareness by informing the different strata of the population on the benefits of gynaecological cancers screening and improving services and research.

Since then, several types of options for care delivery were tested: integration of existing screening in the health system as described above; use of mobile clinics; family planning and cervical cancer screening campaign; and implementation in the primary health care of the algorithm No. 2 of the WHO PEN tool (Package of Essential Non communicable Disease). The following objectives are pursued:

- Testing the feasibility of different patterns of health care services
- Testing different methods for increasing awareness
- Estimate the coverage rate of the population
- Implementing a practical based training process

The results in terms of participation of target populations, rate of positive tests (7.5 to 9%) and care of precancerous and cancerous lesions diagnosed (> 95% for pre-cancerous lesions and 55% for cancer) is very interesting.

Figure 13. Integration of Screening in the Existing Health System

Between 2004 and 2009 11,250 women were examined in the training centre. Among them, 180 carcinomas in situ (CIN) and 420 invasive cancers were found. The number of women treated for CIN was 160 (89%) and the number of women treated for invasive cancer was 252 (60%).

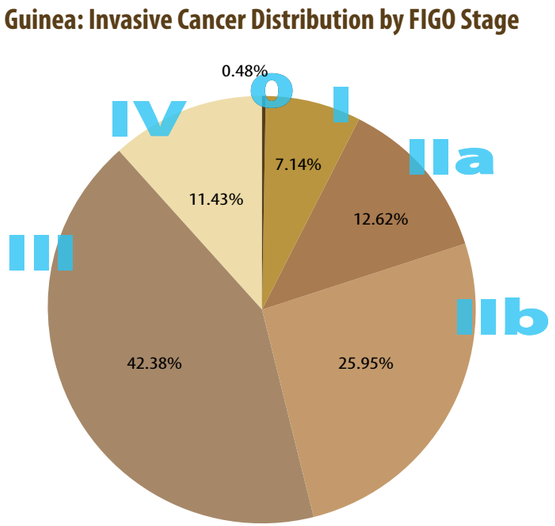


Figure 14. Invasive Cancers Distribution according to the FIGO stage

This figure shows a decrease in stages III and IV at diagnosis, probably due to regular screening activities in Conakry, even if there is still no veritable organised programme.

In 2012 integrated family planning (FP) campaigns and screening for cervical cancer have been started to increase the coverage of the target population. In Conakry, in three days of campaigning, 943 women were examined. Fifty-seven precancerous lesions and 17 cancers were found and treated.

Between September and December 2013, seven administrative regions and Conakry city have been covered by a new campaign integrating FP and cervical cancer screening. The stay in each regional capital was six days; the first three days were devoted to training and last three to the PF and screening activities during the same clinic. Specific objectives were to provide 3,000 women aged 25 to 49 years (300 by region + 900 for Conakry) with cervical cancer screening and to offer to 1,000 women aged 15-49 years (100 by region + 300 in Conakry) FP services.

A total of 5,673 women aged 15 to 60 and over were examined during this campaign, which was 89.1% more than expected. Among these women, 5,110 were aged between 25 and 49 (90.07%), i.e. the target population for screening. The peak of participation was observed among women in the age group of 35-39 years (18.5% of the population). The campaign was followed by a training workshop for regional trainers, which consolidated the gains and favoured anticipation of future campaigns. This training, which lasted ten days in one of the regional capitals, brought together 18 healthcare providers from seven regional hospitals (nine doctors, nine midwives and nurses).

It was planned to repeat this type of campaign once a year to gradually reach all 33 prefectures and thus substantially increase screening coverage across the country. The strategy behind this project was to allow minimum equipment to be available in each city, in order to ensure continuity of screening and timely referrals for treatment. These hospitals would be given the means of diagnosis and treatment of precancerous lesions in a second phase. Unfortunately, the epidemic of Ebola (2013-2015) considerably slowed the implementation of cervical cancer screening in the country. However, the regular daily activity of screening at regional training centres was maintained in Conakry even during the peak of the epidemic.

Other Cancers

There is no formal screening programme for other cancers such as colorectal cancer and prostate cancer. For the latter, some urologists request PSA testing and/or digital rectal examination for some men over 50 years of age who come in consultation for various reasons, but these measures are not systematic and are now known to be ineffective.

The absence of its screening programmes is due to lack of awareness of people but also to scarcity of resources. There is an absence of an effective national mechanism to motivate, organize and coordinate screening activities for other cancer sites. Another difficulty for implementing such prevention programmes is the almost total lack of reference system for confirmed cases towards reference centres. There is only one reference centre for prostate cancer (CHU Conakry), and none for other cancer sites.

Palliative Care

Palliative and rehabilitative care is strongly linked to the management of cancers in national programmes against cancer. Unfortunately, in Guinea, as in large parts of Francophone Africa, health systems face a major challenge: caring for more and more people who suffer from pain, breathing difficulties, nausea, anxiety and depression due to chronic diseases including advanced cancers. Without proper treatments, these symptoms often destroy the quality of life of patients and their families.

Most of these symptoms can be controlled with palliative care. However, these treatments are not accessible to the greatest number. It is estimated that each year about 912,000 people, including 214,000 children, need palliative care in Francophone Africa. Yet 16 Francophone African countries including Guinea (out of 22) do not provide palliative care to patients in need. While the local regulations are favourable to the use of drugs in medical treatment and palliative care, there is to date no real palliative care policy in Guinea. Guinea has signed the 1961 Convention and the 1998-2008 strategic plan implemented by the International Organization of Narcotics Control Board (INCB). The Ministry of Health conducted registration of opiates on the National List of Essential Medicines used in hospitals and different levels of the health pyramid. This represents a significant gain in the context of introducing palliative care in the country.

Cancer and HIV/AIDS in Guinea

Although HIV prevalence in West Africa is much lower than in southern Africa, the sub-region has several serious national epidemics. Thus, if the prevalence of HIV among adults (15-49 years) is less than 1% in Cape Verde, Niger and Senegal, it varies between 1% and 4% the adult population in other West African countries (1.7% in Guinea). The political will supported by the government and development partners has quickly extended the therapeutic management of people living with HIV.

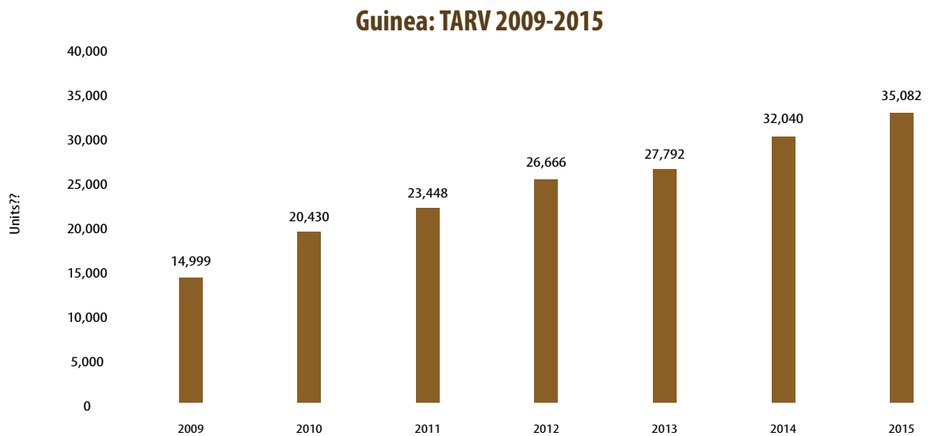


Figure 15. Evolution of Antiretroviral Therapy 2009-2015

Despite the convincing results obtained during recent years in terms of therapeutic coverage and of follow-up, it should be stressed that HIV patients represent a fragile population requiring a very long-term care. This attention should be strengthened among patients with a long therapeutic history due to occurrence of co-morbidities, antiretroviral (ARV) treatments and ageing.

Like in other African countries, the majority of HIV-infected patients followed and treated with ARVs are women and young people. Survival of HIV-infected patients greatly improved when access to antiretroviral treatment was granted at large scale. This improvement in survival is likely to be followed by a change in morbidity with an increasing share of chronic diseases such as cancers.

The association HIV and cervical cancer has been documented particularly in South and East Africa, where the incidence of both diseases is significantly higher than in West Africa. In Guinea there is currently no study covering the entire territory on this association. However some hospital-based studies were made. The most significant studies were carried out in 2006 and 2014 in the centre of management of gynaecological cancers, University Hospital of Donka Conakry. HIV prevalence was almost constant in these two studies: 7.2% in 2006 and 7.5% in 2014.

There are still a lot of unanswered questions on the management of HIV patients diagnosed with cancer. It is in this context screening should target this population.

Cervical cancer screening has been identified as one of 11 specific interventions, in the standards and procedures on Prevention of mother-to-child transmission (PMTCT) published in 2013. It was then recommended to integrate screening activities of cervical cancer in routine tasks of maternal and child health services. The main activities involved are antenatal activities before the 15th week of amenorrhea, post natal

consultations three months after childbirth and family planning (FP) services. This applies to public sector and private health structures having integrated PMTCT services.

The daily management of screening activities should take into account a number of considerations:

- Under the responsibility of human resources activities in health structures concerned, the patient circuit should be developed and integrated into the routine activities of antenatal, post natal and FP consultation ;
- Healthcare providers will be trained and standard procedures will be developed for the realisation of pre-test counselling, cervical cancer screening activities, and management of lesions detected. These procedures will be based on a document developed for this purpose and taking into account the level of the relevant health facility;

Integration involves that providers have the required capabilities to perform screening as well as other integrated activities of PMTCT:

- The cervical screening test should be systematically proposed during the counselling and the offer of HIV testing: during prenatal, post-partum and postnatal examinations
- The patients, (especially HIV Positive) will be more targeted.

During both the prenatal care and the post natal consultations, the principles must be:

- To offer cervical cancer screening to the greatest possible proportion of pregnant women;
- To ensure cervical cancer screening for all HIV-positive patients;
- To ensure a rational management in the implementation of the continuum of care through the proper use of allocated resources;
- To improve the coverage of cervical cancer screening and lighten the workload in PMTCT services. This requires to increase the capacity of awareness and counselling in the community but also in other services.

Results of these integrated activities are planned to be analysed in the coming years in order to measure their exact impact.

Education of Cancer Care Professionals (Human Resources Development)

The country is very backward in the development of human resources and professionals of cancer management. There is only one radiation therapist in training, two haemato-oncologists in function, one medical oncologist and one surgical oncologist. Training specialists is not available locally and requires investments in foreign countries. This is also the case for imaging specialists. Although there are organ surgeons with expertise in the surgical management of cancer, they are very few. There is currently no postgraduate education in this field in the Republic of Guinea.

Given the high incidence of gynaecological and breast cancers, which represent 50% of cancer cases in the country, a degree course for the holistic management of these cancers should be established first. In addition, a reference centre with equipment and financial resources should be created. This is essential to the implementation of an authentic institute of fight against women cancers in Guinea.

The training centre for the prevention of gynaecological cancers was implemented in the early 2000s in the Gynaecology Service of the Donka University Hospital in Conakry, and materialized by a freestanding building in November 2006. In addition to the training of trainers in prevention of gynaecologic cancers, the centre provides permanent care of screening for breast and cervical cancer, and management of precancerous lesions.

NGOs in the Fight Against Cancer in Guinea

Regarding the role played by civil society in the fight against cancer, we must recognise that there are very few NGOs involved in this struggle in the country. A National League was created in the early 2000s; it is not functional due to lack of funding. A few other NGOs have sporadic activities with a very limited impact. There are, among other, the following ones:

- "The Guinean Association for the fight against cancer (AGUICAN)". This NGO organises sensitisation sessions on breast cancer mostly during the global days of the struggle against cancer. To this end, the Guinea Alumina Corporation, a mining company, subsidiary of Emirates Global Aluminium (EGA) has been mobilised by the NGO to be involved in breast cancer screening and to provide some palliative care medicines. The association leads sporadically media activities of information and awareness in online newspapers. It also organised a skin cancer screening campaign for the albinos. This campaign aimed at examining 147 albinos in Conakry and in the surrounding towns. It helped find 15 patients with cancerous lesions, including four with advanced lesions. The latter have benefited from palliative and seven others were treated with the support of the association.

- « Agir tous contre le cancer en Guinée » also organises awareness campaigns. It arranged a special awareness campaign about prostate cancer in partnership with a local bank (UBA). Funds to buy some medicine for treatment were obtained.

- « Fraternité médicale Guinée », without specifically being a NGO to fight against cancer, was involved in 2006 in the community component of the fight against gynaecological cancers with the Guinean Society of Gynaecologists and Obstetricians. It was a punctual activity of community mobilisation of this NGO of young physicians very involved in the fight against HIV/AIDS. Women receiving care for HIV, prenatal care and family planning counselling were sensitised and mobilised to visit cervical cancer screening (VIA/VILI). Screening centres opened in the five municipal hospitals in Conakry with the support of the training centre for prevention of gynaecological cancers.

Although there is a clear commitment of these NGO to improve the well-being of cancer patients, their activities often lack coordination. So it is difficult to measure their real impact on the fight against cancers in the country.

Chapter 161

Kenya

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Kenya is a low income country in Sub-Saharan Africa with a population of 43 million people and an area of 591,971 km^2. There are 10,239 registered medical doctors and dentists in the country. The distribution of the various cadres of health care professionals is given in table 1.

Kenya, like most other developing countries is undergoing an epidemiologic shift of disease patterns characterized by increasing prevalence of cancer and other non-communicable diseases and a double strain on health care resources as shown in figure 1. These emerging lifestyle and genetic diseases previously associated with high income countries are not replacing infectious diseases but adding to them (Etyang et al, 2014; Parkin et al, 2014).

Cancer is ranked as the third most common cause of death in Kenya, after infectious and cardiovascular diseases. The annual incidence is about 28,000 cases with mortality estimated at 22,000 cases (Ministry of Public Health and Sanitation and Ministry of Medical Services, 2011). Over 60% of those affected are below the age of 70 years. In Kenya, the risk of getting cancer before the age of 75 years is 14% while the risk of dying from cancer is estimated at 12%.

Table 1: Registered Healthcare Personnel per 100,000 Population, 2011 – 2014

	2011	2012	2013	2014
Doctors	19	20	21	21
Dentists	2	2	3	3
Basic Degree Nurses	3	4	4	6
Diploma Nurses	80	86	91	96
Certificate Nurses	62	65	64	63
Clinical Officers	25	28	32	37

Cancer prevention and control is jointly done by the Ministry of Health and Private sectors guided by the National Cancer Prevention and Control Strategy 2011-2016. The strategy outlines expansion of existing cancer centres and creation of four other regional centres (Ministry of Public Health and Sanitation and Ministry of Medical Services, 2011-2016) in addition to various strategies for prevention, early diagnosis, appropriate treatments, palliative care and survivorship care. Kenya has also started implementation of the Cancer Prevention and Control act of Parliament 2012 Chapter 246B (Parliament of Kenya, 2012). Some of the aspects covered by this law include 1) to promote public awareness about the causes, consequences, means of prevention and control of cancer 2) to extend to every person with cancer full protection of her/his human rights and civil liberties 3) to promote access to quality and affordable diagnostic and treatment services for persons with cancer and 4) to ensure sustainable capacity for the prevention and control of cancer. Once this law is fully implemented, all cancer prevention and control activities will be under the National Cancer Institute. This is a milestone in cancer control in Kenya.

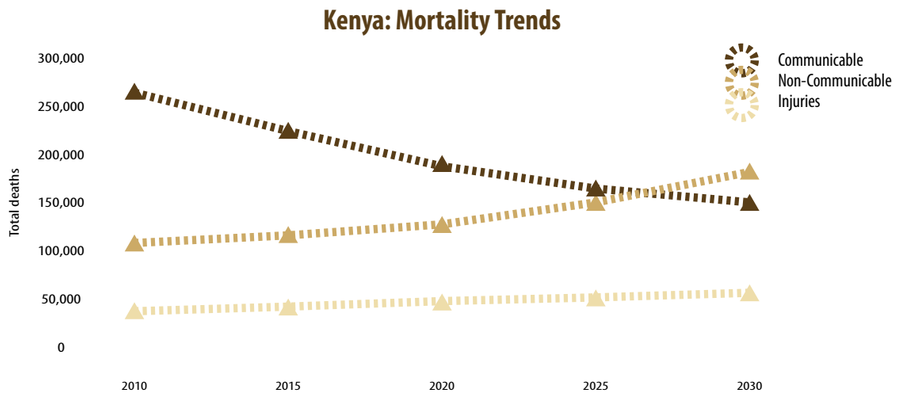

Figure 1: Mortality trends in Kenya

Source: Ministry of Public Health and Sanitation and Ministry of Medical Services, 2011

Cancer Patterns

There are two population-based cancer registries in Kenya based in the urban centres of Nairobi and Eldoret (African Cancer Registry Network). Nairobi City is the Capital of Kenya and has an estimated population of 4 million inhabitants, while Eldoret is a smaller city in Western Kenya. These two registries gather data on cancers cases seen at the two tertiary public referral centres namely Kenyatta National Hospital (KNH) and Moi Teaching and Referral Hospital (MTRH) in Nairobi and Eldoret, respectively.

Nairobi

Figure 2 shows the 16 most common cancer in the Nairobi population men. These 16 cancers account for 69.1% of incident male cancer cases in the registry. The top five cancer sites are prostate, oesophagus, stomach and liver.

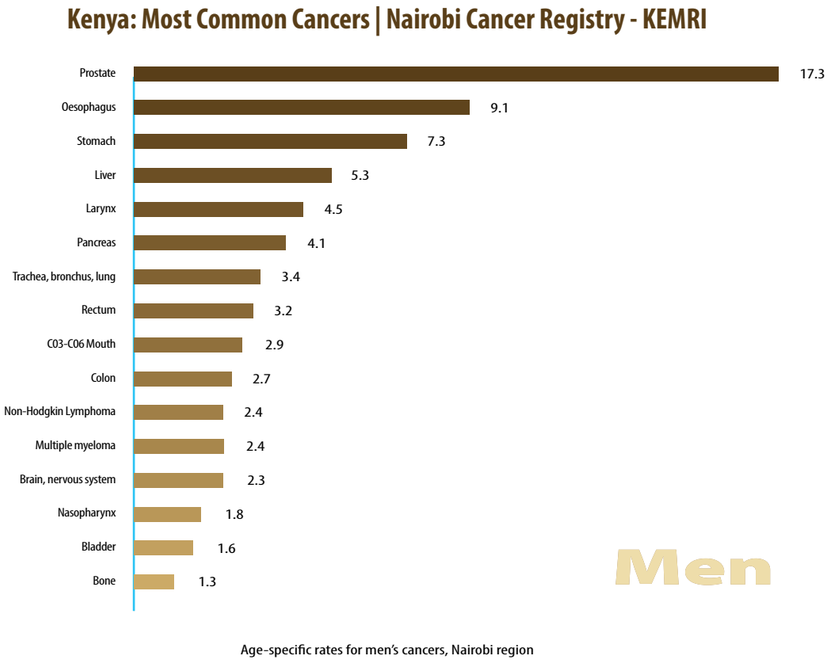

Figure 2: Cancer in Men in Nairobi

The 20 most common cancer sites among Nairobi women are shown in figure 3. These 20 cancers account for 78.1% of incident cancer cases in women within the registry. The commonest are Breast, Uterine Cervix, and Stomach.

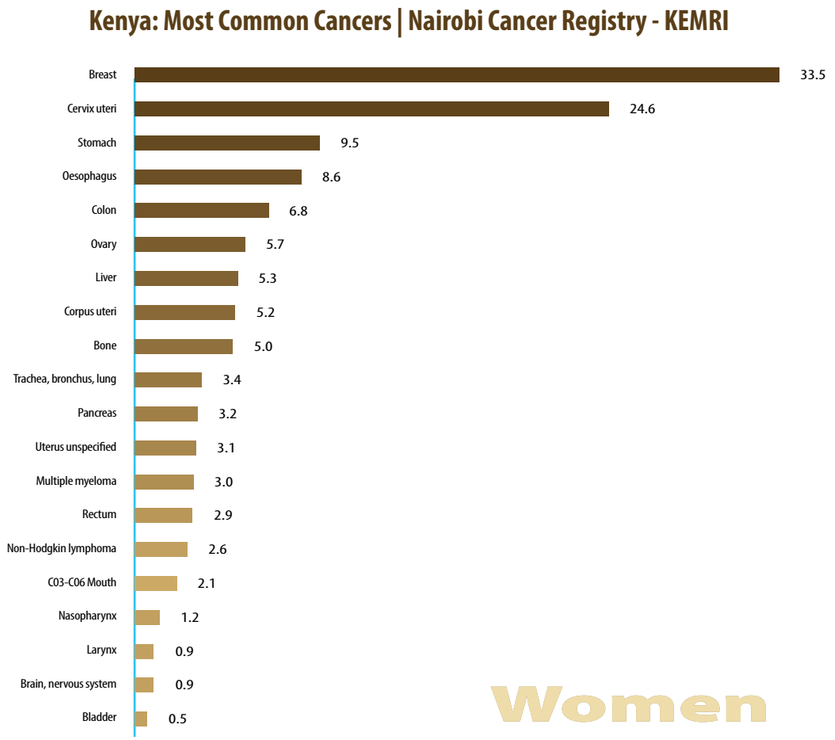

Figure 3: Cancers in women in Nairobi

Childhood cancer in Nairobi are depicted in Figure 4, the most common cancer sites being retinoblastoma, Burkitt's lymphoma, Leukaemia and Nephroblastoma.

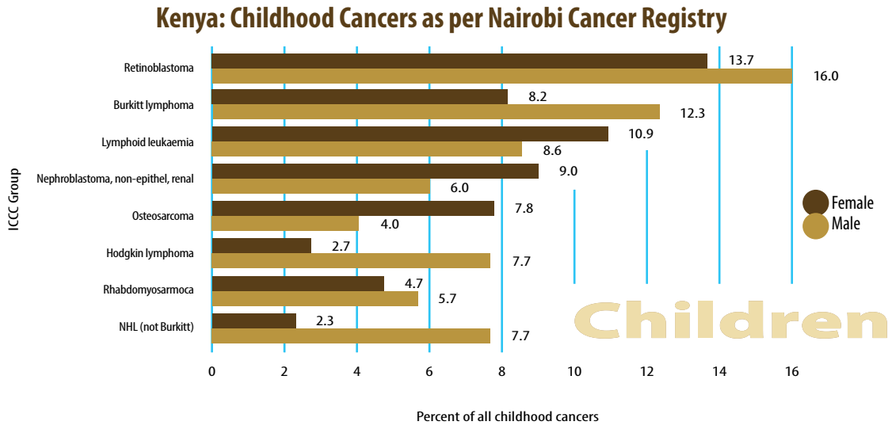

Figure 4: Childhood cancers in Nairobi

Eldoret

In the Eldoret population, the most common cancers in men are Kaposi's Sarcoma (HIV-related), oesophageal carcinoma and non-Hodgkin's lymphoma (Figure 5) while in women the most common cancers are cervical cancer, breast cancer and Kaposi's Sarcoma (HIV-related) (Figure 6). Common childhood cancers include non-Hodgkin's lymphoma, leukaemia and nephroblastoma (Figure 7).

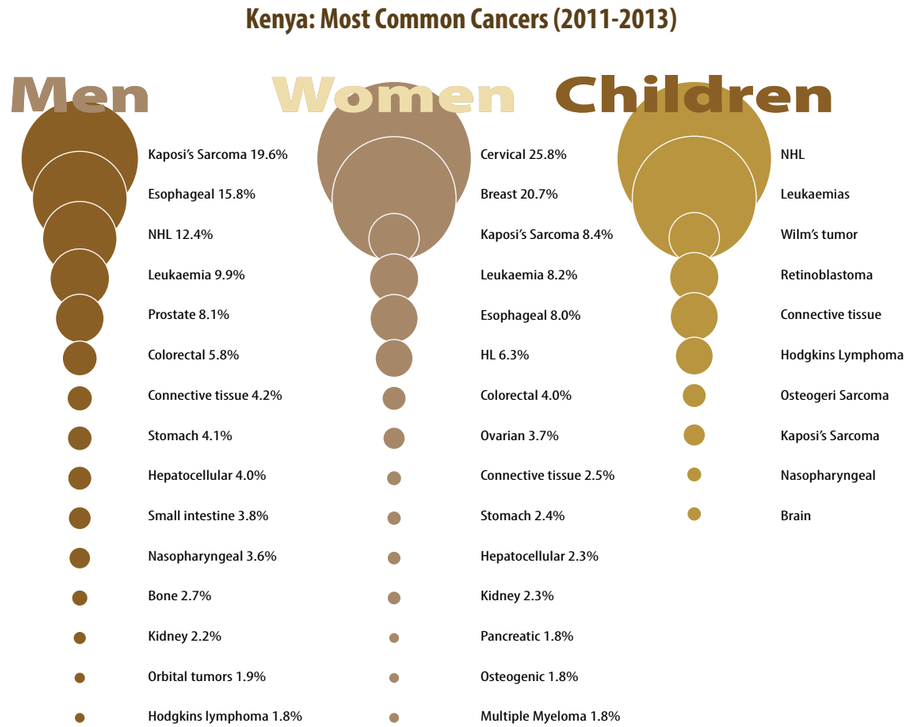

Figure 5-7. Cancers in men, women and children in Eldoret, Kenya

Infrastructure For Cancer Control

There are two public cancer centres in the country based at Kenyatta National Hospital in Nairobi and Moi Teaching and Referral Hospital in Eldoret. The country has nine radiation oncologists, eight medical oncologists and two gynaecology oncologists, all located in Nairobi and Eldoret. Haemato-pathologists also administer chemotherapy in various hospitals. While importation of chemotherapy drugs in Kenya is facilitated by the Pharmacy and Poisons board, making them available anywhere in the country, access to the drugs is limited because of high costs. Kenyatta National Hospital in collaboration with the International Atomic Energy Agency (IAEA) is training radiation technicians. Both Moi University and Nairobi University are developing curriculum to train medical oncologists and oncology nurses. MTRH is already training Medical Oncology Clinical Officers (Higher National Diploma in Medical Oncology) while Moi University in collaboration with Princess Margaret University

in Canada is training gynaecology oncologists (Master of Science in Gynaecology-Oncology). However there is only one cobalt-60 radiotherapy machine at KNH. Plans are underway to install a linear accelerator at KNH and a cobalt-60 machine at MTRH.

In the private hospitals in Nairobi, there are five linear accelerators but access is limited because the cost of treatment is ten to 20 times the cost at KNH. Many public hospitals are negotiating for discounts for their patients but this is a difficult situation because Private hospitals are business enterprises whose survival depends on profit. In an attempt to increase access to healthcare, the government has increased contributions to the national health insurance called National Hospital Insurance Fund (NHIF). While the NHIF policy is to cover all diseases, in practice NHIF does not pay for outpatient cancer services and pays selectively for in-patient services.

Both Nairobi and Eldoret have radiology and imaging equipments for cancer diagnosis ranging from X-rays, ultrasound, CT-scans to magnetic resonance equipment and mammogram equipment. These centres also have pathology departments including immunohistochemistry although frequent delays in specimen processing and reporting are experienced due to frequent shortages.

Cancer Prevention Activities

Carcinogens in Kenya

Environmental carcinogens in Kenya include infectious agents such as human Immunodeficiency virus (HIV), Kaposi's Sarcoma associated herpesvirus (KSHV), human papilloma virus (HPV), hepatitis B and C virus, Epstein-Barr virus and Helicobacter pylori virus. Other carcinogens include alcohol, tobacco products, aflatoxins, solar radiation, processed meat and outdoor air pollution. Genetic pre-disposition to cancer and aging also play a role in carcinogenesis as many of the patients have no known pre-disposing factors.

Because of the high prevalence of infection-related cancers in Kenya, the country is focusing on several approaches to control infections. Kaposi's Sarcoma, non-Hodgkin's lymphoma and cervical cancer are AIDS-defining cancers. HIV still remains a significant public health problem in Kenya with prevalence rates of up to 30% in some regions (Kimanga et al, 2014). Measures to prevent these cancers include scaling up of early diagnosis of HIV/AIDS infections through structured and opportunistic voluntary testing and counselling. In Eldoret, there is a home-based HIV-testing programme targeting individuals who may not be able to go to hospital (Kimaiyo et al, 2010). There is also prevention of mother to child transmission, post-exposure prophylaxis and early initiation of combined anti-retroviral therapy.

Medical circumcision to prevent HIV has also gained widespread acceptance and practice in the country especially among the traditionally non-circumcising communities (Galbraith et al, 2014).

Although cervical cancer is the most common infection-related cancer among women in the country, access to HPV Vaccination is still limited to a few demonstration centres in Eldoret and Nairobi (Vermandere et al, 2015). All accessible children get vaccinated against Hepatitis B as part of the pentavalent vaccine but few adults get the recommended booster doses after every 10 years.

Use of tobacco and alcohol is associated with development of various cancers of the aero-digestive tract. There are laws in the country that restrict advertising, purchasing and consumption of tobacco and alcohol but implementation is not only insufficient but also difficult because these are social-cultural and addictive substances.

Aflatoxin exposure still remains a challenge since most farmers grow and store their own cereals. There is no formal national aflatoxin control strategy.

Models of Universal Access To Cancer Care

The country uses different models of access to cancer care. In Eldoret, integration is preferred where cancer care is provided using infrastructure established for infectious diseases especially HIV-care. Therefore cancer care is part of primary, secondary and tertiary health care. In Nairobi, cancer care is provided independently of the other diseases. While theoretically integration is cheaper, there has been no formal evaluation of the two models. The key to the success of both models is sustainability which depends on availability of cancer-related services, the ability of patients to pay for those services facilitated by an efficient and accountable public health insurance fund (World Health Organisation), the government's commitment towards cancer control efforts, appropriate research and emphasis on manpower development and infrastructure growth.

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Chapter 16j

Malawi

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* This chapter should be referenced as: Masamba L, Mtonga P, Dzamalala C, Chiphangwi N. Malawi. In: Boyle P, Ngoma T, Sullivan R, Ndlovu N, Autier P, Stefan S, Fleming K and Brawley OW. The State of Oncology in Africa 2015. iPRI Scientific Publication 4, iPRI, Lyon, France (2016).

Malawi is a landlocked country in Sub-Saharan Africa located in the southern hemisphere. It is bordered to the north and northeast by the United Republic of Tanzania; to the east, south, and southwest by the People's Republic of Mozambique; and to the west and northwest by the Republic of Zambia. The country is 901 kilometres long and 80 to 161 kilometres wide. The country has many striking topographical features, the biggest being the rift valley which is part of the great east African rift valley. This valley runs the entire length of the country, passing through Lake Malawi in the Northern and Central Regions to the Shire Valley in the south. Malawi has a total area of 118,484 km^2 of which 80 percent is land and the other 20% Lake Malawi.

It is divided into three regions, the Northern, Central and the Southern region. The largest cities in the country are Mzuzu in the North, Lilongwe (Centre), Zomba and Blantyre (South). Lilongwe is the biggest and capital city of the country. Blantyre is the second most heavily populated city in the country and is also considered as the business capital of the country. There are 28 districts in the country. Six districts are in the Northern Region, nine are in the Central Region, and 13 are in the Southern Region (National Statistical Office, 2010).

The population of Malawi is estimated at 17 million as of 2016. The latest population and housing census done in 2008 determined the population to be 13,077,160 (National Statistical Office, 2010). Over half of Malawian population lives in rural areas. The majority of the population is young people with few elderly people (see figure 2). The life expectancy in Malawi is 58 years for men and 61 for women (World Health Organisation, 2013). The country has a free health care system to care for this growing population with a few private hospitals for those who can afford, mostly those on private medical insurance. The majority of the people in the country are poor and earn less than one dollar a day.

The estimated literacy among youth (15-24 years) is 74.3% for men and 70% women in the years 2008-2012. The total adult literacy rate is 61.3% (UNICEF, 2013), with strong differences between urban (82.9%) and rural areas (64.1%; National Statistical Office, 2010).

Malawi's HIV prevalence is estimated to be 9.3-10.8% in the reproductive age group, 15-49 years (UNAIDS, 2014). In women the prevalence is 13% whilst in men the prevalence is 8% within the same age groups.

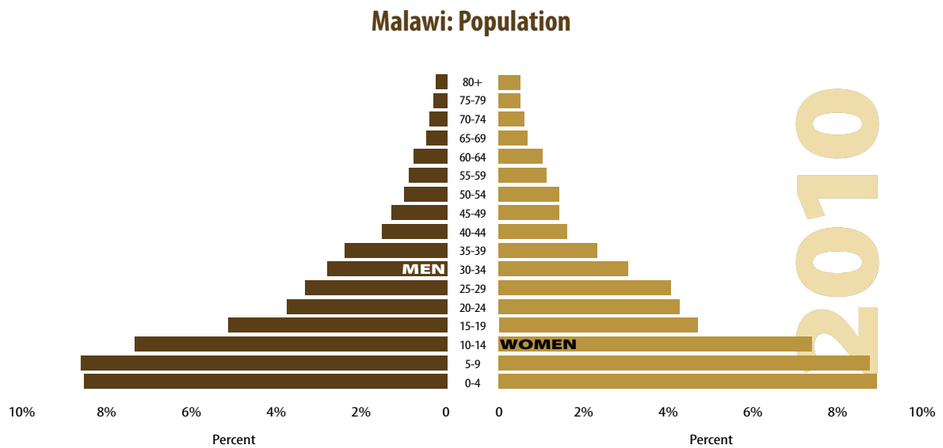


Figure 1: The population pyramid of Malawi

Source: National Statistical Office, 2010

Cancer Epidemiological Data

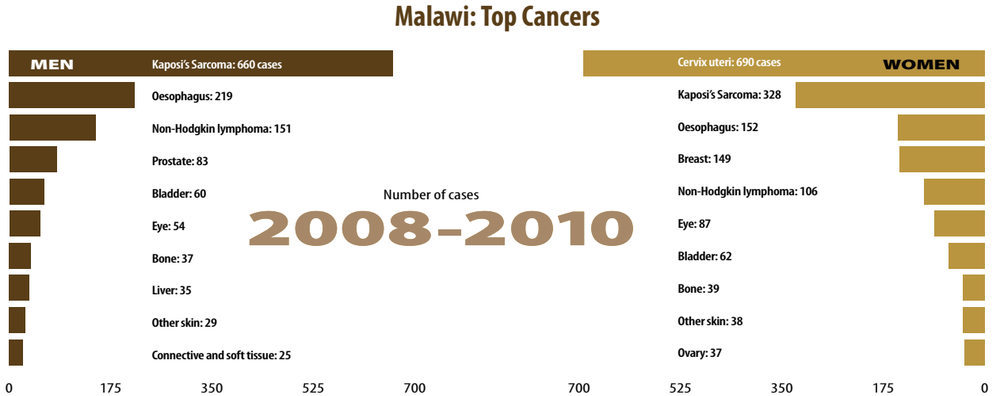
The cancer burden in Malawi is reported to be on the rise. The Malawi national cancer registry recorded 18,946 new cancer cases from the year 2007 to 2010 (Msyamboza et al, 2012). In 2010; 28 government hospitals reviewed 10,300 cancer cases, mostly new cancer cases. The five commonest cancers in the country are Kaposi's Sarcoma, cervical cancer, oesophageal cancer, non-Hodgkin's lymphoma and bladder cancer.

In both surveys, cancer of the cervix was the commonest cancer in women (Figure 3) accounting for 45.4% of all cases followed by Kaposi's Sarcoma (21.1%), cancer of the oesophagus (8.2%), breast cancer (4.6%) and non-Hodgkin's lymphoma (4.1%). In men (Figure 2), of the 8,314 new cases registered in the study led by Msyamboza et al. (2012) in the same period, Kaposi's Sarcoma was the commonest (50.7%) followed by cancer of oesophagus (16.9%), non-Hodgkin's lymphoma (7.8%), prostate cancer (4.0%) and bladder cancer (3.7%).

In children less than 15 years of age non-Hodgkin's lymphoma (mainly Burkitt's) was found to be the commonest cancer accounting for 56.0% followed by Kaposi's Sarcoma which forms 15.0%, cancer of the eye (7.3%), kidney (4.5%) and bone (2.2%).

In new registered cancer cases with ages between 15-59 years, Kaposi's Sarcoma forms the majority of the cases (about 40%), followed by cervical cancer (28%), and cancer of the oesophagus (10%), whereas breast cancer contributes close to 3% (Msyamboza et al, 2012). In those aged above 60 years, cancers oesophagus constitute close to 29% of cases, followed by cervix (24.0%), Kaposi's Sarcoma (10.0%) and prostate cancer (7.7%; Msyamboza et al, 2012).

There is an attempt to histologically confirm most of the cancer diagnoses made at the tertiary facilities. Histopathological confirmation of cancer diagnosis from most patients clinically suspected to have cancer is very high despite some cancers being diagnosed clinically only. All cancers except Kaposi's Sarcoma require to be pathologically (mostly histologically) confirmed before patients can receive chemotherapy.



Figures 2 & 3. Burden of cancer in men and women

Adopted from Malawi Cancer Registry Report 2015

Health Sector Human Resources

The Malawian population of 17 million has a doctor-to-population ratio of 0.2 doctors for every 10,000 people. The nurse-to-population ratio is 3.4 for 10,000 people. This represents one-third of the World Health Organisation's recommended ten nurses per 10,000 people.

There is one medical oncologist, two radiation oncologists (clinical oncologists), four pathologists, two diagnostic radiologists and two haematologists in the country to care for this huge population (Figure 4). Surgical oncology has well-qualified surgeons in some specialty areas but still remains deficient in others fields. Pathology technicians are very few, and there are currently no cancer social workers practicing in the country.

The only nine certified oncology nurses are yet to be registered with the Nurses and Midwives Council of Malawi.

Figure 4: Numbers of cancer related professionals

The majority of doctors are employed by state through Ministry of Health or University College of Medicine. There are few research projects and non-governmental organizations that employ doctors or nurses working to support cancer or treating particular cancers in collaboration with various state facilities. The Doctors Without Borders supports management of Kaposi's Sarcoma with a single agent Bleomycin at Chiradzulu district hospital. The University of North Carolina project supports cancer care at Kamuzu Central Hospital. Partners in Health with Dana Farber Cancer Institute collaboration offers support to Neno district hospital and offers Kaposi's Sarcoma treatment with Paclitaxel chemotherapy. Tiyanjane palliative care clinic, which is externally funded, offers support to some of the Kaposi's Sarcoma patients too.

Infrastructure

Malawi has four central hospitals: Queen Elizabeth Central Hospital (QECH), Kamuzu Central Hospital (KCH), Zomba Central Hospital and Mzuzu Central Hospital. These are general tertiary hospitals with various sub-specialities. It also has 23 District hospitals, 19 community hospitals, 210 Health centres, and 74 dispensaries. The private sector and non-governmental organisations have 129 hospitals. Total number of facilities, both private and public, is 503 offering 13,899 beds. There are both major and minor private hospitals throughout the country with two major private hospitals, Mwaiwathu and Blantyre Adventist Hospital that provide medical oncology services. The third private facility that handles chemotherapy treatment is Lilongwe MASM-MED clinic.

Facilities for Diagnosis

Pathology

There are four histopathology laboratories: one owned by a State University College of Medicine, two owned by public hospitals and one private. The state laboratory facility is at QECH, and the other is at KCH which is run in collaboration with the University of North Carolina. Three of these are in Blantyre City and one in Lilongwe City. Similarly, three pathologists are in Blantyre City and one in Lilongwe City. The Lilongwe histopathology laboratories provide basic immunohistochemistry services however the pathology laboratory at Queen Elizabeth central hospital has been expanded to have a section that can test for Oestrogen Receptors in breast cancer samples.

The histopathology turn around time (TAT) varies from one facility to another in the country. The TAT in private laboratories is significantly shorter than that in public hospitals. In state hospitals, paid for samples take significantly less time than non-paid for samples. This information is well demonstrated by the figure 6 below. The laboratories coded anonymously A, B, C and D have their average TAT of five days, five days, 14 days and 21 days respectively for the paid for samples. The TAT for the non-paid for samples is ten days, 30 days and 40 days for labs A, C and D. In one study on TAT done at the biggest referral hospital in Malawi, the average TAT was 71 days for histopathology samples processed in the year 2010 (Masamba L, 2015).

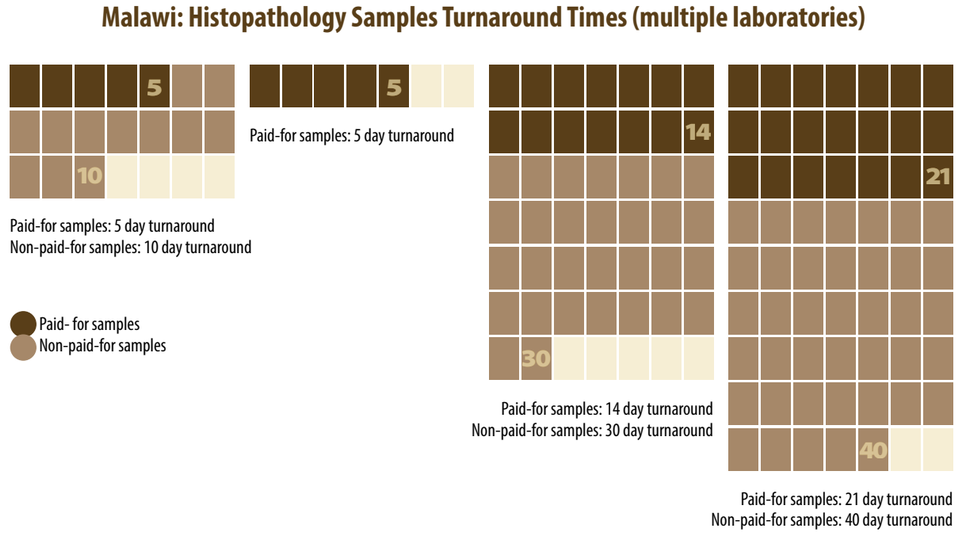


Figure 5: Turnaround times for different laboratories for histopathology samples.

Screening and Early Detection

Cervical Cancer

There is a national cervical cancer screening programme, which was implemented by the Ministry of Health through the sexual and reproductive health unit which being run in most district hospitals in the country. This screen and treat programme for cervical cancer is done using acetic acid, VIA technique. This programme was started in 2004 and targets women aged 30-50 years old. According to the NCR report, by June 2011, 81 health facilities were registered to be providing cervical cancer services of which 50 were providing VIA only, 29 had VIA and cryotherapy whilst two had VIA, cryotherapy, major surgery and loop electrosurgical excision procedure also known as LEEP.

There are no programmes for routine screening of other cancers like breast cancer mammography, colorectal cancer colonoscopies, prostate cancer tumour markers like prostate specific antigen and gastric cancer endoscopies. However, most of the screening tests are available in the major public hospitals upon patient and/or physician request. There is opportunistic clinical breast examination in gynaecology clinics, at ante-natal and VIA clinics. It must be pointed out this is not well structured and hence results or benefits are difficult to document.

Radiology

The country has five working CT scanners, one magnetic resonance imaging (MRI) and conventional and digital radiography. There are frequent break-downs with the CT scans with poor ability to repair them as mostly engineers have to fly from overseas leading to loss of scanning time. There is a new course of bio-medical engineers that is being offered by Malawi University of Science and Technology. This may address the issue and additional problems faced with other medical equipments.

Cancer Policy and Cancer Control Programme

Malawi does not have a National Cancer Control Programme (NCCP) or a cancer plan. In order to put the country on course with the WHO's agenda there is a strong need for the country to have such a programme through the ministry of health. The importance of such a thoroughly set NCCP is in decreasing the incidence of cancer and at the same time improving the lives of cancer patients.

For the first time now there is an oncology chapter in the Malawi Standard Treatment Guidelines (MSTG). This chapter covers some of the most common cancers in the country and a general approach to their management. This document is critical in terms of guiding priority areas of clinical care for the clinical department of the Ministry of Health.

However, good progress is noted in the setting up of a non communicable diseases (NCD) unit and appointment of its manager. This has been spearheaded by the Ministry of Health. This section oversees all NCD activities and helps set and implement cancer policy. The unit has managed to come up with an NCD plan and task forces in different areas of NCDs including cancer. There has been a push for a tobacco and alcohol policy championed by the department of NCDs.

Available Treatment Modalities and Cancer Prevention Services

Medical Oncology Resources

The Centres shown in table 1 provide chemotherapy and surgical oncology services (except MASM-Med) with some cover of oncologists and nurses trained in handling chemotherapy. More capacity is concentrated at KCH and QECH. QECH is the largest facility in the country and is supported by a Medical School. There are other smaller facilities in Zomba and Mzuzu cities. Zomba and Mzuzu Central Hospitals mostly do cancer surgery but do not have established medical oncology. There is limited chemotherapy offered at Zomba and Mzuzu. Chemotherapy is very limited in smaller district hospitals and restricted to managing Kaposi's Sarcoma with vincristine.

Table 1: Chemotherapy Centres in Malawi

Lilongwe City facilities	Blantyre City facilities
Kamuzu Central Hospital (KCH)	Queen Elizabeth Central Hospital (QECH)
MASM-Med clinic	Mwaiwathu Private Hospital
	Blantyre Adventist Hospital.

Radiation Oncology

The country does not have a functioning radiotherapy facility. There are on-going government projects to construct three cancer centres. Construction is to commence in Blantyre and Lilongwe Cities. Most patients requiring radiotherapy are referred to other countries where radiotherapy services are readily available like the Republic of South Africa, Tanzania, Zambia and India.

Surgical Oncology

Surgical oncology services are provided in all the central hospitals of the country and two major private hospitals. However Queen Elizabeth central hospital is the largest referral hospital in the country and has the biggest concentration of surgical specialists. There are neurosurgical specialists, orthopaedic surgery specialists, paediatric surgery specialists, head and neck, Ears / Nose / Throat (ENT) as well as general surgical specialists. Most of the surgical residents are undergoing training in the country, which leads to further increases in the number of surgical specialists. However, there is no specific surgical oncology specialization programme in Malawi.

Cancer surgeries are performed in both public and private the general hospitals. The complicated procedures are done at the four tertiary hospitals and big private hospitals. These procedures are done by respective surgical sub-specialties other than surgical oncologists.

Palliative Care Services

There is an established palliative care centre in Blantyre district at Queen Elizabeth Central Hospital and a palliative care hospital in Lilongwe with several outlets in surrounding districts. There are palliative care consultants with doctors and nurses working for these institutions. Both oral liquid morphine and morphine sulphate tablets are readily available throughout the year for pain relief in cancer patients and other chronic illnesses.

Cancer Registry

The Malawi National Cancer Registry (MNCR) was established in 1985 and is a population based registry. It has its office at the largest referral hospital, Queen Elizabeth Central Hospital in Blantyre. The population component of the cancer registry focuses on urban and rural Blantyre and the surrounding districts. Periodically data is collected from all district hospitals which are secondary health facilities and central hospitals which are tertiary health facilities nationwide. Some data is also collected from private hospitals providing cancer diagnostic services in the country. This cancer registry takes into account both urban and rural populations. The registry was started with support from International Agency for Research on Cancer. The MNCR is affiliated and supported by the African Region Cancer Registry Network. The most recent nationwide data

collection was conducted from September to December 2010 with new cancers being registered from January 2007 and has been included in the IARC Cancer in five continents, Volume 10. (Formon et al, 2013)

There are other registries, in Lilongwe, Zomba and Mzuzu, but these are pathology- or laboratory-based registries. Though these may highlight interesting institutional data, they fall short in terms of their applicability to the community. Their data cannot be used for programming and calculation of cancer survival in the population. The data from the various institutional laboratories feeds into the component of the national-based part of the MNCR.

There is no mandatory reporting of a cancer diagnoses by physicians. Collecting this data is a demanding and costly task for the personnel. Lack of vital statistics, as a legal mandate, is another operational challenge that compromises the accuracy of our cancer statistics. However, the Ministry of Home Affairs and the Department of National Statistics are implementing birth and death registration in the country. This may aid data quality in terms of vital statistics parameters.

Cancer Awareness

The level of knowledge of cancer in the community is suboptimal hence most patients present with advanced disease. Awareness campaigns are carried out in some communities and using media houses. Mostly the awareness targets early recognition of cancer symptoms and early presentation to the hospital. The Cancer Association of Malawi (CAM) which is an umbrella non-profit organization for cancer advocacy run by volunteers spearheads these cancer awareness campaigns. This is done in collaboration with the QECH Cancer Unit and at times MOH-NCD unit.

Training Of Professionals

There is currently no school that has a postgraduate programme for training health care professionals in oncology. Oncology training is mostly done in South Africa. However, a postgraduate programme which will provide lessons in several oncology disciplines is expected in the near future at one of the local universities.

The University of Malawi College of Medicine holds a grant from the Medical Education Partnership Initiative (MEPI, a funding programme administered by the United States National Institutes of Health – NIH) that is helping building the human resources capacity. This grant covers training of pathologists, technicians and public health scientists. Cancer care capacity will be greatly enhanced in Malawi once the trainees supported by this grant graduate.

Health Funding

The main source of funding for cancer screening, diagnosis and treatment is through the State. The various non-governmental organizations outlined above supporting cancer care partner with governmental institutions to deliver care. The majority of the population is not on medical insurance. It is estimated that 15% of the population that is on private insurance accesses private cancer care within and outside the country when necessary.

The estimated cost of treatment for a cancer patient locally is about 1,000$. The cost of treatment for radiotherapy and concomitant chemotherapy is roughly 6,000$ when patients have private insurance or use their own money; and up to 30,000$ when the treatment is State-funded.

Quality of Services and Ideal Requirements and Clinical Outcomes

The patients that are managed within the major state or private hospitals can access most cancer surgeries. Queen Elizabeth Central Hospital and Mwaiwathu Private Hospital provide the largest concentration of surgical expertise in various disciplines. Some of them are neuro-surgery, ENT, Head and Neck Surgery, plastic surgery, paediatric surgery, spine surgery and general surgery. Patients managed within these facilities are mostly managed through decisions made at combined care clinics.

The facilities outlined in Table 1 offer conventional chemotherapy (using older drugs) and selected targeted therapies. All standard protocols for all common solid tumours and some selected haematologic tumours can be prescribed. Imatinib myselate is available for chronic myeloid leukaemia to the state patients using the Glivec® International Patient Assistance Program (GIPAP) programme. Other targeted therapy drugs are available in private hospitals for patients on medical scheme and not easily accessible to public patients because of limited funding. No transplant facility is available in the country.

Collaborative work to determine survival data has just commenced, there is no available analysed data currently on survival for the country.

Research Capacity

Currently, the country is seeing a gradual increase in cancer research capacity in Blantyre and Lilongwe. Part of the research infrastructure has been laid down by the government, MEPI, and other NIH research grants. Currently, there are several research projects going on in both cities, with local and international collaborations. Several local papers have come up addressing local questions, and these have seen work published in the local journal Malawi Medical Journal, other journals and conference journals like AORTIC and SASMO/SASCRO.

Human resources, laboratories and clinicians including pharmacists of Malawi have collaborated with international research organizations like University of North Carolina and University of John Hopkins to deliver particular research projects, of which some are underway as of the preparation of this chapter.

Conclusion

The state of Oncology in Malawi is in its infancy with still so many challenges to be addressed. However, the landscape is quickly changing for the better. The implementation of the radiotherapy projects that are commencing will be a game changer in terms of cancer care and will surely tremendously improve care and outcomes. The implementation of these cancer centres needs to be done in the sphere of comprehensive cancer control to deliver more benefit by addressing all the important aspects of cancer control and fight. There is growing political willpower which if harnessed correctly would augment the scientific and clinical drive to improve the state of Oncology in Malawi. Malawi can definitely improve and address the current cancer challenges.

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Chapter 16k

Mauritania

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* This chapter should be referenced as: Diop MY. Mauritania. In: Boyle P, Ngoma T, Sullivan R, Ndlovu N, Autier P, Stefan S, Fleming K and Brawley OW. The State of Oncology in Africa 2015. iPRI Scientific Publication 4, iPRI, Lyon, France (2016).

Mauritania is a West African country which borders the Atlantic Ocean. It is divided into 15 regions. The main cities are Nouakchott (political capital), Nouadhibou (economical capital), Kiffa on the road of Mali and Rosso on the border with Senegal. The area of Mauritania is 1,025,520 km² of which over 80% is located in the Sahara desert. The population is estimated to around 3,500,000 people as of 2015; 3,105,000 people were recorded in the latest census (2010). The population is 58% rural and 42% urban.

Table 1: General Facts

Source: United Nation Development Programme, 2009

Age distribution (2010)	Under 15: 40.6	15–64: 56.7	65+: 2.7
Median age (2009)	Total: 19.3	Men: (N/A)	Women: (N/A)
Life expectancy at birth (2006)	Total: 58	Men: 55	Women: 60
Birth rate/1 000 population (2005-2010)	33.8		
Under-5 mortality rate/ 1 000 live births (2006)	Total: 125	Men: 134	Women: 115
Maternal mortality ratio/100 000 live births (2005)	820		
Languages	Arabic (official), French , Hassania, Wolof, Soninké, Fulfulde, Bambara		
Literacy (%) (1999-2007)	Total: 55.8	Men: 63.3	Women: 48.3

Health Services

The health system in Mauritania is pyramidal and consists of four levels. The central (national) level includes the Ministry of Health, the body responsible for the purchase of medications (Centrale d'Achat de Médicaments), the National Institute of Public Health Research, the Faculty of

Medicine, the National School for Public Health, and four central hospitals. The regional level consists of four hospitals, and four sub-regional hospitals. The departmental level includes two departmental hospitals, and 67 health centres (12 with a laboratory and more than ten beds, 55 with less than ten beds) and maternity clinics. The peripheral level includes 411 unequally distributed health posts managed by nurses.

Mauritania has a total of 412 physicians, i.e. one per 8,495 people. There are 366 mid-wives, and 2147 nurses. The government allocated 5% of its budget to health, which accounts for almost 75% of total health expenditures in the country. The spending per capita on health is 13$, which remains far below the WHO minimum recommended average (34$). Many people still have no access to health care, and the demand for drugs, which are publically provided, significantly exceeds supply.

Burden of Disease

Communicable diseases remain the highest burden of disease in Mauritania, but non-communicable diseases are increasing rapidly. The top five causes of death are lower respiratory infections, perinatal conditions, diarrhoeal diseases, malaria, and cerebro-vascular disease.

As of 2004, communicable diseases represented 56.1% of all deaths; non-communicable diseases represented 36.9% and cancer 6.3%.

Reflection work and multidisciplinary analyses are in progress. The Ministry of Health is preparing and elaborating a national action plan to fight against cancer. There is currently no cancer registry in Mauritania, and only four pathology registries exist.

Cancer Control Component

Mauritania has one oncology centre (National Oncology Centre (NOC)) in Nouakchott, established between 2006 and 2008. The centre has ten specialized doctors, three general doctors, three radiotherapists trained in Morocco, ten nurses, two MRI machines (one public and one private), and three pathologists. There are four pathology laboratories (two public and two private). Only the NOC pathology lab is able to perform immunohistochemistry analyses. The volume of pathological examinations remains inadequate in terms of availability and capabilities of the laboratory. A partnership with the sub-region is in discussion. This partnership could lead to optimization of the laboratory capability.

Table 2: Incidence of cancer by gender and by category (2008)

Source: International Atomic Energy Agency

Men				Women			
Cancer site	Number of cases	% of cancers	Crude rate ASR	Cancer site	Number of cases	% of cancers	Crude rate ASR
Liver	216	28.8%	23.3	Cervix uteri	364	29.6%	35.1
Prostate	95	12.7%	17.9	Breast	257	20.9%	23.9
Stomach	51	6.8%	6.6	Liver	103	8.4%	10.4
Non-Hodgkin lymphoma	49	6.5%	3.9	Stomach	53	4.3%	5.9
Colorectum	40	5.3%	4.4	Colorectum	44	3.6%	4.3

Men				Women			
Cancer site	Number of cases	% of cancers	Crude rate ASR	Cancer site	Number of cases	% of cancers	Crude rate ASR
Total	749	100.0%	89.2	Total	1229	100.0%	90.3
Total cases: 1978 | ASR: 103							

Table 3: Mortality of cancer by gender and by category

Men				Women			
Cancer site	Number of cases	% of cancers	Crude rate ASR	Cancer site	Number of cases	% of cancers	Crude rate ASR
Liver	212	32.1%	23.5	Cervix uteri	244	27.7%	25.5
Prostate	77	11.6%	15.3	Breast	142	16.1%	14.3
Stomach	48	7.3%	6.4	Liver	101	11.5%	10.9
Non-Hodgkin lymphoma	41	6.2%	3.4	Stomach	50	5.7%	5.6
Colorectum	32	4.8%	3.7	Colorectum	35	4.0%	3.6
Total	661	100.0%	82.1	Total	881	100.0%	90.3
Total cases: 1542 | ASR: 85.5							

The cancer centre has two bunkers. One of which is equipped with a linear accelerator (Varian). About 1,000 radiotherapy sessions are offered every month.

The centre has 40 beds and offers diagnostic and chemotherapy services. As of the end of 2014, the centre treated about 5,000 patients, and reduced the number of patients sent abroad for chemotherapy and radiotherapy by 90-95%.

On the decision of the State, all the diagnostic and treatments are free of charge to all patients. The centre uses standard chemotherapy protocols with virtually all available molecules. Shortages occur in 1 to 5% of cases for some molecules, and are generally resolved within two-three weeks.

Mauritania has signed a partnership agreement with the Roche company in a programme called ACCESS, which will grant access of all targeted therapeutic molecules such as herceptin.

Although there is no National Fight Against Cancer programme, this did not prevent the conduct of occasional campaigns during the last 20 years. These involved screening 500-2,000 women for cervical and breast cancer. These campaigns resulted in reduction of cervical cancer prevalence from 5% in 2000 to 1.8% in 2014 in the district of the capital (1/3 of the Mauritanian population).

Tobacco Use and Control

Mauritania is part of the WHO Framework Convention on Tobacco Control, but does not have a national agency for tobacco control. There is currently no ban in place for smoking in public places, no marketing bans, and no warnings on cigarette packages. Taxes are currently 20.28% of the tobacco price. Prevalence of tobacco smoking is shown in table 4.

Table 4: Prevalence of Tobacco use and exposure

	Adult men	Adult women	Boys	Girls
Tobacco use prevalence (%)	22.3	3.7	20.3	18.3
Youth exposed to second-hand smoke at home (%)	43.8			

Conclusion

In terms of population and financial means, it is clear that Mauritania could easily cope with the difficulties in the fight against cancer. This would require:

- to quickly set up a real cancer registry (African Cancer Registry Network),
- to increase human resources through the training of local oncologists (currently oncologists are all foreigners) and nurses (including palliative care)
- to sustain the means already in place (drugs, consumables for immunohistochemistry, etc.).

However, while the human means and the skills exist, the political will and force of application of all these means by the government are still lacking.

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Chapter 161

Mauritius

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In 2016, the Mauritian population is estimated to lie around 1,278,000 (Including Agalega, Rodrigues and Saint Brandon islands). The cancer incidence in the Republic of Mauritius for the year 2014 represents the new cancer cases registered till December 2014. Data was compiled from multiple sources (Radiotherapy patient register, Laboratory archives, Regional hospitals medical in-patient records and also data from private pathologists) by the cancer registry. 2,387 new cancer cases were registered. The total number of cancer cases among men were 1,068 and 1,319 among women. (Mauritius National Cancer Registry, 2014)

Compared to year 2013, new cases of cancer have increased by 13.0% in men and by 1.4 % in women. This trend is expected to rise and today cancer is the third burden of Mauritian population after diabetes and cardiovascular diseases. The main cancers observed in men are colon, prostate and lung and in women are breast, colon/rectum and cervix (Table 1 & 2). In children the main problem is acute leukæmia. (Mauritius National Cancer Registry, 2014)

Table 1: Most frequent cancers in men

Site	Number	Percentage	ASR(W)/10
Colon/Rectum	130	12.2 %	17.1
Prostate	112	10.5 %	16.2
Lung	100	9.4 %	13.5
Lip, oral cavity and pharynx	65	6.1 %	8.0
Stomach	59	5.5 %	8.4
Bladder	40	3.7 %	5.9
Larynx	31	2.9 %	4.1
Non-Hodgkin Lymphoma	31	2.9 %	4.5
Oesophagus	24	2.3 %	3.4
Kidney	11	1.0 %	1.8

Site	Number	Percentage	ASR(W)/10
OTHERS	465	43.5 %	-
TOTAL	1,068	100 %	136.6

Table 2: Most frequent cancers in women

Site	Number	Percentage	ASR(W)/10
Breast	491	37.2 %	58.2
Colon/Rectum	115	8.7 %	13.5
Cervix uteri	99	7.5 %	11.7
Corpus uteri	63	4.8 %	7.3
Ovary	44	3.3 %	5.3
Stomach	37	2.8 %	8.4
Lung	33	2.5 %	13.5
Lip, oral cavity and pharynx	29	2.2 %	8.0
Brain, nervous system	20	1.5 %	4.3
Thyroid	20	1.5 %	1.4
OTHERS	368	27.9 %	-
TOTAL	1,319	100 %	136.6

The upward trend in incidence could prevail as the country is increasing in its socio-economic level. More than 40% increase in new cases was seen from 1992 to 2014, with colon/rectum for men and breast for women as most common sites. (Nabholtz)

Table 3: Summary statistics of cancer in Mauritius

	Men	Women	Both sexes
Population (thousands)	634	644	1,279
Number of new cancer cases (thousands)	0.6	0.9	1.5
Age-standardised rate (W)	105.9	119.4	110.5
Risk of getting cancer before age 75 (%)	11.2	12.2	11.6
Number of cancer deaths (thousands)	0.5	0.5	1.0
Age-standardised rate (W)	87.7	64.2	73.1
Risk of dying from cancer before age 75 (%)	9.6	6.6	7.9

Source : Ferlay J, Shin HR, Bray F, Forman D, Mathers C and Parkin DM. GLOBOCAN 2008 v1.2, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 10 [Internet]. Lyon, France: International Agency for Research on Cancer; 2010. Available from: http://globocan.iarc.fr, accessed on day/month/year

Table 4: Incidence per 100,000 by age group (period) in men. 2013 Estimated Mid-Year Population (Mauritius and Rodrigues) (Mauritius National Cancer Registry, 2014)

Site	All Ages	Age Unk	0	5-	10-	15-	20-	25-	30-	35-	40-	45-	50-	55-	60-	65-	70-	75-	80-	85+	Crude Rate	(%)	Cum 0-64	Cum 0-74	ASR	ICD (10th)
Lip	0	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.0	0.0	0.00	0.00	0.0	C00
Tongue	16	0	-	-	-	-	-	-	-	2.1	-	-	6.7	10.6	6.5	16.1	9.0	-	48.5	-	2.6	1.6	0.13	0.26	2.1	C01-02
Mouth	16	0	-	-	-	-	-	-	-	-	2.4	4.1	6.7	15.9	3.2	10.8	-	12.6	-	-	2.6	1.6	0.16	0.22	1.9	C03-06
Salivary glands	6	0	-	-	-	-	-	-	-	-	2.4	2.1	2.2	2.7	3.2	-	-	-	24.2	-	1.0	0.6	0.06	0.06	0.7	C07-07
Tonsil	11	0	-	-	-	-	-	-	-	-	-	-	11.2	8.0	3.2	5.4	9.0	-	-	-	1.8	1.1	0.11	0.18	1.3	C09
Other oropharynx	4	0	-	-	-	-	-	-	-	-	-	2.1	2.2	5.3	-	-	-	-	-	-	0.6	0.4	0.05	0.05	0.4	C10
Nasopharynx	4	0	-		-	-	-	-	-	2.1	-	-	2.2	-	3.2	5.4	-	-	-	-	0.6	0.4	0.04	0.06	0.5	C11
Hypopharynx	4	0	-	2.2	-	-	-	-	-	-	-	2.1	-	-	6.5	-	-	-	-	-	0.6	0.4	0.05	0.05	0.6	C12-13
Pharynx unspecified	4	0	-	-	-	-	-	-	-	-	-	-	-	2.7	6.5	5.4	-	-	-	-	0.6	0.4	0.05	0.07	0.5	C14
Oesophagus	24	0	-	-	-	-	-	2.3	2.0	2.1	2.4	-	6.7	5.3	9.7	37.7	9.0	12.6	24.2	65.8	3.9	2.5	0.15	0.39	3.4	C15
Stomach	59	1	-	-	-	-	-	2.3	-		7.1	4.1	6.7	15.9	35.7	69.9	81.0	75.5	48.5	65.8	9.5	6.1	0.37	1.13	8.4	C16
Small intestine	3	0	-	-	-	-	-	-	-	-	-	-	2.2	-	3.2	-	9.0	-	-	-	0.5	0.3	0.03	0.07	0.4	C17
Colon	71	0	-	-	-	-	-	-	2.0	2.1	2.4	12.3	17.9	29.2	48.7	32.3	54.0	113.3	72.7	131.6	11.4	7.3	0.57	1.00	9.3	C18
Rectum	59	0	-	-	-	-	-	-	-	4.2	-	4.1	13.4	21.2	45.5	43.0	45.0	88.1	121.2	65.8	9.5	6.1	0.44	0.88	7.8	C19-20
Anus	3	0	-	-	-	-	-	-	2.0	-	-	-	2.2	-	3.2	-	-	-	-	-	0.5	0.3	0.04	0.04	0.4	C21-
Liver	19	0	2.7	-	2.0	-	-	2.3	-	-	-	2.1	-	8.0	13.0	10.8	36.0	-	24.2	32.9	3.1	1.9	0.15	0.38	3.0	C22
Gallbladder etc.	3	0	-	-	-	-	-	-	-	-	-	-	-	-	-	5.4	9.0	12.6	-	-	0.5	0.3	0.00	0.07	0.5	C23-24
Pancreas	10	0	-	-	-	-	-	-	-	-	-	-	4.5	8.0	6.5	5.4	-	25.2	-	-	1.6	1.0	0.09	0.12	1.2	C25
Nose, sinuses, etc.	3	0	-	-	-	-	-	-	-	-	-	2.1		2.7	3.2	-	-	-		-	0.5	0.3	0.04	0.04	0.4	C30-31
Larynx	31	0	-	-	-	-	-	-	2.0	-	2.4	4.1	13.4	15.9	13.0	32.3	27.0	-	48.5	-	5.0	3.2	0.25	0.55	4.1	C32
Trachea, bronchus and lung	100	3	-	-	-	-	-	2.3	2.0	-	4.7	12.3	35.7	29.2	55.2	69.9	117.0	138.5	97.0	65.8	16.1	10.3	0.73	1.69	13.5	C33-34
Other thoracic organs	1	0	-	-	-	-	-	-	-	-	-	-	-	-	3.2	-	-	-	-	-	0.2	0.1	0.02	0.02	0.1	C37-38
Bone	11	0	-	-	2.0	-	-	-	-	-	7.1	-	2.2	-	10.8	36.0	-	-	-	-	1.8	1.1	0.06	0.29	1.8	C40-41
Melanoma of skin	3	0	-	-	-	-	2.0	-	-	-	2.4	-	-	2.7	-	-	-	-	-	-	0.5	0.3	0.04	0.04	0.4	C43
Other skin	93	24	-	-	2.0	-	2.0	4.6	2.0	2.1	7.1	14.4	11.2	26.5	52.0	32.3	45.0	62.9	72.7	98.7	14.9	9.5	0.83	1.36	12.5	C44
Mesothelioma	0	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.0	0.0	0.00	0.00	0.0	C45
Kaposi's Sarcoma	0	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.0	0.0	0.00	0.00	0.0	C46
Connective and soft tissue	20	0	-	-	-	4.0	-	-	-	-	-	4.1	2.2	8.0	9.7	16.1	9.0	12.6	72.7	32.9	3.2	2.1	0.14	0.27	2.7	C47, C49
Breast	17	0	-	-	-	-	-	-	-	-	4.7	2.1	2.2	15.9	3.2	5.4	27.0	-	48.5	-	2.7	1.7	0.14	0.30	2.2	C50
Penis	1	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.2	0.1	0.01	0.01	0.1	C60
Prostate	112	2	-	-	-	-	-	-	-	-	-	4.1	2.2	19.6	77.9	107.6	108.0	239.2	194.0	296.2	18.0	11.5	0.52	1.99	16.2	C61
Testis	19	0	-	-	2.0	-	10.0	4.6	3.9	8.5	-	2.1	2.2	2.7	-	-	9.0	12.6	-	-	3.1	1.9	0.18	0.22	2.7	C62

Site	All Ages	Age Unk	0	5-	10-	15-	20-	25-	30-	35-	40-	45-	50-	55-	60-	65-	70-	75-	80-	85+	Crude Rate	(%)	Cum 0-64	Cum 0-74	ASR	ICD (10th)
Other male genital organs	1	0	-	-	-	-	-	-	-	-	-	-	-	-	-	5.4	-	-	-	-	0.2	0.1	0.00	0.03	0.2	C63
Kidney	11	0	2.7	-	-	-	-	-	-	-	-	2.1	4.5	-	3.2	26.9	9.0	-	-	-	1.8	1.1	0.06	0.24	1.8	C64
Renal pelvis	0	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.0	0.0	0.00	0.00	0.0	C65
Ureter	1	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	9.0	-	-	-	0.2	0.1	0.00	0.05	0.2	C66
Bladder	40	0	2.7	-	-	-	-	2.3	-	-	-	-	8.9	10.6	13.0	32.3	54.0	37.8	97.0	197.4	6.4	4.1	0.20	0.63	5.9	C67
Other urinary organs	0	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.0	0.0	0.00	0.00	0.0	C68
Eye	1	0	2.7	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.2	0.1	0.01	0.01	0.3	C69
Brain, nervous system	30	0	-	6.6	2.0	4.0	2.0	-	5.9	2.1	4.7	4.1	4.5	15.9	13.0	10.8	9.0	-	-	-	4.8	3.1	0.32	0.42	4.3	C70-72
Thyroid	10	0	2.7	-	-	-	-	-	2.0	2.1	-	-	6.7	5.3	3.2	5.4	-	-	-	-	1.6	1.0	0.11	0.14	1.4	C73
Adrenal gland	0	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.0	0.0	0.00	0.00	0.0	C74
Other endocrine	0	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.0	0.0	0.00	0.00	0.0	C75
Hodgkin disease	6	0	-	2.2	-	-	2.0	-	-	2.1	2.4	-	-	2.7	-	5.4	-	-	-	-	1.0	0.6	0.06	0.08	0.9	C81
Non-Hodgkin lymphoma	31	0	2.7	-	2.0	2.0	4.0	4.6	-	2.1	-	2.1	13.4	8.0	19.5	5.4	36.0	12.6	24.2	-	5.0	3.2	0.30	0.51	4.5	C82-85, C96
Immunoproliferative diseases	0	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.0	0.0	0.00	0.00	0.0	C88
Multiple myeloma	21	0	-	-	-	-	-	-	-	-	2.4	-	6.7	8.0	9.7	32.3	27.0	25.2	-	-	3.4	2.2	0.13	0.43	2.9	C90
Lymphoid leukaemia	9	0	-	2.2	-	-	-	-	-	-	-	-	2.2	-	-	16.1	9.0	12.6	24.2	32.9	1.4	0.9	0.02	0.15	1.4	C91
Myeloid leukaemia	20	0	-	-	-	6.0	-	-	2.0	2.1	-	4.1	-	8.0	13.0	10.8	9.0	25.2	24.2	-	3.2	2.1	0.18	0.27	2.7	C92-94
Leukaemia unspecified	16	0	5.4	-	4.0	8.1	2.0	-	-	-	2.4	2.1	2.2	2.7	6.5	-	-	12.6	-	-	2.6	1.6	0.18	0.18	2.8	C95
Myeloproliferative disorders	7	0	-	-	-	-	-	-	2.0	-	-	-	2.2	2.7	-	5.4	-	12.6	24.2	32.9	1.1	0.7	0.03	0.06	0.9	MPD
Myelodysplastic syndromes	9	0	-	-	-	-	-	-	-	-	2.4	-	2.2	-	3.2	10.8	18.0	12.6	24.2	-	1.4	0.9	0.04	0.18	1.3	MDS
Other and unspecified	128	2	5.4	4.4	2.0	4.0	-	4.6	-	12.7	18.9	12.3	33.5	39.8	61.7	113.0	108.0	125.9	97.0	32.9	20.6	13.1	1.01	2.13	18.1	O&U
All sites	1,068	32	26.9	17.7	18.1	28.2	24.0	30.0	27.4	48.6	77.9	104.8	243.3	360.6	561.7	801.7	999.1	1082.6	1212.4	1151.7	171.5	-	8.09	17.37	149.2	ALL
All sites but C44	975	8	26.9	17.7	16.1	28.2	22.0	25.3	25.4	46.5	70.8	90.4	232.1	334.1	509.8	769.4	954.1	1019.6	1139.7	1053.0	156.5	100.0	7.29	15.98	136.6	AllbC44

Table 5. Incidence per 100,000 by age group (period) in women. 2013 Estimated Mid-Year Population (Mauritius and Rodrigues) (Mauritius National Cancer Registry, 2014)

Site	All Ages	Age Unk	0	5-	10-	15-	20-	25-	30-	35-	40-	45-	50-	55-	60-	65-	70-	75-	80-	85+	Crude Rate	(%)	Cum 0-64	Cum 0-74	ASR	ICD (10th)
Lip	0	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.0	0.0	0.00	0.00	0.0	C00
Tongue	13	0	-	-	-	-	-	-	-	-	-	-	11.0	2.5	5.9	4.4	13.7	8.6	-	15.1	2.0	1.0	0.10	0.19	1.5	C01-02
Mouth	2	0	-	-	-	-	-	-	-	-	-	-	4.4		-	-	-	-	-	-	0.3	0.2	0.02	0.02	0.2	C03-06
Salivary glands	6	0	-	-	-	-	-	-	4.0	-	2.4	-	-	2.5	--	4.4	6.8	-	-	-	0.9	0.5	0.04	0.10	0.8	C07-08
Tonsil	5	0	-	-	-	-	-	-	-	-	-	2.1	-	2.5	-	4.4	-	-	14.0	15.1	0.8	0.4	0.02	0.05	0.5	C09
Other oropharynx	1	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	14.0	-	0.2	0.1	0.00	0.00	0.1	C10
Nasopharynx	1	0	-	-	-	-	-	2.3	-	-	-	-	-	-	-	-	-	-	-	-	0.2	0.1	0.01	0.01	0.2	C11
Hypopharynx	0	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.0	0.0	0.00	0.00	0.0	C12-13
Pharynx unspecified	1	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.2	0.1	0.00	0.02	0.1	C14
Oesophagus	9	0	-	-	-	-	-	-	-	-	2.4	-	-	2.5	8.9	8.8	6.8	-	14.0	-	1.4	0.7	0.07	0.15	1.1	C15
Stomach	37	2	-	-	-	-	-	-	2.0	-	9.7	-	4.4	17.8	17.8	13.3	41.1	34.6	28.0	-	5.8	2.9	0.27	0.56	4.3	C16
Small intestine	1	0	-	-	-	-	-	-	-	-	-	-	-	-	3.0	-	-	-	-	-	0.2	0.1	0.01	0.01	0.1	C17
Colon	78	0	-	-	2.1	-	2.1	-	4.0	4.3	9.7	16.6	15.4	12.7	38.6	39.8	47.9	121.0	56.0	15.1	12.3	6.2	0.53	0.97	9.0	C18
Rectum	37	0	-	-	-	-	-	-	-	-	4.8	4.1	6.6	7.6	35.6	30.9	41.1	8.6	-	15.1	5.8	2.9	0.29	0.65	4.5	C19-20
Anus	6	0	-	-	-	-	-	-	-	-	-	2.1	4.4	-	-	-	20.5	-	-	-	0.9	0.5	0.03	0.14	0.8	C21
Liver	7	0	-	-	-	-	-	-	-	-	2.4	-	-	10.2	3.0	4.4	-	-	-	-	1.1	0.6	0.08	0.10	0.8	C22
Gallbladder etc.	2	0	-	-	-	-	-	-	-	-	-	-	-	-	3.0	-	6.8	-	-	-	0.3	0.2	0.01	0.05	0.3	C23-24
Pancreas	16	0	-	-	-	-	-	-	-	-	2.4	2.1	6.6	10.2	8.9	8.8	13.7	-	-	-	2.5	1.3	0.15	0.26	1.9	C25
Nose, sinuses, etc.	3	0	-	-	-	-	-	-	-	2.2	-	-	-	-	-	4.4	-	-	-	-	0.5	0.2	0.01	0.03	0.3	C30-31
Larynx	2	0	-	-	-	-	-	-	-	-	-	-	-	-	3.0	-	6.8	-	-	-	0.3	0.2	0.01	0.05	0.3	C32
Trachea, bronchus and lung	33	0	-	-	-	-	-	-	-	2.2	-	2.1	8.8	20.4	26.7	8.8	13.7	8.6	28.0	45.2	5.2	2.6	0.30	0.41	3.6	C33-34
Other thoracic organs	1	0	-	-	-	-	-	-	-	-	-	-	-	-	3.0	-	-	-	-	-	0.2	0.1	0.01	0.01	0.1	C37-38
Bone	9	0	-	-	-	4.1	-	-	-	2.2	-	2.1	2.2	2.5	3.0	-	-	17.3	-	-	1.4	0.7	0.08	0.08	1.1	C40-41
Melanoma of skin	2	1	-	-	-	-	-	2.3	-						-	-	-		-	-	0.3	0.2	0.02	0.02	0.4	C43
Other skin	58	13	-	-	-	-	-	-	-	4.3	4.8	6.2	12.7	14.8	14.8	22.1	54.8	17.3	42.0	105.5	9.1	4.6	0.32	0.81	6.5	C44
Mesothelioma	0	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.0	0.0	0.00	0.00	0.0	C45
Kaposi's Sarcoma	0	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.0	0.0	0.00	0.00	0.0	C46
Connective and soft tissue	13	1	2.8	-	-	2.0	-	2.3	2.0	2.2	4.8	2.1	2.2	-	5.9	-	-	-	-	-	2.0	1.0	0.14	0.14	1.9	C47, C49
Breast	491	8	-	-	-	-	-	11.7	15.9	60.4	104.2	126.5	160.7	178.3	219.7	176.7	260.2	198.7	182.0	105.5	77.2	38.9	4.46	6.68	58.2	C50
Vulva	7	0	-	-	-	-	-	-	-	-	2.4	-	2.2	-	5.9	-	-	17.3	14.0	-	1.1	0.6	0.05	0.05	0.7	C51
Vagina	7	0	2.8	-	-	-	-	-	-	-	-	-	4.4	2.5	3.0	4.4	-	8.6	-	-	1.1	0.6	0.06	0.09	1.0	C52

Site	All Ages	Age Unk	0	5-	10-	15-	20-	25-	30-	35-	40-	45-	50-	55-	60-	65-	70-	75-	80-	85+	Crude Rate	(%)	Cum 0-64	Cum 0-74	ASR	ICD (10th)
Cervix uteri	99	1	-	-	-	-	-	-	15.9	13.0	19.4	16.6	35.2	30.6	20.8	35.3	102.7	51.8	56.0	-	15.6	7.9	0.76	1.46	11.7	C53
Corpus uteri	63	0	-	-	-	-	-	-	-	-	7.3	6.2	26.4	7.6	32.7	57.4	47.9	69.1	28.0	15.1	9.9	5.0	0.40	0.93	7.3	C54
Uterus unspecified	13	1	-	-	-	-	-	-	-	-	2.4	4.1	6.6	5.1	5.9	-	6.8	8.6	-	-	2.0	1.0	0.13	0.17	1.5	C55
Ovary	44	0	-	-	-	2.0	-	-	-	2.2	12.1	8.3	24.2	12.7	17.8	26.5	20.5	8.6	-	15.1	6.9	3.5	0.40	0.63	5.3	C56
Other female genital organs	0	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.0	0.0	0.00	0.00	0.0	C57
Placenta	0	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.0	0.0	0.00	0.00	0.0	C58
Kidney	13	0	-	-	-	-	-	2.3	-	-	-	4.1	2.2	2.5	5.9	8.8	13.7	8.6	14.0	-	2.0	1.0	0.09	0.20	1.6	C64
Renal pelvis	0	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.0	0.0	0.00	0.00	0.0	C65
Ureter	1	0	-	-	-	-	-	-	-	-	-	-	2.2	-	-	-	-	-	-	-	0.2	0.1	0.01	0.01	0.1	C66
Bladder	15	1	-	-	-	-	-	-	-	2.2	-	-	-	-	8.9	8.8	-	34.6	42.0	15.1	2.4	1.2	0.06	0.11	1.5	C67
Other urinary organs	0	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.0	0.0	0.00	0.00	0.0	C68
Eye	1	0	-	-	-	-	-	-	-	-	-	-	-	2.5	-	-	-	-	-	-	0.2	0.1	0.01	0.01	0.1	C69
Brain, nervous system	20	0	-	-	-	2.0	-	-	2.0	4.3	7.3	8.3	4.4	5.1	11.9	-	-	8.6	-	-	0.0	1.6	0.23	0.23	2.5	C70-72
Thyroid	20	0	-	-	2.1	-	2.1	-	2.0	4.3	9.7	4.1	4.4	5.1	11.9	4.4	-	-	-	-	0.2	1.6	0.23	0.25	2.5	C73
Adrenal gland	0	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	2.4	0.0	0.00	0.00	0.0	C74
Other endocrine	0	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.0	0.0	0.00	0.00	0.0	C75
Hodgkin disease	6	0	-	-	2.1	2.0	2.1	-	-	-	-	-	2.2	-	-	8.8	-	-	-	-	0.9	0.5	0.04	0.09	0.9	C81
Non-Hodgkin lymphoma	20	0	2.8	-	2.1	-	-	2.3	-	2.2	-	2.1	8.8	5.1	5.9	13.3	13.7	17.3	-	-	3.1	1.6	0.16	0.29	2.7	C82-85, C96
Immunoproliferative diseases	0	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.0	0.0	0.00	0.00	0.0	C88
Multiple myeloma	13	0	-	-	-	-	-	-	-	-	2.4	-	4.4	5.1	3.0	8.8	13.7	-	14.0	30.1	2.0	1.0	0.07	0.19	1.4	C90
Lymphoid leukaemia	2	0	-	-	-	2.0	-	-	-	-	-	-	-	-	-	-	6.8	-	-	-	0.3	0.2	0.01	0.04	0.3	C91
Myeloid leukaemia	19	0	-	-	-	-	2.1	4.7	-	2.2	2.4	4.1	2.2	5.1	3.0	17.7	13.7	8.6	-	15.1	3.0	1.5	0.13	0.29	2.5	C92-94
Leukaemia unspecified	7	1	2.8	-	-	-	-	2.3	4.0		2.4	-	-	-	-	-	-	-	-	15.1	1.1	0.6	0.07	0.07	1.1	C95
Myeloproliferative disorders	2	0	-	-	-	-	-	-	2.0	-	-	-	-	-	3.0	-	-	-	-	-	0.3	0.2	0.02	0.02	0.2	MPD
Myelodysplastic syndromes	5	0	-	-	-	-	-	-	-	-	-	-	4.4	-	8.9	-	-	-	-	-	0.8	0.4	0.07	0.07	0.6	MDS
Other and unspecified	108	1	5.5	2.3	2.1	4.1	4.1	2.3	7.9	15.1	7.3	20.7	28.6	30.6	44.5	39.8	89.0	69.1	14.0	45.2	17.0	8.6	0.88	1.53	1.35	O&U
All sites	1,319	30	16.5	2.3	10.4	18.4	12.3	32.6	61.6	123.0	222.9	244.7	396.3	402.4	593.9	569.8	862.7	725.8	588.0	467.0	207.5	-	10.94	18.26	157.7	ALL
All sites but C44	1,261	17	16.5	2.3	10.4	18.4	12.3	32.6	61.6	118.7	218.1	238.4	389.7	389.7	579.1	547.7	807.9	708.5	546.0	361.6	198.3	100.0	10.58	17.45	151.1	AllbC44

Mortality observed in 2014 in Mauritius accounts for 1,177 deaths. 597 deaths occurred in men and 580 in women. (Mauritius National Cancer Registry, 2014)

This figure is projected to increase to approximatively 1,900 in 2030 (*GLOBOCAN estimates).

Table 6: The most common causes for mortality in 2014 in men

Site	Number	%	Crude mortality rate/10	ASR(World)/10
Lung	123	20.6 %	19.7	16.8
Prostate	82	13.7 %	13.2	11.8
Colon/Rectum	73	12.2 %	11.7	9.9
Stomach	52	8.7 %	8.3	7.4
Pancreas	47	7.9 %	7.5	6.5
Lip, oral cavity and pharynx	34	5.7 %	5.5	4.6
Oesophagus	24	4.0 %	3.9	3.3
Eye, brain and other C. N. S.	23	3.9 %	3.7	3.0
Liver and intra-hepatic bile ducts	19	3.2 %	3.1	2.7
Bladder	16	2.7 %	2.6	2.2
OTHERS	104	17.4 %	16.7	-
TOTAL	597	100 %	95.8	83.0

Table 7: The most common causes for mortality in 2014 in women

Site	Number	%	Crude mortality rate/10	ASR(World)/10
Breast	150	25.9 %	23.6	16.9
Colon/Rectum	60	10.3 %	9.4	6.3
Cervix uteri	49	8.4 %	7.7	5.6
Ovary	37	6.4 %	5.8	4.4
Trachea, Bronchus and Lung	37	6.4 %	5.8	3.8
Stomach	28	4.8 %	4.4	2.9
Leukaemia	27	4.7 %	4.2	3.4
Pancreas	24	4.1 %	3.8	2.6
Liver and intra-hepatic bile ducts	23	4.0 %	3.6	2.7
Corpus uteri	17	2.9 %	2.7	1.9
OTHERS	128	22.1 %	20.1	-
TOTAL	580	100 %	91.2	64.9

In developed countries, there is a rapid evolution towards the integration of extremely potent biology-oriented therapies (anti-HER2, tyrosinekinase inhibitors, immunotherapies). It has been shown that advances in standard care and the impact of new biologic drugs have already allowed a significant improvement of cancer survival and quality of life with an accelerating trend. (Nabholtz)

As a consequence, in countries in transition, there is a strong need to anticipate this evolution in order to minimize the foreseeable increasing gap between developed countries and countries in transition.

Current Status For Cancer Services In Mauritius

Mauritius has implemented since 2010 a national cancer control program action plan. Several goals at different stages of implementation have been identified by the National Cancer Control Program (NCCP):

1. Reducing exposition to risk factors of cancer
2. Promoting early screening
3. Ensuring timely access to diagnosis and treatment
4. Improving the patient and family experience of cancer care
5. Supporting an efficient Mauritius Cancer Register

In terms of public information, different campaigns through the media are conducted as regards to preventive health measures and adoption of healthier life-styles.

As regards to screening, the government is working on the elaboration of mobile clinics to give access to breast and cervical screening to all Mauritian women. At the level of the Central Health Laboratory free services are provided for testing of circulating tumour markers and Immunohistochemistry markers. Since 1995, a computerised system for all paraffin blocks is available; besides the paraffin blocks have been archived for at least the past two decades.

National screening and early detection programs exist for cervical (Pap smears) and breast cancer, (clinical palpation and diagnostic mammography) together with community-based awareness campaigns.

Medical and surgical management of cancer is undertaken in all 5 public hospitals and all private clinics. Multidisciplinary meetings are held for cases of breast, brain and paediatric tumours. There has been much progress done in the country from imagery through biopsy to laboratory analysis. For radiation therapy, one centre is present at Victoria hospital with technical access to 1 linear accelerator and 2 cobalts.

For systemic cancer treatment, all care including chemotherapy, hormonotherapy are delivered in several sites. In terms of treatment, patients have access to various infrastructures in Public and Private sectors. The Ministry of Health provides free of charge more than 40 different chemotherapy drugs, mainly generic drugs, beyond the recommended WHO essential chemotherapy list of drugs.

For palliative care, it is primarily hospital-based. Pain management has also improved. Access to opiates is possible in oral and parenteral forms but limited to a ten day outpatient repeat prescription by the Dangerous Drug Act. Emergency palliative radiotherapy is also offered. A very efficient cancer registry is allowing a clear vision of cancer Mauritius.

Today, in Mauritius, there is no clinical and translational research. This is an important point for the integration and access to novel major drugs including new biological therapies. Cancer management needs implementation of research in order to optimize patient care. Even if standards of treatment are good in Mauritius, the trend in incidence might be expected to rise.

There is much effort from the public administration and several stakeholders who are committed to reduce this ascending trend of new cancer cases by putting more emphasis on the preventive aspect of cancer control and to provide the best possible care.(Mohith et al., 2015)

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Chapter 16m

Mozambique

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* This chapter should be referenced as: Carvalho-Fumane JM. Mozambique. In: Boyle P, Ngoma T, Sullivan R, Ndlovu N, Autier P, Stefan S, Fleming K and Brawley OW. The State of Oncology in Africa 2015. iPRI Scientific Publication 4, iPRI, Lyon, France (2016).

Mozambique is located on the coast of Southern Africa with a total area of 799,380 km². The country as a long coastline of 2,515 km and is divided into 11 provinces and 152 Districts. According the National Statistic Institute, the 2015 total population is 26.423 million, based on projections from the 2007 census. There is a slight preponderance of women and the urban population represents 32% of the total population. The population is relatively young, with 40% being below 15 years of age and 16.6% under 5 years. The population annual growth rate is 2.7% (Figure 1).

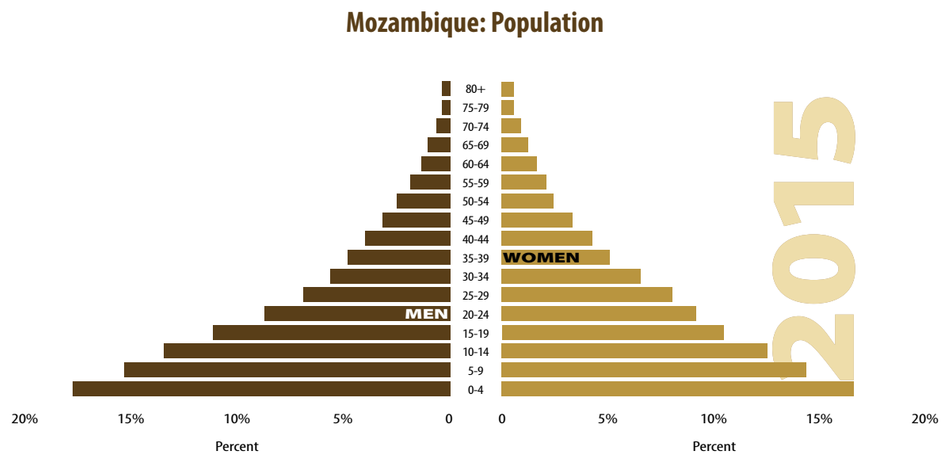


Figure 1: Population Pyramid by Age Group and Gender, 2015 (National Statistics Institute, 2015)

The adult literacy rate in Mozambique is 49.9% according the 2015 National Statistic Institute data. Only 35% of the population has access to safe drinking water. Work force is largely concentrated in the agricultural sector (81%).

The National Health System

The National Health System covers approximately 60% of the population and is heavily dominated by the public sector. The private health care providers are mostly concentrated in big cities. Additionally, many National and International non-governmental organizations (NGO) provide preventive and curative care at rural and district level. The Government is revitalizing the community health workers networks, as a mean to improve access to health care.

Non-communicable diseases (NCD) are considered a major public health problem by the Ministry of Health of Mozambique since 2008. Cardiovascular diseases, diabetes, cervical cancer, breast cancer, prostate cancer and trauma are included in priority interventions for the health sector, according the 2014-2019 Health Strategic Plans (Table 1).

Table 1: Organisation of Health Care Network

Level	Category of health unit (HU)	Beds	Types of care provided
I	Health centres I and II urban and rural	10,180	Primary (preventive and curative) care
II	Rural and district hospitals	4,590	First reference, with admission and surgery
III	Provincial hospitals	2,202	Surgery, obstetrics, gynaecology, paediatrics, internal medicine, orthopaedics and dentistry
IV	Central Hospital and psychiatric hospitals	3,042	Multiple specialities and some subspecialities; most advanced HU
Total		20,014	

Cancer Registration and Overview of Cancer

A population-based cancer registry in Mozambique was started in early 1960s by Prates and Torres and stopped in 1965, shortly after the start of the Mozambican war of independence. This registry was placed at Miguel Bombarda Hospital (presently the Maputo Central Hospital) and covered an area of 60 km^2. During this period the burden of cancer was dominated by liver cancer, in both genders (Table 2).

Table 2: Cancer Incidence/100,000 hab

Lourenço Marques, 1956-1960

Site	Cases (all ages)	%	Age-adjusted incidence rate
Men			
Liver	264	65.5	101.7
Bladder	24	6.0	17.1
Non-Hodgkin's lymphoma	18	4.5	17.1
Non-melanoma skin	13	3.2	7.6
Prostate	10	2.5	9.5
All sites	403	100	184
Women			
Liver	61	31.0	31.4
Cervix	42	21.3	29.1
Bladder	21	10.7	14.0
Mouth	10	5.1	7.0
Non-melanoma skin	9	4.6	7.6
All sites	197	100	122

In 2006, Ferro implemented a pilot project of population-based cancer registry in Beira city which was unfortunately stopped in 2007 (African Cancer Registry Network, 2016). The data presented a strong burden of AIDS-related cancers dominated by Kaposi's Sarcoma (Figure 2).

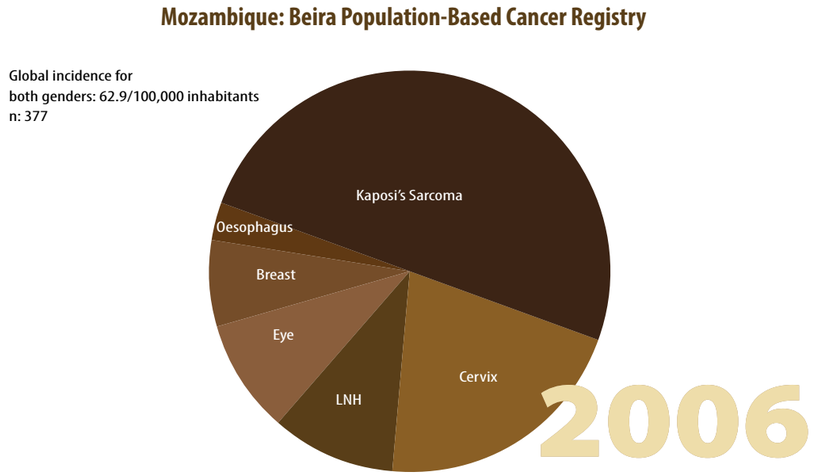


Figure 2: Population Based Cancer Registry of Beira (African Cancer Registry Network, 2016)

In Maputo Central Hospital, a hospital-based cancer registry has been implemented since 1991 and a total of 13,710 cases were reported until 2008, with 57% of cases in women and 43% in men. A total of 2,446 cases of cervical cancer and 798 cases of breast cancer were reported. In men, a total of 955 cases of prostatic cancer were registered. Kaposi's Sarcoma was responsible for 1,500 cases, with male predominance (Figure 3).

Mozambique, Maputo City: Most Frequent Cancers

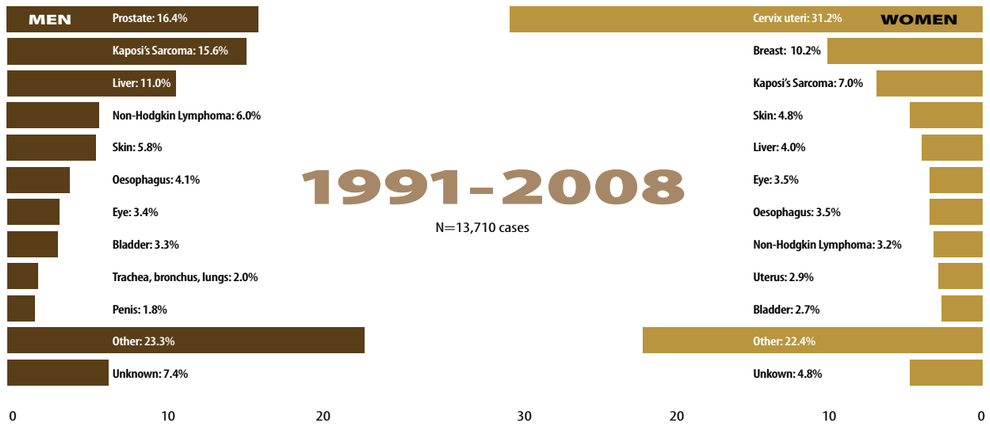
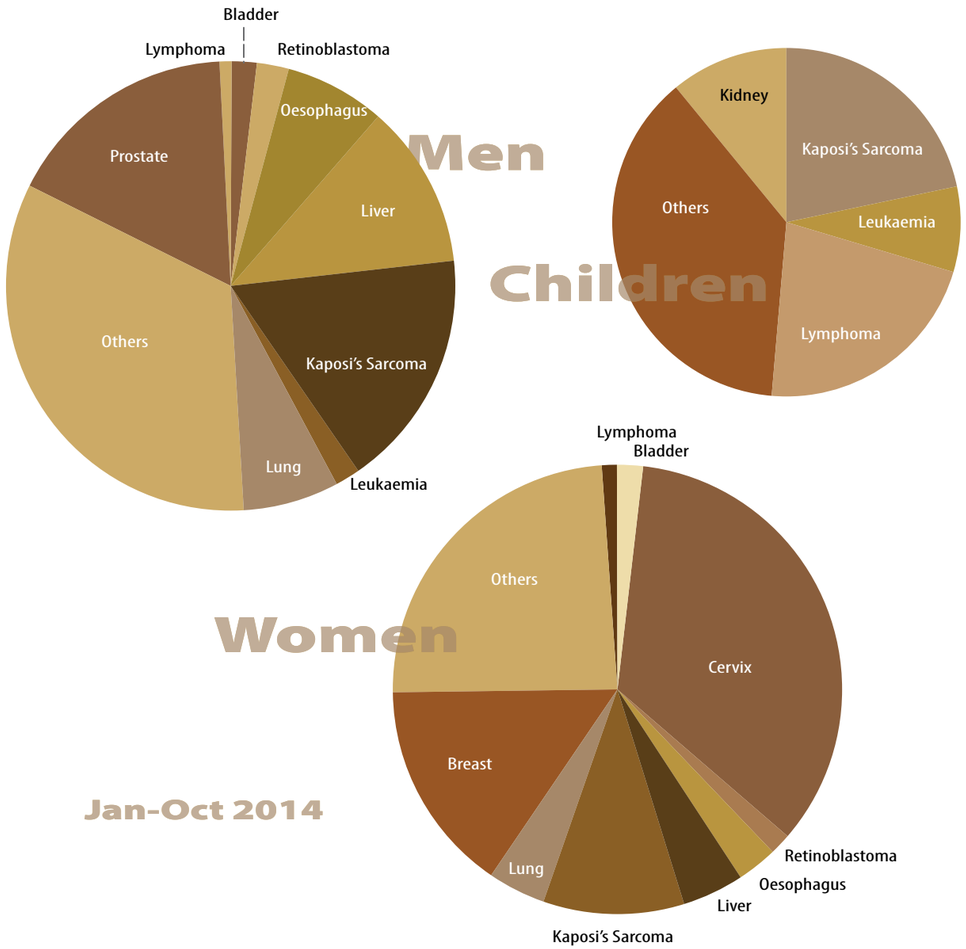


Figure 3: Distribution of the ten most frequent cancer in Maputo city, 1991-2008

In 2014, the registry system was updated and modernized; in 2015 a population-based registry was started in Maputo City. Data analysed from January to October 2014, presents a total of 759 cases (62% in women). Prostatic cancer and Kaposi's Sarcoma were the leading cancer sites in men (Figure 4), cervical cancer in women (Figure 5) and lymphoma in children (Figure 6). Liver cancer is also predominant in men (12% of cases in adult men).

Mozambique: Maputo Population-Based Cancer Registry



Figures 4-6. Cancer in Adult Men, Women and Children

Cancer Centres

There are two cancer treatment centres in Mozambique, at Maputo Central Hospital. In addition to these, there are chemotherapy units at the Nampula Central Hospital. The role of private units in cancer management is very limited. The only radiotherapy centre is being refurnished in order to fulfil international requirements. The planned equipment includes a linear accelerator, a high dose brachytherapy unit and an appropriate simulator room. There is currently no radiotherapy treatment provided in Mozambique. All patients requiring such treatment have to go to South Africa or India, either at their own expense or with the financial support of the government.

Pathology Resources

Histopathology services are located in three main Central Hospitals (Maputo, Beira and Nampula), Maputo being the referral centre. It is planned to extend the pathology facilities in provincial hospitals. The service at Maputo Central Hospital Department of Pathology is very good, and a quality assurance programme is in implementation in order to obtain international accreditation. Immunohistochemistry and hormone receptors for breast cancer are available at Maputo Central Hospital.

Tumour markers are available at Maputo Central Hospital, and occasionally in Beira and Nampula. The following are usually available: CEA, CA125, CA19-9, PSA, AFP, beta HCG and CA15-3. Molecular biology is not available in the public setting.

Available Oncologists

The radiotherapy centre (under refurnishment), has two radiation oncologists, two medical physicists and four technicians. Four clinical oncologists are located in Maputo and one in Nampula. In addition, there are four haemato-oncologists including one paediatric haemato-oncologist in Maputo Central Hospital.

There are also resident doctors in training in radiation oncology/clinical oncology in the local residence programme at Maputo Central Hospital. Additionally, there are collaboration programmes with the Brazilian National Cancer Institute (INCA), the Institute of Pathology in Porto, the hospital Pedro Ispano, the Hospital São Joao and the Portuguese Institute of Oncology (all in Portugal), for training human resources for cancer treatment.

A radiation safety programme is in place in the country, with scheduled screening for radiation doses for all personals exposed, not only in oncology field but also in radiotherapy catheterization laboratories and other facilities using radionuclides.

The National Cancer Control and Prevention Programme (NCCP)

Cancer was recognized as a Public Health problem in 2008. Since then, a screening programme was started for breast, cervical and prostatic cancers. A comprehensive Strategic Plan for Cancer Control is in elaboration, with involvement of different stakeholders, including civil society. The Strategic Plan for Health Sector 2014-2019, includes cancer as one priority area.

Prevention and Early Detection

Like in most African countries, the increasing incidence of cancer in Mozambique was linked with several risk factors, including infectious agents and lifestyle-related factors such as tobacco, alcohol, unhealthy diet and physical inactivity. A study was carried out to identify risk factors associated with liver cancer, whose burden is particularly high in Mozambique. Food contamination with aflotoxin was identified as the leading cause (Prates et al, 1965). An appropriate preventive programme was set up, not only for early detection through screening, but also with strong public education and information as well as legal measures.

Unfortunately, many cancers are diagnosed in advanced stage, due to a lack of information and weak detection capacities of the health system. A community programme including pain management, nutritional and psychological support was organised in collaboration with a NGO in order to deal with patients requiring palliative care.

Mozambique adopted the International Framework Convention for Tobacco control. Both legal measures and educational programmes are in place for strongly controlling tobacco consumption. Advertising tobacco use and smoking in closed environments are forbidden by law. However, strong tobacco lobbies are playing an important role and try to avoid the implementation of more aggressive legal measures.

Mozambique created a strong programme against abusive alcohol consumption. Selling alcohol to people less than 18 years is illegal. Additional legal measures were adopted to control the public selling of alcohol. However, the implementation of those measures is very weak, due to several factors, including the weak auditing system, commercial interests and lobbies.

Infectious risk factors which promote cancer (HIV, HPV, Hepatitis B and C, EBV, Helicobacter Pylori and Schistosomiasis) are monitored. Promotion of interventions such as safe sex, eradication of the schistosoma parasite and hepatitis B vaccination are part of measures being taken to reduce these risk factors.

Many programmes aiming at reducing HIV transmission are in place. General behavioural changes, condom use, access to treatment and prevention of mother to child transmission are promoted.

Mozambique launched in 2014 a HPV vaccination programme for reducing the prevalence of cervical cancer. A national immunization programme includes hepatitis B vaccination as part of the routine health care.

Cancer Screening Services

In 2008, Mozambique adopted a cancer screening programme for early detection of breast, cervical and prostatic cancer as a priority intervention in Cancer Control Programme. A manual breast examination is encouraged for all women, and an education programme was set up to introduce this behaviour in communities. However, mammography is available in only three central hospitals. Fine needle biopsy is available in central hospitals and in few provincial hospitals.

Cervical cancer screening using visual inspection with acetic acid (VIA) is the most disseminated programme in cancer control in Mozambique. It is done in all districts at primary health care centres by trained nurses. Cryotherapy is done in all central and provincial hospitals and in some district hospitals. Pap smears are available in all three central hospitals.

Drugs

Mozambique adopted a National Drug List (including oncology drugs) since the early 1970th, which is revised regularly. The availability of drugs for cancer control is warranted by a central medicine storage directorate which is responsible for acquiring drugs for the public health system. Oncologists and oncology-related medical personnel are involved in the definition of the drug list and prioritization of the necessary items. Of note, the Maputo central hospital has the autonomy to acquire small amounts of drugs for selected and justified clinical cases.

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Chapter 16n

Nigeria

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* This chapter should be referenced as: Ogunbiyi OJ, Soyannwo O, Tunde-Odukogbe A. Nigeria. In: Boyle P, Ngoma T, Sullivan R, Ndlovu N, Autier P, Stefan S, Fleming K and Brawley OW. The State of Oncology in Africa 2015. iPRI Scientific Publication 4, iPRI, Lyon, France (2016).

Nigeria is a Western African country with a total area of 356,667 square miles (923,768 km^2). Nigeria has a rich ethnic diversity, with more than 250 ethnic groups, including Hausa and Fulani (29%), Yoruba (21%), Igbo (18%), Ijaw (10%), Kanuri (4%), Ibibio (3.5%) and Tiv (2.5%).

The most widely professed religions are Islam (50%) and Christianity (40%), with a minority of indigenous beliefs (10%).

The literacy rate is approximatively 59.6%, with a rate of 69.2% and 49.7% in men and women, respectively (2015 estimate).

The total and per capita gross domestic product were estimated at $478.5 billion ans $2,800 in 2013, respectively. Nigeria has a high growth rate (6.2%), inflation (8.7%) and unemployment (23.9%). Arable land represents 39.0% of the country area.

Regarding agriculture and farming, the main resources are cocoa, peanuts, palm oil, corn, rice, sorghum, millet, cassava (tapioca), yams, rubber, cattle, sheep, goats, pigs, timber and fish.

The labour force represents 51.53 million people. Based on 1999 estimates, people mainly work in the agricultural sector (70%) followed by services (20%) and industry (10%).

The main industries include crude oil, coal, tin, columbine, palm oil, peanuts, cotton, rubber, wood, hides/skins, textiles, cement and other construction materials, food products, footwear, chemicals, fertilizer, printing, ceramics, steel, small commercial ship construction and repair. The natural resources are natural gas, petroleum, tin, columbine, iron ore, coal, limestone, lead, zinc and arable lands.

The population was estimated in 2014 at 177,155,754 with a growth rate of 2.47%, a birth rate of 38.03 per 1,000, and an infant mortality rate of 74.09 per 1,000.

The population is relatively young with a majority under 25 years-old (62.39%; 2015 estimates).

In 2015, the male/female ratio in the total population was slightly higher than 1.04, and remained consistently above one, except for older age categories. The male/female ratio is 1.06 at birth, 1.05 for ages 0-54 years, 0.95 for 55-64 years and 0.91 for over 65 years of age. As of 2015, life expectancy is 53.02 years for the total population (52 for men and 54.1 for women, respectively).

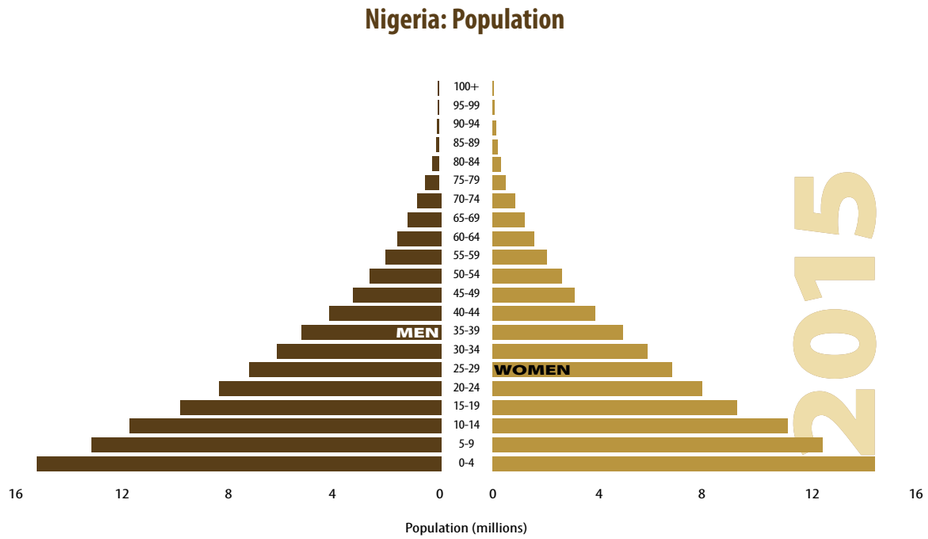

Figure 2: Population Pyramid by Age Group and Gender

About 47.8% of the population lives in urban communities and the urban migration rate is about 4.6% annually.

The largest cities in Nigeria (2011 estimates) are Lagos (11.223 million); Kano (3.375 million); Ibadan (2.949 million); Abuja (Capital city; 2.153 million); Port Harcourt (1.894 million) and Kaduna (1.524 million).

The health expenditure was about 4% of GDP as of 2013 and the adult HIV prevalence rate was approximatively 3.17% in 2014.

In 2015, 68.5% of the total population had access to drinkable water, and 31.5% had not. The improvement of access to water was mainly observed in urban areas, where 80.8% of the population had access to drinkable water, vs. 57.3% in rural areas.

Cancer Registration and Overview of Cancer

Nigeria has three recognised population based cancer registries (PBCR) in Ibadan (South West zone), Calabar (South South zone), and Abuja (Central zone). The Ibadan Cancer Registry is the oldest PBCR in Nigeria, and the second oldest sub-Saharan Africa. It is considered as the most reliable population-based cancer registry in Nigeria by many international organisations such as the International Agency for Research on Cancer

and the African Cancer Registry Network. The registry has contributed significantly to the development of cancer registration and surveillance in sub-Saharan Africa by providing useful data for the GLOBOCAN reports. The registry has also helped in the training of new registrars in centres trying to develop cancer registries.

The PBCRs in Ibadan, Calabar, and Abuja generate data that is comparable to other international PBCRs in terms of coding methods used, definitions of incidence dates and multiple primaries.

Following the review of the registry databases and exclusion of unsuitable submissions, findings from the Abuja and Ibadan population-based cancer registries as well as 11 Hospital-based cancer registries (HBCRs) were published in two separate journal articles in 2012 (Jedy-Agba et al, 2012a; Jedy-Agba et al, 2012b). The PBCRs reported on the age-standardized incidence rates (ASR) of the most common cancers in Nigeria (Jedy-Agba et al, 2012a). In women, the most common cancers were breast (54.3/100,000) and cervix (34.5/100,000). In men, the most frequent cancer was prostate (19.1/100,000). Information on the number of cases by site and gender, most valid basis of diagnosis as reported by 11 hospital-based cancer registries in Nigeria has also been published (Jedy-Agba et al, 2012b).

Table 1: Most common cancers and age standardized rates in Nigeria in 2012

Table from Jedy-Agba et al. (2015)

Men	Total cases*(ASR/100,000)	Women	Total Cases* (ASR/100,000)
Prostate	11,944 (30.7)	Breast	27,304 (51.5)
Liver	7875 (15.2)	Cervix	14,089 (29.2)
Non-Hodgkins Lymphoma	2328 (3.7)	Liver	4172 (8.2)
Colorectal	2164 (4.5)	Colorectal	2008 (4.0)
Kaposi's Sarcoma	982 (1.5)	Non-Hodgkin's Lymphoma	1778 (2.8)
All Sites but Skin	37,540 (79.5)	All Sites but Skin	64,622 (122.8)

Combined Estimates derived from Ibadan, Abuja, and Calabar

The most reliable data on cancer incidence in Nigeria derive from the three working population-based registries in Ibadan, Abuja, and Calabar. A report on the data from especially Ibadan (IBCR) and Abuja (ABCR) was published in 2012 in the journal Cancer Epidemiology (Jedy-Agba et al, 2012a). The following paragraphs are based on this article.

The age standardized incidence rate for all invasive cancers from the IBCR was 66.4 per 100,000 men and 130.6 per 100,000 women. In ABCR it was 58.3 per 100,000 for men and 138.6 per 100,000 for women. A total of 3,393 cancer cases were reported by the IBCR. Of these cases, 34% (1,155) were seen among men and 66% (2,238) in women. In Abuja over the same period, 1,128 invasive cancers were reported. 33.6% (389) of these cases were in men and 66.4% (768) in women. Mean age of diagnosis of all cancers in men for Ibadan and Abuja were 51.1 and 49.9 years respectively. Breast and cervical cancer were the commonest cancers among women and prostate cancer the most common among men. Breast cancer age standardized incidence rate (ASR) at the IBCR was 52.0 per 100,000 in IBCR and 64.6 per 100,000 in ABCR. Cervical cancer ASR at the IBCR was 36.0 per 100,000 and 30.3 per 100,000 at the ABCR. The observed differences in incidence rates of breast, cervical and prostate cancer between Ibadan and Abuja, were not statistically significant.

Table 2. Most Frequent Invasive Cancers < 45 years

Most Frequent Invasive Cancers < 45 years			
Ibadan		Abuja	
Men	Women	Men	Women
1. Liver 30 (8)	Breast 390 (45.5)	NMSC 22 (14.5)	Breast 217 (55.6)
2. NMSC 27 (7.2)	Cervix 110 (12.8)	Kaposi's Sarcoma 21 (13.8)	Cervix 31 (8)
3. NHL 27 (7.2)	Ovary 33 (3.8)	Liver 15 (9.8)	NMSC 17 (4.4)
4. Connective & soft tissue 26 (7)	Thyroid 27 (3.1)	Connective & soft tissue 11 (7.2)	Ovary 16 (4.1)
5.Nasopharynx 26 (7)	NMSC 20 (2.3)	Nasopharynx 8 (5.2)	Kaposi's Sarcoma 14 (3.6)

Most Frequent Invasive Cancers = and > 45 years			
Ibadan		Abuja	
Men	Women	Men	Women
1. Prostate 250 (32.1)	Breast 527(38.2)	Prostate 103 (46.1)	Breast 163 (45.7)
2. Colorectal 63 (8.1)	Cervix 430 (31.2)	Colorectal 12 (5.4)	Cervix 86 (24.1)
3. NMSC 47 (6)	Colorectal 47 (3.4)	Liver 12 (5.4)	Ovary 16 (4.2)
4. Liver 40 (5)	Corpus uteri 36 (2.6)	NMSC 11 (5)	Colorectal 12 (3.4)
5. Larynx 35 (4.5)	Ovary 35 (2.4)	NHL 8 (3.6)	Unspecified site 6 (1.7)

Number of cases and proportions (n(%)) of the 5 most frequent cancers in each registry by sex, stratified by age group. (NMSC: Non Melanoma skin cancer; NHL: non-Hodgkin's lymphoma)

There was a steady rise in age-specific incidence rate of all invasive cancers from age 0–4 years to 65 years and greater in men in both registries. Among women, the age specific incidence rate for all invasive cancers peaked at 55–64 years in both registries.

Nigeria: Age-Specific Rates for all Cancers

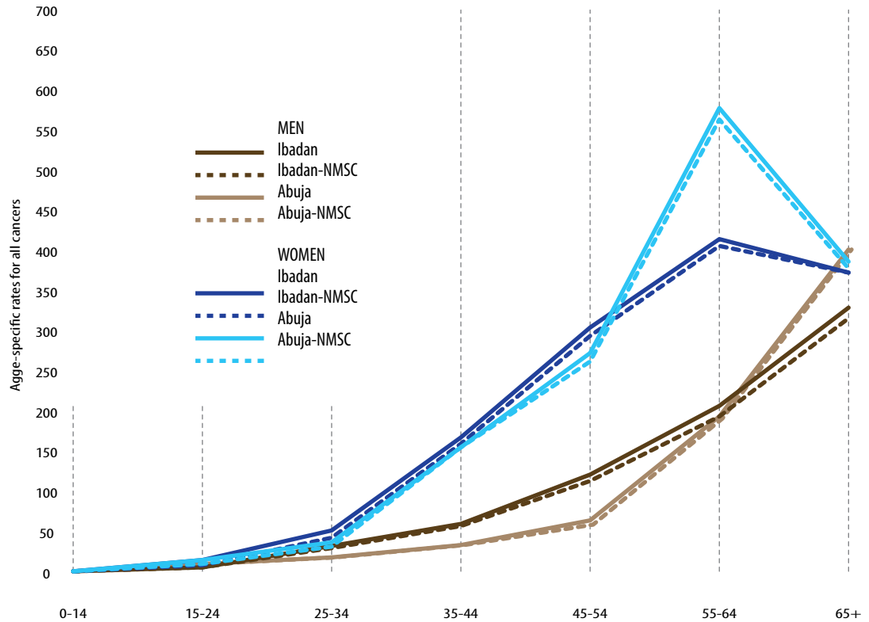

Figure 3: ASR for Cancers in Nigeria

Childhood cancers (age 0-14) represented 3.6% of all the cancers recorded in 2013. A total of 236 childhood cancers were registered. They occurred in 123 (52.1%) boys and 113 (47.9%) girls. The five most frequent cancers (n (%)) in boys classified according to the ICCC system were lymphoma 21 (17.0%), soft tissue sarcomas 20 (16.3%), leukaemia 17 (13.8%), retinoblastoma 15 (12.2%) and renal tumours 13 (10.6%). In women, the five most frequent were renal tumours 22 (19.5%), soft tissue sarcomas 16 (14.2%), lymphoma 13 (11.5%), retinoblastoma 12 (10.6%) and leukaemia 11 (9.7%). Kaposi's Sarcoma accounted for 41.7% of the soft tissue sarcomas in both boys and girls.

Cancer Mortality

In terms of percentages, cancer mortality in Nigeria is very close to the incidence. There is no national screening programme for cancer and the majority of cancers are diagnosed at late stage regardless of them being preventable or not.

Data on survival is scanty because of challenges experienced with the follow-up of cancer patients (including the inadequacies of death registration in the country) but there is a renewed drive to ensure this information is captured.

Medical Oncology Resources

In Nigeria, cancer therapy is provided by surgical oncologists and radiation oncologists. There are no trained medical oncologists working in Nigeria. There are however haematologists who administer chemotherapy for haematologic malignancies. In addition, there are paediatric oncologists in some centres.

There is limited availability of chemotherapy drugs in the public sector. Most patients acquire drugs at their own expenses. The cost of these medicines is prohibitive for the vast majority of the population. Even in the private sector, there are shortages of chemotherapy drugs. These factors commonly lead to disruptions and delays in the treatment of patients and may possibly result in poor treatment outcomes.

Radiotherapy Resources

The use of low dose, manual after loading Caesium brachytherapy was introduced for treating gynaecological malignancies in the 1960s at the University College Hospital Ibadan. About the same time or very shortly after it, the Lagos University Teaching Hospital introduced the use of ionizing radiation for the treatment of superficial tumours with ortho-voltage therapy. The Lagos University Teaching Hospital (LUTH) commenced frank radiotherapy with a cobalt -60 machine. In 1987 the University College Hospital Ibadan also acquired a colbalt-60 machine. Since then, seven other centres have been established.

There are a total of 50 qualified radiation oncologists in Nigeria, and many others are currently in training.

The present radiotherapy resources in Nigeria are thus:

- Five Linear accelerators (only two are presently functional)
- Three TeleCobolt-60 megavoltage (only two are presently functional)
- Four brachytherapy machines
- Two low-dose rate (LDR) after loading Caesium brachytherapy machines (none presently functional)
- One high dose rate (HDR) Cobalt machine (presently non-functional)
- One high dose rate Iridium machine (presently non-functional)

There are nine radiotherapy centres in Nigeria (Lagos University Teaching Hospital, University College Hospital Ibadan, University of Benin Teaching Hospital, University of Nigeria Teaching Hospital Enugu, Usman Danfodiyo University Teaching Hospital, Sokoto, National Hospital Abuja, Ahmadu Bello University Teaching Hospital, Zaria, Gombe Teaching Hospital and Eko hospital (a private centre).

In each centre, there is a dedicated simulator, 2D planning system. Appropriate dosimetry and quality control equipment for external beam radiation therapy (EBRT) and HDR brachytherapy are available in all centres. Other related equipment are the brachytherapy TPS for each unit, and dedicated C arm.

Drugs

There is no control on the acquisition and use of chemotherapeutic drugs in Nigeria. Practitioners prescribe by preference and based on pharmaceutical representatives or drug importations of patients themselves. Some drugs are sometimes available free of charge from donors through research endeavours or donations from philanthropists.

The National Cancer Control and Prevention Programme (NCCP)

In recognition of cancer being a major cause of morbidity and mortality, the Nigerian Federal Ministry of health established a National Cancer Control Programme with a Cancer Plan for 2013-2018. The purpose of that five-year plan was 'to draw attention of all stakeholders and to bring to the fore the types of cancer in our environment and the interventions required to reverse the alarming trend'.

The plan included ten goals designed to focus attention on the priority areas, strategies and activities to address the challenges:

1. Increase Cancer information dissemination, education, and cancer outreach services nationwide.
2. Increase opportunities for cancer training for relevant healthcare providers and advocates
3. Improve the clinical services for cancer prevention, early detection, diagnosis, an treatment
4. Improve the documentation of the location and quality of existing cancer facilities, manpower and services
5. Develop and establish policies and regulations for quality cancer care and services
6. Increase funding for research activities in cancer control
7. Create a systematic framework for the dissemination of national and international cancer research
8. Improve the cancer surveillance system to delineate public health priorities as well as plan and monitor comprehensive strategies for cancer control
9. Facilitate effective communication and collaboration among public and private cancer stakeholders nationwide
10. Ensure quality palliative care services including pain control.

The document was crafted through extensive consultative processes involving national and international stakeholders and was coordinated by the National Cancer Control Strategy Committee.

Following this plan, an increasing activity in the field was observed with pockets of screening programmes based on NGO activities or church-related activities. However, there is still no national screening programme for any cancer in place.

Breast Cancer

Mammography is available in a few teaching hospitals and a couple of private diagnostic services in about five major urban cites. The current available mammography capacity is far below what would be needed for national coverage of women at risk. There is a gradual increase in the prevalence of clinical breast exams due to the activities of NGOs especially rooting for the prevention and early detection of breast cancer. Many of these accesses are funded from international bodies including the NCI and other philanthropic organisations from abroad. Still, the number of people getting breast examinations is very low.

Awareness of the importance of breast self-examination still needs to be prioritized together with instruction on the technique of how to perform such self-examinations.

Cervical cancer

Cervical cancer still forms over 60% of cases of gynaecological cancers in Nigeria. There is no established population-based screening system for its prevention. Opportunistic screening occurs in some public and private hospitals/clinics and recently in some religious centres. Many NGOs

are attempting to raise awareness levels about the disease, its prevention through lifestyle alterations, the newly introduced vaccines and the measures to detect early and treat its pre-invasive lesions.

Because of its high cost and the need for highly trained histo-pathologists, the more specific Pap smear test is available in few centres in urban areas. Human papilloma virus (HPV) testing and colposcopy are even less available. The less specific although more sensitive visual inspection methods which use acetic acid and/or Lugol's iodine are having wide publicity and advocacy especially because of the benefits of single visit, 'see and treat' approach using cryotherapy when abnormalities are seen, and the low cost.

Although awareness appears to be increasing gradually, severe limitations of our health care system still make utilisation of even the low-cost visual inspection services to be grossly suboptimal.

Other Cancers

Only *ad hoc* screening measures are available for all other cancers. For prostate cancer digital rectal examination (DRE) is not routinely offered by the majority of health workers and most public hospitals do not offer PSA screening, although the latter is sometimes offered at awareness events throughout the country.

The situation is similar for other cancers such as colon cancer. There is recognition of the prohibitive costs of screening services, absence of an effective national mechanism to motivate, organize and coordinate cancer screening activities and a sound referral system of referral centres with capacity to take up the cases as they are identified.

Palliative Care

Palliative care was first introduced in Lagos, Nigeria in 1991. By 1993, Hospice Nigeria was registered and major advocacy efforts included support from visiting Dr. Anne Merriman, founder of Hospice Africa, Uganda. The current movement commenced in1996 when a team of health professionals in Ibadan led by Prof. Olaitan Soyannwo formed the Cancer Pain Group. Its goal was to address the pain and suffering experienced by cancer patients and the unavailability of strong opioid analgesics. This movement resulted in the establishment of holistic palliative care service in many parts of the country.

This led to the inauguration of Society for the Study of Pain (SSPN) in 1998 as a chapter of the International Society for the Study of Pain (IASP), and Palliative Care Initiative Nigeria, which was later registered as a Non-governmental organization: Centre for Palliative Care, Nigeria (CPCN) in 2005 (Wright et al, 2006). The Federal Ministry of Health includes palliative care as one of the goals of the National Cancer Plan.

Centre for Palliative Care Nigeria (CPCN) has facilitated training of pioneer palliative care initiators and in-country educational workshops with the support from international agencies especially Hospice Africa United Kingdom, Hospice Africa Uganda, Help the Hospices United Kingdom and African Palliative Care Association. The Federal Ministry of Health, University College Hospital (UCH) and University of Ibadan also funded staff development.

In 2007, in collaboration with CPCN, UCH established the first palliative care unit in a teaching hospital in Nigeria. This unit provides holistic palliative care for patients in the hospital, on day care and home-based care basis; and also offers Clinical placement for training of students and staff from other institutions within and outside Nigeria. Functional palliative care units/teams have subsequently been established in other tertiary

and secondary health institutions including the teaching hospitals in Zaria, Enugu, Ilorin, Port Harcourt, as well as the Federal Medical Centre (Abeokuta), the National Hospital (Abuja), Ladoke Akintola University teaching hospital, LAUTECH Osogbo, and recently the General Hospitals in Umuahia and Makurdi (figure 4). All these hospitals provide palliative care service and training. Pain and palliative care issues are also being incorporated into undergraduate and postgraduate curriculae (Oliver et al, 2011).

Palliative care services are largely based in urban and large hospitals (in-patient and day care clinics), but the home-based care and referral systems reach some of those in neighbouring communities (Omoyeni et al, 2014).

Nigeria: Functional Palliative Care Teams

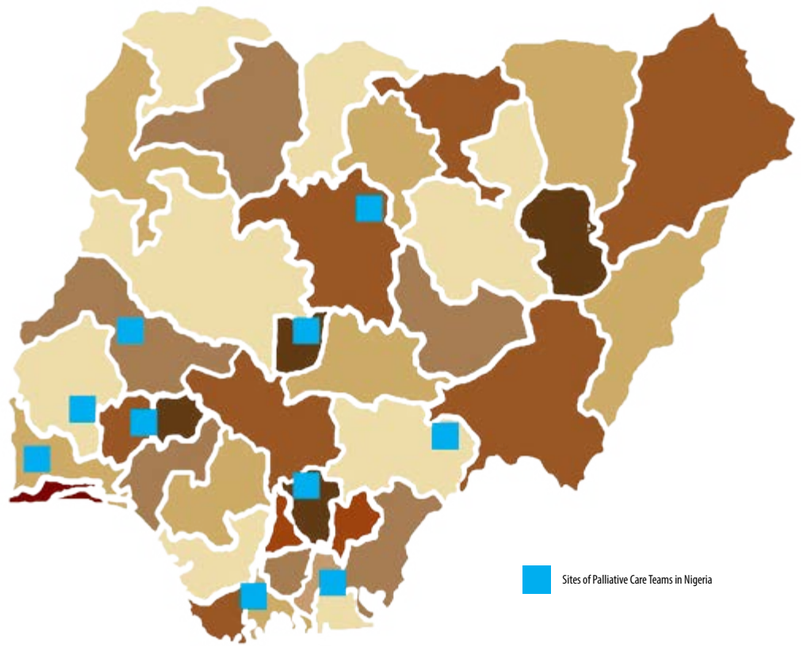

Figure 4: Sites of functional palliative care teams

The palliative service in Nigeria caters for both adult and paediatric patients, mostly those with late stages of cancer as well as patients with other life-limiting illnesses including HIV/AIDS, Sickle cell disease, neurological diseases, late stage organ failures and the elderly. There is no stand-alone hospice in the country but doctors, nurses, pharmacists and social workers drawn from 29 of the 36 States have been trained (mostly in

Hospice Africa Uganda and Nigeria). Almost 100 have attended the five weeks palliative care initiators course of Hospice Africa Uganda. A few of them further obtained postgraduate qualifications such as Diploma, BSc, MSc and MPhil in palliative Medicine. All the centres are also currently involved in educating both professionals and non-professional health care providers for the country. The UCH palliative care unit has become a recognized service model for clinical placement of undergraduates, post-graduates and continuing education students including students from The Gambia (sponsored by APCA), Sierra-Leone, Canada and Sweden. The Ibadan centre also serves as an external examination centre for the Makerere University BSc and Diploma Palliative care courses.

The Federal Ministry of Health is the only legal source for controlled drugs for both public and private health facilities in Nigeria. Along with the National Agency for Food and Drug Administration and Control, it established in 2010 a standing committee on the availability of opioid analgesics. By early 2012, the Ministry, in collaboration with the Global Access to Pain Relief Initiative, initiated an emergency procurement of opioid analgesics as a means of improving access to drugs for pain. A full-time staff member was employed within the Ministry to focus on pain relief and opioid availability issues. This project aimed to empower trained pharmacists in designated Federal Government tertiary hospitals in the six geo-political zones, to access morphine powder from the central medical stores in Lagos and to prepare oral morphine solution for palliative care patients at cheaper cost.

Opioid availability has been erratic in Nigeria since the late 1990s. South Africa consumed 71% of the opioids in the Africa region (International Narcotics Control Board, 2011) with only 205 kg of opioids consumed per year by the remaining countries. This was enough to treat only about 2.8% of the estimated 1.17 million annual painful deaths from cancer or HIV/AIDS. The average annual morphine-equivalent opioid analgesic consumption in Nigeria from 2007 to 2009 was 1.3 kg (International Narcotics Control Board, 2011).

The Ministry is also moving to establish the manufacture of oral morphine at the Federal Pharmaceutical Manufacturing Laboratory at Yaba, Lagos—a manufacturing facility owned by the Federal government.

Vaccination and Cancer in Nigeria

Hepatitis B virus (HBV) vaccination was incorporated into an extending programme of immunization, but the coverage is still extremely low.

The Federal Government funds the vaccination of individuals at risk in the health sector. However the uptake is low and the vaccine is not always available. In many other situations, people have to pay for these vaccines, which are not particularly cheap.

There is a more recent talk on the introduction of the Human Papilloma Virus (HPV) vaccine in schools, but again this is slow in taking off.

Education of Cancer Care Professionals (Human Resource Development)

Training of cancer data abstractors takes place as institutions become interested. There is no national programme for the employment, training and coordination of activities of cancer data abstractors. The offices of vital statistics are also mostly unreliable sources for information on cancer deaths within communities.

Training of radiation oncologists, radiographers and recently medical physicists and oncology nurses is available in Nigeria and as stated earlier on. There are a total of 50 qualified Radiation Oncologists and many others in training.

The Cancer Community

There is an increasing number of local voluntary organizations that are involved in cancer efforts in Nigeria. Most are related to breast cancer, but there is also the one interested in skin cancers because of the high prevalence of Albinism in some parts of the country.

Apart from the one in Ibadan, a few hospices are also now developing in different parts of the country albeit with limited facilities and means.

Conclusion

Palliative care, being a new concept in Nigeria is developing at a steady pace. As government interest and support increases, the population will be more adequately informed about the role and benefits of palliative care. It is also essential that palliative care is incorporated into the national health system to extend service and ensure improved quality of life for those with life-limiting illnesses in both urban and rural areas of the country.

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Chapter 160

Senegal

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* This chapter should be referenced as: Diop MY. Senegal. In: Boyle P, Ngoma T, Sullivan R, Ndlovu N, Autier P, Stefan S, Fleming K and Brawley OW. The State of Oncology in Africa 2015. iPRI Scientific Publication 4, iPRI, Lyon, France (2016).

Senegal is a low income country of west Africa, with a population of 14 million. A bit more than half of the population lives in rural areas (58%). Despite this, most health care resources are concentrated in big urban areas specially in the capital city. Life expectancy at birth was measured to be 59 in 2006. The literacy rate is around 40%. The country is divided into 14 regions. Peanut production accounts for around 40 % of cultivated land, taking up to two million hectares, and provide employment for as many as one million people. Peanut oil is processed industrially mainly for exportation and locally for direct regular consumption.

Healthcare is not free for its citizens, meaning that less than 20% of the population can afford some form of coverage. Cancer patients are required to pay for oncology treatment. The healthcare system is generally weak and fragmented with three parallel systems (public, military and private sectors) and state expenditure on health *per capita* is around 5% of the GDP.

In this context of low resource settings it seems to commend improvisation due to the distance from the knowledge generation centre and the inadequacy between the recommended strategies and the available resources. Intrinsic obstacles, lack of reliable data and human resources, poor quality and lack of standardized medical records, deficient registration of the causes of death (most deaths occurring at home), and poor administrative and financial management of health care facilities, constitute major drawbacks to the development of Senegalese NCCP.

Cancer Registration

There is no mortality registry in Senegal and no population-based cancer registry. However, the cancer control strategic plan includes the development of a national population-based cancer registry that will start in main public hospitals of Dakar with a low cost method using software engineering Win Dev that will allow to register online with different level access and automatic generation of statistics. The registration sheet can be electronically filled or downloaded and printed. ICD-books have been integrated to reduce any risk of error.

Table 1: Cancer incidence in Senegal, GLOBOCAN 2008, Total: 6,646

Men				Women			
Cancer site	Number of cases	% of cancers	ASR(W)	Cancer site	Number of cases	% of cancers	ASR (W)
Liver	713	27.8%	23	Cervix uteri	1,197	29.3%	34.7
Prostate	359	14.0%	18.1	Breast	853	20.9%	23.7
Stomach	175	6.8%	6.6	Liver	338	8.3%	10.5
Non-Hodgkin lymphoma	170	6.6%	3.8	Stomach	167	4.1%	5.7
Colorectum	127	4.9%	4.2	Colorectum	147	3.6%	4.4
Total	2,566	100.0%	88.4	Total	4,080	100.0%	90.2

Table 2: Cancer mortality in Senegal, GLOBOCAN 2008, Total: 5100

Men				Women			
Cancer site	Number of cases	% of cancers	ASR (W)	Cancer site	Number of cases	% of cancers	ASR (W)
Liver	697	31.3%	23.1	Cervix uteri	795	27.5%	25.5
Prostate	288	12.9%	15.3	Breast	472	16.3%	14.5
Stomach	165	7.4%	6.4	Liver	330	11.4%	11
Non-Hodgkin lymphoma	142	6.4%	3.2	Stomach	158	5.5%	5.5
Colorectum	101	4.5%	3.5	Colorectum	115	4.0%	3.7
Total	2,230	100.0%	80	Total	2,896	100.0%	90.2

According to figures from GLOBOCAN 2008 (Publication of the International Agency for Research on Cancer - IARC), the estimated ASR(W) cancer incidence (World Age-Standardized rate) in men is 88.4/100,000 (2,566 new cancer cases), and for women 117.1/100,000 (4,080 new cancer cases). Leading cancers in men are liver (27.8%), prostate (14.0%), stomach (6.8%), non-Hodgkin lymphoma (6.6%), and colorectal cancers (4.9%). In women, cancers of the cervix (29.3%), breast (20.9%), liver (8.3%), stomach (4.1%) and colorectal cancers (4.4%) are the most common. The ASR(W) cancer mortality (world age-standardized rate) according GLOBOCAN is 80.0/100,000 (2,230 death) for men and 90.2/100,000 (2,896 death) for women. Cervical cancer is the leading cause of cancer mortality in the country. Local experts maintain that these figures do not accurately reflect reality and incidence and mortality rates are in fact underestimated (Tables 15.1.1 and 15.1.2).

Cancer Control Programme

The strategic plan is not supported by adequate budgetary resources, around 100,000 US dollars per year. However, it appears that the MoH recognizes the importance of integrating cancer into NCDs and the prevention and control of NCDs are included in the 2009-2018 National Health and Social Development Plan. There is even an NCD focal point (a public health specialist) established at the MoH.

Lack of human resources is one our biggest issues, they need to be upgraded and spread out. Besides, surgical organ specialists, the 4 surgical oncologists, two radiotherapy oncologists, one medical oncologist work in the single Dakar Cancer Centre at Aristide Le Dantec hospital. All eight pathologists, public and private, are located in the capital city.

The scarce cancer diagnosis and treatment services available are mainly concentrated in Dakar too. The majority of patients (around 70 %) present with very late stage disease. However, in practice, the main focus is on treatment oriented approaches that are not linked to early detection and palliative care programmes.

Primary health care centres do not provide cancer prevention, early detection or palliative care services.

Because of late presentation, chemotherapy is frequently used as first or only treatment but the cost is entirely the responsibility of patients. In Senegal, less than 20 % of population have health insurance or can access to the government Medicare programme. However, after years of advocacy, the government has committed to put in next budgetary plan, $2 million subsidy to make chemotherapy accessible.

Table 3 : Overall Cost of Cancer Management (CFA, US dollars)

Chemotherapy	200,000 F CFA - 1,500,000 F CFA	$ 400 - 3,000
Surgery	300,000 F CFA	$ 600
Radiotherapy	150,000 F CFA	$ 300
Diagnosis and Staging	300,000 F CF	$ 600
Total	950,000 F CFA - 2,250,000 F CFA	$ 1,900 - $ 4,500

Partnership Policies

Senegal has developed strong partnership policies to strengthen the cancer control action plan.

INCA France: A cooperation agreement has been set up in 2011 for three years including:

- Contribution of French experts to elaborate a new NCCP
- Short term practical training in French cancer centres for oncology specialists and nurses
- Specific training courses like colposcopy and cervical precancerous lesions management for gynaecologists
- Study of HPV prevalence in Senegalese women

NCI United States: With the assistance of NCI, we have set up a national cervical cancer screening programme based on HPV rapid testing developed by QIAGEN and proposed as a donation programme. Senegalese MOH has already committed to this method in order to start with a pilot project in the health district of Thies, 70 km from the capital city.

International Atomic Energy Agency: many kind of useful support at different levels have been provided for many years:

- Specific training for radiotherapy oncologists and physicists
- Radiation control and diagnosis devices like the single gamma camera of the country
- Impact mission in 2010 which purpose was to collect all information needed in order to supprt more appropriatly Senegalese NCCP

World Health Organization: WHO has specially contributed in tumour registry elaboration by achieving a workshop in 2009, giving softwares Can Reg four and ICD-O books but because of lack of political willingness to implement the programme, we have been working to set up an online registration method.

Primary Prevention

Prevalence of tobacco use is intermediate, about 24 % compared to other African countries but it is increasing among women and adolescents. Senegal has signed the WHO Framework Convention and the law has been enacted but there is no implementation so far.

Vaccination against hepatitis B has been included in Expanded Vaccination Program for free since 2001 but measures need to be taken to prevent cereal aflatoxin contamination especially in rural areas.

Vaccines against HPV are available in drugstores but they are too expensive, their prescriptions are so far individually based but Senegal is applying to the GAVI programme in order to include these vaccines in cervical cancer prevention programme.

Early Detection

Senegal does not yet have systematic, well-established early detection programmes. The present early detection activities are not well organized or well-coordinated. There is some opportunistic early detection of cervical and breast cancer. Early detection for cervical and breast cancer are prioritized in the former strategic plan 2007-2011. Local NGOs raise awareness of the need for cancer early detection but there has not been much coordination with the clinical services required for patients with suspected cancer.

There is also a project with NCI-USA on cervical cancer screening using low-cost HPV testing that has to be implemented in Thies district area. This programme is based on age patterns of cervical cancer natural history, low cost and rapid testing which accuracy and effectiveness have been proven by randomized clinical trials in rural India and China.

Premenopausal women aged 35 and older will be tested followed by immediate cryotherapy to treat HPV positive women. Before cryotherapy, visual inspection using acetic acid (VIA) should assess eligibility for cryotherapy. However, because of recent information from our partners of NCI-USA that Qiagen donation programme has been suspended, Senegal will probably start VIA followed by cryotherapy in a single visit programme.

Regarding breast cancer which is the 3rd most common cancer, NGOs like LISCA (Ligue Sénégalaise Contre le Cancer) achieve workshops on breast cancer management for physicians of community health centres in order to get them involve in self breast examination promotion. In addition to these actions, Senegal is studying possibility of private-public partnership to set mobile multidisciplinary teams to use mammography for breast cancer screening but this programme will need mutualization of both available human resources and equipments.

Diagnosis and Treatment

The majority of cancer patients in Senegal have very limited access to diagnosis and treatment services. This is mainly due to the fact that specialized services are scarce and mainly concentrated in Dakar (and then principally at the cancer centre in Aristide Le Dantec Hospital, the biggest public hospital in the country which is out of date and cramped, but other large hospitals in the city offer some specialized services as well),

leaving the rest of the country virtually devoid of specialized services. In addition, patients have to pay out-of-pocket and, more often than not, cannot afford the costly procedures and, frequently, ever a simple curse of chemotherapy.



Figures 1-3

Regarding costs of treatment and in addition to governmental funding, there are efforts from NGOs to provide financial support and reduce the cost of treatment by raising funds through donations. "Ligue Sénégalaise Contre le Cancer" (LISCA) covered from to 2010 to 2012 an average $10,000 USD for each patient treated.

Patients sharing beds to receive chemotherapy or waiting outside facilities.

Human resources available for cancer diagnosis and treatment are restricted. There is only one pathologist at Aristide Le Dantec hospital which includes the cancer centre and results might take over six weeks to be ready. It is possible, and it happens quite often, that samples are sent to be analysed by a pathology lab in France, resulting in increased cost for patients.

The cancer centre in HALD has one operating Teleradiotherapy C0 60 unit and one HDR brachytherapy machine. The cobalt machine is a donated second hand machine, thanks to the support the Institut National du Cancer de France (INCA). The HDR machine is a donation too, thanks to Radiating Hope, a United States association based in Utah but because of inadequate infrastructures, this HDR machine was put in the cobalt bunker and used only for cervical cancer under local anaesthesia. There is no computer-assisted planning system or adequate quality control and assurance equipment. The unit treats around 50 patients per day. The majority are cervical and breast cancer patients.

Figure 4: Cobalt machine

Figure 5: HDR brachytherapy machine

Aristide Le Dantec hospital has a paediatric oncology unit that was created ten years ago and that was reinforced in 2005 thanks to the support of UICC programme, "My Child Matters". The unit sees 150 patients per year. It is estimated that only 20% of paediatric patients have access to treatment. There is no radiotherapy service available for children. Drugs for paediatric patients are offered as donations by GFAOP.

Conclusions

Senegal NCCP has been strengthened by the technical assistance and support provided by WHO, IAEA and other partners. However, there are important gaps and barriers that need to be addressed in order to achieve significant progress in the fight against cancer in the coming years. MOH should increase budgetary resources dedicated to cancer control programme in order to:

- Set up a sustainable tumour registry
- Prevent tobacco use specially among young people
- Develop accurate and cost effective early detection method to prevent cervical and breast cancer
- Put in place affordable chemotherapy regimens

Chapter 16p

Sudan

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Sudan was, until recently, the largest country in Africa, with an area of about one million square miles (2,505,810 km²) and a population of nearly 40 million, of which about 15% live in Khartoum, the capital city. In July 2011, the country split into two countries following the vote for independence of South Sudan. The northern Sudan is now officially called the Republic of the Sudan, the third largest country in Africa (after Algeria and the Democratic Republic of the Congo) and also the third largest country in the Arab world (after Algeria and Saudi Arabia). The country is bordered by Egypt to the north, the Red Sea, Eritrea, and Ethiopia, to the east, South Sudan to the south, the Central African Republic to the southwest, Chad to the west and Libya to the northwest. This country sits between North Africa, Sub-Saharan Africa, and the Middle East. It has an ethnic mosaic of about 700 tribes and a broad climatic diversity. Sudan is divided into 18 states, further divided into 133 districts.

In Sudan's 2008 census, the population of Northern, Western and Eastern Sudan was recorded to be over 30 million, putting present estimates of the population of Sudan after the secession of South Sudan at a little over 30 million people. The population density is markedly uneven. The current average of 10.2 persons per square kilometre would imply that the country is sparsely populated, but in fact, there are densely populated areas and vast areas that are almost or completely uninhabited. The population structure is young, with 40.8% under 15 years old (Sudan Demographic and Health Survey 1989/1990, 1991), 20.2% between 15 and 24 years old, 31.8% between 25 and 54 years old, 3.9% between 55 and 64 and 3.3% of 65 years old and above (2014 estimates). The male/female ratio is higher than 1 for most age categories with 1.03, 1.07, 1.13 and 1.21 for the age categories of 0-14, 15-24, 55-64 and 65+, respectively. For the 25-54 years old category, the male/female ratio was 0.94 (2014 estimates).

There has been a relatively small but significant increase in life expectancy, from 36.3 and 39.1 years in 1955 for men and women respectively, to 55.6 years for men and 58.4 years for women in 1999.

The epidemiological profile is largely dominated by communicable diseases such as malaria and tuberculosis, as well as diarrheal diseases and respiratory infections. In addition to the burden of communicable diseases, Sudan is also experiencing a rapidly increasing burden of non-communicable diseases. Of these, diabetes mellitus, cardiovascular diseases and cancer have been among the top ten causes of hospital admission and deaths in Sudan since 1998, according to the Federal Ministry of Health.

While infectious diseases are still the main concern of the healthcare system, Sudan, as most sub-Saharan African countries, needs to face a predicted increment in cancer incidence because of the progressively rising life expectancy, the wide diffusion of cancer-related infections, the mounting pollution due to urbanization and the spread of intensive agriculture and industrialization.

Burden of Cancer

Sudan has no national population-based cancer registry. The main sources of data on cancer are the hospital-based case series at the only two oncological centres of the country, both located in the densely populated Central Sudan, i.e., the Radiation and Isotope Centre in Khartoum (RICK), Khartoum State, and the National Cancer Institute of the University of Gezira (NCI-UG) in Wad Medani, Gezira State. In addition, a newly established centre in the north of Sudan (Shandi) is operating at small scale and providing chemotherapy only.

RICK is the main referral centre, treating the largest number of cancer cases in Sudan. Almost fifty per cent of female cancers seen at RICK are breast (25-30%) and cervix (12%). The predominantly prevailing male cancers are prostate (17-20%), head and neck (10-12%) and cancers of the oesophagus. The department of radiation oncology has four external beam machines (two linear accelerators, two Cobalt-60). The staff comprises 25 radiation oncologists, 65 radiation technologists, 10 medical physicists and 10 biomedical maintenance engineers. Regarding nuclear medicine, RICK is equipped with a SPECT gamma camera, a radioiodine facility, isolation rooms, and staffed with four nuclear medicine specialists and 16 nuclear medicine technologists. In the diagnostic radiology department, RICK has two conventional X-ray machines, an ultra-sonography machine, CT machine, three radiologists and five technologists.

There are an estimated 500 paediatric cancer cases per year in Sudan, of which 40 percent are treated at RICK, where there are 14 paediatric beds available and where roughly 30 paediatric patients are seen per day.

For chemotherapy, 80 beds are available for male and female patients. Chemo-radiation is being used for 25 patients daily. Overall, 140 - 150 patients receive chemotherapy daily.

The NCI is based in Wad Madani, roughly three hours from Khartoum. It provides medical care for cancer patients from Gezira State as well as the surrounding states in the central region of Sudan. NCI is composed of two buildings, one of which is currently undergoing a US $18 million construction for expansion of the hospital. The new building will be comprised of five floors and 120 beds. Once completed, the centre will have capabilities in chemotherapy, surgery, radiation, operation theatres, palliative care and iodine therapy (as a part of nuclear medicine). Regarding radiotherapy, the centre is equipped with two Cobalt-60 machine operating daily from 8:00 a.m. to 6:00 p.m. treating 60 to 90 patients daily. The centre has a conventional simulator and a treatment planning system. It had purchased a linear accelerator machine but, due to embargo imposed on the country, this unit has not been operational since installation. The staff is made up of 4 clinical oncologists, a paediatric oncologist, 12 radiographers, 3 medical physicists, and 3 biomedical engineers.

The centre is equipped with 15 dedicated chemotherapy beds and chemotherapy is provided free of charge for the patients. An average of 40 patients is seen daily.

The nuclear medicine department is equipped with one gamma camera and one SPECT. The staff is composed of one specialist, four radiographers, two pharmacy technicians and one radio-pharmacist. NCI also has a well-equipped molecular laboratory with four machines for tissue typing, used primarily for renal and liver transplant.

The radiology department is equipped with two ultrasound machines testing 40 patients daily. A mammography unit as well as conventional radiology are also available. The radiology department staff includes two specialists and six radiographers.

The Shandi Cancer Centre is a University-based centre, with one clinic, the 'older' Shandi Centre, treating an estimated number of 375 new cancer cases per year (an estimated 75 of these cases are referred from RICK). The centre has a chemotherapy service that is run by one clinical oncologist who travels from Khartoum once per week, typically examining 30 patients per visit. The service is a day care service with 15 beds. Radiology services include conventional X-ray, ultrasound and CT scan; a radiologist and three technologists make up the staff. The nuclear medicine service is located in the cancer unit. The facility is equipped with a gamma camera and staffed by two technologists, one medical physicist and one nuclear medicine physician (currently training in Egypt). There is currently no radiotherapy service at the centre. Two oncologists are currently in training. A new campus is under construction at the Shandi Cancer Centre, consisting of five buildings and will soon open, although it is not yet ready to receive cancer patients.

In 2006, the NCI-University of Gezira, supported by the International Agency for Research on Cancer (IARC), established the first population-based cancer registry in Sudan. It uses the Can-Reg5 format. Table 1 and 2 show unpublished data on the cancer incidence per 100,000 population by age group among men and women for the period 2005-2012.

Recently, with the support from the Ministry of Health, a population-based national cancer registry (NCR) was established in Khartoum. The main goal of the NCR is creating a system that integrates regional and local data into an accessible central registry. The NCR has managed to report on 6,771 cancer cases among the Khartoum State residents, for the period 2009-2010, using passive and active approaches to collect data on cancer diagnosed by all means.

Rates were age-standardized to the 2010 Sudan Standard Population and 1966 and 2000 World Standard Population and expressed per 100,000 persons. Among the 6,771 new cancer cases registered for 2009-2010, 3646 (53.8%) cases were in women and 3125 (46.2%) were in men.

The most commonly diagnosed cancer among women was breast cancer followed by leukaemia, cervix, and ovary. Correspondingly, for men, the most commonly occurring cancer was prostate cancer followed by leukaemia, lymphoma, oral, colorectal, and liver cancers. In children less than 15 years of age, leukaemia was the most common cancer followed by lymphoma, cancers of the eye, bone, kidney, and the brain cancers.

The overall age-standardized rate (ASR) per 100,000 population was higher in women (124.3) than in men (90.8) using the 2010 Sudan Standard Population. Similarly, it was higher in women (188.6 and 206.3 per 100,000 population) than in men (145.4 and 160.0 per 100,000 population) using the 1966 and 2000 World Standard Population, respectively.

Regarding histopathology services in Sudan, there is shortage in these services, very few States have histopathology laboratories. Federal hospitals with such laboratories are Suba, Khartoum, Omdurman, military hospitals, and Khartoum North hospital. 5 out of 18 states hospitals have histopathology laboratories, the remaining states refer to the central lab in the laboratories directorate. This lab also receive biopsies from different public and private hospitals. Beside these few governmental laboratories, there are about 11 private histopathology laboratories in Khartoum state and two in Gezira state.

Table 1: Gezira Cancer Registry, Sudan (2005-2012) – Male population

Site	All age	Age UNK	0-	5-	10-	15-	20-	25-	30-	35-	40-	45-	50-	55-	60-	65-	70-	75+	Crude rate	(%)	CUM 0-64	CUM 0-74	ASR	ICD (10th)
Lip	53	0	-	-	-	-	-	0.3	0.1	0.2	0.5	0.2	0.6	1.7	2.6	2	4.7	4.6	0.4	1.3	0.03	0.06	0.5	C00
Tongue	18	0	-	-	-	-	0.1	0.1	-	0.1	-	0.4	-	1.3	0.6	0.5	1.4	1.1	0.1	0.4	0.01	0.02	0.2	C01-02
Mouth	70	0	-	-	-	0.1	-	0.1	0.1	0.4	0.5	0.7	1.1	2	4.8	3.4	5.7	4.2	0.5	1.7	0.05	0.09	0.7	C03-06
Salivary glands	19	0	-	-	-	0.1	-	0.1	-	-	0.2	0.2	0.4	0.7	0.6	0.5	1.4	1.8	0.1	0.5	0.01	0.02	0.2	C07-08
Tonsil	6	0	-	-	0.1	-	0.1	-	-	-	0.2	0.4	0.2	-	-	-	-	-	0	0.1	0	0	0.1	C09
Other oropharynx	2	0	-	-	-	-	-	-	-	-	-	-	-	0.3	-	-	-	0.4	0	0	0	0	0	C10
Nasopharynx	150	0	-	-	0.5	0.5	1	0.6	0.6	0.7	2	3.6	3.2	4.6	3.5	4.4	5.7	3.2	1	3.6	0.1	0.15	1.4	C11
Hypopharynx	36	0	-	-	0.1	0.1	0.1	0.2	0.2	0.2	0.2	1.1	0.6	0.3	1.3	2	0.9	1.8	0.2	0.9	0.02	0.04	0.4	C12-13
Pharynx unspecified	2	0	-	-	-	-	-	-	-	0.2	-	-	-	-	-	-	-	-	0	0	0	0	0	C14
Oesophagus	183	0	-	-	-	0.1	0.3	0.6	0.4	0.6	1.1	1.4	4.9	6.3	6.1	13.7	11.8	12.3	1.2	4.4	0.11	0.24	1.9	C15
Stomach	148	0	-	-	-	-	-	0.2	0.2	0.4	1.8	1.8	3.4	4.3	6.1	9.3	10.9	10.2	1	3.6	0.09	0.19	1.6	C16
Small intestine	10	0	-	-	-	-	-	0.1	-	-	0.2	0.2	0.6	-	-	1	0.5	0.4	0.1	0.2	0.01	0.01	0.1	C17
Colon	134	0	-	-	0.1	-	0.6	0.4	0.4	0.8	2.6	2.5	3.9	4.3	3.5	6.4	5.2	5.3	0.9	3.2	0.1	0.15	1.4	C18
Rectum	125	0	-	-	-	-	0.4	0.6	1.2	1.2	2.3	2	3.9	4.3	3.9	3.9	3.8	3.2	0.9	3	0.1	0.14	1.3	C19-20
Anus	23	0	-	-	-	-	-	0.1	0.2	-	0.8	-	0.4	1.3	0.6	1	1.4	0.7	0.2	0.6	0.02	0.03	0.2	C21
Liver	294	0	0	-	-	0.1	0.2	0.2	0.9	0.7	1.5	4.9	4.5	11.3	13.8	16.7	18.4	23.3	2	7.1	0.19	0.37	3.1	C22
Gallbladder etc.	12	0	-	-	-	-	-	-	-	-	0.2	0.2	0.4	1	-	1.5	-	0.7	0.1	0.3	0.01	0.02	0.1	C23-24
Pancreas	78	0	-	-	-	-	-	0.1	0.1	0.2	0.8	1.1	1.5	2.7	5.1	5.4	4.7	3.9	0.5	1.9	0.06	0.11	0.9	C25
Nose, sinuses etc.	23	0	-	-	0.1	-	-	-	0.2	-	0.3	0.9	-	1	0.3	1	0.9	1.8	0.2	0.6	0.01	0.02	0.2	C30-31
Larynx	70	0	-	-	-	0.1	-	-	0.1	0.2	0.2	0.9	2.4	3	3.5	5.4	2.8	4.2	0.5	1.7	0.05	0.09	0.8	C32
Trachea, bronchus and lung	100	0	-	-	-	-	-	-	0.4	0.2	0.8	1.4	2.1	4.3	4.5	6.9	7.6	5.3	0.7	2.4	0.07	0.14	1.1	C33-34
Other thoracic organs	3	0	-	-	-	-	-	-	-	-	0.2	-	-	-	0.6	-	-	-	0	0.1	0	0	0	C37-38
Bone	82	0	0	0.2	0.3	1.1	0.6	0.2	0.5	0.1	1.1	0.4	1.7	1	1.3	2.9	1.9	1.4	0.6	2	0.04	0.07	0.7	C40-41
Melanoma of skin	23	0	-	-	-	-	-	-	-	-	-	0.2	0.6	1	1	2.5	0.9	2.1	0.2	0.6	0.01	0.03	0.3	C43
Other skin	108	0	-	-	0.2	0.1	0.2	0.3	0.6	0.8	1.1	2	1.5	2	2.6	3.9	7.6	8.1	0.7	2.6	0.06	0.11	1	C44
Mesothelioma	0	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0	0	0	0	0	C45
Kaposi's Sarcoma	11	0	-	-	-	-	-	-	-	-	0.2	-	0.4	-	-	1.5	0.5	1.4	0.1	0.3	0	0.01	0.1	C46
Connective and soft tissue	93	0	0.2	0.1	0.1	0.2	0.4	0.3	1.1	1.3	0.5	0.9	1.7	2	2.6	4.9	4.3	1.4	0.6	2.3	0.06	0.1	0.9	C47,C49
Breast	68	0	-	-	-	-	0.2	-	0.6	0.4	0.5	1.1	2.1	1	1.3	3.9	6.1	3.9	0.5	1.6	0.04	0.09	0.7	C50
Penis	4	0	-	-	-	-	-	-	-	-	-	-	-	-	-	0.5	-	1.1	0	0.1	0	0	0	C60
Prostate	615	0	-	-	-	-	-	-	0.1	-	0.2	0.9	4.3	9.3	19.3	41.2	70.9	93.8	4.2	14.9	0.17	0.73	6	C61
Testis	48	0	0.1	0	-	0.1	0.4	0.5	0.4	0.2	1.4	0.5	1.1	0.3	1	1.5	1.4	0.4	0.3	1.2	0.03	0.04	0.4	C62
Other male genital organs	0	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0	0	0	0	0	C63
Kidney	95	0	0.6	0.2	0.1	0.1	-	0.1	-	0.6	0.5	0.7	2.6	4	2.9	4.4	4.3	3.9	0.6	2.3	0.06	0.1	0.9	C64
Renal pelvis	0	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0	0	0	0	0	C65
Ureter	0	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0	0	0	0	0	C66
Bladder	126	0	-	0	-	-	0.1	0.2	0.6	0.2	1.4	1.3	3	4.6	4.8	5.9	11.3	7.1	0.9	3.1	0.08	0.17	1.3	C67
Other urinary organs	0	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0	0	0	0	0	C68

Site	All age	Age UNK	0-	5-	10-	15-	20-	25-	30-	35-	40-	45-	50-	55-	60-	65-	70-	75+	Crude rate	(%)	CUM 0-64	CUM 0-74	ASR	ICD (10th)
Eye	36	0	0.6	0	0.1	0.1	0.1	0.2	-	0.1	0.2	0.4	0.2	1.3	0.6	0.5	0.9	1.4	0.2	0.9	0.02	0.03	0.3	C69
Brain, nervous system	127	0	0.5	0.6	0.4	0.4	0.2	1.1	0.7	0.8	0.9	2	3.2	3.3	1.6	2	3.3	2.1	0.9	3.1	0.08	0.11	1.1	C70-72
Thyroid	45	0	-	-	-	0.1	0.2	0.1	0.1	0.5	0.3	1.4	0.4	1.3	2.3	1.5	0.9	2.8	0.3	1.1	0.03	0.05	0.5	C73
Adrenal gland	3	0	-	-	-	-	-	-	-	-	0.2	-	0.2	-	-	-	-	0.4	0	0.1	0	0	0	C74
Other endocrine	2	0	-	-	-	-	-	0.1	-	-	-	0.2	-	-	-	-	-	-	0	0	0	0	0	C75
Hodgkin disease	101	0	0.2	0.6	0.5	0.6	0.7	0.6	0.7	0.7	0.6	0.9	0.4	2	1.3	2	2.8	2.5	0.7	2.4	0.05	0.07	0.8	C81
Non-Hodgkin lymphoma	326	0	0.6	1.1	0.6	0.6	0.6	1.6	1.1	2.9	3.1	3.8	4.7	7.6	9.3	17.7	13.2	12.7	2.2	7.9	0.19	0.34	3.1	C82-85,C96
Immunoproliferative diseases	0	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0	0	0	0	0	C88
Multiple myeloma	101	0	0	-	0.1	0.1	0.2	0.3	0.1	0.6	0.9	2.4	2.4	3.3	3.9	3.9	7.1	4.2	0.7	2.4	0.07	0.13	1	C90
Lymphoid leukaemia	148	0	0.6	0.4	0.4	0.4	0.8	0.6	0.1	0.1	1.2	1.4	1.9	5	5.1	3.4	7.6	5.3	1	3.6	0.09	0.15	1.3	C91
Myeloid leukaemia	232	0	0.4	0.3	0.4	0.6	1	1.4	1.6	2.8	2.8	5.1	4.9	4.6	2.9	6.4	9.5	4.6	1.6	5.6	0.14	0.22	2.1	C92-94
Leukaemia unspecified	87	0	0.2	0.7	0.7	0.2	0.5	0.5	0.4	0.6	0.2	0.5	1.5	1	1.3	2.5	0.9	2.5	0.6	2.1	0.04	0.06	0.7	C95
Myeloproliferative disorders	3	0	-	-	-	-	-	-	-	-	-	-	-	0.7	-	0.5	-	-	0	0.1	0	0.01	0	MPD
Myelodysplastic syndromes	0	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0	0	0	0	0	MDS
Other and unspecified	193	0	0.1	0.2	0.2	0.2	0.4	0.5	0.5	2.1	1.8	2.4	2.8	6.6	5.5	12.3	11.3	8.5	1.3	4.7	0.12	0.23	1.9	O&U
All sites	4236	0	4	4.8	4.5	5.7	9.1	12	14.5	21.4	34.8	52.3	76.2	116.7	132.2	210.3	254.8	259.7	28.8		2.44	4.77	41.3	ALL
All sites but C44	4128	0	4	4.8	4.3	5.7	8.9	11.7	13.9	20.6	33.8	50.3	74.7	114.8	129.6	206.4	247.2	251.5	28.1	100	2.38	4.65	40.3	ALLbC44

Table 2: Gezira Cancer Registry, Sudan (2005-2012) – Female population

Site	All age	Age UNK	0-	5-	10-	15-	20-	25-	30-	35-	40-	45-	50-	55-	60-	65-	70-	75+	Crude rate	(%)	CUM 0-64	CUM 0-74	ASR	ICD (10th)
Lip	13	0	0	-	-	0.1	0.1	0.1	-	-	-	-	0.2	-	0.7	-	1.5	1.3	0.1	0.3	0.01	0.01	0.1	C00
Tongue	28	0	-	-	-	0.1	-	0.2	0.1	-	0.1	0.5	0.6	1.5	1	1.8	2.1	1.3	0.2	0.6	0.02	0.04	0.3	C01-02
Mouth	43	0	-	0.1	-	-	-	0.1	-	0.2	0.4	1.2	1	1.8	1.4	1.8	2.6	3	0.3	0.9	0.03	0.05	0.5	C03-06
Salivary glands	21	0	-	-	-	0.1	0.1	0.1	-	0.2	0.1	0.4	0.8	-	0.3	0.6	2.1	0.9	0.1	0.4	0.01	0.02	0.2	C07-08
Tonsil	6	0	-	-	-	-	-	-	-	-	0.1	0.4	-	-	0.3	-	1	-	0	0.1	0	0.01	0.1	C09
Other oropharynx	7	0	-	-	-	-	-	-	-	-	0.1	0.2	-	-	0.3	-	1	0.9	0	0.1	0	0.01	0.1	C10
Nasopharynx	96	0	0	0.1	0.3	0.3	0.6	0.4	0.7	0.7	1	1.1	2.1	3.7	2.7	3	2.1	2.6	0.6	1.9	0.07	0.09	0.9	C11
Hypopharynx	51	0	-	-	-	-	0.1	0.2	0.4	0.7	0.8	1.6	1.3	1.1	1.4	2.4	0.5	0.9	0.3	1	0.04	0.05	0.5	C12-13
Pharynx unspecified	1	0	-	-	-	-	-	-	-	-	0.1	-	-	-	-	-	-	-	0	0	0	0	0	C14
Oesophagus	241	0	-	-	0.1	-	0.2	0.4	1	1.3	2.2	4.1	5	3.7	10.6	19.7	14.9	18.5	1.6	4.8	0.14	0.32	2.7	C15
Stomach	73	0	-	-	-	-	0.2	0.2	-	0.5	0.8	0.9	1.9	2.9	1.7	4.8	7.2	3.5	0.5	1.5	0.05	0.11	0.8	C16
Small intestine	5	0	-	-	-	-	-	-	-	0.1	0.1	0.2	-	-	0.3	0.6	-	-	0	0.1	0	0.01	0.1	C17
Colon	87	0	-	-	-	0.1	0.5	0.2	1	0.4	0.8	2	1.7	1.1	2.4	4.2	6.2	2.6	0.6	1.7	0.05	0.1	0.8	C18

Site	All age	Age UNK	0-	5-	10-	15-	20-	25-	30-	35-	40-	45-	50-	55-	60-	65-	70-	75+	Crude rate	(%)	CUM 0-64	CUM 0-74	ASR	ICD (10th)
Rectum	85	0	-	-	-	-	0.5	0.4	0.8	0.7	0.7	1.6	2.7	0.7	2.7	3	5.2	2.2	0.6	1.7	0.05	0.1	0.8	C19-20
Anus	12	0	-	-	-	-	0.1	-	0.1	-	-	0.2	0.4	0.4	-	1.8	0.5	0.9	0.1	0.2	0.01	0.02	0.1	C21
Liver	117	0	0.1	0.1	-	0.2	-	0.2	0.2	0.7	0.7	1.6	2.9	2.9	4.4	7.8	8.2	8.6	0.8	2.3	0.07	0.15	1.3	C22
Gallbladder etc.	36	0	-	-	-	-	-	0.1	0.1	-	0.6	0.4	0.8	1.5	1.4	0.6	4.6	2.6	0.2	0.7	0.02	0.05	0.4	C23-24
Pancreas	61	0	-	-	-	-	0.1	0.1	0.4	0.2	0.1	0.7	1.5	1.8	3.1	6.6	5.7	2.2	0.4	1.2	0.04	0.1	0.7	C25
Nose, sinuses etc.	15	0	-	-	-	0.1	0.1	-	0.2	0.1	0.1	-	0.4	0.4	0.3	1.8	0.5	0.4	0.1	0.3	0.01	0.02	0.2	C30-31
Larynx	13	0	-	-	-	0.1	-	-	0.1	-	-	-	0.4	0.4	0.3	2.4	-	1.3	0.1	0.3	0.01	0.02	0.2	C32
Trachea, bronchus and lung	67	0	-	-	-	-	0.2	-	0.1	0.3	0.6	0.7	1.3	2.9	2.7	7.2	4.6	3.9	0.4	1.3	0.04	0.1	0.8	C33-34
Other thoracic organs	4	0	-	0.1	-	-	-	-	-	-	-	-	-	0.4	-	0.6	0.5	-	0	0.1	0	0.01	0	C37-38
Bone	51	0	0	0.1	0.5	0.5	0.1	0.5	0.1	0.3	0.4	0.2	0.2	1.5	1	1.8	1	0.9	0.3	1	0.03	0.04	0.4	C40-41
Melanoma of skin	19	0	-	-	-	-	-	0.1	-	0.1	-	0.4	0.4	1.1	0.3	1.8	1.5	1.3	0.1	0.4	0.01	0.03	0.2	C43
Other skin	88	0	-	-	-	0.2	0.5	0.2	0.4	0.6	0.6	1.2	1.3	2.6	3.8	6	4.1	5.6	0.6	1.8	0.06	0.11	0.9	C44
Mesothelioma	1	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.4	0	0	0	0	0	C45
Kaposi's Sarcoma	6	0	-	-	-	0.1	-	0.1	0.2	0.1	-	0.2	-	-	-	-	-	-	0	0.1	0	0	0	C46
Connective and soft tissue	69	0	0.1	0.1	0.1	0.1	0.6	0.4	0.3	0.8	0.4	1.1	1	1.5	1	3	3.1	1.7	0.5	1.4	0.04	0.07	0.6	C47,C49
Breast	1598	1	-	-	-	-	0.9	4.1	12.8	26	34.1	46.5	35.9	43.4	36.2	50.2	36.6	38.8	10.5	31.9	1.2	1.63	15.6	C50
Vulva	38	0	-	-	-	0.1	0.1	-	0.2	-	0.1	0.2	1.3	1.5	1.7	6	3.6	-	0.2	0.8	0.03	0.07	0.5	C51
Vagina	5	0	-	-	-	-	0.1	-	-	0.1	-	0.2	-	0.4	0.3	-	-	-	0	0.1	0.01	0.01	0.1	C52
Cervix uteri	254	0	-	-	-	-	0.1	0.2	0.6	1.4	2.1	3.2	6.7	13.2	9.2	20.9	17	14.7	1.7	5.1	0.18	0.37	3	C53
Corpus uteri	93	0	-	-	-	-	0.1	0.1	0.1	0.3	0.8	2	2.3	2.6	5.1	6.6	7.7	4.3	0.6	1.9	0.07	0.14	1.1	C54
Uterus unspecified	101	0	-	-	0.1	-	0.1	0.1	0.2	0.1	1.5	1.8	1.7	4.4	6.8	6	4.6	6.5	0.7	2	0.08	0.14	1.2	C55
Ovary	404	0	-	0.1	0.3	0.8	0.7	1	1.3	4.5	6.5	8	7.5	15.4	13.3	23.9	16	10.4	2.6	8.1	0.3	0.5	4.2	C56
Other female genital organs	15	0	-	-	-	0.1	-	0.3	0.3	0.2	-	0.5	0.2	-	-	0.6	-	-	0.1	0.3	0.01	0.01	0.1	C57
Placenta	18	0	-	-	-	0.1	0.3	0.4	0.3	0.2	0.1	0.2	-	-	-	-	0.5	-	0.1	0.4	0.01	0.01	0.1	C58
Kidney	83	0	0.7	0.2	0.2	0.1	0.1	0.1	0.6	0.3	0.3	1.6	1.3	2.9	2.7	3.6	2.1	3	0.5	1.7	0.05	0.08	0.8	C64
Renal pelvis	2	0	-	-	-	-	-	-	-	0.1	-	-	-	0.4	-	-	-	-	0	0	0	0	0	C65
Ureter	1	0	-	-	-	-	-	-	-	-	-	-	-	0.4	-	-	-	-	0	0	0	0	0	C66
Bladder	66	0	-	-	-	-	-	0.2	0.1	-	0.4	0.4	1.7	2.6	3.4	6	5.7	4.7	0.4	1.3	0.04	0.1	0.8	C67
Other urinary organs	0	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0	0	0	0	0	C68
Eye	38	0	0.9	0.1	0.1	-	-	-	0.1	-	0.3	-	-	0.4	1	0.6	0.5	2.6	0.2	0.8	0.01	0.02	0.3	C69
Brain, nervous system	97	0	0.2	0.8	0.2	0.2	0.3	0.2	0.1	0.8	1.4	1.6	2.7	2.6	0.3	3.6	2.1	1.3	0.6	1.9	0.06	0.09	0.8	C70-72
Thyroid	121	0	-	-	0.1	0.2	0.1	0.4	0.6	1	1	2.3	2.5	0.7	4.8	9	8.2	6	0.8	2.4	0.07	0.15	1.3	C73
Adrenal gland	0	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0	0	0	0	0	C74
Other endocrine	3	0	-	-	-	-	-	-	0.1	-	0.1	-	-	-	-	-	-	0.4	0	0.1	0	0	0	C75
Hodgkin disease	53	0	0.1	-	0.2	0.5	0.3	0.1	-	0.5	1.1	0.7	0.8	0.7	1	-	2.1	1.3	0.3	1.1	0.03	0.04	0.4	C81
Non-Hodgkin lymphoma	197	0	0.6	0.6	0.4	0.4	0.5	0.5	0.7	1.5	1.1	1.8	3.5	5.5	5.8	8.4	12.9	7.3	1.3	3.9	0.11	0.22	1.9	C82-85,C96
Immunoproliferative diseases	0	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0	0	0	0	0	C88
Multiple myeloma	54	0	-	-	-	-	0.1	-	0.1	0.2	0.7	0.9	1.5	3.3	2.4	1.8	3.1	3	0.4	1.1	0.05	0.07	0.6	C90

Site	All age	Age UNK	0-	5-	10-	15-	20-	25-	30-	35-	40-	45-	50-	55-	60-	65-	70-	75+	Crude rate	(%)	CUM 0-64	CUM 0-74	ASR	ICD (10th)
Lymphoid leukaemia	88	0	0.2	0.4	0.2	0.1	0.1	0.5	-	0.1	0.7	0.7	1	2.9	3.4	6	3.6	5.6	0.6	1.8	0.05	0.1	0.9	C91
Myeloid leukaemia	223	0	0.2	0.5	0.9	0.4	1.1	1.3	1.6	2.9	1.5	4.3	2.7	5.1	3.4	7.2	6.7	5.6	1.5	4.4	0.13	0.2	1.9	C92-94
Leukaemia unspecified	43	0	0.3	0.4	0.1	0.1	0.1	-	0.1	0.4	0.4	0.5	0.8	0.7	0.3	0.6	1.5	1.3	0.3	0.9	0.02	0.03	0.3	C95
Myeloproliferative disorders	8	0	-	-	-	-	0.1	-	-	0.1	0.1	-	-	-	0.3	0.6	1	0.4	0.1	0.2	0	0.01	0.1	MPD
Myelodysplastic syndromes	0	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0	0	0	0	0	MDS
Other and unspecified	186	0	0	0.1	0.1	0.1	0.4	0.4	0.9	1.2	2.6	3	4	5.5	5.5	11.4	11.3	9.5	1.2	3.7	0.12	0.23	2	O&U
All sites	5105	1	3.7	3.4	3.6	4.7	9.6	13.6	27.2	50.1	68.3	101.1	105.9	148.5	151.6	255.8	227.8	194.1	33.4		3.46	5.87	51.6	ALL
All sites but C44	5017	1	3.7	3.4	3.6	4.5	9.1	13.5	26.8	49.5	67.7	99.9	104.7	145.9	147.8	249.8	223.7	188.5	32.9	100	3.4	5.77	50.7	ALLbC44

Cancer Management

Cancer management started at the Khartoum teaching hospital decades ago. In 1967, the Radiation and Isotope Centre (RICK) was established as a specialized cancer management centre. The efforts of the highly qualified physicians in the field laid the foundation for the present cancer control program. Nevertheless, there is a rising trend in the reported cancer cases, attributed to the growth and aging of population, increased exposure to cancer risk factors, and increased knowledge and public awareness.

Risk factors for cancer are prevalent in Sudan, as shown by the Khartoum State, stepwise risk factor survey, where the prevalence of current tobacco smoking in adults of 25 years and above was 24.7% and 2.9% in men and women, respectively. The snuff use was 25.8% in the same age group. The prevalence of overweight or obesity in adults over 25 years, was 41.4%, and 62.5% in men and women, respectively. Moreover, the respondents were interviewed about their physical activity, 58.6% stated that they were physically active. Only 25.4% had regular activity while 33.2% had irregular physical activity. 41.4% never had any physical exercise.

Sudan is experiencing many challenges that are characteristic of developing countries, including high incidence of advanced, difficult-to-treat disease at presentation and high cancer burden that is related to infectious diseases. Cancer is a major cause of morbidity and mortality in Sudan, ranking second as the most common cause of death after infectious diseases (mainly malaria and tuberculosis). Current cancer control efforts are fragmented and lack consistency. These efforts include prevention, early detection, diagnosis and treatment.

Prevention

Tobacco use, obesity and infections are prevalent in Sudan. Public awareness regarding cancer prevention and control is poor and expenditure on health tends to be skewed mainly towards curative and hospital care. Therefore, cancer preventive activities are limited.

For instance, hepatitis B vaccination in infancy started in 2006. Guidelines on prevention and early detection of the most common cancers, such as breast, cervix, and oral cancers was developed, in parallel with training of a few health care providers. They were developed by the National Cancer Council in 2008, when the Council had formed a dedicated committee for 'Prevention and Early Detection'. "Guidelines on prevention and early detection of most common cancers in Sudan – Breast, Cervix, and Oral Cancers" were published in a report by the Federal Ministry of Health in September 2010. They are intended for the primary health care level and are available in Arabic and English.

Early Detection

Health education activities are scant, primary health care workers are rarely provided with sufficient education about early signs of cancer, and about when and where to refer. There are no other cancer control activities at primary health care level. There is an absence of mass screening programmes, but projects for breast cancer and cervical cancer screening are under development. This situation leads to delay in presentation which is often due also to a variety of factors, including lack of awareness of the signs and symptoms of cancer and lack of money to travel to a hospital and cover the costs of diagnosis and treatment, thus leading many to seek traditional treatments instead.

Over 70% of patients present with advanced stages, with most at stage III and IV. At the time of RICK's inception (1967), an estimated 85-90% of cancer cases presented late, and this trend has not changed noticeably in the 45 years since its opening.

At these stages of the disease, treatment is more expensive and complicated involving multiple modalities of treatment, including surgery, radiotherapy, chemotherapy and hormone therapy, and has a markedly low chance of a good outcome.

Several factors were found to be associated with late stage presentations. These factors include a general lack of awareness and knowledge about cancer among the population and even among some medical staff, which is more serious than the former in determining early presentation. This situation could be explained by inadequate education and poverty. Also, the unequal distribution of medical/health resources in Sudan and their concentration in urban areas impede many patients seeking diagnosis and treatment.

Another factor playing a role in late presentation is the stigma associated with cancers in local communities. In fact, there is a common perception that cancer is transmissible, which results in the isolation of the patients and in the breakdown of marriages, leading patients to hesitate to disclose their symptoms and to seek proper care. In women, a barrier to early presentation are traditional healers. They usually keep women with possible breast cancers on herbal/other medications for long periods before the patient and/or the family decides to seek professional medical services.

Efforts are being made by the government to scale up cancer services at the primary health care level, notably in prevention and early detection. A pilot project started in 2012-2013 with the aim of integrating cancer services in seven states into primary health care. Training tools, provision of supplies and training courses are included in this plan. Currently, there are only 15 mammography units in Sudan, 13 of which operate in the private sector. In general, despite the high level of commitment demonstrated by the medical staff and NGOs to enhance early detection activities, these efforts are episodic and not yet sustainable

Diagnosis

Another significant problem in combating cancer is that, even if the sign and symptoms of cancers are discovered early, the diagnostic facilities are both limited and expensive. There is shortage in histopathology services, very few States have them. Moreover, training is needed to improve the quality of histopathology reports. The Federal hospitals with histopathology laboratories (31.2%) are Suba, Khartoum Teaching hospital, Omdurman teaching, military hospitals, and Khartoum North hospital. The main problems that need to be addressed are the shortage of dedicated resources, the extremely low number of pathologists and pathology departments, the geographic distances involved, the poor SOPs used

in sample handling, and the need for developing logistic systems for sending specimens from peripheral hospitals to centralized pathology laboratories.

Radiology services are available in almost all States especially conventional X-ray machines and ultra-sonography units. However, CT scanners and MRI machines can be found only in big cities. The national insurance covers the cost for state employees, but the rest of the patients have to cover the costs themselves, which remains impossible for the majority.

Treatment

Treatment of cancer is expensive and complicated especially in developing countries – where there is limited or no access to health insurance – simply many patients cannot afford to pursue treatment.

In Sudan, many patients and their families have to bear the full costs of their treatment. However, governmental hospitals offer admittance, investigative techniques, blood samples, scans, the drugs used to treat the cancer, as well as other treatment options such as surgery, chemotherapy and radiotherapy, at affordable cost or at no cost for state employees who are covered under the national insurance corporation. Missing diagnostic investigations are referred to private centres, which can be up to 300 times more expensive. Some tests have a waiting list of up to three weeks.

Another critical problem in Sudan is the lack of oncologists and specialized cancer nurses in each State. Oncology and palliative care are only available in the previously mentioned three cancer centres. Also, access to radiotherapy is limited; there are only two linear accelerators and four Cobalt-60 machines in working order for a population of over 30 million. These machines are present in only two centres in two adjacent states (Khartoum and Gezira) and do not cover the whole population.

Large distances that patients must travel across Sudan to seek treatment as both RICK and NCI are located in the central Sudan obviously limit the access for those who live far from them; many patients may not have the financial means to support transportation costs. Furthermore, patients and families must have sufficient financial resources to arrange for accommodation and other requirements for the duration of treatment in Khartoum or Wad Madani.

Approximately 10,000 new cancer patients are diagnosed each year in Sudan. RICK receives an estimated 7,000 – 8,000 patients while another 1,500 are seen in NCI. There are published treatment protocols for breast and prostate cancers. In 2004, a group of surgeons, pathologists, oncologists and radiologists agreed to have general guidelines for the Gezira State (Gezira Guidelines for Management of Breast Cancer). These guidelines, updated in 2006 and 2010, were published and distributed to all those who are involved in the management of breast cancer patients in Gezira State. Although these protocols are widely distributed to oncologists and surgeons, and urologists, recommendations are often not followed. Although many practicing doctors who are actively involved in the management of breast cancer are currently aware of these 3 documents or at least of the last one, variation in management remains and reflects major deviation from the national /international guidelines. This can be explained by the multiple reasons. Firstly, the number of facilities for diagnosis of breast cancer is limited. Triple assessment cannot be done in most parts of the country because of limited number of mammography machines and radiologists. Most of the diagnostic facilities and trained personnel are in the capital. Secondly, access to histopathology facilities is also limited. The extreme shortage of pathologists and laboratory technicians is a major issue that hinders proper diagnosis and hinders initiation of appropriate treatment.

Thirdly, persons who are involved in breast cancer management have different educational bases. For example, surgeons who are among the first medical specialists to meet patients, are very much different in their training and exposure to such conditions. The majority of surgeons are not specialized in a certain branch of surgery and practice general surgery; few of them are interested in breast surgery.

Moreover, there is an extreme shortage of well-trained oncologists, radiotherapy units and chemotherapeutic agents. Above all, there is a very small number of combined breast clinics where the multimodalities management of breast cancer is applied. Finally, there is no enforcement of management guidelines.

Not following national/ international guidelines results in lack of consistency in treating the same cancer at the same stage in different centres. The need for standard care management protocols is obvious. For other types of cancers there is effort underway to formulate national management guidelines.

Status of Radiotherapy in Sudan

According to GLOBOCAN 2008 data, there are an estimated 21, 860 new cancer cases in Sudan each year. As it is estimated that 60% of patients will require radiotherapy during the course of treatment, approximately 13,116 cancer patients will need treatment annually.

Currently, Sudan has two linear accelerators and four Cobalt-60 machines in working order for a population of over 30 million. The government has a plan to establish 5 new radiotherapy centres which will ease the need and relief the pressure on the existing centres. The department of Radiation Oncology at RICK has four external beam machines (two linear accelerators, two Cobalt-60). The external beam machines work in three shifts starting from 6:00 a.m. to 2:00 a.m. On a typical day, 190 - 200 patients are treated on all machines. The waiting period ranges from one day to three months depending on curative or palliative intent. Seventy per cent of patients are treated with palliative intent and the remaining 30 per cent with curative intent.

Repair and maintaining uptime of radiotherapy equipment is a challenge. As there is neither a maintenance contract nor budget for maintenance of equipment, machines can sometimes be out of order for several months at a time leading to insufficient radiotherapy provided to cancer patients. A quality assurance program for radiotherapy is in place at RICK.

NCI is equipped with two Cobalt-60 machines operating daily from 8:00 a.m. to 6:00 p.m. which treats 60 to 90 patients daily. The waiting list is one week for patients beginning radiation therapy. Treatment and dose schedules are radical and curative for half of the patients and palliative for the remaining half. The centre does not have a brachytherapy machine and a request to the IAEA has been put forth for a high-dose rate brachytherapy machine. There are no budgets or maintenance contracts in place for the majority of equipment at NCI, but a quality assurance program for radiotherapy is established.

Status of Chemotherapy in Sudan

At RICK, 80 beds are available for male and female patients in chemotherapy. Chemo-radiation is being used for 25 patients daily. Overall, 140 - 150 patients receive chemotherapy daily.

NCI is equipped with 15 dedicated chemotherapy beds. Chemotherapy is provided free of charge for an average of 25 patients daily. NCI has 47 inpatient beds for men and women. The centre has also two paediatric oncologists who are treating 100 patients annually.

For male and female patients receiving treatment at NCI, a 50-bed boarding house located in the vicinity of the hospital is made available for longer-term stays. The house hosts a kitchen for patients and families staying at the facility, and offers patients (who sometimes travel from neighbouring countries) a chance to finish treatment while remaining on site.

Although NCI was established more recently (1994) and it has small number of doctors and machines in comparison with RICK, the centre is more stable in terms of providing radiotherapy and chemotherapy and it continues to prove itself an effective back-up for RICK.

Shandi centre has a chemotherapy service run by one clinical oncologist who travels from Khartoum once per week, typically examining 30 patients per visit. It is a day care service with 15 beds and a centralized area for chemotherapy preparation. One clinical pharmacist and three nurses treat 10-12 patients per day.

The problems related to chemotherapy, hormonal therapy and new agents as targeted therapy: these problems include a lack of knowledge of the real needs, their availability and sustainability, their rising cost, the rising number of patients, the inadequate budget for supporting poor patients, the inadequate number of well trained staff –pharmacists, chemotherapy nurses and inadequate facilities to prepare chemotherapy agents.

Status of Palliative Care in Sudan

A British palliative care nurse living in the United Kingdom volunteered to conduct a series of lectures on palliative care for nurses working at Radiation & Isotopes Centre Khartoum (RICK) and Soba University Hospital (SUH). A clinical oncologist and a nurse from SUH attended the comprehensive 5 weeks training of palliative care (PC) in Hospice Africa Uganda in October 2009. Subsequently, a series of introductory palliative care courses were conducted at RICK and SUH by trainers from outside Sudan. In January 2011, the palliative care ward was opened with special funding from Africa Palliative Care Association, representing the site for Sudan's first palliative care service. From here, palliative care is spread to the other two centres (SUH & NCI). The service includes: an out-patient clinic, a ward with 9 beds and a palliative care unit.

The out-patient clinic opens daily five days a week and accepts patients from other oncology units at the centre or from outside the hospital. The ward with 9 beds acts as a demonstration site for holistic nursing care, continuity of care, networking, and effective communication with patient and family members. Patients are usually admitted for symptom control or end of life care, the majority of admissions are for duration of less than five days. In the palliative care unit, the nurses and doctors train the care givers in how to look after and perform dressing of fungating wounds, giving medications, physiotherapy for bed ridden patients, healthy nutritional advices and general care for bed ridden patients.

Since their inception, palliative care services at RICK introduced major changes in the hospital/doctors' practices. For example, symptoms burden in patients with advanced cancer (emotional and spiritual distress) are being addressed and talked about. Also, psychosocial issues of the patients such as wives being abandoned because husbands believe their cancer is incurable or even contagious or the fear of touching their chest after mastectomy or wash that area for long time, are being addressed. Care givers are facing stress to look after their beloved ones. Continuity of cancer care is ensured (including for example contacting patients by phone). Metronidazole crushed tabs is used for fungating wounds (a practice exported from Hospice Africa Uganda). Patients and their care givers are trained to perform wound dressing simply at home. Good communication skills and creating long-standing, strong and good relationship between patients and PC team members help patients understanding their prognosis and empower them to follow treatment and make life decisions. Telling the truth on the prognosis gives patients a chance to disclose very important issues in their lives and breaks any conspiracy of silence at those important days of life. It is also important to prevent any futile care, and avoid continuously looking for costly treatment in the country or abroad without any evidence of benefit.

All these interventions lead to better outcomes and improved quality of life. With the introduction of palliative care principles, patients and families receive proper care and greater level of support, to a degree that patients ask when they can be transferred to the palliative care unit (PCU).

To July 2014, 1,249 patients have been referred and offered Palliative Care services and 700 patients have been admitted to the PC ward. As breast cancer is the most common cancer among women in Sudan, all patients referred during the mentioned period were reviewed regarding breast cancer diagnosis. Breast cancer was found in a total of 107 patients, among which 104 were referred permanently to the PCU, and only three patients were jointly taken care of with the oncology department. 52 patients were referred with pain, three patients were referred for end of life care, eleven patients were referred because of cessation of curative treatment and eight patients were referred for psychological support.

In spite of the urgent need for Palliative Care in Sudan, the available services exist only in three Institutes. There are limited PC services at RICK, SUH, and NCI. International PC associations have a strong hand in backing these services. Also, the lack of oral opioids elsewhere limits pain management. Palliative care in Sudan is a fairly new concept but has proved worthwhile in alleviating patients' symptoms and helping families of patients with cancer. A lot of effort is requested from stakeholders to expand and cover all those who are in need.

Sudan National Cancer Strategy

Sudan developed a 'National Cancer Strategy 2012-2016' that incorporates most major components of a comprehensive approach to tackle cancer. The strategic document has laid a strong foundation for what could be the next phase of planning, where action items, timelines and budgets for activities are developed.

Conclusion

Many factors facilitate successful implementation of the National Cancer Control Program in Sudan. These are a strong commitment to fight cancer, especially during the last years and due to the increased number of patients diagnosed each year. Infrastructure exists; it can be strengthened and further developed to be used in different aspects of cancer control.

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Chapter 169

Tanzania

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* This chapter should be referenced as: Ngoma M, Malichewe C. Tanzania. In: Boyle P, Ngoma T, Sullivan R, Ndlovu N, Autier P, Stefan S, Fleming K and Brawley OW. The State of Oncology in Africa 2015. iPRI Scientific Publication 4, iPRI, Lyon, France (2016).

Tanzania is an East-African country located within the African Great Lakes region. It has a total area of 945,087 km^2 (364,900 square miles). The area of Tanzania includes the islands of Mafia, Pemba, and Unguja; the latter two form a semi-autonomous region called Zanzibar, which is part of an official union with the republic of Tanzania. In 2014, Tanzania had a population of 51.82 million, with a male/female ratio of 0.99. Tanzania's population is characterized by a young age structure, with 43.9% of the total population below age 15 years and only 5.6 % of the Tanzanian population aged 60 years and above. Also, life expectancy is 60.85 years. The majority of Tanzanians (69%) live in the rural areas. According to 2010 statistics, the adult literacy rate is 67.8%.

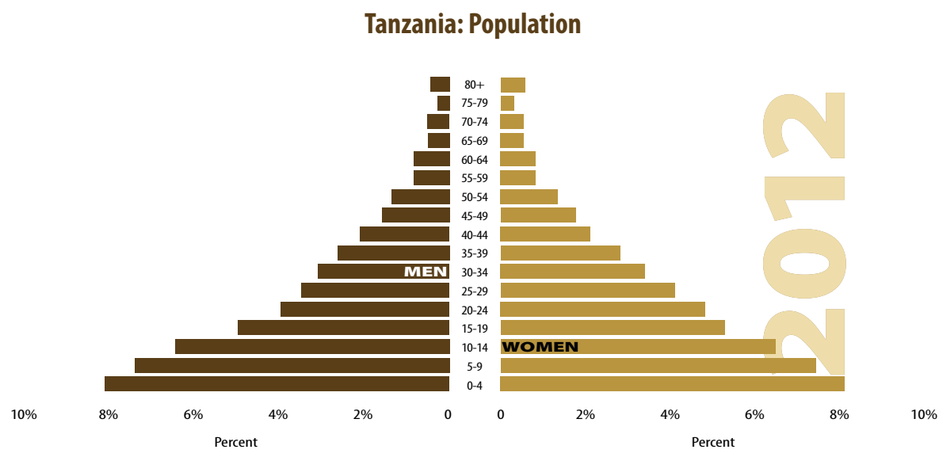

Table 1: Population Pyramid (Five-Year Age Groups) (National Bureau of Statistics, 2012)

Cancer Incidence and Mortality

Currently there is no established population-based cancer registry existing in Tanzania. However, there are institutional registries (hospital based registries) at Ocean Road Cancer Institute (ORCI) and Kilimanjaro Christian Medical Centre (KCMC)

Figure 2 presents trends of cancer incidence and mortality from the ORCI registry for patients who were attended from 2006 to 2014.

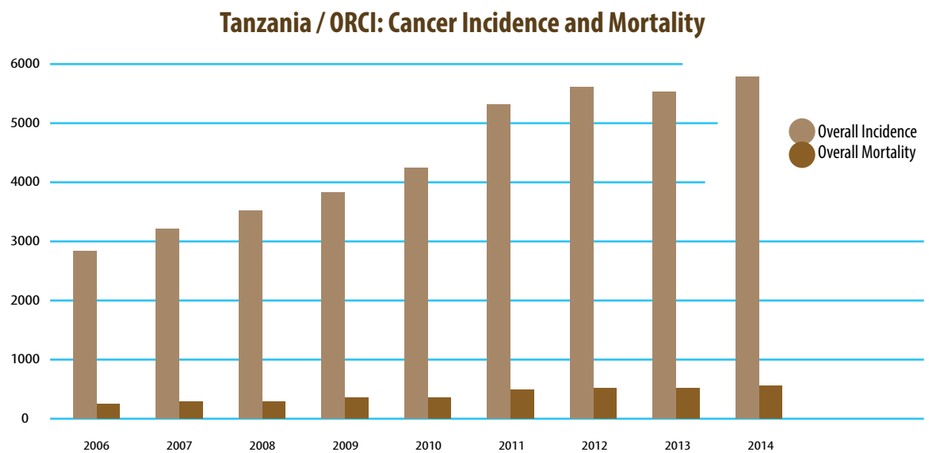

Figure 2: Cancer Incidence and Mortality trend at ORCI presents patients who were attended at ORCI from 2006 – 2014 (Ocean Road Cancer Institute)

As it can be clearly observed, the number of new cancer cases is increasing every year.

This data does not show the true picture on the ground, because most of cancer patients do not reach ORCI for treatment, and some are treated at Bugando Medical Centre and the Aga Khan hospital. Moreover, a great percentage of patients do not come back for follow up after treatment.

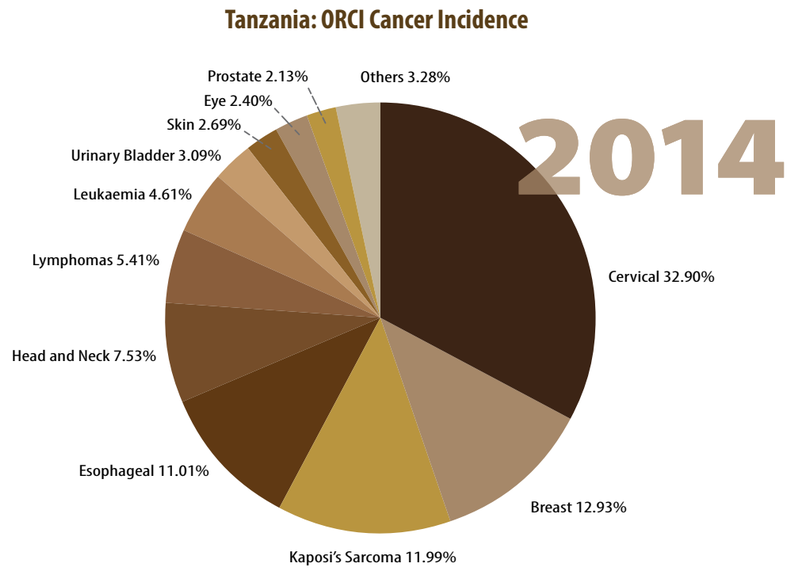

Figure 3: ORCI 2014 Cancer incidence in % (Ocean Road Cancer Institute)

The most frequently occurring cancers among Tanzanians are cervix cancer (32.9%), Kaposi's Sarcoma (11.99%), breast cancer (12.93%), oesophageal carcinoma (11%), head and neck cancers (7.53%), lymphoma (5.41%), leukaemia (4.61%), urinary bladder cancer (3.09%), skin cancer (2.69%), eye cancers (2.40%) and prostate cancer (2.13%). The other cancers account for 3.28%.

Cancer Centres in Tanzania

Currently, Tanzania has a one radiotherapy centre, the Ocean Road Cancer Institute in Dar es Salaam, located along the Indian Ocean, about 200 meters from the beach. This health facility is one of the oldest health institutions in Tanzania having been founded in 1895 by the German colonial government. It receives cancer patients from all over the country, having an inpatient bed capacity of 257 people and 190 people for outpatient. However, the hospital is sometimes forced to deal with much larger numbers.

There is an Oncology paediatrics ward at Muhimbili National Hospital, with an inpatient bed capacity of 23 people. The national hospital is about 4 kilometres from Ocean Road Cancer Institute.

Bugando Medical Centre is a consultant and teaching hospital for the lake and western zones of Tanzania. It is situated along the shores of Lake Victoria in Mwanza, in North-Western Tanzania. It has 900 beds and over 900 employees. It is a referral centre for tertiary specialist care for six

regions, serving a population of approximately 13 million people. The hospital has a newly established Oncology Department which provides care for all patients with histopathologically proven cancers.

Nevertheless, the department does not currently provide radiotherapy services. As a result, patients requiring radiotherapy have to travel long distances to receive this treatment method at ORCI.

The other consultant hospital providing cancer care but no radiotherapy is the Aga Khan Hospital, a private hospital located in Dar es Salaam.

Regional Referral hospitals that provide pathology services for diagnosis of cancer diseases are the Kilimanjaro Christian Medical Centre (KCMC) which is a referral hospital for over 15 million people in Northern Tanzania. The hospital is a huge complex with 500-800 inpatients in 630 official beds.

Mbeya Consultant Hospital is a tertiary healthcare facility for the southern Highland zone in Tanzania covering the regions of Ruvuma, Rukwa, Iringa and Mbeya. This hospital provides only pathology services, therefore diagnosed patients have to go elsewhere for treatment.

Tanzania Oncological Resources

Oncological resources in Tanzania are generally minimal and unevenly distributed throughout the country, Most of the resources are located within the city centres i.e. Dar es Salaam and Mwanza.

Newly diagnosed cancer patients need pathology, surgery, chemotherapy and/or radiation therapy. The number of oncologists needed is therefore based on the number of patients.

Figure 4: Laboratory at Ocean Road Cancer Institute (Dar es Salam)

Figure 5: Linear accelerator

Figure 6: Simulator machine

Figure 7: HDR intra-cavitary machines

Medical Oncology in Tanzania

Hospitals currently providing Chemotherapy services

Chemotherapy is provided at Ocean Road Cancer Institute, Bugando Medical Centre, Muhimbili National Hospital-Paediatric Ward and in private hospitals.

Chemotherapy Drugs

Usually, there is shortage of chemotherapy drugs in public hospitals. If available, the chemotherapy is free of charge, but if case of drug unavailability at a government hospital, the patient is given a prescription to buy the drug in private pharmacies. If a patient has health insurance, they can acquire the drugs through their insurance. If not, they have to buy it at their own expenses which represents a huge burden because most of them can't afford it.

Radiotherapy Sources

Radiotherapy services started in 1980s; and nowadays, about 90% of cases require radiotherapy. At ORCI, there are two Cobalt-60 machines, and two Linear Accelerators are expected very soon. There is also one simulator machine.

There are also Brachytherapy services at ORCI. Brachytherapy is mainly used for treatment of cervical cancer. ORCI has currently two HDR intra-cavitary machines.

Pathology Resources in Tanzania

There are about twelve pathologists in the country, among which six are at the Muhimbili National Hospital. Out of these six pathologists, 3 are retired, 1 is part of the administration, leaving two full-time working pathologists. The other six pathologists are distributed as follows: two in the Mbeya referral hospital, two in the Bugando Medical Centre, one in the Ocean Road Cancer Institute and one in the Kilimanjaro Christian Medical Centre.

These human resources are not enough compared to the number of new cancer patients per year. Turnaround time is about 4 to 7 days for soft tissue tumours and about 3 days for Fine Needle Aspiration Cytology.

There are few Histo-technology laboratories in the country: three at Muhimbili National Hospital, two at KCMC and two at Mbeya Referral Hospital. There is no available Molecular Lab in the country, but immunopathology tests are available for breast cancers, lymphoma and some soft tissue tumours but they are not done for all the patients mainly because of their high costs; most patients cannot afford them and the Government doesn't subsidize them.

Oncologists in Tanzania

In Tanzania, doctors are trained to be clinical oncologists in contrast to other countries where the functions of medical oncology and radiation oncology are clearly separated and defined. This is done accordingly to the recommendations of the International Atomic Energy Agency (IAEA)

for developing countries, which consist in training Radiation/Clinical Oncologists who can prescribe both radiation and chemotherapy for the common solid cancers, instead of separate medical and radiation oncologists.

Currently at ORCI, there are 21 Clinical oncologists, with the majority of them having been trained in the country. The Mmed Clinical oncology program started in 2010 under MUHAS having its department at ORCI. In BMC, there is one medical oncologist and one radiation oncologist, while in the private sector, Aga Khan Hospital has one Medical Oncologist.

Also, there are two Paediatric Haemato-oncologists at Muhimbili National Hospital working in the oncology paediatrics ward.

The National Cancer Control Strategy

Since the day that Tanzania got its independence, there have been efforts in dealing with issues that were a threat to the country's development including diseases such as cancer, one of the leading causes of deaths. It is estimated that 109 new cancer cases and 89 cancer deaths occur every day in Tanzania.

The Government through the Ministry of Health recognized the importance of establishing cancer services in the country since the 1970s. One of the key milestones was to establish a National Cancer Institute, the Ocean Road Cancer Institute (ORCI), in 1996, through an act of Parliament.

The ORCI managed to establish a hospital-based cancer registry, access to cancer awareness education to the public, facility-based as well as outreach-based cervical and breast cancer screening services, palliative care services and perform local and multi-centre researches.

To further strengthen efforts to fight cancer, the Government through the Ministry of Health formulated the National Cancer Control Strategy 2011-2016.

The formulation process was coordinated by the appointed national steering committee in closer consultation with various stakeholders and the public.

Hence, the national strategy reflects a shared commitment to reduce the incidence of cancer, to improve the quality of life of those who develop cancer, and to integrate cancer control and intervention services in the existing healthcare infrastructure.

Prevention and Early Detection

Cancer is still one of the serious concerns in most developing countries including Tanzania, where the incidence continues to escalate. Numerous factors have been identified to be causes of cancer in all its forms, which include among other the use of tobacco, alcohol consumption, the unhealthy diet, physical inactivity and obesity, chronic infections, hazardous materials and waste.

The only solution for the threat of increasing cancer in Tanzania is prevention. In the case prevention is not possible, other solutions are early detection, diagnosis and treatment.

In efforts to prevent the disease, the Tanzanian government has deliberately taken various measures including educating the public on various causes and prevention measures for cancer; the establishment of the Ocean Road Cancer Institute (ORCI) in Dar es Salaam; and also arrangements to sponsor health experts for specialized courses on cancer and related dieses treatments.

However, more efforts needs to be done so that the initiatives are widely spread.

For example, public education should cover schools, villages, districts, all regions, hospitals and worshipping areas. Also, establishing more cancer centres in various parts of the country is needed.

Tobacco

Tobacco is associated with three of the top five cancers at ORCI i.e. cervical cancer, oesophageal cancer and head and neck cancers. Tanzania produces about 9,600 tons of tobacco annually; about 50% is exported to industrialized countries while about 20% is processed locally into cigarettes. About 90% is cultivated by small-scale farmers and the rest by large-scale farmers. Tobacco is the sixth foreign exchange earner for Tanzania, contributing 4% of the foreign currency earnings (BOT annual report, 2004). Tobacco industry contributes about 30 million dollars annually in the form of taxes to the Government of Tanzania.

According to a study conducted in Tanzania in 2002, the number of people smoking was increasing with 27% in the male population and 5% in the female population.

Looking at the threat of this growth, the Tanzanian government passed in 2003 the law that among other actions made smoking in public illegal. However, enforcement to implement this law has not been strong enough, making the situation worse.

Additionally, companies and businesses dealing with tobacco have taken advantage of the inactive systems and regulations set by the government by increasing advertisements of cigarette brands all around the country, hence making enormous profits out of people's ill-health.

Currently, the strongest intervention to warn smokers and non-smokers on the harms of tobacco smoking and also avoiding secondary smoking, is the Tobacco Regulation Act (2003). This Act clearly indicates that "Smoking seriously damages your health, Smoking cause cancer, lung diseases, smoking causes heart and fatal diseases".

It is therefore important that all the necessary measures are taken to create more awareness, specifically among the youth, through teaching the risks of tobacco use and also to prohibit its use in public areas and its sale near schools.

Unhealthy Diet, Physical Inactivity and Obesity

Unhealthy diets, physical inactivity, and obesity are associated with risk of several cancers such as colon, endometrial, postmenopausal breast and pancreatic cancers.

There is an increase of obesity in Tanzania which has mostly affected the population in the urban areas. The main cause for this has been consumption of unhealthy foods and less physical activity in daily life. In the past, it has been thought that obesity affects only adults, but now this health condition affects also to the large extent children and youth.

Engaging in physical activities and/or sports contributes greatly to a healthy life. Hence, it is important that individuals are motivated to participate in physical activities which are the basis of building a good health and mind.

Hazardous Materials and Waste

Increasingly hazardous waste mismanagement and general environmental pollution are issues of concern in Tanzania. Formerly, these issues were not given much attention mainly because of the limited awareness and also due to financial and technical constraints. Tanzania has suffered severe consequences, in particular, the increased number of cancer cases arising from hazardous waste and environmental mismanagement. Key hazardous materials and waste in Tanzania include industrial, constructions, agrochemical, mining, mineral processing, health facilities etc.

Various initiatives have been taken by the Government of Tanzania in addressing this particular challenge, including establishment of policies, legislations and regulations, being part of the Basel Convention on the Control of Trans-boundary Movements of Hazardous Waste and their Disposal, and Bamako Convention on the Ban of the Import into Africa and the Control of Trans-boundary Movement of Hazardous Wastes within Africa. Despite existing challenges, the country is obliged to take necessary measures to ensure sound management of its environment through community awareness programmes.

Infections

In Tanzania infectious agents have been the major causes of the most diagnosed cancers such as cervix, liver, and bladder cancers and Kaposi's Sarcoma. In 2012, for example, Tanzania had 33,884 new cancer cases among which infection-associated cancers represented a great proportion.

However, the link between cancer and infectious agents also means that the problem is potentially preventable and the rates of cancer could be reduced through awareness campaigns, education on infection prevention and further insurance of an extensive accessibility of vaccines. Early screening and detection is key to enhance survival and quality of life of cancer patients.

Cancer Control in Tanzania

Prevention

Prevention services include the use of health protection, health promotion and disease prevention strategies to alert the population to cancer risks, promote healthier lifestyles and create healthier environments that aim to reduce potential cancer risks.

Liver Cancer

Primary liver cancer is mostly attributed to Hepatitis B virus. It is estimated that by the age of 15, about 80% of children in Tanzania show signs of being infected with Hepatitis B virus and approximately 10% become chronic carriers. It has been found that the majority of infections are acquired between the age of 6 months and 5 years. Hepatitis B is a major risk factor for primary liver cancer although the number of new patients seen at ORCI is less than 50 per year. A large number of patients seen in consultant hospitals are not referred to ORCI due to limited treatment options. Hepatitis B viral infection can be prevented by vaccination with Hepatitis B vaccine, and this could help prevent liver cancer and other liver diseases such as liver cirrhosis. Currently, Tanzania provides this vaccine in its Expanded Program on Immunisation (EPI).

Cervical Cancer

Cervical cancer is caused by Human Papilloma Virus (HPV). The majority of women are exposed to the virus once they become sexually active. The ideal way to prevent HPV infection would be through vaccination prior to exposure. In developing countries, girls are vaccinated with HPV vaccines design to protect against infections with high risk types (HPV16 and HPV18), starting at the age of 9. However the cost remains high and it is not affordable to the majority of people, unless it is included into EPI in developing countries. Currently, in Tanzania, HPV vaccines are available commercially in private hospitals although the cost is high.

Other Cancer Prevention Measures

Other primary cancer prevention measures in Tanzania, although conducted in a limited capacity include: education on increased daily intake of vegetables, increased percentage of people eating fruits every day, decreasing daily intake of fat, reducing intake of alcohol to modest amounts, and well informed sexual and reproductive behaviour.

Early Detection, Screening and Diagnosis

Efforts have been made by the Ocean Road Cancer Institute to create public awareness campaigns on signs and symptoms of the common cancers. The unique challenge to these efforts are of financial nature. This could eventually lead to information not reaching a wider audience.

Screening

In 2001, the ORCI in collaboration with IARC and INCTR introduced a cervical cancer screening program using Visual Inspection with Acetic Acid (VIA) and/ or Lugol's Iodine (VILI). This screening clinic located at ORCI is run free of charge. By December 2010, a total of about 19,000 women were screened for cervical cancer, and about 20 to 25 women were screened per day. The program faces a number of constraints, especially concerning advertisement and encouraging women to attend the clinic.

In 2006, ORCI received funds from the Government in order to conduct nationwide cancer control activities. These focused on cervical and breast cancer screening using VIA and BCE, respectively, in the regions in Tanzania. A total of 45,000 women were screened in 13 regions.

There are other individual-based screening programs conducted by cancer specialists in government as well as private clinics for different types of cancers. However, the screening is done on an *ad-hoc* basis due to various challenges, including a shortage of mammography machines.

Diagnosis

In Tanzania, there are no laid-down guidelines for the diagnosis and referral of cancer patients. This situation might be the cause for late cancer detection and delays in treatment.

Treatment

In Tanzania, options for cancer treatment include surgery, radiotherapy, chemotherapy and hormonal therapy. Treatment options may also depend on the type of cancer and stage at presentation. At the moment, ORCI is the only specialized centre for cancer treatment offering

chemotherapy, radiotherapy, and hormonal therapy. Consultant hospitals, major private hospitals, regional hospitals and some district hospitals may perform cancer surgery.

Palliative care

In Tanzania, 80% of cancer patients present at advanced stages of disease when showing up for treatment, where the most that can be offered is palliative care.

It is observed increasingly that a great number of HIV-infected individuals develop HIV-related cancers such as Kaposi's Sarcoma, lymphomas, cervical cancer and leukaemia. Consequently, Tanzania saw the need of having these palliative services in order to attain quality of life with minimal suffering among patients with incurable diseases as well as those who are terminally ill patients.

The major palliative care services in Tanzania can be found at Ocean Road Cancer Institute. Other palliative care centres include Muheza Hospice Care (offers hospital-based care for HIV/AIDS and cancer patients), Pastoral Activities and Services for People with AIDS in Dar es Salaam (PASADA; offers care for HIV/AIDS patients), Selian Lutheran Hospital Hospice in Arusha and Winmware Hospice in Mbeya.

Drugs

The Tanzania Food and Drugs Authority (TFDA) was established under the Tanzania Food, Drugs and Cosmetics Act 2003, Cap 219, with the mission of protecting and promoting public health by ensuring quality, safety and effectiveness of food, medicines, cosmetics and medical devices. One of the TFDA functions is to conduct pre-marketing evaluation of the regulated products to ensure that they meet standards of quality, safety and effectiveness before they are registered i.e. being officially allowed into the market.

All medicines in Tanzania are imported to the country by the following categories after being given permission from Tanzania Food and Drug Authority: Government and Non- Governmental institutions, pharmaceutical wholesalers, pharmaceutical manufacturers, clinical trial sponsors and principal investigators and recipients of donations.

However, individuals and hospitals can be authorized in extraordinary circumstances to import pharmaceuticals for personal and hospital use, respectively.

The Government pays for health care in public facilities, where they exist. Treatment of cancer is free in Tanzania, for patients treated at Ocean Road Cancer Institute, the only Cancer Institute in the country. Cancer chemotherapy drugs are procured by the Medical Store Department (MSD) and delivered to ORCI. When the drugs are out of stock, then patients must buy drugs from private drug stores at their own expense. The National Health Insurance Fund (NHIF) also buys cancer drugs for their beneficiaries.

Cancer and HIV/AIDS in Tanzania

In Tanzania, 5.1% of adults aged 15 – 49 are infected with HIV. The prevalence has dropped slightly in the country from 5.7% in 2008/2009 to 5.1% in 2011/2012, although the infection rate has remained higher for women than for men, according to the Tanzania HIV/AIDS and Malaria Indicator Survey report for 2011/2012.

HIV is a known risk factor for cancer, with a number of cancers now being known as HIV-related malignancies. Kaposi's Sarcoma, cervical cancer, and malignant lymphoma are cancers often associated with the HIV infection. The role of HIV in the pathogenesis of these malignancies is not well understood, and few studies have been done to determine any general increase in cancers after the onset of the HIV epidemic.

The introduction of Anti-retroviral therapy (ART) in Tanzania had a big impact in the reduction in incidence and prevalence of these cancers; this is evidenced by a study done in Tanzania at Ocean Road Cancer Institute in Dar es Salaam. This study examined the changes in proportions of Kaposi's Sarcoma to all cancers over the period of increased AIDS management by ART (2006-2011).

The management of HIV-related cancers has been a challenge mainly due to the lack of proper treatment. Moreover, current guidelines do not support the use of standard therapy (chemotherapy and radiotherapy) to this group of patients, due to lacking evidence. Also, issues of drug toxicity and interactions with ART need further research.

While HIV-related malignancies have declined globally with ART, including Tanzania, the rates of Non Aids defining cancers (NADCs) are believed to have increased i.e. rectal cancer, squamous cell carcinoma of the conjunctiva, and Hodgkin's Lymphoma. This is evidenced by a study done at Ocean Road Cancer Institute in Dar es Salaam Tanzania, showing an increase of NADCs over the past 11 years (2002 – 2012) among the HIV-positive patients.

This has brought an increasing burden in Tanzania, and other low and middle-income countries which led to the development of integrated programs for cancer prevention, control and HIV therapy. There is a need to identify and implement preventive measures for HIV related cancers through prevention of HIV infection.

The National HIV Prevention Strategy for Tanzania Mainland is based on the nine main strategic HIV Prevention objectives stated in the National Multi – Sectoral HIV/AIDS Strategic Framework, Established in 2009/ 10 – 2012. The focus is on promoting safer sexual behaviour among youth, preventing the mother to child Transmission PMTCT, reducing the risk of HIV transmission by HIV testing and counselling, increasing the proportion of sexual active adults who use condoms consistently and correctly, and increasing the number of people who know their HIV status and adopt appropriate measures to protect themselves and their partners.

Training, Education, Research, and Human Resources Development

Cancer research is necessary in order to add more scientific knowledge regarding epidemiology, curative outcomes, psychological and behavioural patterns in Tanzania. In Tanzania, the majority of cancer research has focused on epidemiological aspects and very few on laboratory and clinical aspects.

Training and human resources development has not been a major priority in the management of cancer in Tanzania due to lack of resources. This has made career development as well as improvement in cancer care throughout the country a major problem. Currently, in Tanzania, a university program offering specialized training for cancer treatment i.e. MMED clinical oncology training and a Bachelor's degree in Radiation Therapy Technology have been established at Muhimbili University of Health and Allied Sciences.

The Cancer Society

The Tanzania Cancer Society was established in 1991 with the priority of advancement and dissemination of knowledge concerning cancer, encouragement of research concerning cancer, promotion of cancer prevention, cancer screening, early diagnosis, treatment and good care for all patients suffering from cancer and improvement of training and treatment facilities in the field of cancer medicine. The association was formed as a non-charitable non-profit organization. The head office of the association was situated at ORCI and the association started with about 35 members with different professional backgrounds. However, the association has been dormant for the past 3-4 years due to a number of reasons including lack of funds and lack of commitment by the members after establishment of ORCI in mid-1990s.

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Chapter 16r

Uganda

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Uganda has a strong history of medical and cancer research. This dates back to the days of missionary doctor Sir Albert Cook often regarded as the father of modern medicine in Uganda (Savage, 2007). His meticulous records (1897-1904) formed the basis of establishing cancer registration leading to the current world renowned Kampala cancer registry (KCR) (Orem et al, 2009). In 1958, the discovery of Burkitt's lymphoma, a childhood cancer, was another landmark in cancer research from Uganda inspired by the legacy of Sir Albert Cook. The establishment of the Uganda Cancer Institute (UCI) in 1967 as a dedicated cancer research centre was the culmination of this great history and tradition. Since its inception, the Uganda Cancer Institute has been at the frontline of cancer diagnosis, treatment and prevention efforts through research in Uganda and the Eastern Africa region (Olweny, 1980).

Cancer Burden in Uganda

Uganda is one of the countries with very high morbidity and mortality due to cancer. Cancer is becoming a major challenge affecting people of all walks of life with the impact felt at all levels; individuals, families and communities. The cause of the rise in cancer incidence is multifactorial ranging from environmental agents, lifestyle, infection and the HIV epidemic (Mbulaiteye et al, 2006).

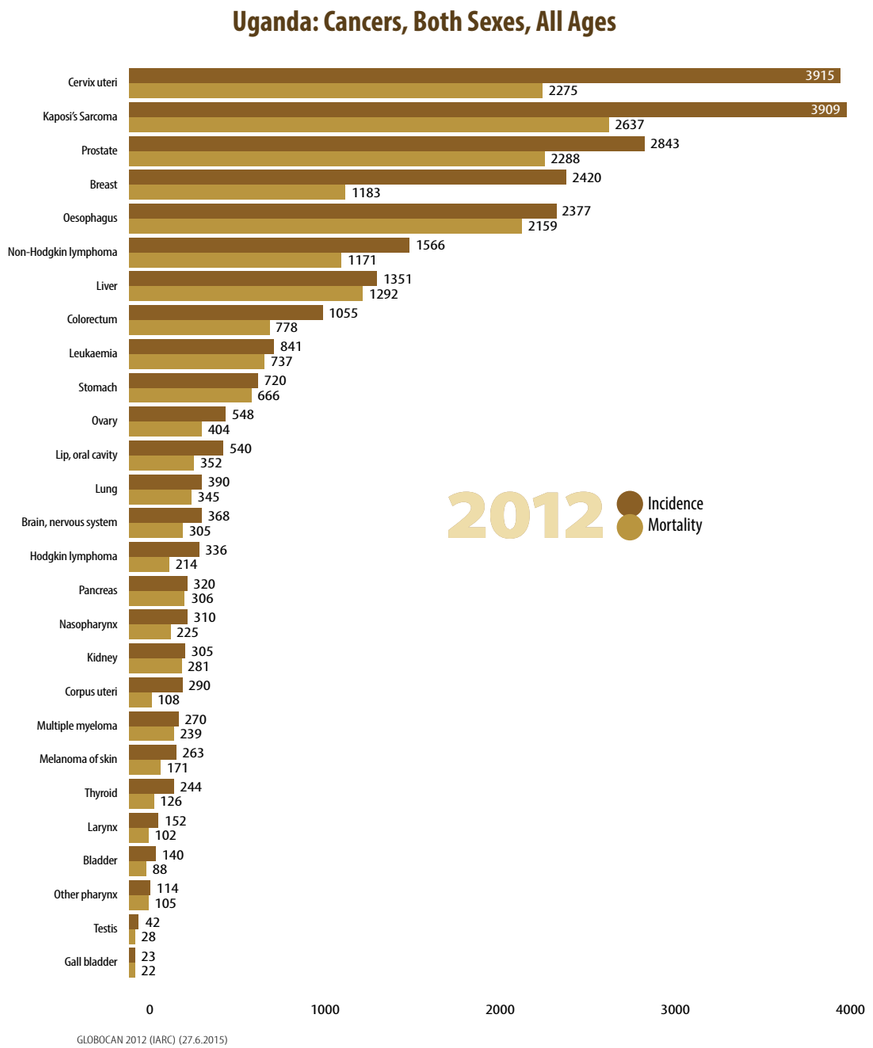

Figure 1: Common Cancers in Uganda

There are more than 200,000 cases of cancer per year in the country, of which 60,000 are incident cases. Each year about 46, 970 deaths occur in Uganda due to cancer. In addition, the risk of cancer before the age of 75 years is 17.8%. It is estimated that in the next five years there will be 300,000 cancer cases in the country. This alarming trend is confirmed by data from the Kampala Cancer registry and at the Uganda Cancer Institute (Coghill et al, 2013; Wabinga et al, 2014).

Currently four thousand newly diagnosed cases of cancers are seen at the Institute per year, and this is only 4% of new cases in the whole country (Okuku et al, 2013). Also, the number of revisits by patients at the Institute is more than 46,000 per year. Currently, sixty percent (60%) of the cancer burden in the country is directly attributed to HIV. Moreover there is no access to funding for these cancers from HIV funds at the moment. It has been over two decades since the emergence of HIV, a disease with one of the most profound impacts on the practice of medicine globally. Cancers seen in the context of HIV are very common in Uganda (Coghill et al, 2013).

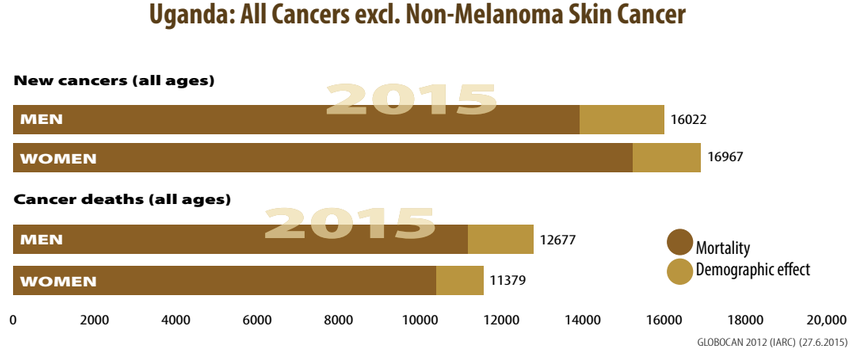

Figure 2: New cancer cases and deaths in Uganda, 2015.

The Ministry of Health Strategy for a Comprehensive National Cancer Control Program

Uganda has taken steps in line with the WHO recommendations to adopt a planned response to the cancer crisis by initiating the Comprehensive National Cancer Control Program CNCCP (Orem et al, 2009). The key components of this will be: Cancer Prevention, a comprehensive care delivery with a comprehensive Cancer Service network, a National Cancer Centre of Excellence at the centre, Cancer service support system, Cancer Research, cancer training, Collaboration and partnership and, finally, a strong national policy backed by legislation.

The Uganda National Development Plan (NDP) 2010 and further amplified in NDP 2 clearly states that, despite the increasing burden of cancers and other NCDs, there is inadequate capacity for specialized units such as the UCI, mainly due to lack of framework to handle these diseases. It therefore proposes the need to strengthen these specialized entities with enhanced specialized human resource capacity and upgrade of

infrastructure. This is further echoed by the Uganda National Health Policy 2010. They encourage improved access to quality services by strengthening the development of specialized care such as those offered at the Uganda Cancer Institute and other tertiary care facilities. In line with this, the Health Sector Strategic and investment plan 2010/11-2014/15 came up with plan to establish national infrastructure and human resource capacity building for NCDs. This is further echoed in the recently launched National Health Strategic plan 2015-2020.

Update on Cancer Service Provision in Uganda

The Uganda Cancer Institute is currently the only dedicated centre for cancer treatment in the country. It is an institute of the Government of Uganda's Ministry of Health with a fourfold mission and vision: research into the causation, treatment and prevention of common cancers in Uganda; provision of optimal clinical care that is guided by results of research, provision of training for health care professionals using the cancers seen at the UCI as the foundation for improved cancer treatment and clinical research skills; and lastly coordination of cancer prevention and control through implementation of comprehensive National Cancer Control Program (NCCP), a key requirement for holistic cancer care.

A major process of transformation of the UCI in line with the above outline role is underway; through major investment in infrastructure. First and foremost, the Government of Uganda has embarked on the construction of a new radiotherapy block adjacent to the completed six level wards. Secondly, two projects have been completed; a six level cancer building comprising an imaging centre, clinical laboratory, intensive care unit, chemotherapy infusion centre (Figure 3) and three levels of ward space have been completed and the process of equipping and furnishing is in progress. A community cancer clinic has been developed in a rural district of Mayuge; it will serve as pilot project in understanding the cancer burden in a rural population.

Figure 3: New cancer building at the Uganda Cancer Institute

Thirdly, a project is underway in partnership with the Fred Hutchinson Cancer Research Centre in Seattle and the USAID; it will house a modern outpatient, a research laboratory and training centre. The UCI/HCCA is a partnership between the UCI and Fred Hutchinson Cancer Research Centre (Fred Hutch) that seeks to reduce the global cancer burden through the prevention, early detection, diagnosis and treatment of cancer, infectious diseases and other health-related concerns in Uganda.

The new state-of-the-art UCI-Fred Hutch Cancer Centre was commissioned by the President of Uganda, Yoweri Kaguta Museveni, on the 21st May 2015.

Figure 4: The commissioning of the new UCI-Fred Hutch Cancer Centre - a state-of-the-art cancer care centre

Integration of Services

Despite statistics showing the increasing burden, cancer services provision in Uganda has not improved substantially over time. The occurrence of cancer and feedback from patients 'experiences show inequalities between services for cancer. A great number of cancer deaths are undiagnosed; this is reflected by the very low cancer survival rate in the country and also by the increasing number of patients accessing care abroad. This is the main reason behind initiating the comprehensive cancer service network core to a functional comprehensive cancer control program. This approach is already being implemented, with the assumption that the public sector, non-governmental organizations, academia, and the private sector can share with each other skills, knowledge, and resources in implementing cancer control. This network model of services integrate community, hospitals, regional and national cancer centres with a coordinating oversight being provided centrally at the Uganda Cancer Institute. The service points of the network are located in community health centres, district hospitals, regional cancer centres and national cancer centres of excellence.

It is envisaged that an increasing level of sophistication and well trained personnel will develop over time with an integrated system, with a leadership and organizational structure and a cancer care pathway linking the primary care services to the established regional and national cancer care centres, as a conduit along which patient traffic will flow back and forth. This organization of cancer services will ensure that patients receive the highest standards of care possible and that their care doesn't depend on where they live or who they are. The population should be aware that the presence of services and sharing of expertise should be the hallmark of the network.

Cancer Prevention

Cancer prevention is part of the health promotion, a component of public health that tackles the major determinants of health to achieve health and social changes that can improve the health of the whole population. The high rate of infection-related cancers in Uganda makes cancer

prevention and control a priority. In Uganda, Hepatitis -B has now been included in the routine national immunization schedule available to all children. In addition, there are Hepatitis-B immunization policies for all patients at risk or those exposed as a result of their occupation or workplace environment. HPV vaccination is in the roll-out phase, and in the next five years, all districts in the country would be covered. There is a great deal of similarity between chronic non-communicable diseases and communicable diseases, which is best exemplified by the cancers of infectious origin. This provides the best opportunity for harnessing the advances that have been made in the control of communicable diseases to work for control of non-communicable diseases. There are possibilities at various levels of intervention from primary, secondary and tertiary levels which fit well within well-planned national cancer control strategies. Prevention should proceed through steps of disruption of transmission, improvement of disease recognition and diagnosis, and prompt effective treatment. This principle should work for both infection and the resultant cancer.

A stringent anti-tobacco law has been passed by Parliament of Uganda that will curtail the availability of cigarettes, hence protecting the population from the harmful effects of tobacco. If it is not controlled, smoking will substantially contribute to cancer burden in the country in the future; 75% of patients with oral cancer had a history of smoking, with the number of years of smoking ranging from two to 33 years. Almost a quarter of Ugandan men (22%) aged between 15 and 49 are smokers, while 4% of women are smokers. Exposure to second hand smoke is known to increase the risk of lung cancer by 20-30%.The Ministry of Health is encouraging lifestyle changes aimed at mitigating diseases such as cancer, through its Non-Communicable Disease program. Increasing fruit and vegetable consumption is being encouraged as a strategy to reduce risk of cancer. Reduction in consumption of alcoholic beverages is another strategy being promoted as a measure to prevent the risk of cancers of liver, oral cavity, pharynx, larynx and oesophagus among others.

General Cancer Awareness and Cancer Screening

Cancer screening is being encouraged in the country, even if at the moment most screening are being done opportunistically. Population-based screening will be the goal and strategy in the future. The UCI is the spearhead of this encouragement through its Comprehensive Community Cancer Program (CCCP). This program, started in 2009, empowers communities with knowledge in cancer prevention, early detection, diagnosis and treatment so that they can play their rightful role in cancer control. The main objectives are to raise cancer awareness, to improve cancer prevention, to increase early diagnosis and to achieve compliance among those already diagnosed with cancer. Since most cancers are diagnosed at advance stage, it is hoped that the screening program will lead to early detection and increase prospects for the implementation of curative therapy for more cancer patients. Greater awareness should encourage early recognition of disease, preferably before development of symptoms, hence effective treatment and better outcome. Already common cancers are particularly targeted with specific interventions; cervical cancer (*see and treat*), breast cancer (breast awareness), prostate examination among others. We hope to reinforce our awareness program with increased access to cancer information targeting both the public and health professionals with electronic and other media platforms.

Partnerships, Collaborations and the Role of Civil Society

There is a need to provide holistic support to cancer patients and families by dealing with emotional and practical challenges of the disease. This includes the reduction of level of distress due to cancer regardless of prognosis. A significant part of this work in Uganda has been done by the NGO sector. They have however been working hand-in-hand with government in implementing their agenda. This is most visible in palliative and hospice services in the country which are being run almost entirely by civil society organizations. This has led to practical support being rendered to hundreds of individuals and families dealing with everyday concerns related to cancer. There is however still need to expand these roles by developing a more structured partnership with the NGO to ensure provision of services as complementary to government services. A code of practice should be developed for NGOs in cancer support through an umbrella body such as the Uganda Cancer Society to help with

implementation and development of best practices for cancer support groups and NGO.NGOs working on cancer are active under the umbrella of the Uganda Cancer Society which, in turn, is part of the Uganda Non-communicable Disease Alliance (UNCDA).

Overview of Cancer Care Network

A comprehensive cancer service network is being developed, comprising all modalities for cancer management with a referral system linking lower health levels and higher health centres progressively from district to regional and National centre of excellence.

National Centre of Excellence

This will consist of Clinical care team; Surgical oncology, Gynaecological oncology, Medical oncology, Paediatric oncology, palliative care specialists and Radiation oncology. Within this will be a National Cancer Diagnostic Centre with the following components: the cancer reference laboratory, the National Cancer Imaging Centre, the National Tumour Biobank and Resource Centre. Other services to be offered will include supportive and palliative care.

Regional Cancer Centres

Regional cancer centres will be developed with services increasing specialization and presence of multidisciplinary team. Regional cancer centres shall be rolled out in phases and shall constitute infrastructure, human resources and equipment necessary to ensure a functional multidisciplinary cancer care team. We envisage that regional centres will have a radiotherapy unit equipped with a Cobalt-60 tele-therapy unit, a simulator, a high dose rate Brachytherapy unit, a planning unit and a linear accelerator.

Research

Cancer research best exemplifies research being a key factor in promoting health, combating disease, reducing disability and improving quality of care. Cancer research is an essential component in the development, implementation and evaluation of a national cancer control programme. The scientific basis for identifying the causes of cancer and for specifying effective strategies for the prevention, treatment and control of cancer, as well as for evaluating overall programme performance, rests with cancer research. The scope of cancer research is wide, extending over a number of key areas: Epidemiological research, Prevention research, Laboratory research, Clinical research, Translational research and Health services research. One of the key aspects of research with implication to cancer control is the Kampala Cancer Registry. Established in 1951 and based at the Makerere Medical School, it has collected a unique data set that has been instrumental in improving understanding of cancer in Uganda and informing health policymaking and planning. These data comprise demographic information, diagnosis information, and the source of the data. The KCR has provided data to global publications, catalysed collaboration and research opportunities with universities and other organizations, supported training, and guided design of cancer control programs.

Cancer Training and Capacity Building

The East African Centre of Excellence in Oncology at Uganda Cancer Institute in collaboration with Makerere University proposed a project for cancer training. The main aim of this project is to strengthen and expand the Education mandate and role of the Uganda Cancer Institute as a centre of excellence in higher education in oncology education in East Africa. The main objectives of this project are to improve the level of care and research through trained man power, to improve the quality of care through higher education and professional development in oncology

and to contribute towards prevention and control of cancer in the region through higher education. Of note is the key training collaboration with several African countries being spearheaded by IAEA/WHO through the imPACT program, the VuCCNet with proposed secretariat at the UCI in collaboration with Makerere University.

Conclusion

With a strong historical background in medical and cancer research as a basis for current practice, Uganda is in a better position to face the current upsurge in cancer burden, compared to many countries in the region. The Ministry of Health Strategy for a Comprehensive National Cancer Control Program shall take the right steps in line with the WHO recommendation to respond to the cancer crisis. The key components of this will be Cancer Prevention, a comprehensive care delivery with a National Cancer Centre of Excellence at the centre, a comprehensive Cancer Service network, Cancer service support system, Cancer Research, cancer training, partnership and finally, a strong policy. Given its clear and focused mission and mandates at the centre of NCCP, the Uganda Cancer Institute is a major asset in the hands of Ministry of Health.

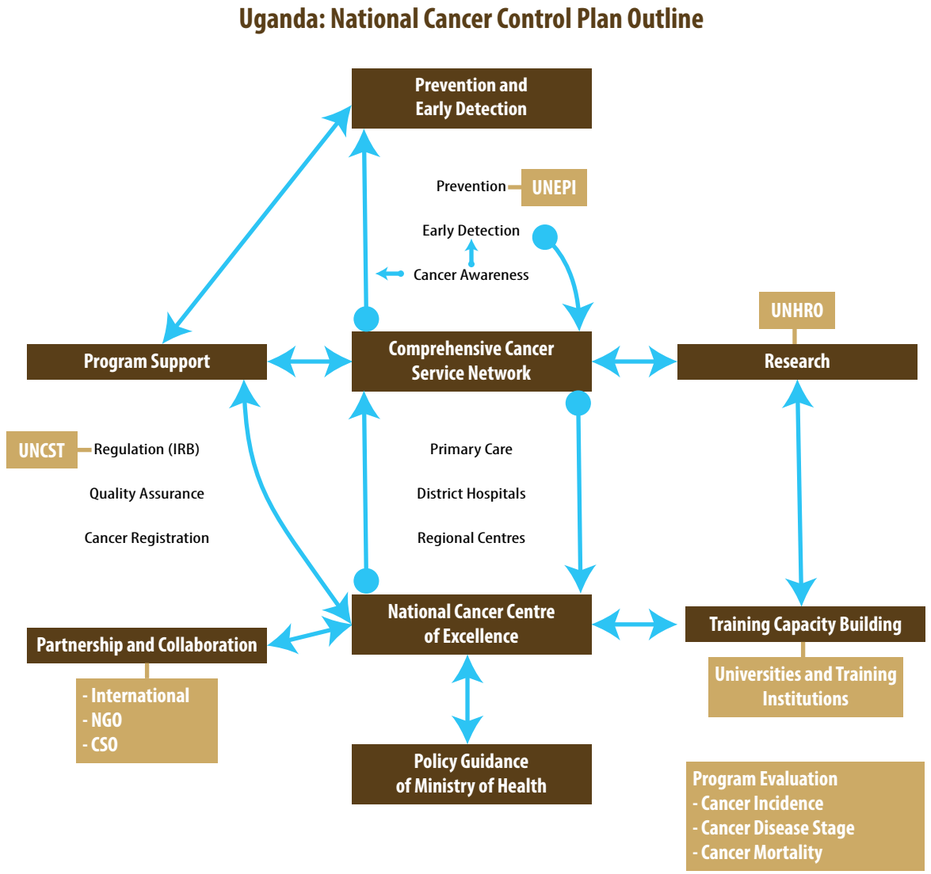

Figure 5: Outline of comprehensive national cancer control program for Uganda

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Chapter 16s

Zimbabwe

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Zimbabwe is a southern African country with a total area of 390,757 km², divided into 10 provinces. According to the 2012 census, Zimbabwe has a total population of approximatively 13 million, with a slight preponderance of women. The population is relatively young, with 41% being below the age of 15 years and only about 4% being 65 years and above. Life expectancy from birth is 58 years old. The vast majority of the population (65%) lives in rural areas, and 58% of the population is married. People of African ethnic origins make up for almost the entire population (98%).

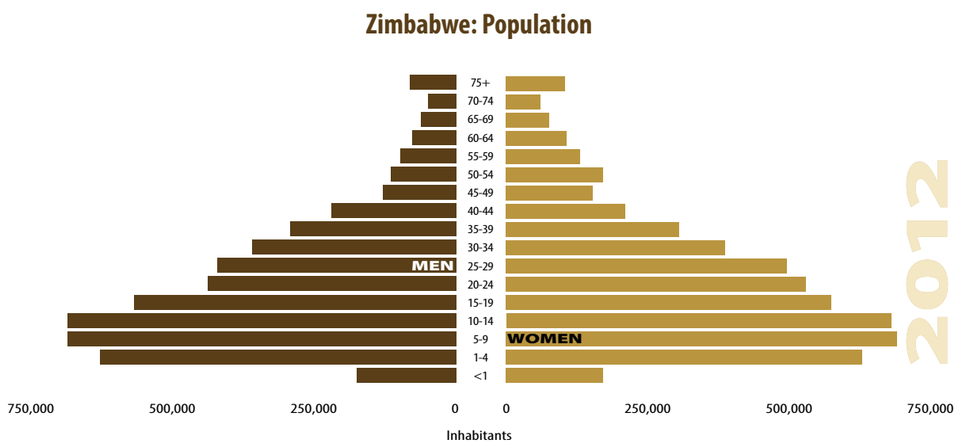

Figure 1: Population Pyramid by Age Group and Gender, 2012 (ZIMSTAT)

According to the most recent global literacy list (Unesco Institute for Statistics, 2013), the adult literacy rate in Zimbabwe in 2011 was 83.6%.

75% of households have access to potable water that is either piped or comes from boreholes and protected wells.

Cancer Registration and Burden of Cancer

Zimbabwe's National Cancer Registry is nowadays considered a model for African population-based registries by many international organisations such as the International Agency for Research on Cancer or the African Cancer Registry Network.

The registry has contributed significantly to the development of cancer registration and surveillance in sub-Saharan Africa by providing technical support to other registries in the region.

Zimbabwe: Registration of Cancer Data

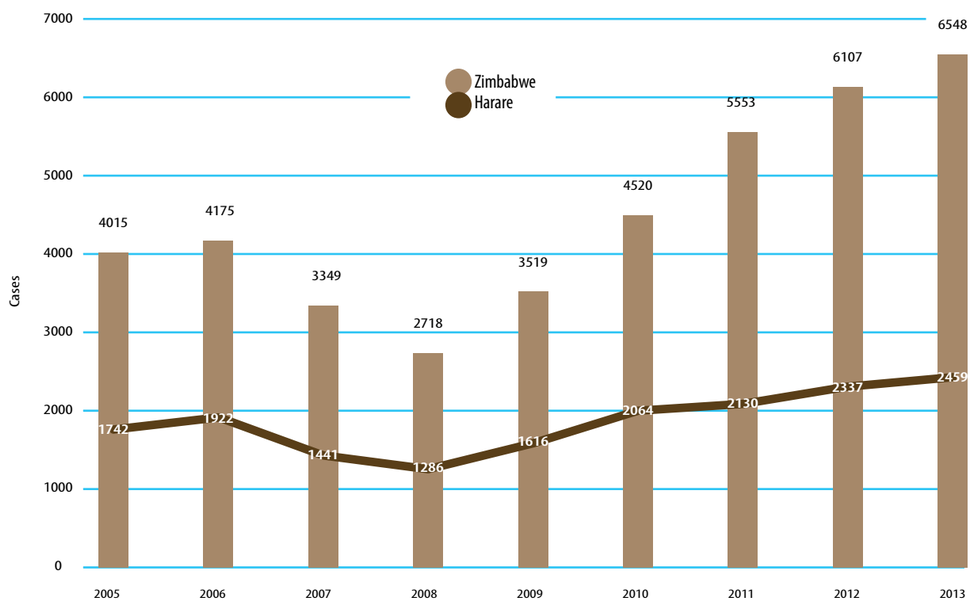

Figure 2: Registration of Cancer Data: 2005-2013 (ZNCR)

The burden of cancer is increasing in Zimbabwe, following the regional and global trend. The Zimbabwe National Cancer Registry (ZNCR) reported more than 6 000 new cancer cases diagnosed in 2012 and over 6 500 new cases in 2013.

Generally, trends in the last decade show a steady increase in the incidence of cancer. This has been attributed mainly to a continued increase in HIV-related cancers and lifestyle related factors.

The same tendency applies also for some individual cancers such as prostate cancer, which is the most common cancer in Zimbabwean men (See Figure 3).

Zimbabwe: Prostate Cancer Trends

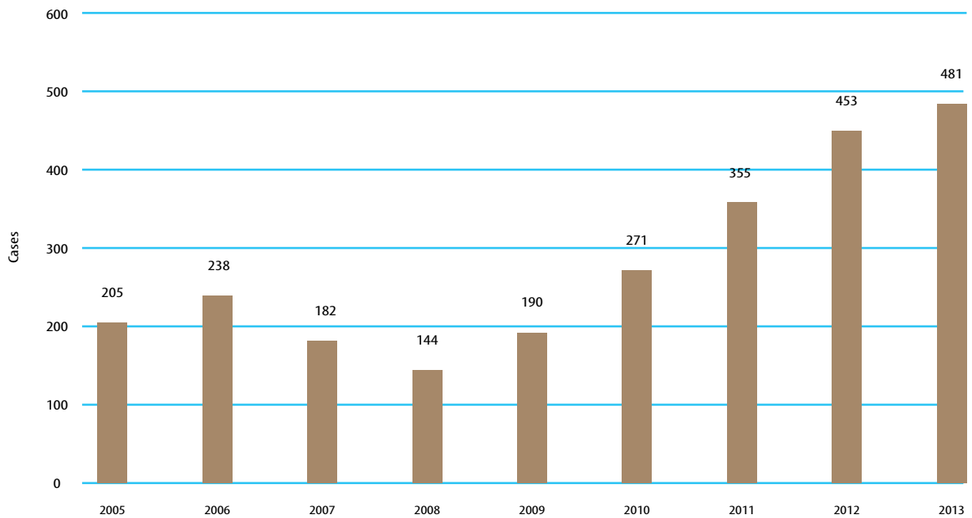

Figure 3: Prostate Cancer Trends in Zimbabwe: 2005-2013 (ZNCR)

Cancer Incidence

The most frequently occurring cancers among Zimbabweans of all races were cervix uteri (18%), Kaposi's Sarcoma (10%), prostate cancer (7%), breast cancer (7%), non-Hodgkin lymphoma (6%), non-melanoma skin cancer (6%), oesophageal carcinoma (4%), colorectal cancer (4%) and eye malignancies (3%). The other cancers accounted for 35% of the registered cancers as shown in Figure 4.

In 2013, the five most common cancers among Zimbabwean black men were: prostate cancer (17.8%), followed by Kaposi's Sarcoma (14.8%), non-Hodgkin lymphoma (NHL) (8.6%), oesophageal cancer (5.8%) and liver cancer (4.9%).

The five most common cancers among black women were: cervical cancer (32.1%), breast cancer (12.5%), Kaposi's Sarcoma (6.9%), NHL (5.4%) and eye malignancies (3.4%).

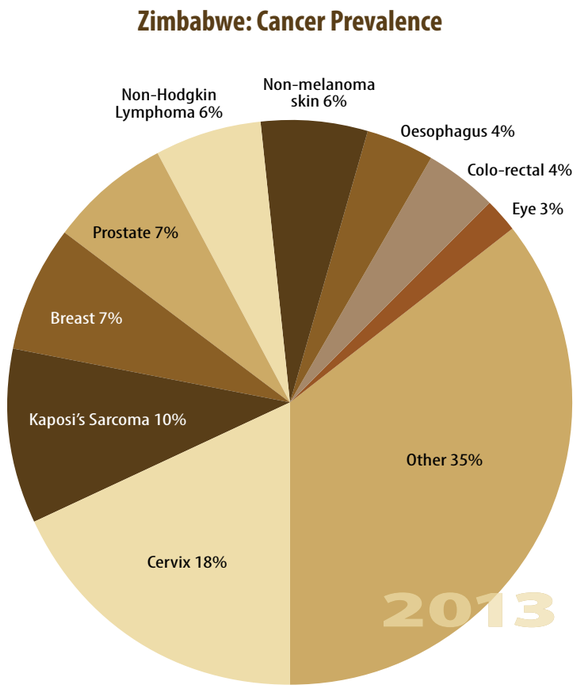

Figure 4: Cancer Prevalence in Zimbabwe 2013 (ZNCR)

As expected in a tropical environment, non-melanoma skin cancer was the most frequent cancer among Zimbabwean non- black men (52.8%) in 2013. The second most common cancer was prostate cancer (12.1%), followed by colon cancer (4.8%), cancer of the rectum (4.3%) and lung cancer (2.6%). The five most frequent cancers in non-black Zimbabwean women were: non-melanoma skin cancer (43.7%), breast cancer (21.3%), colon cancer (7.5%), lung cancer (6.3%) and non-Hodgkin lymphoma (2.9%). Melanoma skin cancer ranked sixth in both men and women of non-black origin (2.6 and 2.3% respectively).

In 2013, childhood cancers represented 3.6% of all the cancers recorded. A total of 236 childhood cancers (age 0-14) of all races were registered. They occurred in 123 boys (52.1%) and 113 girls (47.9%). The five most frequently occurring cancers in boys classified according to the ICCC system were lymphoma (17.0%), soft tissue sarcomas (16.3%), leukaemia (13.8%), retinoblastoma (12.2%) and renal tumours. For the girls, the five most frequent cancers were renal tumours (19.5%), soft tissue sarcomas (14.2%), lymphoma (11.5%), retinoblastoma (10.6%) and leukaemia (9.7%). Kaposi's Sarcoma accounted for 41.7% of the soft tissue sarcomas in both boys and girls.

Cancer Mortality

Mortality of cancer in Zimbabwe almost mirrors the incidence in percentages per type of cancer. This might be an indication of non-robust screening programs such that deaths from curable cancers remain common. It is also well known that the majority of cancers are diagnosed late, regardless of them being preventable or not. In such circumstances, any intervention would not yield outcomes related to improvement of survival.

Liver and lung cancer emerge however as the 7th and 8th causes of cancer mortality respectively, due to their relative resistance to treatment.

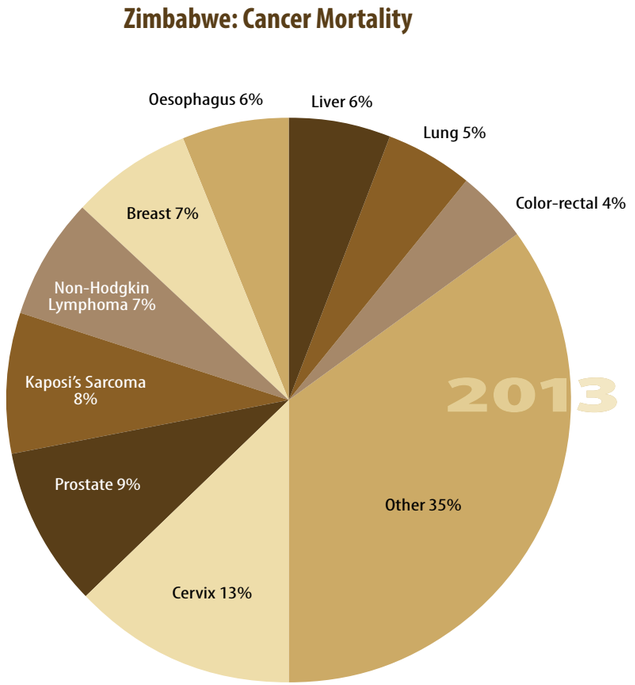

Figure 5: Cancer Mortality in Zimbabwe 2013 (ZNRC)

Cancer Centres

There are two major cancer treatment centres in Zimbabwe, serving both northern and southern parts of the country. These are at the Parirenyatwa Group of Hospitals in Harare (northern part) and at the Mpilo Central Hospital in Bulawayo (southern part). In addition to these, there are a few chemotherapy administration units in the private sector.

Medical Oncology Resources

Contrary to other countries where medical and radiation oncology are clearly separated and defined, the model of clinical oncology is used in Zimbabwe.

There are however, haematologists who practice hemato-oncology and administer chemotherapy for hematologic malignancies. In addition, there is a Kaposi's Sarcoma clinic run by physicians interested in the disease who administer chemotherapy for this condition only.

Chemotherapy is administered at Parirenyatwa and Mpilo Hospitals and a few other private institutions. There is limited availability of chemotherapy drugs in the public sector and most patients acquire them at their own expense. The cost of these drugs is prohibitive since free access is often not provided.

Even in the private sector, there are shortages of chemotherapy drugs. These factors commonly lead to disruption of patients' treatment and may possibly lead to poor treatment-related outcomes.

Radiotherapy Resources

Radiotherapy treatment was introduced in Zimbabwe in the 1960s with the installation of one Cobalt-60 machine at the Parirenyatwa Group of Hospitals and another one at Mpilo Central Hospital. As early as 1987, a BBC Dynaray CH-6 accelerator was installed at Parirenyatwa Hospital, followed by two CLINAC 2100C accelerators installed in 1996 (one in Harare, one in Bulawayo), in conjunction with corresponding XIMATRON Simulators with CT-Option.

Currently, the two cancer treatment centres have a total of five state of the art medical linear accelerators (LINAC) for external beam treatment (EBRT). Two additional LINACs that were decommissioned to make way for the new ones are in useable state and await construction of housing when they will be refurbished and reinstalled.

Figure 6: One of the linear accelerators at Parirenyatwa Hospital Radiotherapy Centre

Figure 7: The wide-bore dedicated oncology 16 slice CT scanner

Figure 8: Digital Simulator

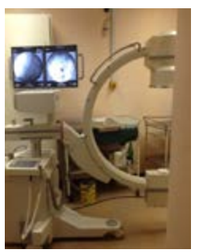

Figure 9: One of the HDR brachytherapy rooms

Figure 10: The "Gynaesource" brachytherapy equipment with 5 channels

In each centre, there is a radiotherapy digital simulator, a dedicated oncology wide bore 16slice CT scanner, 2D and 3D treatment planning and oncology information systems. Appropriate dosimetry and quality control equipment for EBRT and High Dose Rate (HDR) brachytherapy are available in both centres. Brachytherapy services are provided in both centres. Although the main use of this method of treatment is for intra-cavity treatment of cancer of the uterine cervix, the equipment has some other applications. Brachytherapy is to be introduced for prostate cancer, interstitial brachytherapy and endo-cavity brachytherapy for oesophageal cancer. However, plans still need further development before

their implementation. Equipment available for brachytherapy consists of 3 HDR 60 Cobalt brachytherapy units, two of which are in the Harare Oncology centre. One of these is a dedicated gynaecologic HDR unit. Other related equipment are the brachytherapy TPS for each unit, dedicated C arm and 3D CT based planning system.

Pathology Resources

Histopathology services are centralized in Harare and Bulawayo. These services are found in both private (5 laboratories) and public sectors (1 laboratory).

It takes between 48 hours and 6 weeks to get a histology result. A number of reasons influence such time factors, including distance of the specimen collecting centre from the main hospital, time taken to approve results before dispatch and need for additional specialized tests at another institution.

Services are also greatly affected by shortage of skilled staff, with only seven pathologists for the whole country (2 in Bulawayo and 5 in Harare). It is estimated that 48 pathologists are needed for the whole population of Zimbabwe if one pathologist is to service 250 000 people.

Appropriate preservation of the specimen is needed and involves prompt immersion in formalin. Sometimes this can be challenging, especially in outlying areas where alternative means may be used and therefore may distort results.

Due to a limited number of pathologists, quick-frozen section diagnosis is not readily available. Fine needle aspiration is readily available in all hospitals, having had a recent re-emergence from the introduction of Interventional Radiology.

Immunohistochemistry is available but the cost is prohibitive for most patients. The immunohistochemistry tests are carried out in batches in order not to waste resources. This is one of the factors that may lead to delays in obtaining results within a short period of time.

Tumour markers whilst not always available in the public sector, they are readily available in private. The following markers are usually available: CEA, CA125, CA19-9, PSA, AFP, beta HCG and CA15-3. Molecular biology is not available in the public setting. Some private laboratories offer access to tests such as BCR-ABL PCR.

Oncologists Available

The two Radiotherapy Centres in the country have eight Radiation Oncologists/Clinical Oncologists and four hemato-oncologists who treat haematological malignancies.

There are also ten resident doctors in training in Radiation Oncology/Clinical Oncology in the local Master's program run by the University of Zimbabwe - College of Health Sciences.

The National Cancer Control and Prevention Program (NCCP)

In recognition of cancer being a major cause of morbidity and mortality, the Zimbabwe National Cancer Prevention and Control Strategy (2014-2018) was formulated and adopted by the Ministry of Health and Child Care (MOHCC) to advocate a comprehensive cancer control policy and programme.

The document was crafted through extensive consultative processes involving national and international stakeholders and coordinated by the National Cancer Control Strategy Committee. The strategy was officially launched in February 2014.

The overall goal of the strategy is the reduction of cancer morbidity and mortality through implementation of evidence-based cost-effective prevention and control interventions and providing palliative care to improve quality of life of people living with cancer and their families by 2017. The Goal Areas are Programme Strengthening, Primary Prevention, Early Detection, Diagnosis and Treatment, Palliative Care/Rehabilitation and Surveillance and Research.

The strategy focuses on reform and reorganisation of the way cancer services are delivered in order to ensure future services that are consistent and associated with good clinical outcomes. It also seeks to ensure that cancer prevention and care across the whole country is equitable and is at the highest possible standards.

Prevention and Early Detection

The main risk factors contributing to the increasing incidence of cancer in Zimbabwe (as in most African countries) include infectious agents and lifestyle related factors such as tobacco use, harmful alcohol use, unhealthy diets and physical inactivity. Prevention becomes, therefore, the most cost-effective intervention, an approach that has been adopted in Zimbabwe.

Many of the cancers are diagnosed at an advanced stage in Zimbabwe and a great number of African countries. Moreover, due to limited resources, the current cancer treatment and palliation services are greatly burdened. A focus on screening programmes is therefore warranted.

The oncology community (including the Cancer Association of Zimbabwe) conduct cancer awareness programmes but they might not reach places where they are most needed, outside the towns of Harare and Bulawayo.

Tobacco

In Zimbabwe, cigarettes are the most common use of tobacco, smoked or chewed in various forms. Tobacco consumption is six times more common in men than in women. Exposure to passive smoking is quite common as there is no enforcement for people to smoke in designated areas. It is believed that about a quarter of adolescents in Zimbabwe are exposed to second hand smoke.

The strong commercial interests behind tobacco consumption are a major drawback to the efforts at individual and mass education against its use. The International Framework Convention for Tobacco control has remained a blue print for effective control of tobacco, outlining articles on protecting populations from exposure to tobacco smoke, implementing graphic warning signs and passing comprehensive bans on tobacco advertising, promotion and sponsorship.

Nonetheless, the Framework Convention for Tobacco Control has not yet been ratified by Zimbabwe and tobacco remains a major cash crop in Zimbabwe. Also, legislation for tobacco use exists but its implementation lags behind.

Alcohol Consumption

Ethanol is the most widely used and abused agent throughout the world. The Zimbabwe STEPwise survey in 2005 revealed that current alcohol consumption is very high with a prevalence of 58% in men and 13.5% in women. This numbers are most probably underestimated due to under reporting as a result of cultural effects, especially in women. Several measures have been adopted to try to reduce the consumption of alcohol, such as the restriction of the places and times alcohol is available, the raise of the minimum legal age at which alcohol is purchased and the increased taxation on alcoholic beverages.

Diet and Exercise

Obesity is increasingly becoming a concern in Zimbabwe as is the reduction in physical activity. Correspondingly with other developing countries, eating habits are changing. This is seen as a shift from natural, traditional wholesome foods to a more Westernized diet low in fibre, high in fat and less of plant protein. The message of losing weight and exercising to help reduce the risk of developing cancer is promoted through various media.

Occupational and Environmental Exposure

In Zimbabwe, lessons are being drawn from industrialized countries in identifying and assessing existing and potential occupational exposures that can lead to the development of cancer in workers and in the community. Therefore, measures to ensure reduction of such exposure are important. Surveillance of workers who are potentially exposed is promoted. There is existing legislation on exposure to the majority of occupational carcinogens. This includes the following acts of Parliament: Pneumoconiosis Act, Radiation Protection Act and Environmental Management Act.

Infections

Infectious risk factors associated with cancer in Zimbabwe include HIV, HPV, Hepatitis B and C, EBV, Helicobacter Pylori and Schistosomiasis. Promotion of interventions such as safe sex, eradication of the Schistosoma parasite and hepatitis B vaccination are part of measures being taken to combat these factors.

Many programmes are in place aiming at reduction in HIV transmission through promotion of general behavioural change, condom use, access to treatment and prevention of mother to child transmission. This has reduced HIV prevalence from about 24% to 15%.

HPV vaccination was approved in 2009 and supported by the Global Alliance on Vaccines and Immunisation (GAVI), which requires sharing ability to vaccinate an adolescent population. In 2014, Zimbabwe implemented the HPV vaccination demonstration project in the towns of Marondera and Beitbridge. Vaccination was conducted in 10 year old girls using the school based strategy. In 2014, there were 4450 girls vaccinated whilst in 2015, a total of 4950 girls were vaccinated. The future plan is the roll out of the vaccine for 9 – 13 year old girls by 2016.

Chronic infection with hepatitis B and C causes hepatocellular carcinoma which was responsible for 6% of all cancer deaths in 2013 in Zimbabwe. In 1999, MOHCC reintroduced HBV vaccination targeting children less than 5 years. Since 2007, the HBV vaccine has been administered in combination with diphtheria, pertussis, tetanus and haemophilus influenza type B as a 5 in 1 vaccine (Pentavalent) under the extended program of immunization. A good coverage of 87% was reported as achieved in 2010.

Exposure to ultraviolet radiations is responsible for the development of both melanoma and non-melanoma skin cancers. This is very important in a tropical country with a significant non-black population such as Zimbabwe. Non-melanoma skin cancer prevalence is over 40% of all cancers in both non-black men and women Zimbabweans. Education in avoiding sun exposure especially at peak intensity is given to the white skinned and albino populations. Also, use of protective clothing and sunscreen lotions is promoted for populations at risk. The cost of these lotions can however be prohibitive for daily use.

Cancer Screening Services

The majority of cancer patients (80%) in Zimbabwe are diagnosed with late stage disease (stage 3 and 4) resulting in poor treatment-related outcomes and increased premature deaths from cancer. Nevertheless, national cancer screening and early detection programmes are generally still at an early phase.

Breast Cancer

Most public hospitals do not provide mammography due to lack of the necessary equipment and skilled personnel. The current available mammography capacity is far below what would be needed for national coverage of women at risk. Women rarely have a clinical breast exam unless they are symptomatic. This is due to the lack of information on its importance as well as the fact that this service is not routinely proposed in clinics. Priority is given to the presenting condition when women visit health institutions and there is no set routine to accommodate screening activities generally. Awareness of the importance of breast self-examination still needs to be prioritized together with instruction on the technique of how to perform this self-examination.

Cervical Cancer

Visual Inspection with Acetic Acid (VIA) was pioneered by a team of researchers from the Department of Obstetrics and Gynaecology, University of Zimbabwe, in collaboration with researchers from Johns Hopkins Programme for International Education in Gynaecology and Obstetrics (JHPIEGO). They demonstrated in a randomized controlled trial that cryotherapy was a reasonable option to treat cervical intraepithelial neoplasia (CIN) compared to loop excision (LEEP). The former has been the preferred method of screening for cervical cancer in Zimbabwe since.

Demonstration projects with VIA and treatment with cryotherapy were successfully launched by UZ researchers in Mutoko, Gwanda and Chiredzi and they were based on the "see and treat" principle. To date, the government has 66 sites providing VIAC (visual inspection with acetic acid and cervicography). Several non-governmental organizations also provide a number of sites for VIAC with most of these services being centralized in urban areas.

PAP smears are available in private institutions but the cost is prohibitive for the majority of patients. Even among those who can afford them, there has been insufficient awareness campaigns to encourage people to be screened. PAP smear services are generally centralized and not available to the majority population. Most medical insurers do not provide cover for screening services.

Other Cancers

Only ad-hoc screening measures are available for all other cancers. For prostate cancer, digital rectal examination (DRE) is not routinely proposed by the majority of health workers and most public hospitals do not provide PSA screening, although the latter is sometimes offered at awareness events throughout the country.

The situation is similar for other cancers such as colon cancer. The main problems are the recognition of the prohibitive costs of screening services, the absence of an effective national mechanism to motivate, organize and co-ordinate cancer screening activities and also, the absence of a referral system to centres with capacity to take up the cases as they are identified.

Palliative Care

Palliative care and rehabilitation are well recognized as essential elements in the continuum of care for cancer patients in Zimbabwe. While some elements of both adult and paediatric palliative care have been implemented as part of medical and household interventions for patients, palliative care was formally introduced in 1979. This has contributed significantly to the improvement of the quality of life for patients and family members facing the diagnosis of cancer and other life-threatening or life-limiting illnesses.

Zimbabwe has a long history of providing palliative care, with Island Hospice Service being one of the first hospice organizations to provide hospice and palliative care not only in Zimbabwe but in Africa, since 1979. The service has grown and 17 regional branches were established throughout the country by 1997. Approximately 13 organizations were providing palliative care by 2004.

This growth in palliative care provision has been a result of several initiatives and factors that have necessitated and facilitated the provision of palliative care in Zimbabwe. Initially, a small minority of the population generally accessed palliative care services and the disease focus was cancer. However, with the growth of the disease burden due to HIV and AIDS, palliative care provision has widened to include those living with and experiencing HIV and AIDS and other chronic illnesses.

The result was the increase of community-based services throughout the country provided by both hospice organizations and community home-based care organizations. The community and home-based care programme national review of 2006 reported that there was at least one community and home-based care programme in each of the 62 districts of Zimbabwe.

Notable initiatives have facilitated palliative care service provision in the country. In 1992, the MOHCW established the Prevention and Control of Cancer Committee in Zimbabwe comprising relevant stakeholders and professionals. The committee oversaw the development of a ten-year plan for the National Cancer Control Programme for Zimbabwe (1994-2004) with the overall aim to formulate, plan and implement a coordinated and cost effective programme for the prevention and control of cancer in Zimbabwe. Aspects of palliative care policy were incorporated in this plan.

Within this period the post of a Programme Officer for Cancer and Palliative Care was filled in 1994, funded by the World Health Organization (WHO). Palliative care training was established in the eight provinces and the two cities of Harare and Bulawayo during the same period. However, due to lack of funds coupled with the economic challenges, the programme was not sustained. In 1999, a national Hospice and Palliative Care Association of Zimbabwe (HOSPAZ) was registered to support and promote palliative care services in collaboration with the MOHCW.

In 2004, through a pilot project in five African countries which included Zimbabwe, WHO estimated that a total of 208,600 people were dying from HIV and AIDS or cancer annually in Zimbabwe. The proportion of people needing palliative care was estimated at 1 in 60. Those dying from HIV and AIDS or cancer and suffering pain were estimated at 56,900. The report noted that the number actually needing palliative care was much higher, because it should also include those suffering from serious illnesses but not dying during the same year, as well as those suffering from diseases other than cancer or HIV and AIDS. In addition, palliative care should not only be provided at the end of life. In light of these considerations, WHO estimated that at least 1% of the country's population will need palliative care. The WHO report noted the long tradition in provision of palliative care in Zimbabwe but also the low level of integration of palliative care into the health system.

The National Health strategy and Palliative Care Standards provision of palliative care is already effective. The National Palliative Care Policy and National training curriculum was finalized in 2013.

Analgesia is an important component of cancer care, particularly in an environment like Zimbabwe where patients tend to be diagnosed with advanced stage disease. Shortage of opioid analgesia is very common leaving patients with uncontrolled pain. Morphine, which is an essential medicine in management of cancer pain, has not been in stock at Mpilo for several years now. The morphine supply at Parirenyatwa Group of Hospitals has been erratic over the years.

Drugs

The medicines control authority of Zimbabwe (MCAZ) is a statutory body established by an Act of Parliament, The Medicines and Allied Substances Control Act of Zimbabwe (MASCA) (Chapter 15.03). Its mandate is to protect public health ensuring that medicines on the market are safe, effective and of good quality through enforcement of adherence to standards by manufacturers and distributors.

All medicines sold in Zimbabwe must be registered as stipulated under the Medicines and Allied Substances Control Act and Regulations. There is however a provision in the Act (section 75) for named patients who have received a valid prescription from a registered prescriber to import unregistered lifesaving medications. This enables cancer patients to be able to import any drug that is deemed lifesaving by their doctor.

Subsidized drugs are sometimes available from the Cancer Association drug donations, drug subsidies at the public hospitals such as the Parirenyatwa hospital pharmacy, donations from philanthropists and drugs leftovers from paying patients.

Cancer and HIV/AIDS in Zimbabwe

HIV/AIDS and cancer causes problems needing special consideration in Zimbabwe. Evidence is available regarding HIV as a risk factor for cancer with a number of cancers now being known as HIV-related malignancies. Zimbabwe has been in the epicentre of the HIV/AIDs epidemic and 60 to 80% of cancers reported in Zimbabwe in the last decade were HIV-related. Cases of non-HIV related malignancies have coexisting HIV infection matching the prevalence of HIV infection in the general population. HIV is associated with cancers such as Kaposi's Sarcoma, squamous cell carcinoma of the conjunctiva, cervical cancer and non-Hodgkin's lymphoma, that have a high prevalence in Zimbabwe.

The recognition of the impact of HIV infection on cancer has led to calls for the integration of HIV and cancer control programs for better outcomes. The National Cancer Strategy is now directing focus towards integrating HIV and cancer prevention services as controlling HIV will assist in controlling cancer.

The impact of antiretroviral therapy (ART) on the incidence of HIV-related cancers is generally observed as that of a reduction in incidence and prevalence of these cancers with improved ART coverage. It can be therefore assumed that as ART coverage improved in Zimbabwean adults between 2004 and 2012 (Fig. 11) this would result in lowered incidence of HIV-related cancers.

There remain many unanswered questions on the management of HIV-related cancers and other cancers occurring in the presence of HIV. There are no clear treatment guidelines as there is insufficient evidence to support what is current standard therapy in this population of patients. Drug interactions and toxicity to both chemotherapy and radiotherapy need to be further studied. As more patients with HIV survive longer, the problem of development of cancers in this population can only escalate. Research in this area is therefore warranted.

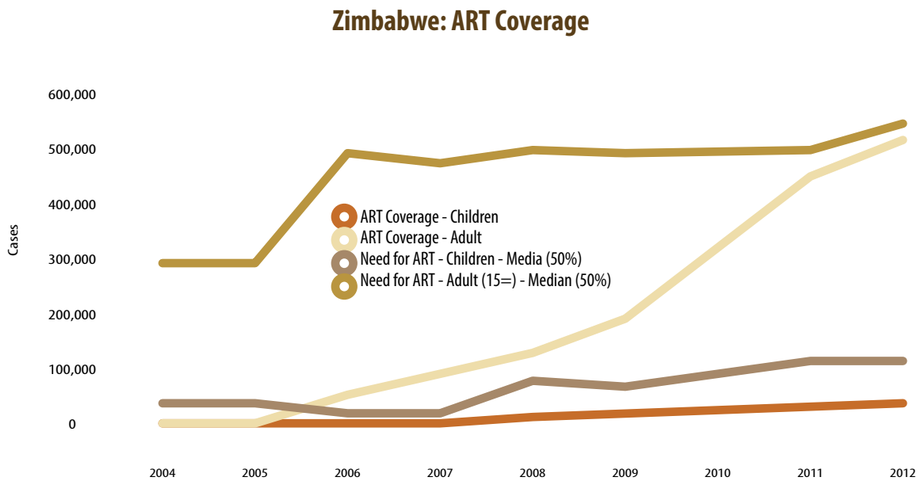

Figure 11: Adult and Paediatric ART Coverage Scale-up (ZIMSTAT)

Unfortunately this is not the case with cervical cancer as shown in Figure 12. However, a shift has been observed in the case of Kaposi's Sarcoma. In black men, Kaposi's Sarcoma was the most prevalent cancer (23.8%) and second most prevalent in women (11.9%) in 2006. A decline to 14.8% (second in prevalence) in black men and only 6.9% (third in prevalence) in black women has been observed by 2013.

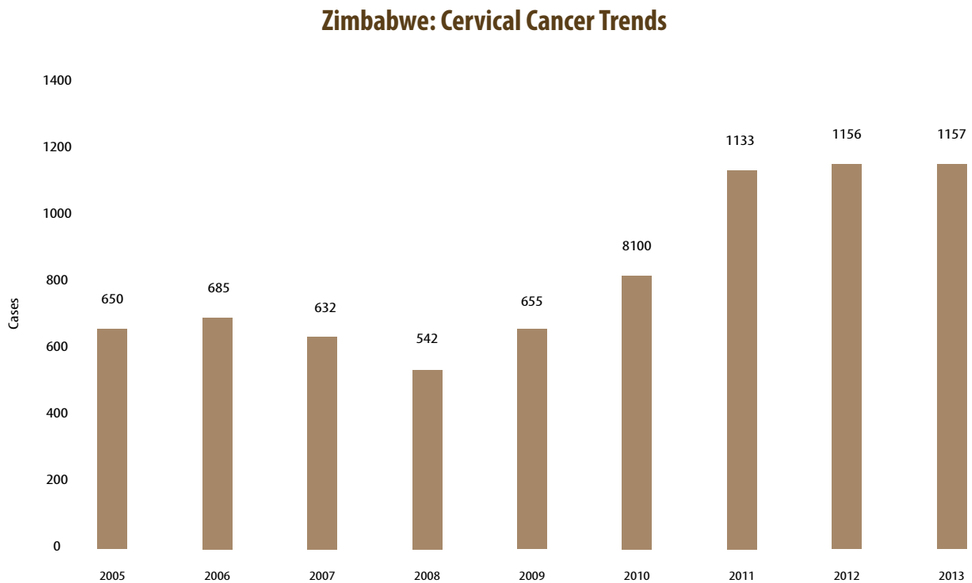

Figure 12: Cervical Cancer Trends in Zimbabwe: 2005-2013 (ZNCR)

As with other preventable cancers, a call to identify and implement preventive measures for HIV-related cancers is important. Within the Zimbabwe National Strategic Plan 2010-2015, several HIV prevention strategies have been adopted. The focus is on promoting safer sexual behaviour and on a package of health sector interventions such as PMTCT, HIV testing and counselling. HIV prevalence has declined over the past decade from 29.3% (1998) to 15.6% (2007). Such measures will also have an impact on the reduction in transmission of the human papilloma virus (HPV) and will add to the control of other cancers such as cervical cancer.

Male voluntary circumcision is another measure that has been adopted in Zimbabwe. Randomised controlled trials from Uganda, Kenya and South Africa demonstrated a reduction in the risk of female to male transmission of HIV with this practice. Additionally, studies have shown that male circumcision also reduces the chances of occurrence of penile cancer and cervical cancer. It is estimated that around 11% of Zimbabwean men are circumcised. It is undertaken for religious reasons among Chewa and Muslims, for cultural reason in other groups such as Xhosa, Tonga or Binga but also for medical reasons.

Education of Cancer Care Professionals (Human Resource Development)

It has been through efforts in human resource development of cancer care professionals that the effect of migration of skills has been cushioned. Training of Radiation Oncologists, Radiographers and recently Medical Physicists and Oncology Nurses is available in Zimbabwe. The postgraduate training of Radiation Oncologists (MMed Rad & Onco) and other specialties that are essential for a robust multidisciplinary approach to cancer management e.g. various surgery disciplines, pathology, internal medicine, gynaecology is done by the University of Zimbabwe - College of Health Sciences (UZ-CHS). Radiation oncology training was set up in the early 90s through a WHO funded regional initiative. The UZ-CHS also offers undergraduate programs Diagnostic and Therapy Radiography (BSc Hons.).

The School of Radiography is an Associate College of UZ-CHS and offers Radiography training at diploma level within the same teaching hospital. Oncology nursing is facilitated by the School of Nursing. These 2 schools are run by the MOHCC.

The training of Medical Physicists was commenced in 2015 at the National University of Science and Technology.

The Cancer Community

There are a number of local voluntary organizations that are involved in cancer efforts in Zimbabwe. These include The Cancer Association of Zimbabwe, KIDZCAN, Island Hospice, National Cancer Alliance of Zimbabwe, Brain Tumour Association and Breast Cancer Alleviation of Zimbabwe. They complement government efforts in cancer prevention and early detection through advocacy and health promotion.

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Chapter 16t

Northern Africa

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* This chapter should be referenced as: Eser S. Northern Africa. In: Boyle P, Ngoma T, Sullivan R, Ndlovu N, Autier P, Stefan S, Fleming K and Brawley OW. The State of Oncology in Africa 2015. iPRI Scientific Publication 4, iPRI, Lyon, France (2016).

North African countries bordering the Mediterranean (Morocco, Algeria, Tunisia, Libya and Egypt) have a combined population of around 190 million. Between 3.8% (of the population of Tunisia) and one third (of the population of Libya) live below the poverty level: the other countries are around 20%. Where data are available, the percentage of GDP spent on Health is low (less than 5%).

Life expectancy figures generally do not differ so much from the figures in more developed parts of the world in contrast to the lower life expectancy figures in the other African regions and Tunisia has the highest, Sudan has the lowest life expectancies at birth in Northern Africa (Figure 14.3.1 on the next page) (World Health Statistics, 2009).

Over the last few years, Cancer Registries in North Africa (Morocco, Algeria, Tunisia, Libya and Egypt) have increased in number from one (Setif, Algeria) to nine (Morocco: Rabat, Casablanca; Algeria: Alger, Setif; Tunisia: Northern Tunisia, Sousse (Centre), Sfax (south); Libya: Benghazi; Egypt: Gharbiah, Aswan, Minia, Damieta) and currently covers 13% of the total regional population and are producing quite good, acceptable quality, according to available indicators (American Cancer Society, 2011; Zanetti et al, 2010; Tazi, Benjaafar and El-Raki, 2005; Benider et al, 2004; Hamdi Chérif et al, 2008; Parkin et al, 2005; Institut National de Santé Publique Registre des Tumeurs d'Alger, 2006 ; Ben Abdallah et al, 2006 ; Korbi et al, 2008 ; Sellami et al, 2007 ; El Mistiri et al, 2004a ; El Mistiri et al, 2004b ; Amal et al, 2008 ; El Mistiri et al, 2007 ; Inrahim and Mikhall, 2010 ; Seif Eldein et al, 2007 ; Barchana et al, 2009 ; Registre des Cancers de la Région du Grand Casablanca, 2007 ; Tazi, El-Raki and Benjaafar, 2013 ; Missaoui et al, 2010).

These quite reliable data made it possible to prepare this section. There are some other registries also in the region with less reliable data, i.e. Oran Cancer Registry in Algeria. Two reports prepared using data of different years (1998-2005 and 2006) which has released from this registry contain contradictory results (i.e. lung cancer AAIRs (Age adjusted incidence rate on World Standard population) in men 21.4 and 6.8 in 1995-2005 and 2006 reports respectively) (Fouatih et al, 2008; Ferlay et al, 2010). The figures considered as less reliable were not used in this chapter.

Despite to the reported relatively low incidence and mortality rates at present in Africa, the cancer burden is projected to almost double in coming decades due to the aging and population growth. Furthermore it seems likely that the cancer burden will be even higher because of the

changes of behaviours and lifestyles in the region towards more risky ones associated with economic development, such as smoking, unhealthy diet and less physical activity (American Cancer Society, 2010).

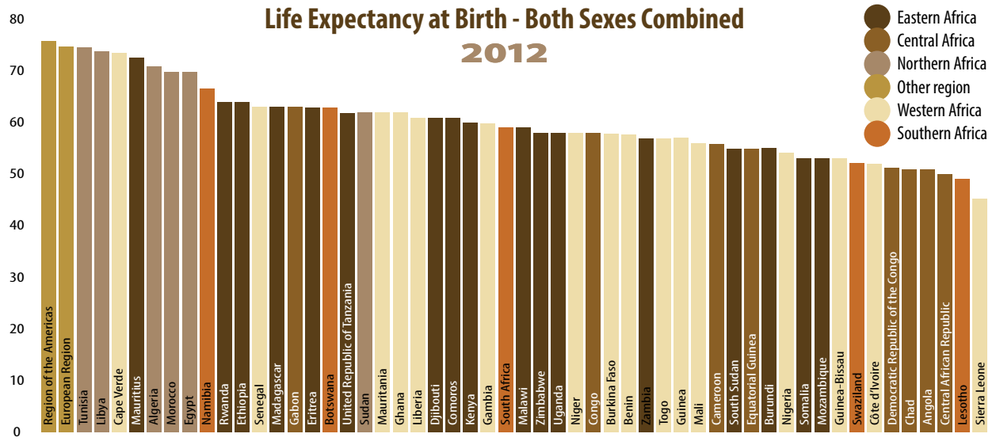


Figure 1: Life expectancy at birth, both sexes combined

In consequence of the differences in exposure to the most common risk factors, diagnostic possibilities (lack of diagnostic and screening services), public awareness of early signs and symptoms, and availability of treatment, not only the incidence, mortality and survival rates but type of major cancers and stage at diagnosis as well in Africa, vary significantly from that in developed parts of the world. For instance, the infection related cancers such as Kaposi's Sarcoma, liver, cervical cancers dominate the patterns while cancers such as lung, breast and colorectal cancers associated with behaviours related with economical development (i.e. smoking, less activity, obesity) or cancers like prostate cancer related with overdiagnosis have lower incidence rates than shown in the developed populations.

It looks like the differences between Africa and the developed world in cancer incidence and mortality patterns actualize also across regions within Africa depending on the regional differences in socioeconomic, cultural and other environmental factors that effect the exposure levels to the known risk factors (American Cancer Society, 2010).

In Northern Africa in both sexes, cancer pattern by type of major cancers resembles to the pattern in developed world with only remarkable exceptions of colorectal cancers with low frequency and liver cancer with high incidence rates, rather than that in the rest of Africa where infection-related cancers are the most frequent. The commonest cancers are lung, liver, bladder, colorectal, NHL (Non-Hodgkin Lymphoma), leukaemia, and prostate cancers in men; breast, uterine cervix, colorectal, NHL, liver, thyroid and ovary cancers in women (Figures 14.3.2 & 14.3.3, Tables 14.3.1 & 14.3.2).

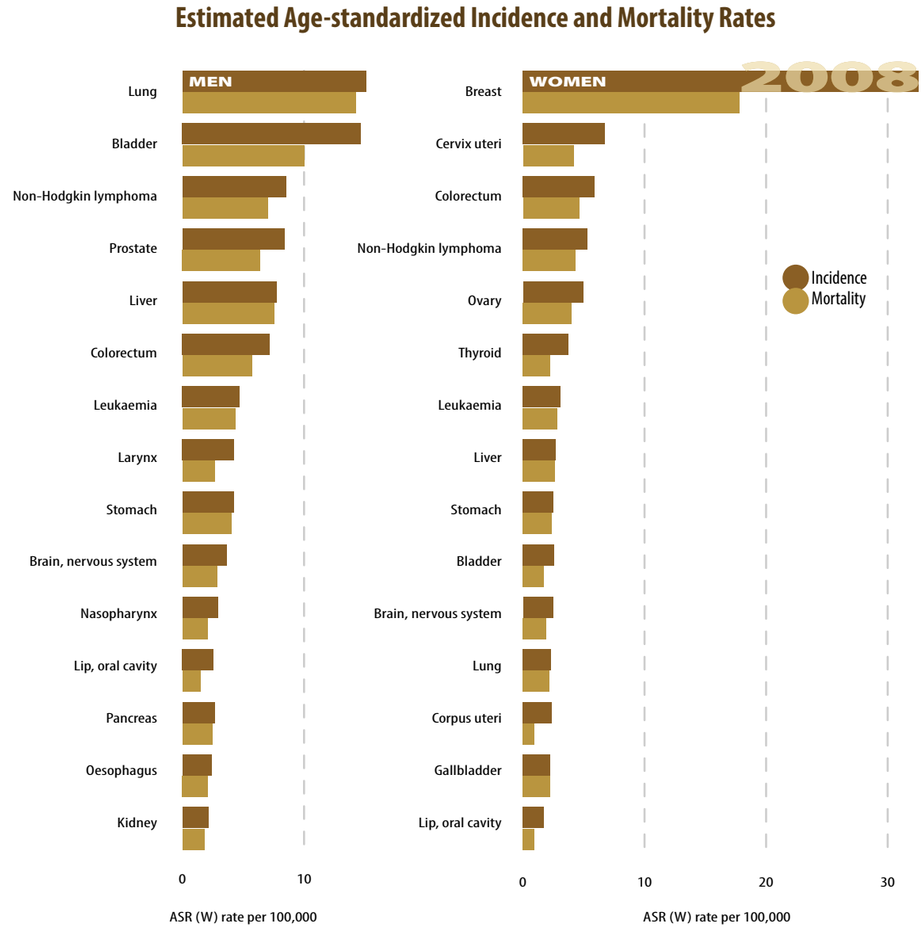


Figure 2: Estimated age-standardized incidence and mortality rates: men

Source: Ferlay J, Soerjomataram I, Ervik M, et al. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Available from: http://globocan.iarc.fr, accessed July 7, 2014.

Table1: Estimated incidence, mortality and 5-year prevalence: men

Cancer	Incidence		Mortality	
	(%)	ASR (W)	(%)	ASR (W)
Lip, oral cavity	2.1	2.3	1.1	1
Nasopharynx	2.7	2.7	2.1	1.7
Other pharynx	0.9	0.9	0.9	0.8
Esophagus	1.8	2	2.1	2
Stomach	3.6	3.9	4.1	3.7
Colorectum	6.6	7	6.3	5.5
Liver	6.6	7.5	8	7.4
Gallbladder	0.9	1	1	0.9
Pancreas	2	2.3	2.4	2.2
Larynx	3.4	4	2.4	2.4
Lung	12.7	14.9	14.7	14
Melanoma of skin	0.3	0.4	0.2	0.2
Prostate	6.4	8.1	6.1	6.2
Testis	0.7	0.6	0.5	0.3
Kidney	1.8	1.9	1.8	1.5
Bladder	12.5	14.5	10.1	9.9
Brain, nervous system	3.5	3.3	3.3	2.5
Thyroid	1.1	1.1	0.9	0.8
Hodgkin lymphoma	2.1	1.7	2.1	1.4
Non-Hodgkin lymphoma	8.4	8.4	8.4	6.9
Multiple Myeloma	1.5	1.7	1.7	1.6
Leukaemia	4.6	4.4	5.3	4.1
All cancers excl, non-melanoma skin cancer	100	109.2	100	89.5

Incidence and mortality data for all ages, 5-year prevalence for adult population only
ASR (W) and proportions per 100,000

Table 2: Estimated age-standardized incidence and mortality rates: women

Cancer	Incidence		Mortality	
	(%)	ASR (W)	(%)	ASR (W)
Lip, oral cavity	1.6	1.6	1	0.8
Nasopharynx	1.1	1	1	0.6
Other pharynx	0.7	0.8	0.9	0.6
Esophagus	1.5	1.6	2.1	1.5
Stomach	2.3	2.4	3.2	2.3
Colorectum	5.8	5.8	6.6	4.5
Liver	2.3	2.5	3.4	2.5
Gallbladder	1.9	2.1	2.7	2
Pancreas	1.2	1.3	1.8	1.3
Larynx	0.2	0.2	0.2	0.1
Lung	2	2.2	2.8	2
Melanoma of skin	0.3	0.3	0.3	0.2
Breast	33.8	32.7	26.3	17.8
Cervix uteri	6.4	6.6	5.6	4
Corpus uteri	2	2.2	0.9	0.7
Ovary	4.8	4.8	5.3	3.7
Kidney	1.4	1.4	1.7	1.1
Bladder	2.2	2.4	2.2	1.6
Brain, nervous system	2.5	2.2	2.8	1.7
Thyroid	3.6	3.4	2.7	1.9
Hodgkin lymphoma	1.4	1.1	1.7	0.9
Non-Hodgkin lymphoma	5.1	5	6.1	4.1
Multiple Myeloma	1.1	1.2	1.5	1.1
Leukaemia	3.2	3	4.5	2.8
All cancers excl. non-melanoma skin cancer	99.9	98.9	100	68.2

Incidence and mortality data for all ages.
ASR (W) and proportions per 100,000.

In men, lung cancer was the most commonly diagnosed and the leading cause of cancer deaths according to Globocan 2008 estimates in the region. However with the observed significant increase in incidence and mortality of liver cancer, particularly in Egypt based on data from Garbiah registry (Amal et al, 2008; Seif Eldein et al, 2007), it can be expected that the liver is the most common cancer site in the region at present. Chronic infections with hepatitis C virus (HCV) in Northern Africa are the major causes of liver cancer. Schistosoma is a prevalent parasite (blood fluke) in the region which caused chronic liver disease and bladder cancer especially during 1960s, 1970s mainly in Egypt. As a result of HCV contaminated injection equipment during mass treatment campaigns against Schistosoma, HCV associated liver cancer has become the major cancer in Egypt. Bladder cancer is one of the common cancers in the region. Egyptian men have had the highest bladder cancer incidence rates worldwide (Parkin

et al, 2005). Bladder cancer is caused by smoking and occupational chemical exposure in Schistosoma-free regions, i.e. developed countries, while about 40% of the disease in most parts of Africa is caused by Schistosoma haematobium.

The incidence and mortality rates of Kaposi's Sarcoma (an HIV-associated cancer caused by human herpes virus) in Northern Africa are 20 times lower than in Eastern Africa due to the lower HIV/AIDS prevalence (Pakin et al, 2005).

In women, breast cancer is the most frequent cancer and the leading cause of cancer death among women in the region. Based on data from the Algeria (Setif) cancer registry, breast cancer incidence rates have nearly doubled over the past 20 years, though the rates still remain about one-fifth those in the Western countries (El Mistiri et al, 2007; Ibrahim and Mikhall, 2010). Cervical cancer is the second most common diagnosed and second leading cause of cancer death in the Northern Africa in contrast to Eastern Africa where the cervical cancer is the most common and leading cause of cancer with very high incidence and mortality rates due to the high prevalence human papillomavirus (HPV) infection and lack of Pap test screening services for prevention and early detection of the disease (Parkin et al, 2005).

The cancer pattern does not show substantial diversity across the region among the countries. Across the North-African Region, breast cancer is the most common cancer and leading cause of cancer deaths among women. In men, lung is the commonest cancer in Algeria, Libya, Morocco and Tunisia while liver in Egypt and NHL in Sudan are the most frequent diagnosed cancers (Table 14.3.3). The distribution of the different cancer sites seems quite homogeneous across the region, with a few exceptions (Tables 14.3.4a and 14.3.4b):

- High level of liver and bladder cancer incidence in Egyptian men (particularly in Gharbiah)
- High rates of non-Hodgkin lymphomas in both sexes in Gharbiah, Egypt
- High breast cancer incidence rates in women in Algiers and Aswan.
- High rates of cervical cancer in the west of the region, namely in Algeria and Morocco

Lower incidence rates of nasopharyngeal cancers in both sexes in Egypt. The rates of nasopharyngeal cancer are intermediately high in all the North African countries (but Egypt), compared to those observed in developed countries. Nasopharyngeal carcinoma has a strong relation with Epstein-Barr virus primarily in endemic regions.

Table 3: Most frequent cancer sites by gender in Northern African countries

Country	Men	Women
Algeria	Lung	Breast
Egypt	Liver	Breast
Libya	Lung	Breast
Morocco	Lung	Breast
Sudan	NHL	Breast
Tunisia	Lung	Breast

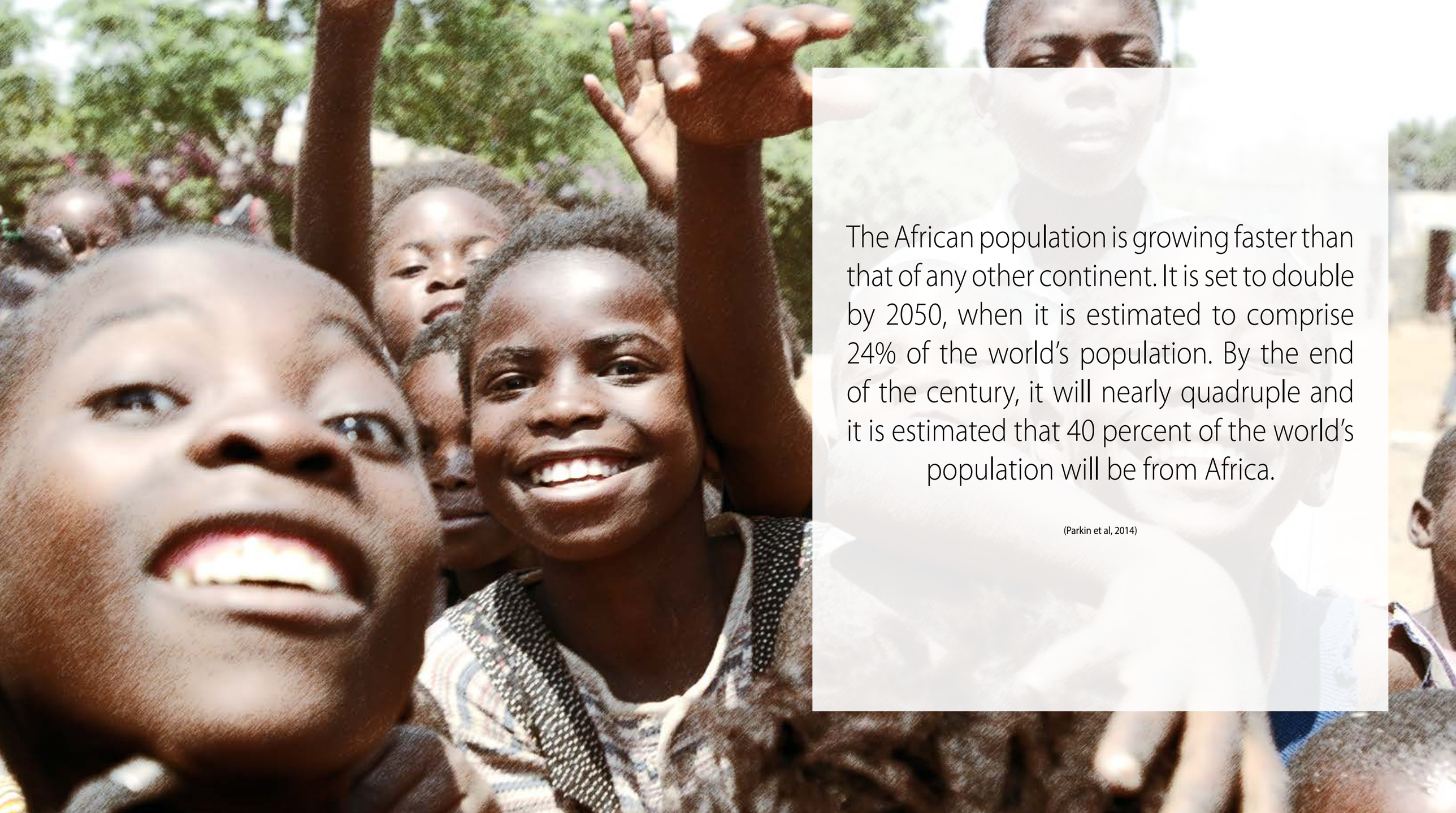
Table 4: Incidence rates (per 100,000 age-standardized on world population) of major cancers in the regions of North African Registries, Men

	Se'tif, Algeria (1998-2002)	Algier, Algeria -2006	Gharbiah, Egypt (2000-2002)	Aswan, Egypt -2008	Casablanca, Morocco -2004	Rabat, Morocco (2006-2008)	Benghazi, Libya -2004	Northern Tunisia (2004-2008)	Sfax, Tunisia (2000-2002)	Sousse, Tunisia (2003-2006)	Sudan (Globocan 2008)
Population (M)	684,636	1,478,947	1,873,805	539,617	1,828,291	332,556	832,346	2,382,720	417,3	250,5	20,817,000
Nasopharynx	5.4	3.7	1.1	1.1	4.2	2.3	4	3.6	3.8	2.8	2.8
Stomach	7.1	7.9	3.1	4.1	4.8	5	4.5	6.1	3.9	4.4	2.5
Colorectum	6.6	14.8	7.1	5.5	8.1	12	14.3	11.6	11.5	12.4	5.4
Liver	1.1	1.2	21.7	17.4	0.7	2.1	4.9	n.a	1.9	2.2**	5.6
Larynx	2.8	6.3	4	6	6.1	3.7	5.3	5.6	4.6	4.9	2
Lung	19.9	24.2	13.6	11.2	25.9	24.9	26.7	32.5	24.6	32.6	2.4
Prostate	7.5	11.2	8.8	9.2	13.5	22.9	9.8	11.8	11.5	11.2	9
Bladder	4.5	16.7	26.9	18.6	8.7	9.7	12.6	13.7	16.9	16.9	3.1
NHL	5.3	3.6***	17.1	2.2	7.2	8.2	6.4	5.5	7.6	6	8.2
Leukaemia	n.a.	2.4***	6	7.7	2.7	4	5.1	3.1	7.2	n.a.	6
All sites but C44	86.3	143	154.8	140.7	113	132.3	126.8	133.2 *	123.7	143.8	81.6

Table 5: Incidence rates (per 100,000 age-standardized on world population) of major cancers in the regions of North African Registries, Women

	Se'tif, Algeria (1998-2002)	Algier, Algeria -2006	Gharbiah, Egypt (2000-2002)	Aswan, Egypt -2008	Casablanca, Morocco -2004	Rabat, Morocco (2006-2008)	Benghazi, Libya -2004	Northern Tunisia (2004-2008)	Sfax, Tunisia (2000-2002)	Sousse, Tunisia (2003-2006)	Sudan (Globocan 2008)
Population (F)	680,852	1,455,244	1,823,660	534,514	1,883,970	309,444	799,705	2,318,400	403,3	244,3	20,529,000
Nasopharynx	1.7	1.8	0.3	0.2	1.2	1.3	1.4	1.5	0.9	0.9	1.4
Stomach	3.1	7.4	2	3.4	2.7	3.2	2.1	3.7	3	2.5**	0.9
Colorectum	6.6	11	4.7	5.1	5.8	9	12.3	9.5	9.1	10.1	3
Liver	0.8	0.1	4.2	8.7	0.6	1.5	2.5	n.a	0.6	0.7**	2.4
Breast	18.8	60.5	41.9	63.9	36.4	43.4	23.3	31.8	28	28.3	24.6
Cervix uteri	11.6	9.5	2	0.9	15	13	3.5	4.2	2.3	4.9	7
Ovary	2.1	7.3	5.2	9.1	5.3	3.2	3.9	4.3	3.7	4.6	5.8
Thyroid	3.6	8.6	2.5	4.5	6.7	3.9	3.9	3.3	3	2.6	2.3
NHL	3.8	1.2***	9.9	1.6	4.7	4.2	4.5	3.8	4.1	4.7	3.7
Leukaemia	n.a.	1.5***	4.6	6.6	2	2.7	5.5	2.3	4.4	n.a.	2.5
All sites but C44	80.3	164	118	164	11.7	112.5	102.5	101.4 *	89.1	102	82.2

* All sites including C44 n.a. not available at the source | ** 1998-2002 | *** 1993-97



The African population is growing faster than that of any other continent. It is set to double by 2050, when it is estimated to comprise 24% of the world's population. By the end of the century, it will nearly quadruple and it is estimated that 40 percent of the world's population will be from Africa.

(Parkin et al, 2014)

Data from the Kenyan Ministry of Health projects that by the year 2025, NCDs will overtake infectious diseases.

Chapter 17

The Eldoret Model

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* This chapter should be referenced as: Busakhala N, Asirwa FC, Loehrer PJ. The Eldoret Model. In: Boyle P, Ngoma T, Sullivan R, Ndlovu N, Autier P, Stefan S, Fleming K and Brawley OW. The State of Oncology in Africa 2015. iPRI Scientific Publication 4, iPRI, Lyon, France (2016).

The prevalence of cancer is higher in low and middle income countries (60%) compared to high income countries and these figures are projected to rise by over 75% by the year 2030 unless intervention is done. In some low income countries, the rise may be by 93 % (Bray et al, 2012; de Martel et al, 2012; Parkin et al, 2014).

Kenya, like most other developing countries is undergoing an epidemiologic shift of disease patterns characterized by increasing prevalence of Cancer and other Non-Communicable diseases and a double strain on health care resources. As shown in Figure 1, these emerging lifestyle and genetic diseases previously associated with high income countries are not replacing infectious diseases but adding to them (Ministries of Medical Service, 2011; Mutuma GZ, 2006). Cancer is ranked third among causes of death in Kenya, after infectious and cardiovascular diseases. The annual incidence is about 28,000 cases with mortality estimated at 22,000 cases (Etyang et al, 2014). Data from the Kenyan Ministry of Health projects that by the year 2025, NCDs will overtake infectious diseases as shown in Figure1.

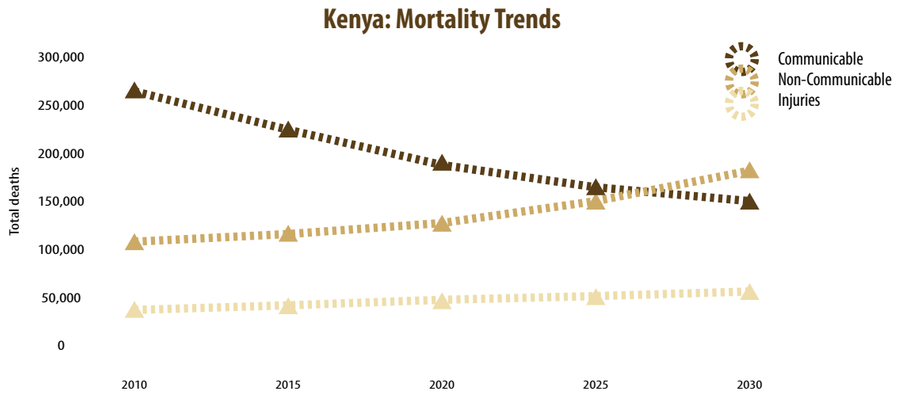

Figure 1: Mortality trends in Kenya

Source: Ministries of Medical Service, Public Health and Sanitation, Comprehensive National Health Policy Framework, 2011

We describe development of a cancer control and prevention program at Moi Teaching and Referral Hospital (MTRH) /Moi University, leveraging the infrastructure initiated by the Academic Model Providing Access to Health care (AMPATH) Program for treatment of HIV/AIDS.

What is AMPATH?

The acronym AMPATH was initially derived from the Academic Model for the Prevention and Treatment of HIV/AIDS (Einterz et al, 2007). As the name indicates, the initial goal of the program was provision of HIV care at a time when the epidemic was at its peak but hardly any care existed. The program was initiated in 2001 as a partnership between Moi University School of Medicine, Indiana University School of Medicine, and Moi Teaching and Referral Hospital (American Cancer Society, 2010). Moi Teaching and Referral Hospital (MTRH) is the second largest Public Hospital in Kenya serving the entire western Kenya where about 50% of Kenya's population live. Over the years, AMPATH has expanded to include primary health care and chronic disease management including cancer. AMPATH currently treats over 140,000 patients for HIV in 60 Government of Kenya's Ministry of Health facilities in western Kenya as shown in Figure 2. In addition to HIV care, AMPATH educates orphaned children and partners with volunteer lawyers and other legal experts to provide free legal services to HIV-positive patients. All AMPATH programs are initiated and led by Kenyans in a collaborative partnership.

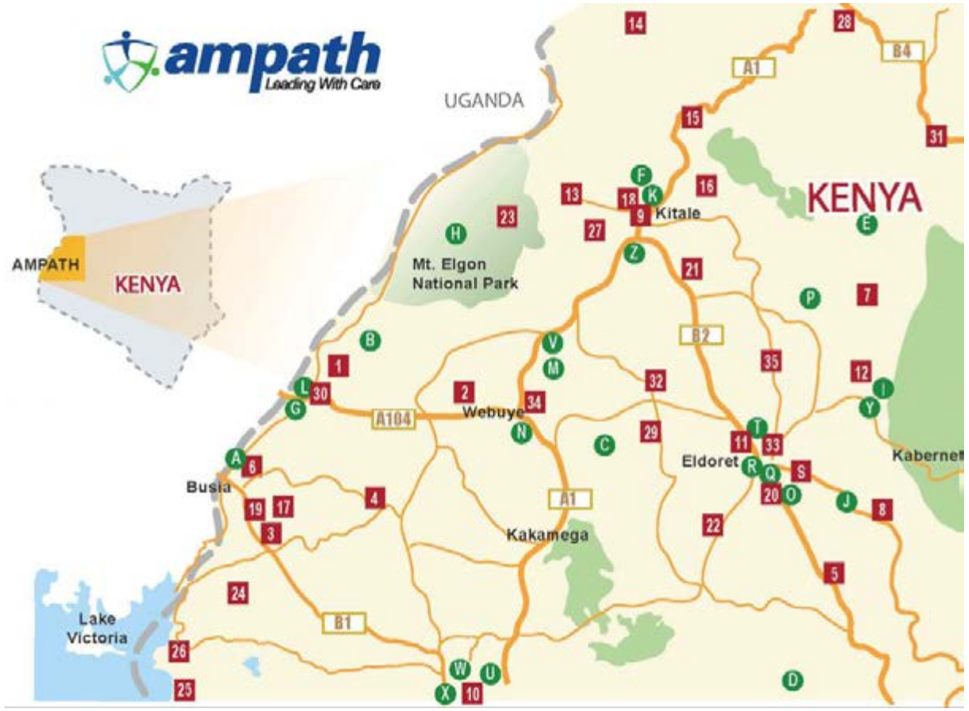

Figure 2: AMPATH sites

To achieve sustainability, AMPATH has enrolled over 10,000 patients in income security programs including Agricultural extension services, micro-finance and small business initiatives. In partnership with the UN Food Program, it feeds 31,000 patients daily. Once an AMPATH nutritionist finds that a patient is food insecure, they are provided with a nutrition prescription assuring access to 50% of daily nutrition requirements for themselves and their dependents for up to 1 year or until they regain their strength to provide for themselves. To ensure sustainability, patients are trained on profitable farming techniques on their farms. Successful farmers are contracted by AMPATH to sell food to the nearby AMPATH clients with vouchers.

To encourage patients to raise capital, Project officers initiate the creation of self-regulating savings groups. Groups are made up of 15 - 30 self-selected members who meet regularly and save money through the purchase of shares which form a loan fund. At the formation stage of the group, members are expected to draft a Group Constitution that stipulates group regulations and mandates operational structures of the group. The groups issue loans to members with a 10% interest rate. Income is also generated from fines paid by members due to lateness for meetings or loan re-payment. At the end of one cycle (12 months), each member is refunded their shares, and interest earned from loans is divided among the

group members. Since 2010, most of the groups have shared out twice. To date this project has 6,484 clients (81% female, 19% male), 338 groups, a cumulative savings of $101,945, a social fund of $11,829 and interest earned of $41,000. The outstanding loan amount is $103,675. Clients with a good loan repayment history and who are operating a business are being linked and endorsed by AMPATH to access interest-free loans from KIVA ZIP. KIVA ZIP is a web-based non-profit organization with a mission to connect people through lending to alleviate poverty. Leveraging the Internet and a worldwide network of microfinance institutions, KIVA lets individuals lend as little as $25 to help create opportunity around the world. A borrower on KIVA ZIP has the opportunity to access a community of lenders who can serve as brand ambassadors and potential customers for their business.

Imani workshop is another AMPATH enterprise for HIV positive artisans which produces high quality crafts for income generation. Imani employees earn a living by producing handmade goods such as jewellery, fabric bags, handmade paper and beadwork.

In partnership with Proctor and Gamble, AMPATH is able to provide water treatment packets to patients, establish safe community water wells and educate communities on safe drinking-water practices. In 2015, Maji Safi International, AMPATH's safe water business model, was launched with the help of Purdue University Centre for Entrepreneurship, Indiana University Kelley School of Business, and Dow Agro Sciences. The business was created in hopes of creating a sustainable means to providing access to safe drinking water in resource-constrained settings.

AMPATH Oncology Institute

HIV-related cancers mainly Kaposi's Sarcoma, Cervical Cancer and Non-Hodgkin's Lymphoma led to the development of Oncology services within AMPATH. Functional structures were developed by MTRH/Moi, Indiana and Brown Universities. In 2008, the service was upgraded to a formal department of Haematology and Oncology by MTRH and elevated into a full division in 2012. The AMPATH- Oncology Institute (AOI) was formed in 2010, bringing on board all members of the AMPATH fraternity with each member volunteering on specific roles.

The mission of the AMPATH Oncology Institute is to be the premier cancer centre in Sub-Saharan Africa, which is noted for excellence in prevention, treatment and palliative care. The vision is that the AOI will become the model for international collaboration in cancer care, education and research in resource-constrained settings.

Organizationally, the AOI has three Clinical Pillars:

1. Screening and Prevention – identification of at-risk populations, active reduction of risk through screening and early intervention will be the focus of this theme. Approaches include implementation of screening and prevention programs in both adult (e.g. cervical and breast cancers) and paediatric populations (e.g. retinoblastoma screening). Key elements include building a screening and early detection infrastructure, immunization as well as education of practitioners and at-risk populations.

2. Diagnosis and Treatment – this clinical pillar is potentially the most expansive, and covers coordination of clinical care services to establish a standard for oncology care, and to create a research engine that is capable of redefining that standard regularly. Currently, the AOI prioritizes diagnosis and treatment programmes by those diseases with the highest impact on quality of life and lost life-years.

3. Palliative Care – with the majority of patients presenting with very late-stage disease, a major focus of this pillar is the expansion of an effective palliative care and home hospice program.

For each of these Clinical Pillars, there is substantial need for resources and intellectual effort to create a sustainable organization for the development of a premiere cancer program in sub-Saharan Africa. To focus upon construction of this effort, the following cross-cutting areas direct the development of the AOI:

- Care delivery –Chemotherapy and other medical supplies, pathology support (immunohistochemistry stains, microscopes), imaging (CT scans, mammography, and ultrasound), transportation and temporary housing are required to enable delivery of care for patients from a wide catchment area.

- Physical infrastructure – The development of the physical infrastructure is needed for the AOI to adequately deliver the care and to address the clinical mission. This includes the outpatient (for screening, prevention and treatment (chemotherapy and radiation therapy)) and inpatient facilities. The new outpatient facility was opened in 2015. An improved and dedicated inpatient ward is almost complete for optimal treatment of adult cancer populations. Paediatrics is still housed in the general paediatrics hospital buildings.

- Human capital – Expansion of the personnel with specialized education is required to adequately deliver care. Curriculum has been developed for various programs. Our focus is towards the development and the training of medical, radiation, and surgical oncologists; nurses; pathologists; and support staff for optimizing health care delivery and research in limited resource settings.

- Research – The research and educational infrastructure must focus on relevant clinical, translational and population research to impact and optimize health care delivery. This includes training opportunities in clinical research trials with opportunities for pilot projects relevant to the population in the catchment area of western Kenya. This is also pursued by AMPATH Oncology Institute.

- Medical informatics – Informatics infrastructure is under development to support both the clinical and research missions of AOI including an annotated tumour registry.

- Patient advocacy and education- The stigma and myths about cancer and the futility of treatment abound. Development of an active patient advocacy program that can assist in the dissemination of knowledge throughout the catchment area is required. Patient support groups for breast cancer and colorectal cancers has been established.

Structure of Services within the AOI

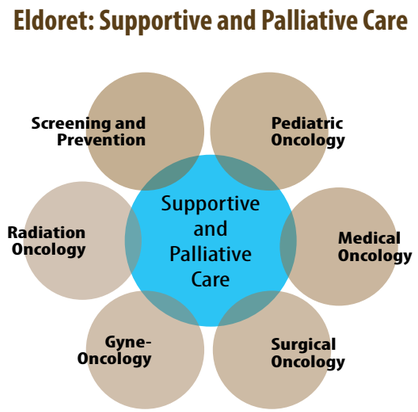

Figure 3: Supportive and Palliative Care

The AMPATH-Oncology Institute (AOI) relies on limited intra-institute services and personnel and extensive coordination with existing AMPATH, and de facto, Moi Teaching and Referral Hospital/Moi University, clinical services and core facilities. At present there are 6 clinical services within the AOI – four of which are already well established cancer programs (Medical Oncology, Paediatric Oncology, Gynaecology Oncology, and Screening Services). Surgical and Radiation Oncologic services are developing programs. There is some overlap between the clinical services – for example, screening services would be informed by both Gynaecology Oncology (cervical cancer), Medical Oncology (breast cancer), and Paediatric Oncology (retinoblastoma).

The AOI has additional Core Services, shared by the Clinical Services, including: the Oncology Pharmacy, Pathology and Cancer registry, Data and Clinical Trials management, Nutrition, Oncology Nursing, and Radiotherapy. The Oncology Pharmacy has also been well established as a functional Chemotherapy Service and Dispensing Pharmacy; the capacity as a Research Pharmacy is growing with current focus on pharmacovigilance. A number of other services exist in which the AMPATH Oncology Institute will need to coordinate for the delivery of clinical care as well as research. This will help to streamline the interface between the AOI and the broader AMPATH-supported resources and core facilities minimizing redundancy and maximizing efficiency.

Public-Private Partnerships

The support of key donors has to date allowed a dramatic expansion of services through AMPATH-Oncology. Nearly 10,000 patient visits to AMPATH-Oncology occur each year with approximately 10-12,000 women also being screened for breast and 20,000 for cervical cancers annually. The AOI has been highlighted by the NCI Centre for Global Health (NCI Center for Global Health, 2015) and has been recognized as the model for comprehensive cancer care in low to middle income countries as highlighted by Dr. Peter Boyle and the International Prevention Research Institute (Conversation with The Cancer Letter, 2014; The State of Oncology, 2013). AMPATH has been the site for three consecutive ASCO Multidisciplinary Care Management Conferences in 2012, 2013 and 2016, and NCI Grant Writing Workshop in 2013. This underscores the tremendous return on

investment created by the support of industrial partners and other philanthropists. We will continue to work with these and other international partners to provide funding for patient care costs and working with the Kenyan Ministry of Health to provide more sustainable support through insurance plans for cancer patients in Kenya. Towards this end, the National hospital insurance fund (NHIF), has in 2016, started re-imbursement of cancer services especially chemotherapy treatments for up to USD 250 per cycle. This is augurs well for the sustainability of our programs.

Organizational Structure of AOI

Functionally, the top level of organization of the AOI is the Steering Committee comprised of representatives from Kenya and the North America/European Partners. Field operations are headed by the Co-Directors (Drs. Chite Asirwa (Indiana University Simon Cancer Centre), Busakhala (MTRH) and Omenge (MTRH)) on ground in Kenya. The Co-Directors have the ultimate responsibility of both implementing the multi-year plan, as well as reporting on progress and difficulties to the Steering Committee. Additionally, the Co-Directors are responsible for the interface with other AMPATH, MTRH and Moi University organizational entities.

Leadership of AOI

Administration and oversight is provided by the AOI steering committee which is composed of representatives from collaborating institutions. The steering committee holds monthly teleconferences and communicates continuously through email. Departmental heads submit monthly reports to the two Co-Directors who present them to the steering committee.

The steering committee also works through sub-committees which hold additional monthly teleconferences. These include the Finance committee, Research Working group, Radiation Oncology working group and Paediatric Oncology working group.

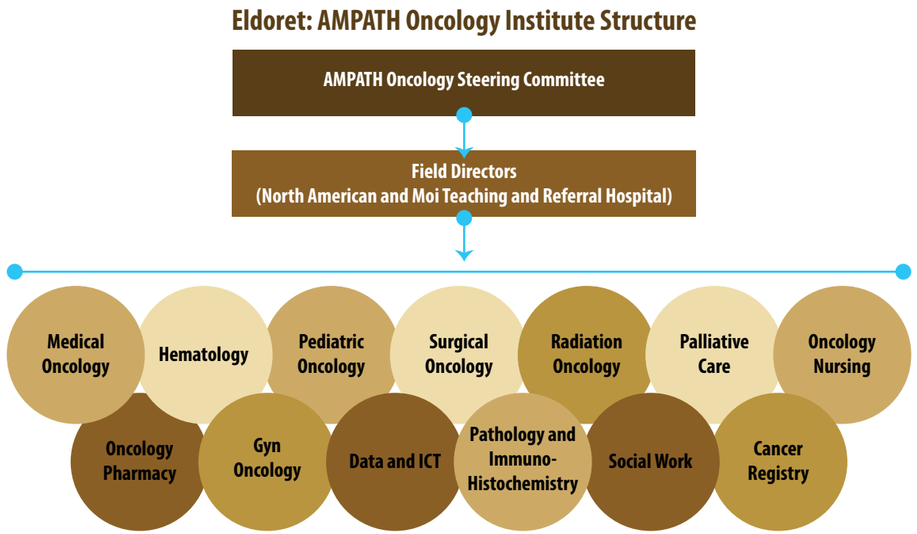

Figure 4: Organizational Structure of AMPATH Oncology Institute

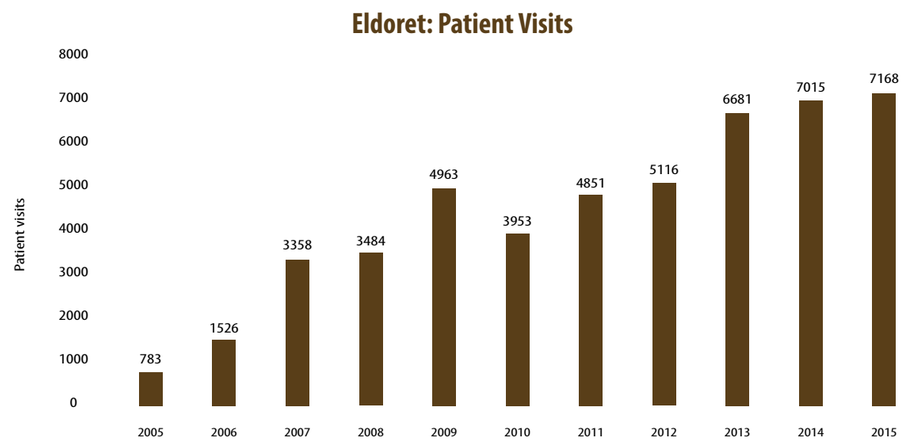

Figure 5: Growth of AMPATH Oncology Institute

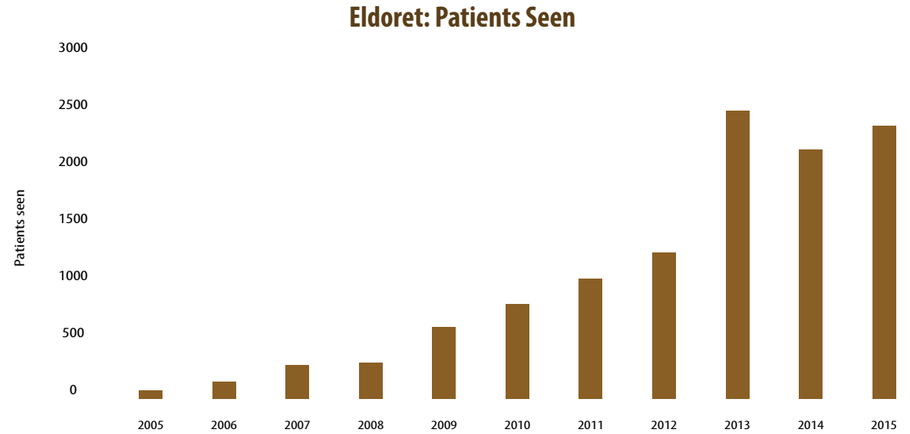

Figure 6: Actual number of patients seen

By 2014, AOI had treated over 5,000 patients and screened over 30,000 people for Cancer.

Strategic Planning

All aspects of the program are protocol-based with intense programmatic monitoring and evaluation, allowing rapid response to the changing needs of our patient population. The program has had approximately 20% annual growth for the last several years (refer to Figure 4 and 5). We expect to continue to grow minimally at this rate, and so expect the need for, and cost of, chemotherapy to rise proportionally. We have balanced sustainability of service provision and access to services through provision of chemotherapy to patients at cost and a credit system for patients who cannot afford chemotherapy. The money is managed by the AMPATH Research and Sponsored Projects Office (RSPO).

We have successfully contained costs through several processes:

- Care Rationing – based on expert opinion, cancer presentations in Kenya were divided into low priority diseases, medium priority diseases, and high priority diseases, based on expected response rates, expected benefit, and volume of patients seen with that presentation.
- Protocol-based Therapy – based on expert opinion and literature review, all chemotherapy to be purchased and offered through AOI are developed in consultation, based on the market-cost of drugs, local availability of drugs, and expected benefits.
- Bulk purchasing –the department has been able to project needs, and make bulk quarterly purchases based on predicted needs.
- Integration of Haematology and Oncology services

- Weekly tumour boards and multi-disciplinary clinics where clinicians discuss and adapt accessible standard practice.
- Active participation in Clinical trials and research which allows participants to receive study-provided treatment.
- Task-Shifting where general nurses and clinical officers are trained to perform specialized oncology duties.
- Promoting enrolment in the National Health Insurance Scheme (NHIF). NHIF is a state corporation that recently extended insurance cover to cancer.

Training

Through AOI, curriculum developments and establishment of training programs has been done for Medical Oncologists, Gynaecology Oncologists, radiation oncologists, radiotherapy technicians, Oncology clinical officers and a radiation physicist. In addition, curriculum for Medical Oncology is at advanced stages of approval in Moi University. Nursing Oncology training begins later this year.

Challenges

- Lack of local research funding
- High rates of loss-to-follow up of Patients making it difficult to have accurate treatment outcomes data.
- Lack of radiation services
- Donor dependency
- Lack of training facilities

Lessons learned

1. Once Cancer services are established, they attract both governmental and non-governmental support
2. Integration of cancer services with existing infrastructure should be done where possible. Some Professional bodies now provide guidelines based on available resources (American Cancer Society, 2010; Farmer et al, 2010; Kerr et al, 2010).
3. Research is important in addition to provision of care.
4. Collaborative networks are vital for provision of cancer services

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Levels of knowledge about the magnitude of the cancer burden remain inadequate in most countries in Africa.

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Chapter 18

South-South Knowledge Exchange

Cancer Care And Control South-South Knowledge Exchange

Miriam Schneidman, Joanne Jeffers, Kalina Duncan*

* This chapter should be referenced as: Schneidman M, Jeffers J, Duncan K. Cancer Care and Control South-South Knowledge Exchange. In: Boyle P, Ngoma T, Sullivan R, Ndlovu N, Autier P, Stefan S, Fleming K and Brawley OW. The State of Oncology in Africa 2015. iPRI Scientific Publication 4, iPRI, Lyon, France (2016).

Currently 80 percent of the disability-adjusted years of life (DALY) lost to cancer is in low- and middle-income countries (LMICs), but only 5 percent of global cancer resources are spent in these countries. This disparity will grow dramatically as changing lifestyles, increasing urbanization, and aging populations lead to a projected doubling of the incidence of cancer in Africa in the next five years. In 2010, the economic costs of productivity losses combined with treatment costs for cancer were estimated to be US$1.6 trillion, approximately two to four percent of global Gross Domestic Product (GDP). If action is not taken now, future costs will be exorbitant. While some cancer control programs have been initiated, including cervical cancer screening, human papillomavirus (HPV) vaccination, and cancer specialty care centres, comprehensive coverage with the full range of services remains low across Africa. Cancer control programs should be rolled out to advance progress towards the WHO non-communicable diseases (NCD) Global Targets for 2025, that call for a 25 percent reduction in premature mortality from NCDs, including cancer, a 30 percent drop in tobacco use, and 80 percent availability of affordable drugs and technology. Given that African countries face common challenges and can benefit from sharing knowledge and learning from one another's experiences developing and implementing critical interventions to address the growing burden of cancer, a South-South Knowledge Exchange (SSKE) was initiated by the World Bank.

The Cancer Care and Control South-South Knowledge Exchange

The Cancer Care and Control (CCC) South-South Knowledge Exchange was a collaborative effort of the World Bank and the United States National Cancer Institute (NCI)/National Institutes of Health (NIH), designed to support knowledge sharing and networking among participants and global technical experts through a series of knowledge exchange activities. Botswana, Kenya, Rwanda, Uganda and Zambia were selected to participate

in the CCC SSKE because they are each at a different stage in the development and implementation of CCC programs, have different strengths, and have much to learn from one another's experiences.

Effective Cancer Care and Control Interventions

Comprehensive CCC programs provide a range of services that meet the evolving needs of patients along the cancer continuum, from prevention to treatment to palliative care, as noted below.

- Primary Prevention - HPV and Hep B vaccination campaigns; behaviour change campaigns to promote healthy lifestyles; anti-tobacco and no smoking campaigns; and "sin" taxes to curb tobacco and alcohol use.
- Secondary Prevention (screening) - information and education campaigns to encourage breast and cervical cancer screening; cytology (Pap) screening; visual inspection with acetic acid (VIA); and HPV DNA testing.
- Secondary Prevention (treatment) - increased access to cryotherapy; loop electrosurgical excision procedure (LEEP); and cone biopsy.
- Cancer Treatment – provision of specialized care for early and late stage treatment, including standard surgical techniques, radiation, and chemotherapy.
- Palliative Care – palliative, home based or institutional care programs and expanded access to opioids and radiation.

Effective systematic implementation of these interventions requires a health system in which surgery, radiotherapy, chemotherapy, and pain management are well integrated at both clinical and community levels. Virtually no country in Africa, save South Africa, has capacity at all these levels. However, several have initiated promising programs to address selective aspects that were covered during the CCC SSKE.

Intervening early in the continuum of care will save lives and resources. There is growing evidence that many of the interventions in the continuum of care are cost effective. Immunization with the HPV vaccine and cervical cancer screening can reduce deaths from cervical cancer by 80 percent. Early stage treatment of most cancers increase long-term survival by 50 percent, and palliative care can reduce suffering of terminally ill patients.

Common Challenges and Innovative Solutions

Participants shared innovative approaches to common challenges in the planning, management, implementation, and financing of CCC initiatives. The main themes, key issues, and good practices covered during the CCC SSKE are summarized below.

Improving Surveillance to Better Understand the Burden of Disease

Levels of knowledge about the magnitude of the cancer burden remain inadequate in most countries in Africa. Lack of comprehensive, timely data, and information impedes effective program planning and service delivery. Population-based cancer registries (PBCRs) are vital components in comprehensive CCC programs and document the nature and scope of the cancer burden. PBCRs are used to collect data on new cancer cases

in geographically defined populations. Planners, policy makers, and researchers use this information to better understand the cancer burden and improve treatment and prevention options.

Uganda has one of the longest standing and most comprehensive population-based cancer registries in Africa. A number of key lessons have emerged, including the importance of:

- Ensuring ongoing political commitment, and mobilizing resources to make population-based cancer registration a key component of the national cancer control program.
- Strengthening data reliability by enhanced data verification; standardization; improved hospital data systems, including electronic patient records; and promotion of new technologies such as smart phones for more rapid data transmittal.
- Increasing population coverage to capture data from rural areas with the Kampala Cancer Registry linking its work with four regional cancer registries to expand coverage to almost 30 percent of the population, a representative sample that can be used to estimate the national cancer burden.

Identifying National Leaders to Champion the Program

Highly motivated, visible champions can mobilize support and create opportunities for CCC initiatives. The Zambia program received strong political support from former Zambian First Lady Dr. Christine Kaseba-Sata, a gynaecologist by training. Dr. Kaseba-Sata hosted the 6th Stop Cervical Cancer in Africa Conference and generated a great deal of visibility and political support for CCC initiatives in Zambia, as well as throughout Africa. Similarly, the Kenya Cancer Control Program benefited from the support of Ministers of Health who had personal experiences with cancer.

- Identifying champions and influential stakeholders is critical - Key stakeholders need to be mobilized, including Ministries of Health, advocacy groups; cancer survivor and patient support groups; cancer experts; NCD experts; tobacco control experts; and private sector representatives. Additional allies include officials from Ministries of Finance.

Designing Successful National CCC Plans and Programs

Cancer planning is critical to obtaining political support, prioritizing and costing key interventions, and identifying opportunities for strategic partnerships. Successful national plans are evidence- based and informed by locally-relevant research; developed in a participatory fashion by a diverse group of stakeholders; comprehensive in nature, with a full range of activities that strengthen prevention, diagnosis, treatment, palliative care and survivorship; and include a strong monitoring and evaluation component. A number of common lessons have emerged from the design and implementation of national cancer plans and programs:

- Creating linkages between cancer-specific programs and broad national health programs at the central, regional and district levels as well as between public and private sectors taps potential synergies and efficiencies - Effective linkages need to be established with sexual and reproductive health, maternal and child heath, NCD and HIV/AIDS care and treatment programs. Partnering with the private sector and leveraging their expertise and resources is critical to increasing access and improving quality of care.

- Demonstrating economic impact can facilitate support - Ministries of Health need to make the economic case for investing in cancer, in order to mobilize support and resources.

- Overcoming lack of awareness, stigma, discrimination and denial about cancer is critical to generating broad-based support for the program - While support for CCC initiatives is growing in many countries, as increasingly everyone knows someone who is affected by the disease, much more needs to be done to improve knowledge and awareness and early detection.

Innovative Approaches for Strengthening Cancer Prevention, Early Detection, Diagnosis and Treatment

With the rapidly growing number of cancer cases, many countries have initiated programs to strengthen prevention, promote early detection, and establish capacity to diagnose and treat early stage cancers. The CCC South-South Knowledge Exchange permitted countries to share their individual successes and promising approaches, inspiring each other to expand the range of interventions along the cancer continuum of care. A number of generic lessons and country specific examples emerged.

- Generating demand for HPV vaccination and cervical cancer screening services is critical to improving uptake of these services and ensuring cases are prevented or found at earlier stages - Countries draw on their national resources and use unique approaches to accomplish this goal in their respective settings. Zambia uses chiefs, churches, traditional marriage counsellors and other community leaders to raise awareness of the importance of HPV vaccination and cancer screening. Botswana uses census data strategically to target program activities, and is in the midst of implementing a national HPV vaccination program. Rwanda has used its extensive network of Community Health Workers (CHWs) to educate women about the importance of cancer screening and improve uptake.

- Raising awareness through innovative social mobilization efforts to reach a younger target population and to overcome misperceptions and traditional beliefs concerning cervical cancer - The Zambia program found that the best advocates are women returning to their communities after receiving care. The program also introduced health clubs at the secondary education level to raise awareness of cervical cancer screening among younger people.

- Using innovative telemedicine and mobile phone communication strategies can increase access to services in sparsely populated areas - One notable example is the innovative use of mobile phone technologies in Zambia to communicate and follow-up with patients and of telemedicine to ensure quality of care and accuracy of diagnoses.

- Promoting innovative human resources strategies is key to building capacity and addressing the acute shortages of trained health personnel – Given the acute shortages of qualified oncology specialists it is critical to not only expand training but also identify opportunities for task sharing. Rwanda, Zambia and Botswana have effectively used task sharing to expand the role of nurses in the provision of cervical cancer screening and introduced quality assurance programs, training, and supervision to enhance their performance. Zambia increased its capacity to provide cervical cancer screening by piggybacking upon an existing, well-functioning infectious disease platform.

- Building pathology capacity can serve as an entry point for cancer care - Pathology capacity and manpower is limited but essential for the provision of quality CCC services. In the absence of accurate diagnosis it is difficult to make informed decisions about treatment options. Several countries have now placed emphasis on establishing pathology services. Kenya has equipped pathology labs at selected sites while a roving pathologist travels from site to site to provide services. The University of Nairobi has developed pathology training programs that are benefitting individuals from both Kenya and neighbouring countries. Zambia is using telemedicine to extend its pathology capacity to rural areas. Uganda, Kenya and Rwanda have developed twinning arrangements with medical schools in developed countries and put in place quality assurance schemes to strengthen their pathology capacity.

- Strengthening the referral system and ensuring patient follow-up is important for quality care - Given the complexities of providing cancer treatment across the continuum of care, it is important to establish a sound referral system. Zambia has implemented a mobile patient tracking system that is effectively used by nurses to remind patients of follow-up appointments. Rwanda uses its network of Community Health Workers to follow up with patients, and Botswana has strengthened its monitoring and evaluation system to ensure patient follow-up and referral work effectively. However, referral systems and patient follow up remain a challenge for most countries in Africa.

- Reducing the time between diagnosis and treatment is key to minimizing risk of loss to follow up – Both Zambia and Botswana have introduced the Visual Inspection with Acetic Acid, "See and Treat" services, because they allow immediate treatment of precancerous lesions on the cervix and represent a cost effective treatment option in low income settings.

- Leveraging ongoing platforms can generate cost efficiencies and contribute to sustainability – Given both cost and physiological considerations it is sensible to piggyback cancer interventions onto existing primary health or communicable disease platforms that are well established. Zambia has strengthened the sustainability of its cervical cancer screening program by integrating the service into the MCH program of the Ministry of Health. Botswana has also strengthened linkages and leveraged resources from other parts of the health system (e.g. HIV/AIDS program) to enhance chances of sustainability. Similarly, Kenya has built an oncology program from health system infrastructure and specialty care centres originally dedicated to HIV/AIDS.

Increasing Access to Palliative Care (PC)

Access to urgently needed palliative care for terminally ill patients is very limited and constrained by legal, regulatory, and procurement issues. Several countries are beginning to tackle this constraint by:

- Mobilizing both public and private sector support and resources for PC - Kenya has increased access to PC by offering services through a range of public and private sector providers and raising awareness of the importance of PC for all life threatening illnesses.

- Increasing access to cost effective drugs - Rwanda and Uganda procure a more cost effective solution of morphine that is dispensed by trained pharmacists and use public private partnerships to increase access to services.

- Authorizing trained nurses to prescribe and better utilizing pharmacists to dispense opioids - Outdated regulations and practices for procuring and dispensing drugs limit access to PC in most countries. Uganda has authorized trained nurses to prescribe morphine thereby increasing access.

Increasing Access to an Essential Cancer Care Package

While most countries in Africa are focused on designing an essential health care package towards Universal Health Coverage, cancer care and control planners and policymakers have largely not been active partners in this process. To this end, there is a need to:

- Identify the most cost-effective essential cancer care package and determine the cost of its implementation as well as its potential impact - Research conducted under the Disease Control Priorities, Third Edition (DCP3) has determined that HPV vaccination programs, tobacco control measures and tobacco taxes are cost effective interventions in cancer control in many country contexts. For example, Kenya has implemented tobacco control measures and Rwanda has successfully achieved national coverage of HPV immunization.

- Use economic analyses to make the case for investing in cancer and mobilize additional resources to support cancer interventions - Economic analyses are effective tools for making the economic case to support CCC programs. Several countries (i.e. Ghana and Tanzania) that did not participate in the Knowledge Exchange had valuable experiences with economic analyses to inform public policy. Ghana has conducted a cost effectiveness analysis to determine the most cost effective way of expanding its breast cancer prevention program and is using the results to mobilize national health care resources to expand the program. Tanzania used a WHO toolkit to assess the cost effectiveness of alternative strategies for providing HPV vaccination to young girls. Uganda has recently conducted an economic analysis of their cancer registry with the United States CDC.

Increasing Engagement of the Private Sector, Including through Public Private Partnerships (PPPs)

While governments need to ensure financing of cancer programs, they do not necessarily need to deliver the services. It may be more cost-effective for governments to purchase services from private sector hospitals and clinics through public private partnerships. In countries with a vibrant private sector, the public sector needs to remove barriers that impede private sector provision of cancer care and establish a strong enabling environment; create incentives to encourage private sector provision of cancer care; and explore opportunities to form public private partnerships.

AMPATH Oncology and Chronic Care Program in Kenya is an example of an innovative public private partnership between government agencies, academic institutions and private companies that provides access to cancer care for a population of 18 million. Several key lessons have emerged from the success of AMPATH.

- Public Private Partnerships function best when they have a flexible structure that allows public, private and academic partners to each play to their strength - In the AMPATH PPP, government agencies, at all levels, ensure oversight and stewardship, support research, and provide an enabling environment; academic institutions contribute scientific and research expertise and negotiate agreements; and private organizations provide in-kind resources such as bioassays, targeted funding, and resource personnel.

- Ongoing education of patients, service providers, policymakers and the community is needed to maintain political support for the program; address misperceptions and increase demand for services; and improve understanding of side effects to enhance treatment compliance and improve quality of care - AMPATH conducts community and patient education and supports the formation of patient support groups; conducts continuing education and other forms of multidisciplinary provider training to improve quality of care; disseminates research findings and best practices; and provides technical expertise to the MOH to improve policies, guidelines and treatment protocols.

- Increasing access to cost effective drug supplies is critical to improving affordability and sustainability of services - AMPATH has worked with pharmaceutical companies to access generic drugs at lower prices; explored the cost implications of including chemotherapy as a benefit in the National Hospital Insurance Fund; researched willingness and ability to pay; formed Public Private Partnerships; and raised awareness among decision makers of the urgent need to prevent and control cancer to mobilize resources and advance philanthropic efforts of groups such as pharmaceutical companies.

Sharing Knowledge, Experiences and Collaborating to Expand Access to CCC

There are important opportunities for countries to collaborate by sharing knowledge and experiences. The CCC SSKE provided an effective platform for sharing information about the design and implementation of various programs and learning what works and what does not work. CCC SSKE participants reported improvements in knowledge and gains from networking with one another as they continue their efforts to mobilize resources and increase access to services in their countries. Participants reported the knowledge gained would enhance policy and program design in their own countries. Beyond sharing information there are also important opportunities for countries to collaborate on joint activities. During the culminating face-to-face meeting in Lusaka, participants discussed possibilities for collaboration in addressing the shortage of qualified personnel; mobilizing resources by making a better economic case for investing in cancer care and control; and conducting joint research to inform policy and generate knowledge of science of delivery. Several countries have developed regional training programs to build capacity for pathology, oncology, and radiation therapy. Participants plan on building on these nascent efforts to continue networking and support one another to tackle the growing cancer burden.

Introduction

Currently 80 percent of the disability adjusted years of life (DALY) lost to cancer is in low-and middle-income countries (LMICs). However, only 5 percent of global cancer resources are spent in these countries. This disparity will grow dramatically as changing lifestyles, increasing urbanization and aging populations lead to a projected doubling of the incidence of cancer in Africa by 2020. Each year, 50 percent of new cancer cases and 77 percent of cancer deaths occur in LMICs. Global health leaders are calling for greater attention to non-communicable diseases (NCDs), including cancer care and control. At the 63rd World Health Organization (WHO) Regional Committee for Africa meeting, Ministers called for action to address cancer. While some programs, including cervical cancer screening, HPV vaccination, and cancer specialty centers are getting underway, much more needs to be done in Africa. Given that African countries face common challenges and can benefit from sharing knowledge and learning from one another's experiences developing and implementing CCC programs, a South-South Knowledge Exchange was initiated by the World Bank.

The Cancer Care and Control South-South Knowledge Exchange aimed to: (i) raise awareness of the growing importance of CCC in Africa, (ii) encourage cross-fertilization of experiences, with an emphasis on cervical and breast cancers, and (iii) facilitate access to information among participating countries. The CCC SSKE was a joint effort of the World Bank and the United States National Cancer Institute (NCI)/National Institutes of Health (NIH), designed to support knowledge sharing and networking among participants and global technical experts through a series of knowledge exchange activities.

The countries that participated in the CCC SSKE include Botswana, Kenya, Rwanda, Uganda and Zambia. They were selected because they are each at a different stage in the development and implementation of CCC programs, have different strengths, and have much to learn from one another's experiences. They have also learned important lessons while addressing HIV/AIDS that can inform their efforts addressing cancer. During a period of 18 months, from August 2013 to February 2015, CCC SSKE stakeholders from the five participating countries attended nine videoconferences during which they benefited from presentations on key issues, discussed common challenges and shared relevant experiences. The CCC SSKE program was developed in collaboration with participants, so that it responded to their needs and concerns and connected them with technical experts who presented current information on evidence-based interventions and recent global developments. The virtual meetings were then followed by a regional workshop in Lusaka, Zambia in February 2015 at which participants learned first-hand of the achievements of Zambia's Cancer Diseases Hospital and the African Centre of Excellence for Women's Cancer Control at the Centre for Infectious Disease of Zambia; and identified future opportunities for collaboration. This document summarizes the highlights of the CCC SSKE presentations and

discussions. It provides a brief overview of cancer in Africa and synthesizes participating country experiences, common challenges, and innovative solutions.

"Thank you for inviting me to the CCC SSKE Taking a Regional Approach Workshop - It was an eye opener in many ways. I believe there is a lot of potential in Africa and we should maximize it. Money alone is not the only solution."

Dr. Zipporah Ali, Executive Director, Kenya Hospices and Palliative Care Association

Overview of Cancer in Africa

Kenya: Mortality Projections

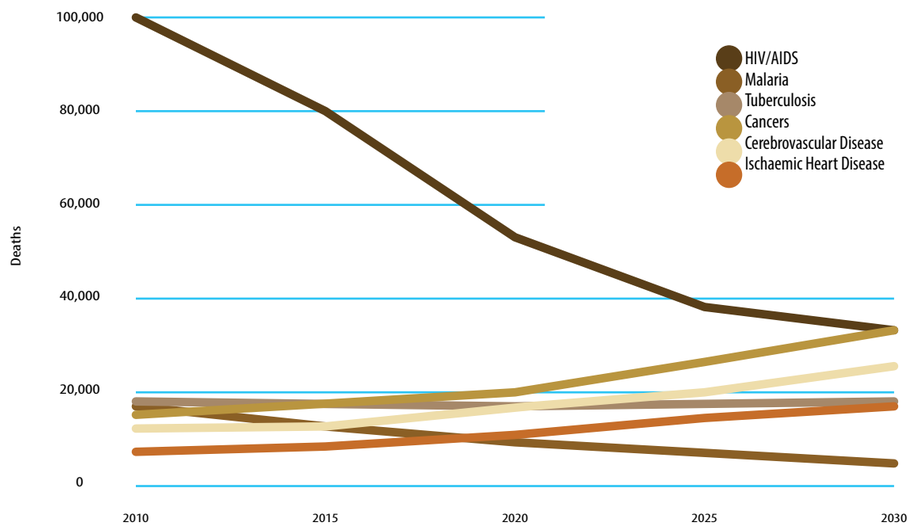


Table 1: Kenya Mortality projections

LMICs in sub-Saharan Africa are shouldering a double burden of disease. While they continue to face high levels of infectious and reproductive health diseases associated with poverty and under development, they are also experiencing rapidly increasing incidence of NCDs. Worldwide, deaths from cancer exceed those caused by HIV/AIDS, tuberculosis and malaria combined, and 70 percent of cancer deaths occur in LMICs. Estimates show that by 2030, LMICs will bear the brunt of the estimated 27 million new cancer cases and 17 million cancer deaths. Much of this morbidity and mortality can be avoided if steps are taken today to strengthen CCC programs.

In addition to presenting a significant burden in terms of morbidity and mortality, cancer also has tremendous economic consequences. Cancer care imposes very high direct costs on health systems, communities, and households. Cancer also exacts very high indirect costs of income foregone by patients, families and caregivers; lost productivity of patients; and premature death and disability. The World Economic Forum lists the burden of chronic disease as one of three leading global economic risks based on potential impact on global productivity and economic growth. In 2010, the economic costs of productivity losses combined with treatment costs for cancer were estimated to be US$1.6 trillion, approximately two to four percent of global Gross Domestic Product. If action is not taken now, future costs will be exorbitant.

Africa: Women's Cancer

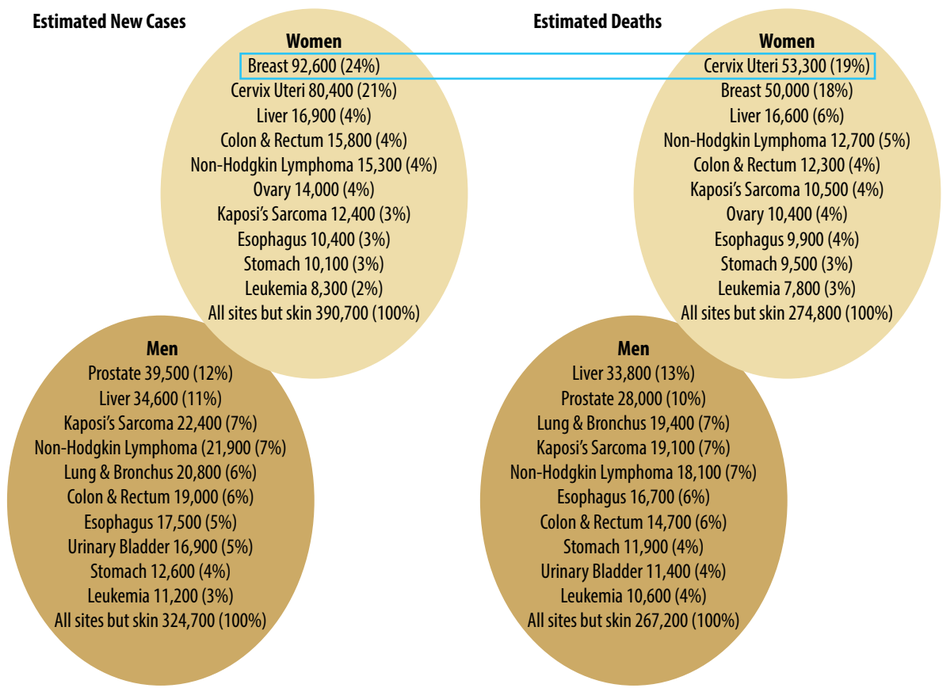


Figure 2: Women's cancer in Africa

In 2012, approximately 715,000 new cancer cases and 542,000 cancer deaths occurred in Africa. Breast cancer contributed roughly 24 percent and cervical cancer 21 percent of all female cancers in Africa. The continent has the highest incidence and mortality from cervical cancer in the world. The most prevalent male cancers are prostrate and liver cancers.

Figure 3: Most Common Female cancers in Africa

There are proven interventions that can prevent some cancers and improve survival. An estimated fifty to sixty percent of cancer mortality in LMICs can be avoided. Most cases of cervical cancer are caused by a viral infection that is sexually transmitted and can be prevented by the HPV vaccine. Liver cancer is often caused by a virus and can be prevented by the Hepatitis B vaccine. Lung cancer is caused primarily by smoking and can be prevented by implementing policies and programs to curb smoking and promote healthy lifestyles. Early detection programs, strengthened care and treatment, and better palliative care can extend cancer survival and improve quality of life. Programs need to be developed to advance progress towards the WHO NCD Global Targets for 2025 that call for a 25 percent reduction in mortality from NCDs, including cancer, a 30 percent drop in tobacco use, and 80 percent availability of affordable drugs and technology.

Cancer Care And Control Continuum

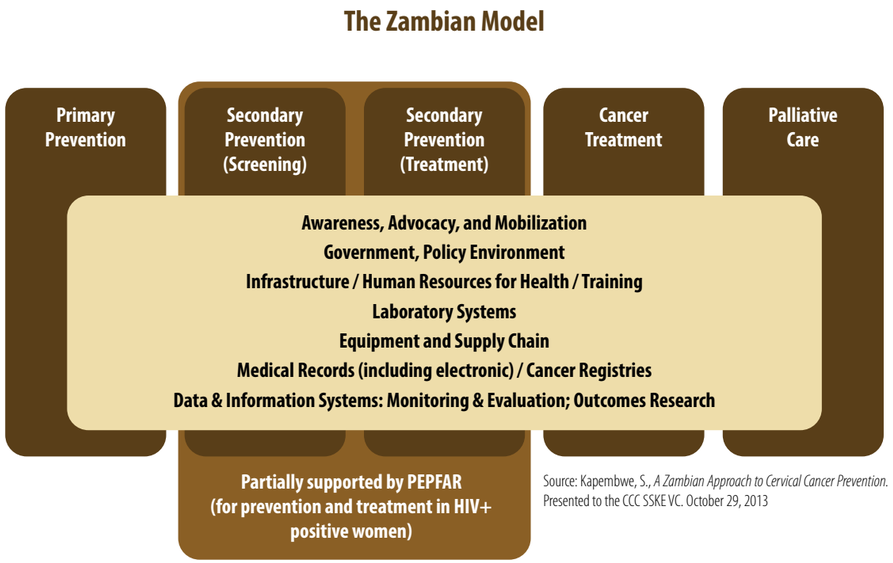


Figure 4: The Zambian Model

Comprehensive CCC programs provide a range of services that meet the evolving needs of patients along the cancer continuum. Cancer prevention and control is crucial because early detection and treatment can cure 30 percent of cancers; prolong survival in another 30 percent; and improve quality of life through adequate disease management and palliative care. As illustrated by the Zambian model above, CCC initiatives can be designed to intervene at different stages of the disease as well as to strengthen specific building blocks of the health system, thereby addressing not only cancer, but also other NCDs. The WHO health system building blocks include information systems; leadership and governance; service delivery; medical products, vaccines, supplies and technology; trained medical personnel; and financing. CCC initiatives can also be integrated into programs that address other aspects of health and/or promote economic development.

Potential areas of intervention along the CCC continuum include:

- Primary Prevention - HPV and Hep B vaccination campaigns; behaviour change campaigns to promote healthy lifestyles; anti-tobacco initiatives and no smoking campaigns; and "sin" taxes to curb tobacco and alcohol use.
- Secondary Prevention (screening) - information and education campaigns to encourage breast and cervical cancer screening; cytology (Pap) screening; visual inspection with acetic acid (VIA); and HPV DNA testing.
- Secondary Prevention (treatment) - increased access to cryotherapy; loop electrosurgical excision procedure (LEEP); and cone biopsy.
- Cancer Treatment- effective linkages with specialized care providing early and late stage treatment, including standard surgical techniques, radiation, and chemotherapy.
- Palliative Care - linkages with palliative care programs and expanded access to opioids and radiation.

There is growing evidence demonstrating that many of these interventions are cost effective; make a significant impact on cancer prevention; prolong survival of cancer patients; and improve quality of life of both patients and their families. To be effective, these interventions require a health system in which surgery, radiotherapy, chemotherapy, pain management and outpatient and acute care services are well integrated. Immunization with the HPV vaccine and cervical cancer screening can reduce deaths from cervical cancer by 80 percent. Early stage treatment of cancer can increase long-term survival by 50 percent and palliative care can reduce suffering in 100 percent of late stage patients.

The five countries participating in the CCC SSKE are at different stages of developing and implementing CCC programs and have a range of experiences. The CCC SSKE activities addressed common challenges and innovative solutions to various aspects of designing and implementing CCC initiatives. Topics included data collection to better document the burden of disease; strategies for designing and implementing successful national CCC programs; innovative approaches for strengthening cancer prevention efforts such as HPV vaccination programs; task sharing and other strategies to build capacity and increase access to cancer screening and treatment; analytical tools for understanding the costs of CCC; financing models, including Public Private Partnerships, to increase access to CCC treatment and care; policy reforms needed to increase access to palliative care; and opportunities for regional collaboration. Highlights of the country experiences shared, common challenges discussed and innovative solutions explored during the CCC SSKE activities are synthesized and presented in the following sections.

Cancer Registries and Information Systems

Population-based cancer registries (PBCRs) are vital components in comprehensive CCC programs and document the nature and scope of the cancer burden. PBCRs are used to collect data on new cancer cases in geographically defined populations. Planners, policy makers, and researchers use this information to better understand the cancer burden and improve treatment and prevention options.

Cancer surveillance provides information on the burden of cancer - incidence, prevalence and survival; identifies priorities for preventive and curative programs; supports investigation into causes of cancer; and can be used to evaluate the effectiveness of cancer control activities.

Coverage of population-based cancer registries needs to be expanded, particularly in LMICs, in order to obtain more complete and reliable data and improve understanding of both current and future cancer burdens as well as site-specific patterns of incidence. There are few population-based cancer registries in Africa. One notable example is the Kampala Cancer Registry (KCR) described below.

Uganda's Experience with the Kampala Cancer Registry

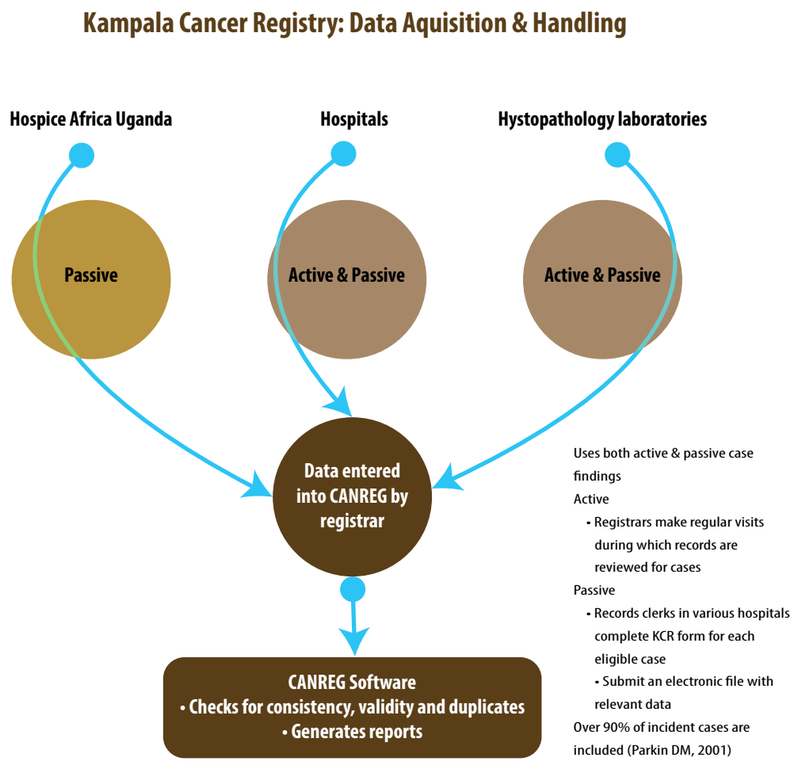


Figure 5: Kampala Cancer Registry

The Kampala Cancer Registry (KCR) was established in 1951 and is based at the Makerere Medical School. It has collected a unique data set that has been instrumental in improving understanding of cancer in Uganda and informing health policymaking and planning. The registry collects: (i) demographic information – name, age, gender; (ii) diagnosis information; and (iii) the source of the data. The KCR has contributed data to global publications; catalysed collaboration and research opportunities with universities and other organizations; supported training; and guided design of cancer control programs. Currently, the KCR is located in the Department of Pathology at Makerere College of Health Sciences

and is staffed by a director and two registrars. It is supported by record clerks at six collaborating hospitals, laboratories and a hospice center and has computerized its data management using the cancer registration software, CANREG5. While other cancer registries have been established in Uganda, none has had the ongoing success of the KCR. This success results from its governance structure as part of Makerere University; its collaborative relationships with the International Agency for Research on Cancer (IARC) and African Cancer Registry Network (AFCRN); continuous effective and committed leadership; a defined mission and clear agenda; and focused approach.

Common Challenges And Innovative Solutions In Information Systems

- Ensuring ongoing political commitment and mobilizing resources - Uganda has made cancer registration a key component of the National Cancer Control Program and charged the Uganda Cancer Institute with its implementation. Recognizing the importance of sustainable population-based data collection to inform their cancer control program, Zambia has partnered with NCI and UICC to hire and train a registry director to develop a PBCR. In Kenya, the MOH, in coordination with the United States Centres for Diseases Control and Prevention (CDC), has developed a tool to determine the cost of registering one case of cancer that it will use to advocate for resources to strengthen and expand the national cancer registry.

- Ensuring reliability - The KCR data collection system has control points for review and verification by both the CANREG5 software and by manual comparison of data entries with hard copy records. KCR staff members maintain collaborative working relationships with clinicians, pathologists, as well as private sector health providers in order to obtain high quality data. They also work to standardize and improve hospital databases, and, when possible, link to electronic patient records. Other strategies to ensure data reliability include using new technologies such as smart phones.

- Increasing population coverage, particularly of rural populations – Uganda increased the personnel and infrastructure of the KCR registry and linked it with four regional cancer registries and a registry at a community cancer treatment centre to reach coverage of 30 percent of the population. This level of coverage is sufficient for estimating the national cancer burden. The community cancer registry is at a cancer treatment centre in Eastern Uganda and collects information about a rural population that is less dynamic than the urban population of Kampala. The Centre aims to collect a time series of information about individual patients so that it can improve its treatment interventions and gain insights into site-specific incidence of cancer in a rural community.

Cancer Control Planning and Programming

National health systems need to address the growing challenge of cancer by: (i) strengthening evidence-based planning to maximize program impact and efficiency; (ii) forming strategic partnerships to leverage resources and expertise; (iii) building capacity; and (iv) developing sustainable cancer control programs. Experience demonstrates that successful national plans are evidence-based and informed by research; have been developed by a diverse group of stakeholders; are comprehensive and include a range of activities that strengthen prevention, diagnosis, treatment, palliative care and survivorship; and include a strong monitoring and evaluation component.

The Kenya Cancer Control Program

Kenya has developed and implemented several landmark policies and strategies to advance its National Cancer Control Programme. These include passage and implementation of the 2012 Cancer Control Act, the 2007 Tobacco Control Act, the 2012 Alcoholic Beverages Control Act, the 2011 National Food and Nutrition Security Policy and the 2013 National Occupational Safety and Health Policy. In addition, Kenya has a number

of official planning documents that guide their national strategy, including: 2011-2016 National Cancer Control Strategy; National Cervical Cancer Programme Strategic Plan (2012 – 2015); National Guidelines for Cancer Management (2013); Palliative Care and Training (2013); and Prevention and Management of Cervical, Breast and Prostate Cancers (2012). These milestones were achieved because the Ministries of Health (MOHs) provided strong leadership and stewardship and mobilized a diverse group of stakeholders, including representatives from academia, the private sector, hospitals, faith-based organizations, civil society organizations and patients' groups, who developed, reviewed, disseminated and implemented comprehensive policies, plans, and roadmaps.

The National Cancer Control Strategic Plan is comprehensive and provides a sound framework for action. Significant strides have been made in each of its seven strategic areas:

- Promote cancer prevention and early detection – Interventions have focused on lowering risk factors by: (i) reducing access to tobacco through smoking bans, increased taxation and advertising limitations; (ii) promoting healthy lifestyles, including improved diet and reduced alcohol use, through behavior change programs; (iii) reducing environmental exposure to carcinogens; and (iv) preventing infectious diseases associated with cancer through HIV prevention and HPV and Hep B immunization programs.

- Improve diagnosis and treatment, including palliative care – Screening interventions have focused on cervical, breast and prostate cancers. Cervical cancer screening programs (VIA and Pap smear) have been expanded and HPV testing, while expensive, is available through private providers. Diagnostic and treatment services are available primarily in Nairobi and large towns and capacity is being expanded to increase geographic access. Since over 80 percent of cancer cases present late, the MOH has established 11 palliative care centers in public regional referral hospitals and several faith-based and private sector organizations provide hospice.

- Promote cancer surveillance, registration and research – Two sites, the Kenya Medical Research Institute (KEMRI) and the Moi Teaching and Referral Hospital (MTRH), have cancer registries and the MOH has developed a cancer registry tool that will be disseminated to expand these efforts. Efforts to develop population-based registries are also underway in Kisumu and Nyeri Counties.

- Promote partnerships and collaboration in cancer control – To ensure that all providers are working toward common goals, they work collaboratively to develop guidelines and conduct joint training programs. Additional work will be done to develop treatment protocols and joint drug procurement systems.

- Advocate for cancer prevention and control legislation – To operationalize the National Cancer Act a National Cancer Institute is being established.

- Integrate cancer prevention and control activities with national health and socio- economic plans – Recently developed strategies and guidelines are being disseminated and implemented at the service delivery level.

- Promote community involvement and participation in cancer control and prevention – Including a diverse group of stakeholders in the development of policies and strategies has ensured buy-in and community participation.

The Uganda Comprehensive National Cancer Control Program

The Uganda Cancer Institute (UCI) and Ministry of Health are implementing the Uganda Comprehensive National Cancer Control Program. The central strategy of this program is a comprehensive cancer service network comprised of UCI, as a National Centre of Excellence, supporting highly specialized Regional Cancer Centres staffed by multidisciplinary teams. UCI's mandate is to research the cause, treatment and prevention of common cancers in Uganda; provide high quality, evidence-based cancer care; provide cancer training using common cancers as models; and reduce the risk of cancer through awareness raising and information. UCI provides oncology services, including chemotherapy and radiation; gynaecology and surgery services; cancer screening services; specialized oncology pharmaceutical services; hematologic clinical care; laboratory and imaging services; physiotherapy services; psychosocial support and training. Both the 2010 Uganda National Development Plan and the 2010 Uganda National Health Policy state the need for increased capacity to address cancer through a specialized unit such as the UCI. A draft cancer policy and a draft bill to establish the UCI by an Act of Parliament are in place.

UCI has collaborated effectively with Makerere University, Mulago Teaching Hospital and the Fred Hutch Cancer Research Centre in its efforts to research and treat childhood lymphoma and other malignancies; research pathogens and their role in causing cancers; and improve strategies for cancer prevention and treatment. UCI also provides countrywide cancer consultation services and trains oncologists. UCI is responsible for many ground breaking scientific discoveries that have enriched the understanding of cancer and led to innovative strategies for more effective prevention and treatment of the disease. It is governed by a board and is a self-accounting government entity under the Ministry of Health. UCI has recently built a six-story facility and its funding has increased from about 5.4 billion Shillings in 2009/2010 to roughly 13.5 billion Shillings in 2013/2014. It was accorded the status of a WHO Regional Centre for Cancer Research in Africa and is currently being reviewed to have that status renewed.

Two outreach regional clinics have been established in Western and North Western Uganda and land has been offered to establish two more. The Comprehensive National Cancer Control Program also includes a Comprehensive Community Cancer Program comprised of community outreach efforts to provide health education and screening for breast, cervical and prostate cancers; cancer awareness and screening at the UCI Centre; continuous medical education for lower level health care workers; television and radio talk shows about cancer; and development and production of information, education and communication materials. The Program also includes satellite surveillance centres that promote cancer research and registration; conduct community level surveillance; raise awareness to promote prevention and early detection; and provide simple treatment and patient follow-up.

The key elements for the success of the UCI and the Comprehensive National Cancer Control Program are effective partnerships, strong coordination, high level leadership, resources and research. UCI collaborates and partners with many international organizations and agencies, including International Atomic Energy Agency, International Agency for Research on Cancer, National Cancer Institute and Fred Hutchinson Cancer Research Centre to achieve several national cancer control goals. Working in partnership with civil society groups, such as the Uganda Cancer Society and the Uganda Non-communicable Disease Alliance, has also been critical for success.

The Rwanda National Strategic Plan for Cancer Diseases

Rwanda's National Strategic Plan for Cancer Diseases aims to improve primary and specialized health care and treatment; increase prevention and control of risk factors; and sensitize the community to change risk behaviours and promote early detection. The Plan focuses on reinforcing primary and specialized health care and treatment by: (i) decentralizing services and training and mentoring lower level health workers to improve screening and early diagnosis; (ii) increasing access to NCD services by strengthening procurement and logistics systems for drugs,

medical supplies, and equipment, and building capacity of one regional hospital to provide radiotherapy and chemotherapy; and (iii) improving quality of NCD services by establishing cancer units inside five regional hospitals, adding radiotherapy services to one regional hospital and increasing the number of pathology units to a total of three nationwide.

Rwanda has five specialized facilities to treat cancer. In the country there is one clinical oncologist, one hemo-pathologist, 1 surgical oncologist and one gynaecologic oncologist. General practitioners provide most cancer care. There are thirty dedicated oncology nurses and ten dedicated histo- technologists. Rwanda has developed national protocols for treating twelve adult cancers, including breast, colon, rectal, gastric, cervical and prostate cancers; and five paediatric cancers, including Burkitt's lymphoma and Hodgkin's lymphoma. There are thirty-one recommended cancer medicines on the Rwanda List of Essential Medicines and in 2014 the country spent close to US$ 630,000 for them.

Rwanda has built the capacity of its cancer program with funding, training and other types of support from many organizations including the Government of Rwanda, Partners in Health, GSK, DfID, CDC, WHO, and GAVI. Over a three-year period, the program has trained 241 doctors on topics such as baseline cancer training, LEEP and VIA/cryo; 406 nurses on baseline cancer training and in-service chemotherapy; and 40 pathology technicians on topics such as pathology outreach. Two pathologists have attended international training. The Rwanda Cancer Program runs monthly inter- facility cancer care symposia to increase cancer awareness among health care providers and enable them to share experiences and harmonize cancer management. To further promote cancer prevention and early detection the Program conducted the National Breast Cancer Symposium, the Breast Cancer Public Awareness Campaign, and the HPV/VIA screening campaign. Finally, the Program has integrated early cancer detection into annual community medical check-ups. To address current gaps the program aims to: extend the cancer registry at the five referral hospitals to also include district hospitals; ensure availability of essential medicines; conduct training in cervical and breast cancer prevention and management; procure screening and diagnostic equipment for additional district-level facilities; and complete expansion of radiotherapy infrastructure.

Cancer Management in Zambia

In 2009 the Ministry of Health developed the National Cancer Control Strategy that aims to provide a comprehensive and coordinated national response to strengthen prevention, awareness, diagnosis, treatment and care of cancer. The strategy focuses on cervical, breast, and prostate adult cancers and retinoblastoma, a childhood cancer. They are currently in the process of renewing and revitalizing this strategy. The next iteration will include policies to prevent cancer, including incorporating HPV vaccination into national policy and developing and implementing a national tobacco control program. The program also aims to strengthen prevention and early diagnosis of cancer by building capacity to conduct cervical cancer screening. Zambia has developed the Centre of Excellence for Women's Cancers as well as the Cancer Diseases Hospital, a Regional Centre of Excellence for Cancer and Oncology Training. Currently cervical cancer screening is available at all provincial hospitals and 31 clinics. Fifteen of these sites provide LEEP and will serve as referral sites at the provincial level. The program has also built breast cancer screening capacity with ten mammography machines, one in each province in the public sector and three in the private sector. Staff members are being trained to conduct breast cancer screening and capacity is being expanded. Finally, the program is beginning to build capacity to provide PSA tests and to perform colonoscopies for early diagnosis of prostate and colon cancers.

Zambia has established the Cancer Diseases Hospital (CDH) to be a regional Centre of Excellence by 2025 and to clinically drive implementation of the national program as well as serve as a hub for workforce training. CDH's mission is to "provide equitable access to cost effective and quality cancer care services as close to the family as possible in order to save, prolong, and contribute to improvement in the quality of life." CDH aims to increase cancer cure rates by 15 percent and reduce late stage presentation of cancer cases in Zambia by 2016. The state-of-the-art facility will include the latest equipment for treatment of cancer with radiotherapy and chemotherapy. To achieve program goals the hospital provides

timely, quality care to reduce morbidity and mortality; develops and implements a cancer early detection and prevention program; effectively manages and develops human resources; mobilizes financial resources to deliver and expand services; provides logistical and administrative support to the program; and develops and implements a comprehensive Health Management Information System to plan, monitor and evaluate program implementation. The hospital developed its 2011-2015 Human Resources for Health Strategic Plan in which it has set the following goals: (i) increase the number employed of specialized personnel and ensure the health workforce is equitably distributed; (ii) increase training outputs and harmonize them to respond to the health sector's needs; (iii) improve performance and productivity of health workers; and (iv) strengthen health systems and structures to support expansion and performance of personnel. Since inception the number of trained health workers has increased and currently the hospital has 35 staff specialized in oncology. The government has been supportive of the program and has funded the hospital to conduct training programs for Radiation Therapy Technology, Clinical Oncology, Radiology and Oncology Nursing.

Common Challenges And Innovative Solutions In Cancer Control Planning And Programming

- Identifying champions, allies, and influential stakeholders who need to be at the table for successful program planning and implementation - Key stakeholders include advocacy groups; cancer advisory boards; survivor and patient support groups; cancer experts; NCD experts; tobacco control experts; private sector representatives; as well as civil society. Other allies can be found in government ministries in many sectors (i.e. education and labor), not to mention, in key Ministry of Health units (i.e. NCD, oncology, family health, and, sexual and reproductive health) at the district, regional and central levels. Finally, it is essential to involve Ministry of Finance officials. The Kenya Cancer Control Program benefited from the support of two very visible champions -- Ministers of both Ministries of Health had personal experiences with cancer and were active supporters of the program.

- Creating linkages between cancer-specific programs and broad national health programs at the central, regional and district levels as well as between public and private sectors - Effective linkages need to be made with sexual and reproductive health, maternal and child heath, NCD and HIV/AIDS care and treatment programs. Also, opportunities to partner with the private sector and leverage their expertise and resources are critical to increasing the impact and effectiveness of CCC interventions.

- Demonstrating economic impact can facilitate support - Ministries of Health need to make the economic case for investing in cancer in order to mobilize support and resources. The Government of Kenya supported the Tobacco Control Program because it recognized that the savings resulting from reduced future expenditures for cancer-related health services, not to mention reduced productivity resulting from disease, far exceed the tax revenues lost from fewer tobacco sales as well as the cost of the program. While there has been some interference from industry, the government has been very supportive in the implementation of the tobacco control program.

- Overcoming lack of awareness, stigma, discrimination and denial about cancer to generate broad-based support for the program - Increasingly, Kenyans have experience with cancer or know someone who has cancer and misperceptions are being dispelled. Continued research, including population-based surveys, such as a module in the Demographic and Health Survey, can help programs track changes in awareness and knowledge; contribute to better designed programs; assist in targeting resources; and help develop effective behavior change and communication programs. Highly motivated visible champions can also mobilize support for programs. While broad base support for CCC initiatives is growing in many countries much more needs to be done to improve knowledge and awareness and early detection.

Cancer Prevention in Africa with a Focus on Cervical Cancer

"Cervical cancer is an African holocaust. Many women in Africa suffer and die from this preventable and treatable disease."

Dr. G. Parham, Co-Director of the Cervical Cancer Screening Programme of Zambia

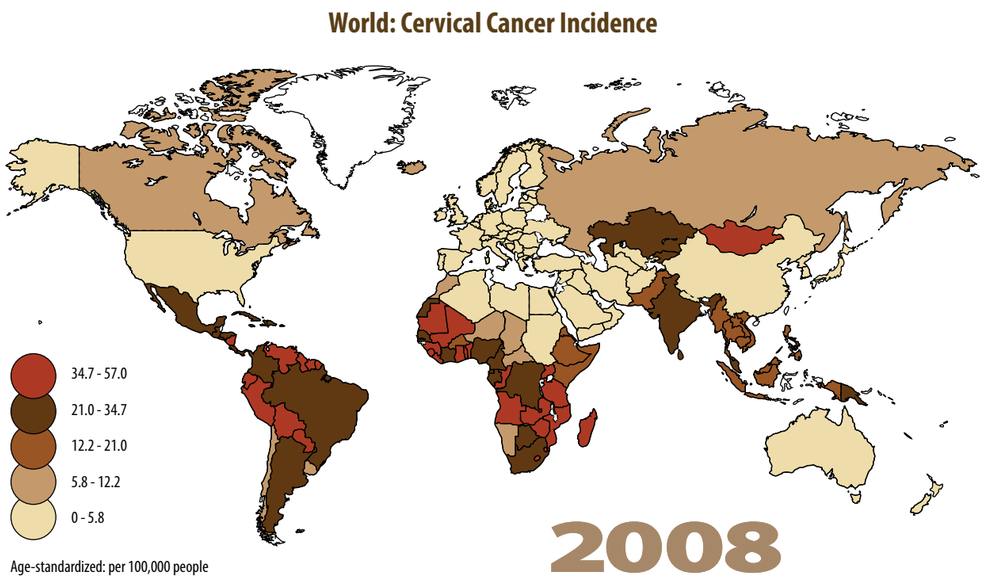


Figure 6: Cervical cancer incidence worldwide

More than 85 percent of the global burden of cervical cancer occurs in developing countries. Cervical cancer accounts for 21 percent of all female cancers in Africa. Cervical cancer is caused by infection with the HPV virus that is transmitted sexually. There are two vaccines that protect against the HPV virus, Gardasil and Cervarix. HPV vaccination programs have been difficult to implement and scale up in LMICs because vaccines and immunization programs are complex and costly when considering the full cost of delivery; social stigma hinders uptake of the vaccines; and reaching adolescent girls is challenging.

Rwanda's Experience Providing the HPV Vaccine

The Ministry of Health spearheaded a Technical Working Group (TWG) to prepare and implement a comprehensive strategy for the HPV vaccination program. The TWG included technical experts, such as clinicians and health professionals engaged in cancer care, and representatives from the Ministry of Education, Ministry of Gender and Family Promotion, the Centre for Treatment and Research on AIDS, Tuberculosis, Malaria

and other Epidemics, and other key development partners. The TWG formed technical subcommittees to address key issues such as monitoring and evaluation; cold chain requirements; strategies for reaching the target populations of girls in and out of school; capacity building for nurses and community health workers; procurement and logistics; financing; education; and social mobilization. A key component of the program was the comprehensive communication strategy. It included a nationwide sensitization campaign that involved all stakeholders; was supported by political and religious leaders; used newspaper, radio and TV; and trained teachers to discuss cervical cancer and the HPV vaccine. The program received support and technical assistance from the Rwanda MOH, the United States Centres for Disease Control and Prevention and the International Centre for AIDS Care and Treatment Programs at Columbia University. Local leaders, community health workers and teachers worked together to implement the program in a "public-private community partnership."

The MOH chose a school-based strategy because 98 percent of Rwandan girls attend school. It included: (i) targeting girls enrolled in Primary 6 to receive the full 3-dose course; (ii) a catch-up phase targeting girls in Secondary 3; and (iii) targeting out-of-school girls age 12. Vaccinations were provided at "health days" and other educational activities at the school. All vaccinations were voluntary and parents provided consent when their daughters received the first dose.

Challenges of the program include adhering to the eligibility requirements and tracing girls who were absent from school. To address these impediments, the program conducted further education to explain the eligibility requirements; used community health workers to trace the girls who were 12 but not enrolled in school; and used the local health centre to vaccinate out-of-school girls. Additionally, there were concerns about the high cost of the program and possibly diverting scarce resources from other priority health programs. To make the program more affordable, Rwanda developed a tiered pricing agreement and negotiated a Memorandum of Understanding (MOU) with Merck pharmaceutical company. By 2012, the program had vaccinated 97 percent of the target population with the required three doses.

The success of the program can be attributed to: (i) a well-established vaccine delivery system with a cold chain, transportation, human resources, and monitoring capacity; (ii) strong national leadership and ownership, including excellent collaboration between public and private institutions; and (iii) a health system with strong outreach capacity. To continue the program, Rwanda developed a favourable pricing agreement with Merck so that each dose of Gardasil cost US$5. It is also increasing access to the vaccine through the private health sector.

Common Challenges and Innovative Solutions in HPV Vaccination

- Debunking myths and misperceptions about cervical cancer and the HPV vaccine - Prior to developing the communication campaign, Rwandan health education experts conducted focus groups to learn about people's knowledge and attitudes towards the vaccine and cervical cancer. There was a great deal of fear that the vaccination could cause sterility and even that it was a plot by the government to slow population growth. There were also questions about why the program targeted only 12 year old girls. This information was invaluable in developing the comprehensive communication campaign that addressed misperceptions and explained cervical cancer and the vaccine at the launch of the program.

- Reaching 12 year old girls, in and out of school - The program was integrated into school-based programs such as health education, hygiene and reproductive health and sought other opportunities throughout the school year during which the second and third doses could be provided. Reaching the entire target population required identifying absent students, vaccinating them, and following up to ensure they received all three doses. It also required close coordination between schools, teachers, and community health workers.

- Monitoring the vaccination campaign - When the first dose was administered, girls received a card to keep and bring back in order to receive the second and third doses. A copy of the card was also kept at the school. Monitoring is important not only to track coverage but also, so that as countries strengthen their cancer surveillance registries, they can measure the impact of the immunization program over time.

Early Detection, Cancer Diagnosis and Treatment

Zambia's Experience Strengthening Cervical Cancer Screening – Using Nurse-Led Screening to Increase Access

In 2005, health officials determined that it would be feasible to introduce a nurse- led VIA-based, "Screen and Treat" program with a referral system of LEEP centres. To ensure quality, the program added digital cervicography. The program initially focused on HIV+ women and was supported by external resources from the United States President's Emergency Plan for AIDS Relief (PEPFAR). To ensure sustainability the services were subsequently integrated into the Maternal Child Health program of the Ministry of Health. Currently, services are provided as part of the gynaecology exam, providing an opportunity to screen for both cervical cancer and HIV. A strong quality assurance system has been put in place, whereby digital images taken by nurses from different areas of the country are systematically reviewed in Lusaka. The MOH pays for staff and facilities and provincial- level MOH staff plan special "gyne" days. While 80 percent of women accepted being treated by nurses, follow-up has been difficult, especially in rural areas. The program added mobile patient tracking so that nurses can remind patients of appointments and follow-up with text messages. Community health workers, marriage counsellors, traditional chiefs and church leaders conduct outreach. The program received strong political support from former Zambian First Lady – Dr. Christine Kaseba-Sata. Dr. Kaseba-Sata is a gynaecologist who has been a highly visible champion for CCC activities, including hosting the 6th Stop Cervical Cancer in Africa Conference that generated a great deal of visibility and political support for the program, not only in Zambia, but throughout Africa.

"I was especially impressed by the organization of the clinic, starting with no missed opportunity for screening. The data managers plus case managers is also an excellent idea."

Dr. Anne Nganga, Program Manager Reproductive Tract Cancers Program, MOH, Nairobi, Kenya

The comprehensive program has all of the key components and provides care nationwide through 31 centres in all provinces. In addition, the program serves as a regional training centre. To date, over 200,000 women have been screened for cervical cancer. Key challenges facing the program include the need to screen more women, faster; decreasing overtreatment rates; improving compliance of patients who have been referred to LEEP; enhancing capacity to perform radical surgery; and transitioning the program to government.

The program's success can be attributed to: (i) piggybacking on an existing, well-funded and well- functioning infectious disease (HIV/AIDS) platform to build capacity for the treatment and prevention of an NCD (cervical cancer); (ii) adapting interventions to the local environment; (iii) assessing all phases of the program during implementation through a rigorous process of quality control and monitoring and evaluation to quickly identify and correct any weaknesses; (iv) investing heavily in surgical excision (LEEP) infrastructure and expanding histology diagnostic services to facilitate management of complex cervical lesions that exceed the therapeutic limitations of cryotherapy; and (v) strengthening the existing healthcare delivery system when weaknesses are identified during program implementation in order to innovate, enhance sustainability, and strengthen long-term success.

Botswana's Experience Strengthening Cervical Cancer Prevention - Using Data and Task Sharing to Streamline Services

Cervical cancer is the second most diagnosed cancer in women 15-49 years old, and the number one cancer killer in Botswana. From 2004 – 2009 the national screening program was Pap–based and suffered from a backlog of PAP smear slides that needed to be read, weak referral services and poor program monitoring and evaluation. In 2012, the National Cervical Prevention Program (NCCPP) developed a new strategy that includes: (i) education and HPV vaccinations; (ii) screening and treatment of pre-cancer; and (iii) cervical cancer treatment. The screening and treatment component continued Pap screening, but also introduced "See and Treat" services at ten locations and in demonstration projects of both HPV DNA testing and the HPV vaccine.

Unlike other countries in the region, awareness of the need for cancer screening among the population of Botswana is high. In order to ensure that the program did not suffer delays, the MOH strengthened planning and used recent census data to estimate the number of women ages 30 – 49 in the different regions and asked political officials and community leaders to inform them of the screening service. The MOH introduced VIA, cryotherapy and LEEP and used task shifting so that women who have been screened with Pap smear and are awaiting cone biopsy treatment by specialists can access treatment at outpatient LEEP clinics run by non-specialized medical officers. Since 2012, the first of eleven "See and Treat" centres has become operational, twenty healthcare workers have been trained at the regional training centre in Lusaka, cryotherapy and LEEP machines have been procured, the program has formed the Botswana-University of Pennsylvania Partnership, and cervical cancer prevention variables have been added to the MOH health management information system.

Current challenges include developing new reporting indicators, streamlining the cumbersome paper-based monitoring system, improving the tracking of referrals, and ensuring staffing and funding. Lessons learned include the importance of leveraging resources and strengthening linkages with other parts of the health system such as Sexual and Reproductive Health, HIV Prevention, the Expanded Program on Immunization and the Infectious Diseases Care Clinic; strengthening planning and strategy development; involving key stakeholders; continuing education and advocacy at all levels of the health system; and strengthening monitoring and evaluation to track performance.

Rwanda's Experience with Building Capacity of Community Health Workers and the Task Shifting Program

The Rwandese health system consists of:- (i) five regional hospitals; (ii) 42 district hospitals in 30 districts; (iii) 474 health centres in 416 health sectors; (iv) 2,148 health community posts; and (v) 14,873 villages with one male and two female community health workers -- one of whom is responsible for maternal and infant health. CHWs are trusted, literate, community members between the ages of 20 and 50 who are elected by the community. They provide community-based prevention, screening and treatment of malnutrition; integrated community case management for malaria, diarrhoea, acute respiratory infection, and malnutrition; community-based maternal and neonatal care; community-based provision of family planning; community direct observation and treatment for tuberculosis; and community behaviour change communication. CHWs report health information about their village through a health management information system (HMIS) called RapidSMS. The information is aggregated from all villages on a monthly basis through the SISCom system. The CHW program uses performance-based financing to create incentives for CHWs to report quality information in a timely manner and support thirteen maternal child health interventions. It also provides community-based health insurance for CHWs. The CHWs are organized into cooperatives that provide opportunities to generate additional income through activities such as pig and poultry farming. The challenges facing the CHW program include need for continual training; providing support and supervision; and ensuring timely supplies of medicines and other commodities. The CHW program has increased coverage of key MCH interventions; benefits from strong political commitment at all levels; has contributed to the empowerment of women; and has helped to implement innovative health financing systems.

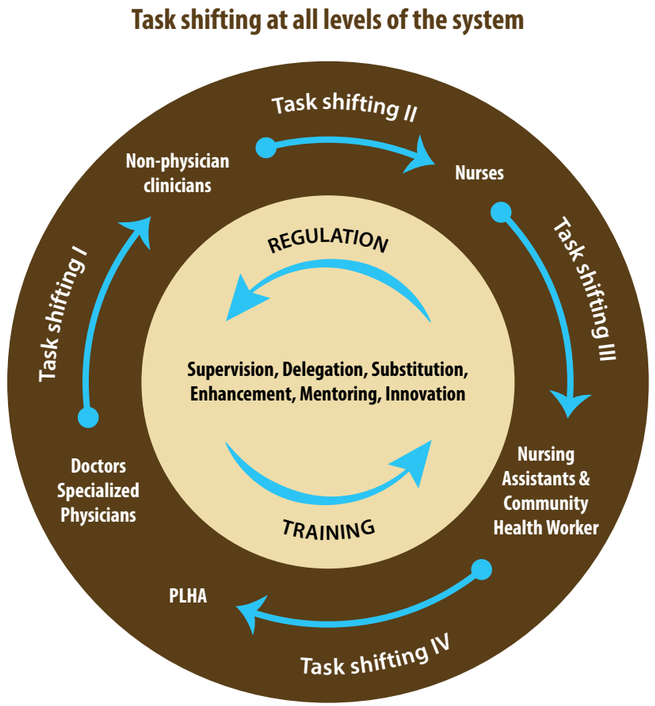


Figure 7: Task shifting at all levels of the system

Rwanda has developed and implemented a Task Shifting Program to fill the gap of trained medical personnel needed to initially address HIV/AIDS, and now being used to address cancer. From 2005-2007 the Ministry of Health and the Treatment and Research Centre (TRAC) on HIV/AIDS worked with Family Health International to develop and pilot test the Task Shifting Program to decentralize services and authorize nurses to prescribe antiretroviral therapy (ART). Nurses were trained to prescribe ART; provide quality HIV/AIDS prevention counselling and testing; teach patients to manage the challenges of compromised immune systems as well as the side effects of the medicines; and provide counselling to prevent maternal to child HIV transmission. The Task Shifting Program was approved by the Minister and scaled up in 2009. The Program shifted responsibilities at every level of the system: from specialized doctors to non- physician clinicians; from non-physicians to nurses; from nurses to nursing assistants and community health workers; and from community health workers to people living with HIV/AIDS (PLHA). The Program required revision of the regulatory framework, a strong quality assurance system, and involvement of service users. Its ongoing success depends upon coordination of all stakeholders at all levels of the health system as well as effective supervision; delegation of authority and responsibility; empowerment; and strong mentoring. Lessons learned include: task shifting and task sharing can strengthen the overall health system; require both a comprehensive regulatory framework that defines tasks and competencies, as well as a coordinated and standardized training program;

and requires a quality assurance system that features ongoing supervision. Task shifting and task sharing are not cost savings strategies but rather strategies for increasing access to services.

Kenya's Experience Training Pathologists

The 2013-2018 Kenya Health Sector Strategic and Investment Plan has set the following 5-year targets for indicators tracking progress towards its objective of "halting, and reversing the rising burden of non-communicable conditions": (i) 75 percent of women of reproductive age are screened for cervical cancer; and (ii) 2 percent of patients are admitted with cancer. Key strategies of the national cancer screening programme are: (i) target diseases should be a common form of cancer with high associated morbidity or mortality; (ii) effective treatment, capable of reducing morbidity and mortality should be available; (iii) test procedures should be acceptable, safe, and relatively inexpensive; and (iv) facilities that can undertake subsequent diagnosis and treatment and follow- up should be available and accessible. The service package includes breast cancer screening and faecal occult blood testing for bowel cancers and breast cancer screening and annual prostate examination for all men over 50 years of age.

Pathology services play a key role in several stages of cancer care and control, including accurate surveillance, reliability of cancer registries, primary prevention, cancer screening, diagnosis and staging, treatment planning, and detection of recurrence. Historically, Kenyan pathologists received their training in 5-year programs in the United Kingdom and were able to specialize in anatomic pathology, cytopathology, haematopathology, chemical pathology, immunopathology, and clinical microbiology. Pathology training capacity has been developed at the University of Nairobi (UON) that now offers a 3-year Master of Medicine General Pathology Training program, experiential mentorship training at the sub-speciality level, as well as professional certificates as a Specialist Pathologist. Since 1986, the UON program has trained 70 pathologists who now work in four teaching hospitals, provincial and district level-level hospitals, and private hospitals, as well as in other hospitals in the East Africa region. In 2006, the Aga Khan University Hospital developed a 4-year pathology residency program that has tracks in anatomic pathology, histopathology, cytology and forensic, as well as clinical pathology (haematology, chemical pathology, immunopathology and clinical microbiology). To date, the program has trained twelve anatomic pathologists and 11 clinical pathologists. In addition, postgraduate cytology programs have been developed and UON now offers a Master of Science in Clinical Cytology. Trainees include technologists and clinicians. This program has built regional capacity and trained pathologists from Malawi, Zimbabwe and Zambia.

UON has collaborated with regional and international professional associations such as the Kenya Association of Clinical Pathologists; the Kenya Society of Haematologists and Oncologists; the Association of Pathologists in East, Central and Southern Africa; and the International Association of Pathologists to develop post MMed Training, fellowships, continuing education seminars and workshops, and teleconferences. Currently, the College of Pathologists in East, Central and Southern Africa (COPECSA) is forming the Regional College of Pathologists and aims to establish standards of pathology training for the region and offer pathology fellowships. UON is also collaborating with the University of Stellenbosch to develop a training and research program.

Kenya is making significant efforts to increase human resources capacity to support cancer diagnosis and treatment follow-up in the region. Several regional opportunities are being developed, however, they face several challenges, including lack of space and infrastructure; shortages of resources and supplies, including teaching microscopes, staining supplies, and reference books; lack of quality assurance schemes; and limited research funding.

Zambia's Experience Training Radiation Therapy Technologists

Zambia has developed a cost effective regional training program in Radiation Therapy Technology. The program uses a mixed model approach that emphasizes both clinical and academic training. It is implemented by the Cancer Diseases Hospital Training College and provides hands on experience through training that is integrated into clinical operations. The program conducted a Training of Trainers in 2010 and developed its curriculum through a collaborative participatory process that involved all key stakeholders. The program has developed an evaluation and quality assurance system and has been accredited. The program graduated two cohorts of students in 2014, including 17 Zambians, 1 Malawian, 2 Eritreans, and 3 Ethiopians.

Common Challenges and Innovative Solutions to Early Detection and Cancer Diagnosis and Treatment

- Generating demand for services - Zambia uses chiefs, churches, and traditional marriage counsellors as advocates and other community leaders to conduct community outreach and educate women about the importance of cancer screening. Botswana used census data to plan outreach efforts and target program activities towards women between the ages of 30 - 49. Finally, Rwanda has used its extensive network of Community Health Workers to educate women about the importance of cancer screening.

- Raising awareness through innovative social mobilization efforts to reach a younger target population and to overcome misperceptions and traditional beliefs concerning cervical cancer - The Zambia program found that the best advocates are women returning to their communities after receiving care. The program also introduced health clubs at the secondary education level to raise awareness of cervical cancer screening among younger people.

- Using innovative telemedicine and mobile phone communication strategies to increase access to services in sparsely populated areas- Zambia uses mobile phones to communicate and follow-up with patients and telemedicine to ensure quality of care and accuracy of diagnoses.

- Building capacity and addressing shortages of trained health personnel - Zambia increased its capacity to provide cervical cancer screening by piggybacking upon an existing, well-functioning infectious disease platform. Countries have used a wide range of strategies for increasing the capacity of their health system staff including: on-the-job training to build capacity for job specific tasks; task shifting and task sharing that reassign tasks to different levels of personnel and, as in the Rwanda experience, require reorganizing policies and procedures throughout an organization or system; reviewing and revising curricula of existing degree programs; and developing new training programs to train nurses, doctors and other levels of health care personnel. Rwanda, Zambia and Botswana have effectively used task shifting and task sharing and developed new training programs to expand the role of nurses in the provision of cervical cancer screening and support their work with quality assurance programs, training and supervision.

- Building pathology capacity - Countries have used several strategies to build their pathology capacity. Kenya has equipped pathology labs at selected sites and uses roving pathologists to travel from site to site and provide services. The University of Nairobi has also developed training programs to train pathologists and now students can pursue a 3-year Master of Medicine General Pathology Training program; a Master of Science in Clinical Cytology; participate in mentoring programs at the sub-speciality level; or receive a professional certificate as a Specialist Pathologist. Since 1986, the University of Nairobi program has trained 70 pathologists who now work in four teaching hospitals; provincial and district level hospitals; private hospitals; as well as hospitals in the region. In 2006, the Aga Khan University Hospital developed a 4-year pathology residency program that offers tracks in anatomic pathology, histopathology, cytology and forensic, as well as clinical pathology (haematology, chemical pathology, immunopathology and clinical microbiology). Zambia is using telemedicine to extend its pathology capacity to rural areas.

Increasing capacity and quality of pathology services is critical to the expansion of CCC services. Many countries have developed twinning arrangements with cancer programs and medical schools in developed countries. For example, Uganda has been working with the Fred Hutchinson Institute in the United States to build its pathology capacity and improve the quality of diagnoses. Kenya, in the AMPATH Program has developed many institutional partnerships with academic and research institutions, including Indiana University and Toronto University. AMPATH is emphasizing quality control during its training to improve the accuracy of its pathology testing. While international collaboration has been critical to the development of pathology capacity, strong quality control during training has been essential to assuring that Kenyan and Ugandan pathologists develop good skills and arrive at diagnoses that are comparable to those of internationally trained pathologists. A recent study showed that 56 percent of diagnoses made by Ugandan pathologists matched those made by United States pathologists.

- Strengthening the referral system and ensuring patient follow-up - Zambia has implemented a mobile patient tracking system that enables nurses to remind patients of the need for follow-up appointments. Rwanda uses its network of Community Health Workers to follow up with patients and Botswana has strengthened its monitoring and evaluation system to ensure patient follow-up.

- Reducing the time between diagnosis and treatment - Both Zambia and Botswana have introduced VIA "See and Treat" services because they allow immediate treatment of precancerous lesions. Zambia has been tracking the stage of disease of patients presenting for treatment and has recently seen an increase in the number of stage two women presenting, indicating that the referral and screening programs are making an impact.

- Leveraging ongoing platforms can generate cost efficiencies and contribute to sustainability - Zambia has strengthened the sustainability of its cervical cancer screening program by integrating services into the MCH program of the Ministry of Health. Botswana has strengthened linkages and leveraged resources from other parts of the health system, including Sexual and Reproductive Health, HIV Prevention, the Expanded Program on Immunization and the Infectious Diseases Care Clinic in order to strengthen sustainability of its cancer-screening program.

Increasing Access to Palliative Care

Palliative Care is "an approach that improves the quality of life of patients and their families facing problems associated with life-threatening illness, through prevention and relief of suffering". PC begins at diagnosis and continues through and beyond treatment. Issues related to palliative and hospice care include limited access to appropriate symptom management and support to sustain function and prolong survival. Appropriate palliative care requires family support; a holistic approach; maintenance of hope and dignity; and open communication for informed decision making.

Opioids are indispensable for the relief of pain and suffering and appropriate policies need to be in place to ensure they are both available for medical use and not abused. Since the early 1960s the United Nations and WHO have worked to develop policies and frameworks that both prevent abuse and diversion and ensure availability of the drugs for medical purposes. In the mid-1980s pharmaceutical companies began manufacturing opioids in sustained release forms that are easier to administer. There is tremendous disparity in the availability and consumption of opioids. In 2010 it was estimated that 16 percent of the world's population living in high-income countries consumed 90 percent of the morphine used globally. In Africa, South Africa has the highest per capita opioid consumption followed by Kenya, Ghana, and Zambia.

In 1990, WHO developed guidelines for using opioids to relieve cancer pain. Despite published guidelines, a 1994 study published in the New England Journal of Medicine found that 42 percent of cancer patients received inadequate cancer pain treatment and minorities, women and older patients were more likely to receive inadequate cancer pain treatment. Barriers to accessing PC and medication to manage pain include lack of knowledge among patients and providers; myths and misperceptions; provider bias; lack of coordination of care and services; procurement policies and supply chain issues; eligibility restrictions limiting facilities authorized to dispense the drugs and health care providers authorized to prescribe them; additional prescription requirements hindering access, such as specialized prescription pads, limits to the length of prescriptions, and referral requirements; general laws that limit access; and lack of accountability.

There are several global and regional frameworks that aim to increase access to PC including the WHO Guidelines for Cancer Pain Relief; the WHO May 2014 PC Resolution that focuses on integration, education, research and funding; and the International Narcotics Control Board efforts to strengthen control and access to narcotics. There are also several North-South Initiatives that are working to develop and advance PC integration as well as expand the evidence base.

Integrating Palliative Care into African Health Programs and Policies

African countries are gaining experience with the integration of PC into existing health services. For example, Uganda formed a Public Private Partnership to provide free access to liquid oral morphine; authorized nurses to prescribe opioids; integrated PC into the curricula for health workers, as well as for diploma, bachelors and masters level students; formed a Country PC Team comprised of both public and private sector stakeholders; and integrated PC into national HIV, Cervical Cancer and Health Sector Strategic Plans. Facilities providing PC services can now be found in 70 percent of Uganda's districts. Swaziland has also made rapid progress in developing a national PC policy and implementation guidelines; developing and implementing a national training curricula and setting up a procurement system for oral morphine with a corresponding monitoring system.

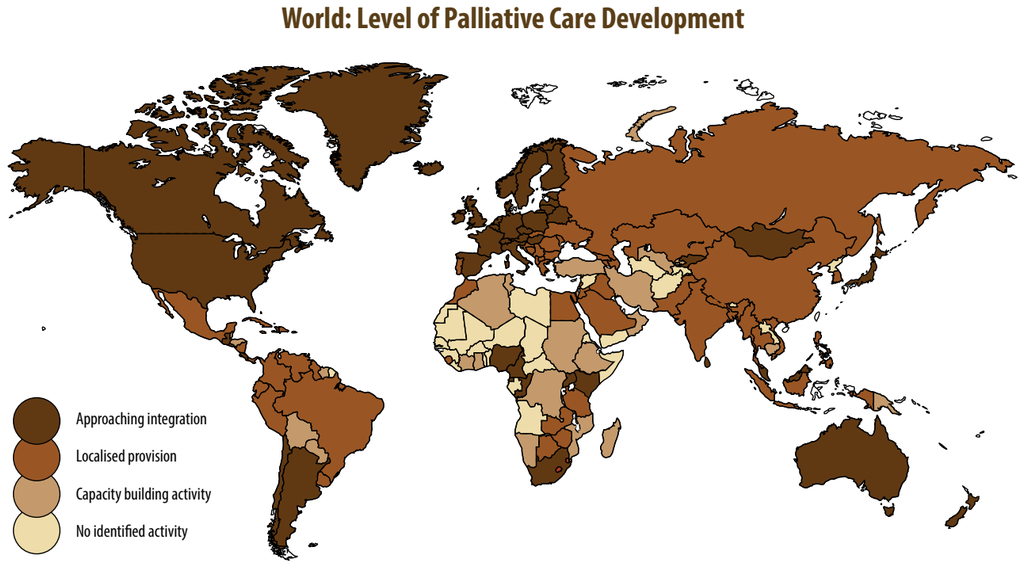


Figure 8: Level of palliative care development

African countries with national PC Policies and Strategies include Tanzania, Botswana, Mozambique, Malawi, Swaziland, Zimbabwe, Uganda and Rwanda. The key components of a PC policy and program include: (i) leadership and governance that include locally appropriate and sustainable policy guidance, information and oversight, collaboration and coalition building, regulation, system design and accountability, especially as pertains to morphine procurement and prescription; (ii) service delivery packages and models that are sustainable, equitable and evidence-based; (iii) financing that promotes sustainable access to an effective mix of preventive, curative, rehabilitative and palliative services; (iv) development of human resources for health that promotes task sharing as well as task shifting; (v) health information systems that are used to inform programming and improve health outcomes; and (vi) access to quality medical products, vaccines and technologies.

The African Palliative Care Association (APCA) is a pan-African organization founded in 2004 that works to improve access to PC in all of Africa and to ensure that PC is well-understood and integrated into health systems at all levels and underpinned by evidence. The APCA works collaboratively with local, national, regional and international partners to: (i) increase knowledge and awareness; (ii) facilitate integration of PC into national policies and education; (iii) ensure access to essential medicines and existing health services; (iv) build the evidence base for PC in Africa; and (v) increase sustainability of programs.

Implementing Palliative Care – Kenya's Experience

Increasing access to PC has been a key component of the Kenya Cancer Control Programme because over 80 percent of cancer cases present late when PC is the only treatment option. To address this growing need and make the best use of scarce resources, Kenya has strategically linked PC to cancer prevention, early detection and treatment for both adults and children. It has also mobilized both public and private sector partners and formed partnerships with key international organizations. The Kenya Hospices and Palliative Care Association has been instrumental in initiatives to establish PC centres and train public and private sector health workers. To date Kenya has established 11 PC centres in public regional referral hospitals; 25 PC centres in county public hospitals; 9 PC centres in hospitals operated by faith-based organizations in various regions; and, established 17 free-standing hospices. PC has been integrated into training provided by most medical and nursing schools, including the Kenya Medical Training College. Five thousand health workers have participated in one-week training courses and 52 health workers have received advanced PC training. Kenya has also mobilized political leaders to support PC and has integrated PC into the 2011-2016 National Cancer Control Strategy and the 2013 National Guidelines for Cancer Management, and promulgated the 2013 National Palliative Care Guidelines. Finally, Kenya is the first African country to have the health minister, a cabinet secretary, include PC in his performance contract in order to ensure continued government action to increase access to PC.

Implementing Palliative Care – Botswana's Experience

In 2003, Botswana participated in a WHO-supported five-country project aimed to improve PC initiatives and the quality of life of people living with HIV/AIDS and cancer. As a result, Botswana developed a comprehensive National Palliative Care Strategy. Its key components include: ensuring access to pain and PC medications at facility and community levels; building local capacity for PC provision in health care settings, hospices, day centres and homes; providing psycho-social support and wrap around care; and improving end-of-life care and bereavement support. The program was launched in 2013.

The MOH is currently implementing the PC Strategy by: (i) addressing misperceptions and improving understanding; (ii) developing guidelines and protocols for PC, as well as for pain management; (iii) implementing 5-day training programs and integrating PC into the undergraduate health curricula; (iv) increasing availability of opioids; (v) forming the Botswana Hospice and Palliative Care Association to improve coordination; (vi) improving continuity of care by strengthening linkages between acute care and PC providers; and (vii) mobilizing resources. Next steps include incorporating PC implementation plans into the National Cancer Control Plan; increasing access to opioids and training health personnel to prescribe them; and reviewing opioid regulations.

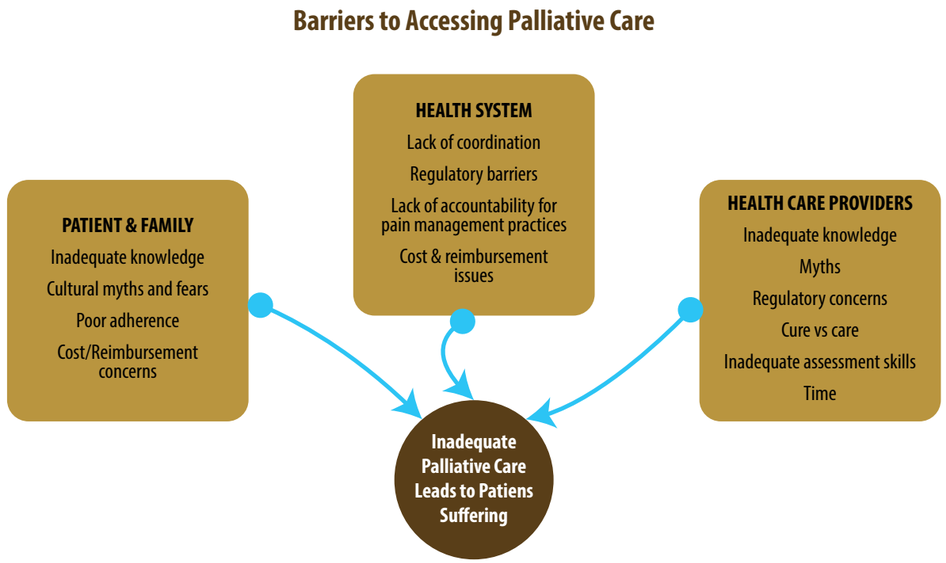


Figure 9: Barriers to accessing palliative care

Implementing Palliative Care – Rwanda's Experience

In 2006, Rwanda's MOH developed a PC program and introduced PC training for hospital and non- governmental organization (NGO) staff. In 2007, PC was added to the clinical care package. In 2008, an advocacy workshop was conducted to strengthen PC delivery and morphine was added to the Essential Drugs List. In 2011 a National Palliative Care Policy was approved, district level hospital workers were trained and the Palliative Care Centre at Kibagabaga was created. In 2013 the National Palliative Care Policy was integrated into the National Strategic Plan. PC is implemented at all levels of the health system and referral, provincial and district hospitals, as well as health centres and health posts provide a clinical care package while community health workers follow-up with patients and support treatment compliance and home-based care. The program uses multidisciplinary teams from provincial and district hospitals and the community to coordinate care.

Priority areas for the PC program include strengthening PC at all levels of the health system; educating health care workers and conducting refresher training of district hospital staff in morphine use and pain management; raising awareness of both patients and health care personnel; improving access to services and quality of care; and conducting research to inform and improve care. Strategies used to expand the program include: (i) gaining government ownership to expand a program initially led by civil society; (ii) using the national health plan to integrate PC into services at all levels of the health system; (iii) using a core team of national trainers at the Provincial Hospital level and a cascade system of training

staff throughout the system; (iv) relying on the national supply chain system to procure and distribute drugs; and (v) establishing a technical working group to advise the Ministry of Health and advocate for continued program support.

Common Challenges and Innovative Solutions in Increasing Access to Palliative Care

- Mobilizing public and private sector support and resources for PC - Public and private sector policymakers need to be educated in the strategic link between PC and cancer prevention, early detection and treatment for adults and children as well as the risks of opioid addiction. In Kenya, the PC program began as a cancer-related program and then raised its visibility by demonstrating that PC services can benefit persons facing all kinds of life- threatening illnesses. It further expanded its services by working with hospice-providers; by improving linkages with cancer prevention and treatment and mobilizing MOH resources to integrate PC into hospital care, and by collaborating with donor organizations interested in improving access to PC.

- Increasing access to drugs - Rwanda and Uganda have procured morphine in an inexpensive solution form and trained compounding pharmacists to dispense it. Both countries have also used Public Private Partnerships to increase access. Finally, global efforts to negotiate with pharmaceutical companies for lower price drugs, as has been done for ART, are needed.

- Authorizing trained nurses to prescribe and better utilizing pharmacists to dispense opioids - It is essential that policy assessments and situation analyses be conducted in each country to understand the laws, policies and guidelines on the books, how they are implemented, and what their impact is on hindering access to PC. Once this information is collected, it is important to involve all stakeholders in the review and revision of regulations and policies to build consensus among doctors, nurses and pharmacists for new prescribing practices that can increase access to PC. Uganda has authorized trained nurses to prescribe morphine.

Increasing Access to an Essential Cancer Care Package

Because cancer care is costly, complex and chronic, identifying strategies for financing the continuum of CCC interventions is challenging and efforts must be made to identify cost-effective interventions. The Disease Control Priorities, Third Edition (DCP3) has for the first time a chapter on cancer that provides the state of the art evidence on cost effectiveness of various interventions. As part of DCP3 a framework has been developed to first analyse the cancer burden in a country; then determine the cost effectiveness of specified health interventions within the country context, and finally estimate the feasibility and potential impact of scaling-up the interventions. This information is then used to identify the most cost effective essential cancer care package and determine the cost of its implementation as well as its potential impact. Global financing to support cancer programs in Africa is limited and programs are typically financed through large out-of-pocket payments with some public sector support. To design a cost effective essential cancer care package the disease burden must be understood; cost effective interventions identified; and the feasibility of scaling up interventions in the specific health care setting assessed.

Cost effectiveness analyses of selected cancer control interventions conducted for the DCP3 demonstrate that HPV vaccination; comprehensive tobacco measures; and tobacco taxes are very cost effective. Similarly, high quality treatment of selected paediatric cancers for patients below age 15 can significantly reduce mortality and be cost effective. The DCP3 estimates that the marginal per capita cost of a comprehensive essential cancer package that includes these interventions ranges from about US$1.7 in low-income countries to roughly US$5.7 in upper middle-income countries.

DCP3 provides a strong economic rationale for financing selected cancer interventions and presents several potential sources of funding the addition of an essential cancer package into current health programs. If the essential cancer package were provided to approximately 5.8 billion people, approximately 3.2 million cancer deaths in people below age 70 would be averted. This would cost 3 percent of public spending for health in upper- middle-income countries; 5 percent in lower- middle-income countries; and 14 percent in low-income countries. Since the per capita income in these countries is growing, more money will become available and cancer interventions can be domestically financed. Funds can also be generated through tobacco taxes. Another important source of funds is international donor support. Currently, global priorities for reducing the costs of the essential cancer package include: (i) lowering the cost of key inputs, such as drugs and vaccines, through large scale purchasing and/or negotiated drug prices; (ii) providing technical assistance; (iii) formalizing communities of practice; and (iv) conducting research. Research priorities include: registries to better understand the disease burden; implementation science; biology; and economics, including costing.

Health system reforms being implemented in many African countries that provide opportunities for increasing access to CCC include: (i) Universal Health Coverage (UHC) to ensure financial protection through pooled, publicly-financed health care; (ii) performance-based financing programs that provide financial incentives to providers and community workers, based on the quantity and quality of services delivered; and (iii) Public Private Partnerships that involve contracts between public and private entities for the provision of services, facilities and/or equipment. When developing strategies for financing CCC programs within the context of these broader health system reforms, it is essential to ensure that all people can obtain health services without suffering financial hardship.

Introducing CCC into Universal Health Coverage Programs

"for cancer to be part of Universal Health Coverage, we need to start building the evidence base. There is urgent need for more information on the burden of disease, on priority interventions, and on the most cost effective ways of delivering services, bearing in mind value for money. This information will be critical to defining benefit packages, and determining what is affordable."

Karima Saleh, Senior Health Economist, World Bank

The World Bank is working with many African countries to support progress towards Universal Health Coverage; a process that depends upon a thorough understanding of the country and its capacity to collect revenues, pool funds, and purchase services. Key considerations for the design of programs to introduce cancer care into UHC programs include: clearly defining the population of beneficiaries who will receive services; determining which services to include in the benefit package; estimating the cost of services to be covered; and developing a strategy for shifting to prepayments and reducing out-of-pocket payments for care. When making these choices it is important to ensure that coverage and use are based on need; to maximize benefits and cost effectiveness by prioritizing policies that generate the greatest sum of health-related well-being in a given population; ensure that contributions are fair and based on ability to pay; and ensure accountability through robust monitoring. Additional research is needed to inform these decisions and better understand the disease burden; the cost effectiveness of interventions; household out- of-pocket spending; and the incidence of catastrophic spending, especially among the poor.

Key lessons from the experiences introducing cancer care coverage into UHC programs in Thailand, Mexico, Columbia, and Peru are: (i) strategies to include cancer care coverage into national health insurance programs need to focus on improving survivorship and reducing out-of- pocket payments for the poor; (ii) separate catastrophic illness funds can be established and revenues can be generated from "sin taxes"; (iii) introduction of benefits needs to be slow, sequenced and structured, focusing first on selected interventions

for high incidence cancers and targeted populations and gradually expanding to include additional services and beneficiaries; (iv) solid data on costs and burden of disease, and efforts to ensure that entitlements translate into effective coverage are essential to success; and (v) political will is key.

Costing of Comprehensive Cervical Cancer Prevention – The Comprehensive Cervical Cancer Costing and Planning Tool

Reducing the burden of cervical cancer requires a comprehensive approach that includes vaccination; screening and treatment of precancerous lesions; detection and treatment of early to mid-stage cancers; and provision of palliative care. To plan for and provide these services it is essential to know both the financial and economic cost, including the cost of training programs; procurement and distribution of vaccines; social sensitization; delivery of services; supervision; monitoring; and program evaluation. To better understand these costs, WHO has supported development of a Comprehensive Cervical Cancer Costing and Planning (C4P) Tool. The tool can be accessed at: www.who.int/immunization/hpv/en/

The C4P Tool facilitates the process of estimating costs and designing a cervical cancer prevention program. It helps decision makers understand the components of various service delivery strategies; compare their costs; estimate their anticipated impact; discuss trade-offs; and clarify policies. It uses population data from the United Nations Development Program (UNDP), vaccine cost data from the Global Alliance for Vaccines and Immunizations (GAVI), data on the number of schools from Ministries of Education, and data on costs of other inputs such as per diem, transport, and allowances from Ministries of Finance. The C4P Tool estimates both investment and recurrent costs; predicts outputs in terms of health systems strengthening and population coverage; and allows users to compare the costs of various strategies and scenarios such as facility-based versus community-based service delivery and school-based versus community-based immunization campaigns.

The C4P Tool has been applied in 12 countries and has shown that: (i) even though financing through GAVI has reduced costs and Gardasil is now available for $4.5 per dose the cost of the vaccine remains significant; (ii) vaccine delivery costs (excluding the cost of the vaccine) are more expensive than those of routine vaccinations largely due to the challenges of reaching girls ages 9-13; (iii) costs for vaccine delivery per fully immunized girl range from $3.9 - $5.8 across countries; and (iv) factors contributing to cost differences include variations in country settings (geography, population etc.) and strategies for administering the vaccines. The C4P Tool has also demonstrated that effective and timely interventions can reduce morbidity and mortality from cervical cancer, however, successful programs require planning and a comprehensive approach.

Cost Effectiveness of Breast Cancer Prevention - Ghana's Experience

In 2012, Ghana's breast cancer diagnosis and treatment program covered ten percent of the population, cost $1.6 million and averted 437 DALYs (disability adjusted life years). The average cost effectiveness ratio was estimated to be $3,745. Currently, the Ghana National Health Insurance Service (GHIS) covers breast (and cervical) cancer diagnosis and treatment for its beneficiaries. However, GHIS only covers 34 percent of the Ghanaian population. Policymakers conducted a cost effectiveness analysis (CEA) to identify the most cost effective way to deliver breast cancer diagnostic services and treatment and explore strategies for increasing financing and expanding access. To conduct a CEA the DALYs resulting from a health condition in a population that can be averted by the health intervention are measured; then the cost of the health intervention is determined; and, finally, the CEA ratio (DALYs averted by the program ÷ the cost of the program) is calculated. The CEA ratios are then used to compare the cost effectiveness of several different health interventions.

Ghanaian policymakers used CEA to compare three components of the breast cancer program, namely, mass media awareness, clinical breast exams, and mammography screening. The CEA indicated that in Ghana, both mass media awareness with a CEA ratio of $1364 and the clinical breast exam if provided with continuity of care with a CEA ratio of $1299 were cost effective. Mammography screening with a CEA ratio of $12,908 was not cost effective in Ghana. The CEA demonstrated that increasing the coverage of the program to 100 percent of the population would cost $16 million and would avert 12,560 DALYs annually. It also demonstrated that a package of interventions that includes mass media awareness, diagnosis, treatment and care is more cost effective than a single intervention for treatment.

Priorities for expanding the breast cancer program in Ghana include: (i) strengthening evidence of the disease burden; the costs and cost effectiveness of key interventions; and the benefits of investments in prevention and early detection; (ii) initiating a dialogue with health finance reformers to expand access to effective interventions and GHIS coverage; (iii) exploring possibilities of purchasing services from established private treatment centres; (iv) continuing to integrate breast cancer and cervical cancer screening into key programs (Maternal and Child Health, Sexual Reproductive Health, and HIV/AIDS prevention) and new initiatives (Every Women, Every Child); and (v) continuing to build service delivery capacity.

Common Challenges and Innovative Solutions in Financing Cancer Care

- Identifying the most cost effective essential cancer care package and determining the cost of its implementation as well as its potential impact - the DCP3 research project has developed a framework for analysing the cancer burden in a country and determining the cost effectiveness of interventions within the country context. The most cost effective interventions in many country contexts are HPV vaccination programs, tobacco control measures and implementation of tobacco taxes. Kenya has successfully implemented tobacco control measures. Additional research is needed to expand the evidence base.

- Using economic analyses to make the case for investing in cancer and mobilize additional resources to support cancer interventions - Economic analyses can be effective tools for generating political support and mobilizing both global and national resources to support CCC programs. Rwanda has mobilized global resources in the form of reduced costs for HPV vaccines. Ghana has conducted a cost effectiveness analysis to determine the most cost effective way of expanding its breast cancer prevention program and is using the results to mobilize national health care resources to increase access to breast cancer screening.

- Introducing cancer care into Universal Health Coverage - strategies to include cancer care coverage into national health insurance programs need to focus on improving survivorship and reducing out-of-pocket payments for the poor. Coverage of cancer care benefits needs to be introduced in a slow, sequenced and structured manner that focuses first on selected interventions for high incidence cancers and targeted populations and gradually expands to include additional services and beneficiaries.

- Assessing the cost effectiveness of alternative delivery strategies—tools can be used to determine the cost effectiveness of delivering critical services using different delivery modes (for example, school-based versus community-based programs to provide the HPV vaccination to girls). This type of analysis is instrumental to making smart decisions in resource-constrained environments.

Public Private Partnerships - The Experience of AMPATH Oncology In Eldoret, Kenya

The AMPATH Oncology and Chronic Care Program is an innovative partnership between: government agencies, academic institutions and private companies. Its flexible structure allows each partner to play to its strength: government agencies support research, provide an enabling environment, and ensure oversight; academic institutions contribute scientific and research expertise and negotiate agreements; and private organizations provide in-kind resources such as bioassays, targeted funding, and resource personnel.

AMPATH is based in Western Kenya and provides CCC services to a population of 18 million. It combines care and research to pursue its mission of "Care Leads the Way." To better meet the increasing needs of its patients, AMPATH expanded its original platform of HIV/AIDS services to provide a range of integrated services. As of 2013, AMPATH Oncology and Haematology Outpatient Clinic provides a variety of services for men, women and children, including for Kaposi's sarcoma, breast cancer, lymphoma, head and neck cancers, gastro intestinal cancers, leukaemia both acute and chronic, breast, cervical and ovarian cancer, and screening for cervical, prostate and breast cancers. AMPATH has developed collaborative relationships with nine academic institutions; multiple United States and Kenyan government agencies; several pharmaceutical companies; foundations and research organizations.

Strategies AMPATH is implementing to address CCC barriers include:

- Improving infrastructure - AMPATH is strengthening pathology infrastructure since cancer treatment can only be as good as the diagnosis. It has improved chemotherapy services by installing chemo prep hoods, improving chemo storage facilities, and installing both hardware and software programs designed to improve management and administration of chemotherapy treatment. AMPATH is also building radiotherapy bunkers in its new cancer treatment centre. Since the majority of patients present with advanced cancers, AMPATH has established a palliative and hospice care unit. To strengthen surveillance, AMPATH has provided hardware and software support and developed a reliable cancer registry. Finally, AMPATH is collaborating with Moi Teaching and Referral Hospital to develop surgery resources dedicated to oncology cases.

- Supporting research and clinical training – AMPATH is supporting collaborative arrangements between Moi, Indiana and Toronto Universities to develop curricula, train trainers, and train medical personnel through both long- and short-term research and clinical training courses.

- Improving affordability and sustainability of services –AMPATH has worked with pharmaceutical companies to provide generic drugs for lower costs; explored the cost implications and possibility of including chemotherapy in the benefits provided by the National Hospital Insurance Fund; researched willingness and ability to pay; formed Public Private Partnerships; and raised awareness of the importance of controlling cancer to mobilize resources and advance philanthropic efforts of groups such as pharmaceutical companies.

- Increasing access to palliative care – AMPATH has improved the acceptability and use of morphine for pain management; explored the possibility of including narcotics on the essential drug list to make them more affordable; developed and conducted multiple short- term trainings on palliative care; and promoted the use of multidisciplinary teams to improve coordination and quality of care.

- Educating patients, service providers, policymakers and the community -Patient education is essential for addressing misperceptions to increase demand for services and improving understanding of side effects to enhance treatment compliance. AMPATH has developed materials on chemotherapy for patients; held multiple meetings and conferences; and disseminated research findings. Provider education through continuing education is essential for improving quality of care. AMPATH has supported chemotherapy administration courses and tumour boards -- multidisciplinary meetings of medical personnel to discuss current cases, to disseminate and promote best practices. AMPATH has also supported the formation of patient support groups that have been very effective in raising awareness and generating demand for cancer screening services. Finally, AMPATH has provided technical expertise to the MOH in support of efforts to develop policies, guidelines and treatment protocols.

Additional areas of capacity building that AMPATH has supported include conducting and disseminating research and using new technologies to improve service delivery and quality of care. Ongoing challenges AMPATH faces include: generating continued political leadership and goodwill; consistent funding; collaboration at all levels in country, especially within the decentralized system; and maintaining access to cost effective drug supplies.

Common Challenges and Innovative Solutions In PPPs

- Improving coordination of public and private sector CCC providers and increasing engagement of the private sector, including through PPPs - While governments need to ensure financing of cancer programs, they do not necessarily need to deliver the services. In countries with a vibrant private sector, it may be more cost effective for governments to purchase services from private sector hospitals and clinics. In some countries, however, there are impediments to private sector provision of cancer care, such as high costs and low demand for services. Policymakers need to explore these issues and work with the private sector to identify ways to increase private sector engagement, including opportunities for Public Private Partnerships. Zambia has used a traditional PPP in which a mining company has sponsored gynaecology days for the wives of employees. Currently Zambia is hoping to form a PPP to add six satellite centres for radiology.

- Advancing research and ensuring that it is relevant and informs local programs - Strengthening the capacity of local Institutional Review Boards for both scientific and ethical reviews is essential to ensuring that research is relevant and useful. Also, including health care providers at all levels of the system, policymakers and other stakeholders in the review of research proposals helps to both ensure its relevance and build ownership of research results.

Opportunities for Regional Collaboration

There are important opportunities for countries to join together and collaborate to address the shortages of qualified personnel and limited training; serious underfunding of programs and the need to maker a better economic case for investing in cancer care and control; and the limited attention to research to inform policy and generate knowledge of science of delivery. Already countries have developed regional training programs to build capacity for pathology, oncology, radiation therapy, and other needed skills. Countries are also building important regional networks of resources to support one another in addressing cancer. Zambia has developed the Centre of Excellence for Women's' Cancers and is rolling out nationwide the HPV screening program. CCC SSKE participants were inspired after seeing the Zambia program in action and commented, "I wish my Minister of Health could visit Zambia and learn from the Zambian government what it takes to allocate resources for cancer care." Another stated, "the Cancer Control Programme for Zambia is a shining example as it has components of prevention at the African Centre of Excellence for Women's Cancers and another Centre of Excellence in Cancer Treatment at the Cancer Diseases Hospital." Rwanda has established the Butero Centre of Excellence on Comprehensive Cancer Care, the first cancer facility in a rural area in Africa. Botswana aims to excel in paediatric cancers. And with support of the African Development Bank, additional centres of excellence are being established. Kenya is developing a Centre of Excellence in renal medicine and Uganda in developing the East Africa Oncology Institute, an East African Centre of Excellence for

oncology training and tertiary education in biomedical sciences. These institutions will collaborate with one another to conduct research, train staff and build CCC capacity in Africa.

CCC SSKE - Sharing Knowledge, Experiences and Collaborating to Increase Access to CCC

The CCC SSKE provided a platform for technical experts and policymakers to share experiences, discuss common challenges and explore innovative solutions to address the rapidly rising burden of cancer in Africa. The World Bank served as convener and organizer of the knowledge exchange. The Bank mobilized the United States National Cancer Institute (NCI)/National Institute of Health (NIH) to participate in the initiative, leveraging technical expertise in highly specialized areas (for example, cancer epidemiology, planning, treatment, pathology). The Knowledge Exchange is in line with the World Bank's role as a knowledge institution, facilitating the sharing of promising approaches and providing a platform for learning. Given the modest technical capacity, limited training and meagre funding allocated to cancer care and control in Africa, the Knowledge Exchange played an important role in inspiring participants to scale up interventions in their own countries, using domestic resources or donor funding when available.

Common challenges discussed during the Knowledge Exchange include: serious shortages of trained specialists; few facilities that provide care; and underfunding of CCC services that leaves families shouldering, not only the tremendous burden of illness imposed by the disease, but also the high costs of seeking care. The CCC SSKE participating countries, Botswana, Kenya, Rwanda, Uganda and Zambia are at different stages in the development and implementation of CCC programs, are gaining experience and have many lessons to share. As one CCC SSKE participant stated: "Regional partnerships are key…countries need to put efforts into supporting each other to ease the patients' burdens."

Many important strides are being made. As has been seen throughout the CCC SSKE discussions, countries are designing and implementing programs and learning what works, and what does not work. CCC SSKE participants said the knowledge they gained through the exchange will enhance policy and program design. As one participant noted, "I have shared the information with my colleagues at work and also with the Ministry of Health….when engaged at the policy level, I will share the knowledge that I gained with the hope that it will help influence policy in my own country."

CCC SSKE participants reported improvements in knowledge and gains from networking with one another as they continue their efforts to mobilize resources and increase access to CCC in their countries. As one participant noted, "I intend to advocate for increased regional capacity for laboratory diagnosis for cancer in Kenya" and another stated, "I plan to hold a stakeholders' workshop to share the experience of Zambia. I will lobby for government support in setting up a cancer treatment centre in Kenya. We are hosting the First Ladies Conference in Kenya this year and we shall use the platform to lobby government for more resources for cancer care." CCC SSKE participants aim to continue sharing and exchanging knowledge and to work together to curb the cancer disease burden in their countries.

CCC SSKE – Main Results, Lessons Learned and Next Steps

In the short to medium term, the SSKE generated important results in terms of learning from promising experiences and identifying opportunities for future collaboration. Most importantly, it established a platform for clients to continue sharing tools, experiences and lessons. While not easy to measure or monitor, in the longer term, the Knowledge Exchange also will contribute to improved policies, greater collaboration, and expanded programs, funded by governments and partners. To summarize, the main results to date are as follows:

- Shared knowledge and experiences on the main building blocks of cancer care and control programs with a full range of topics covered, including:
  - Innovative approaches for strengthening cancer prevention efforts.
  - Strategies for implementing successful national CCC programs.
  - Task shifting and task sharing to increase access to care.
  - Tools for analysing CCC costs.
  - Financing models, including public private partnerships, to increase access to CCC treatment and care.
  - Data collection to better document the burden of disease.
  - Policy reforms needed to increase access to palliative care.

- Established a platform for cross country collaboration. The organizers facilitated communications across countries, to enable continual sharing of tools, experiences and latest research findings.

- Identified opportunities for collaboration (for example, join training, technical support, research) with one another and with institutions in the region such as the Centre of Excellence for Women's Cancers in Zambia, the Butaro Centre of Excellence on Comprehensive Cancer Care in Rwanda and the East Africa Oncology Institute in Uganda. International activity in South-South collaboration was also spurred with coordinating partners like Pink Ribbon Red Ribbon, The National Cancer Institute, and United States academic institutions.

Lessons Learned

- Peer-to-peer learning through a client-oriented, participatory process offers a collegial and collaborative environment for sharing insights, experiences, and lessons. This type of learning is highly valuable, relevant, and timely as reflected in feedback from participants.

- Face-to-face interactions between practitioners and policymakers from the participating countries strengthened understanding of how innovative programs were spearheaded, resources were mobilized, and political commitment was bolstered.

- A demand-driven approach was critical to soliciting views of participants about the most relevant topics to be covered and ensuring the knowledge exchange responded to client needs.

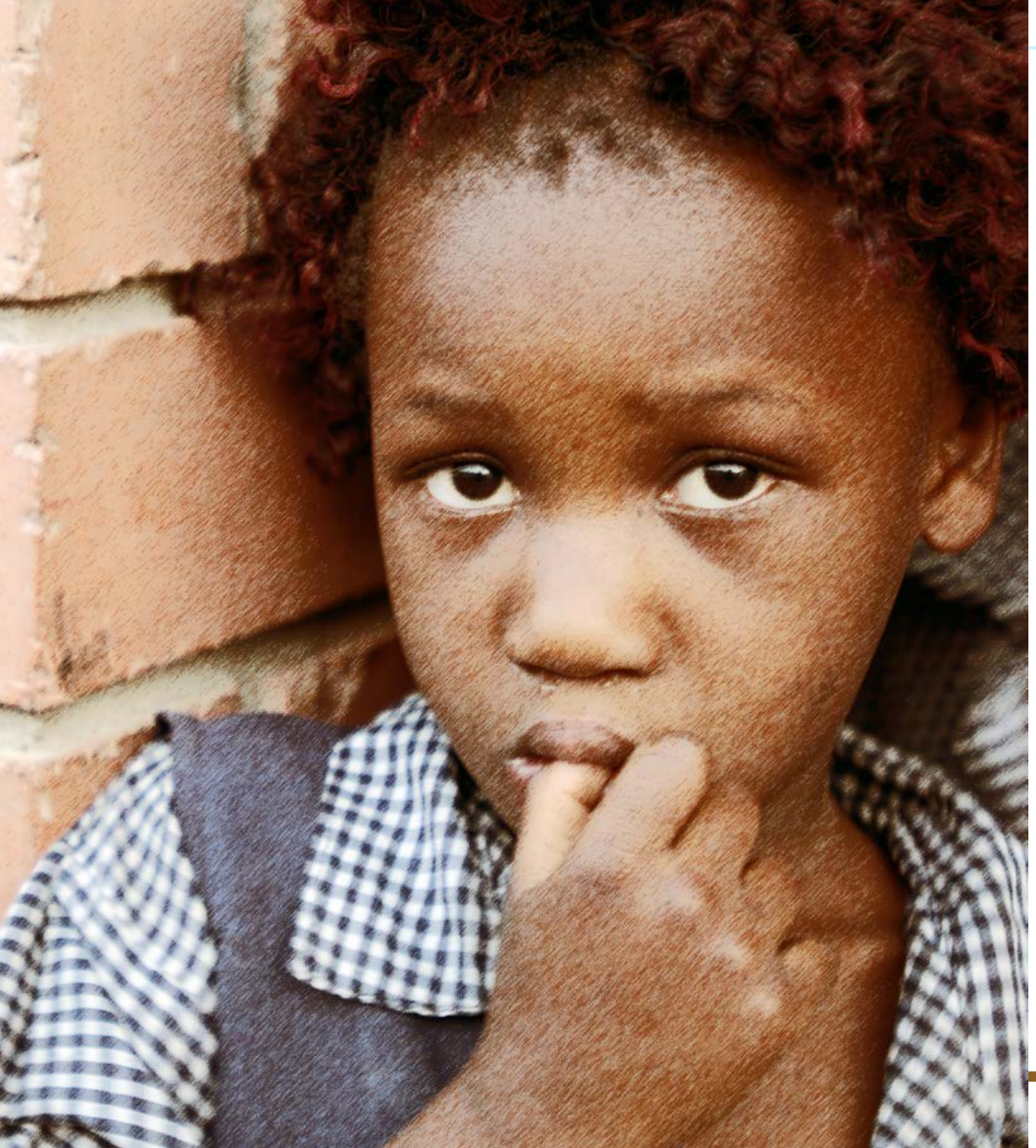
- Strong collaboration with other technical partners was requested by participants and proved highly effective. Technical partners brought a global perspective and offered complementary information which was appreciated by all stakeholders.

- Regional partnerships are key to maximizing learning, tapping comparative advantages of different players, and promoting specialization in delivery of training programs, cancer services and research.

- Strong preparation is essential to success. The knowledge exchange activities need to be well organized, materials need to be concise, and communication channels need to run smoothly, to maximize learning for busy practitioners and policymakers. Soliciting regular feedback from participants is critical to ascertaining views and ensuring that the knowledge exchange is tailored to country demands.

Next Steps

The knowledge exchange established a platform for collaboration and information sharing which continues beyond the formal closing date. Participants are in the process of incorporating lessons learned into their national programs, continuing to exchange information and materials with peers in other countries, and deepening their collaboration with technical partners on several aspects covered during the period (cancer planning, cancer registries). Examples worth noting include: the Bank-funded East Africa Public Health Laboratory Networking Project, which will be used as a vehicle for strengthening the availability of pathology services at project-supported laboratories in Kenya and Uganda; progress in Zambia, Kenya, and Uganda on national cancer control planning, facilitated in part by the regional lessons learned and collaborations highlighted in this paper; progress on cancer registration in Kenya and Zambia, drawing from expertise from Ugandan colleagues and from bi-lateral exchange between the two countries, supported by international organizations like the NCI, CDC and PRRR; and the formation of research networks on niche cancers like Burkitt Lymphoma or oesophageal cancer across countries more heavily affected in this region.



Chapter 19

The Way Forward

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Why this Report?

'The State of Oncology in Africa, 2015' is a unique report about cancer in Africa: it is written by health professionals working in Africa or international colleagues working closely with Africa. Overall, despite painting a depressing and deplorable picture of the current situation regarding cancer, it reflects the reality in Africa. It demonstrates how too many patients do not seek, or cannot access, professional medical services. Those who do, do so when the cancer is at an advanced stage when cure is no longer possible. Africa suffers from a lack of oncologists from all disciplines, oncology nurses and the other necessary health professionals and technicians to support their work. There is a lack of treatment centres. There is a lack of treatments. Most countries do not have any radiotherapy equipment at all. Most countries do not have access to opioid drugs for palliative care and pain control. Most countries do not have many of the cancer drugs on WHO Essential Medicines List. The situation is bound to get worse as the population grows and ages and cancer risk factors imported from high-resource countries begin to have their effect adding to the local risk factors with infections still top of the list.

It is estimated that the annual number of new cases of cancer in Africa will grow to more than one million in the next five years. Together with the immense loss in human life, there is a considerable economic setback attached to this number. However, most African nations are far from adequately scaling up their capacity to control cancer. Stefan (2015) reviewed the published data on the existing cancer control resources in Africa: the first combined effort looking at all resources available on the continent regarding cancer care. The total number of 102 cancer treatment centers, including general oncology centers, gynaecologic oncology or other single-organ malignancy units, and pediatric oncology and palliative care establishments, is not sufficient to cover the increasing needs of the African population affected by cancer (Stefan, 2015).

The evidence is clear. Over the next decades, cancer will cause Africans to suffer and die in greater numbers; much greater numbers than today.

Those professionals who do care for Africa's cancer patients are doing a magnificent job, frequently in desperate circumstances, without adequate resources or infrastructure: they deserve our full respect, admiration and assistance. There is hope from the success of high-quality, sustainable projects such as in Eldoret (AMPATH Oncology) the work of Hospice Africa Uganda, the collaborations between Crumlin Children's Hospital (Dublin, Ireland) and Tanzania, the development by UNC-Zambian colleagues of scalable surgical services for women with cancer and the Breast Health Global Initiative (BHGI). Unfortunately, it is not enough. Significantly, these extraordinary examples rely on international charitable donations rather than governmental funding or structural funds from official development assistance (ODA).

Cancer treatments have improved substantially. Surgery is less mutilating; Radiotherapy is less morbid and more effective; Chemotherapy is also more effective; Nutrition of patients is improving. However, many patients in Africa do not have access to these modern therapy regimes for a variety of reasons which encourage the growth of this disparity. The big question is how to get these advances to African patients?

The fact that in Africa access to health care is a major problem, cancer awareness is limited, cultural barriers are plenty, patients present with advanced disease and there is lack of the fundamental infrastructure that is required to be able to copy what is being done in developed countries compels African countries to develop alternative strategies in the treatment of cancer.

Since the development and implementation of these strategies extends beyond the current capacity of African countries, sustainable external assistance is required. An opportunity has been created by The Breast Health Global Initiative (BHGI). Among other breast cancer developments (Boyle et al, 2013), the Breast Health Global Initiative (BHGI), co-sponsored by Fred Hutchinson Cancer Research Centre and Susan G. Komen for the Cure has developed evidence-based, economically feasible, and culturally appropriate Guidelines for breast cancer for low- and middle-income countries (LMICs) to improve breast health outcomes and access to breast cancer screening, detection and treatment. These guidelines which were developed making sure that they are not defining a "lower" standard of care for that country are readily available and user friendly (Anderson et al, 2006; Anderson, 2008). African countries should therefore put in place proper strategies to implement the guidelines to the greatest extent possible.

External assistance also comes in the form of sustainable, external collaborations. There are many other commendable academic, Governmental and charitable collaborations with African Institutions. Yet surely improvements in the situation would come faster if there was some form of coordination of all these efforts, all of which come from the goodwill of individuals and institutions. Harnessing the power of the immense goodwill available would be of major significance for cancer control in Africa.

Cancer in Africa is not a Recent Phenomenon.

Many people are surprised when they discover that there is cancer in Africa. The documentary which accompanies this Report (Cancer is... Attacking Africa) interviewed 100 people on the streets of Washington DC regarding causes of death from chronic disease in Africa. Only one respondent mentioned Cancer.

In fact, there is a rich history of cancer and cancer research in Africa with some outstanding discoveries having been made there.

Sir Albert Ruskin Cook (1870-1951) was a British born medical missionary in Uganda and founder of Mulago and Mengo Hospitals. Together with his wife, Katherine Cook (1863-1938), a missionary nurse, he is widely regarded as the father of modern medicine in Uganda. Early in his sojourn in Uganda, he noted that the perceived absence of cancer was an artefact of the overwhelming burden of infectious disease and the lack of any referral system within the rudimentary health care system.

Cook kept meticulous records including a mention of a tumour of the jaw in a young boy. These records formed the basis of establishing cancer registration leading to the current Kampala Cancer Registry (KCR) and allowed Davies et al (1964) to examine the complete records from 1897 to 1956. Davies et al. (1964) noted that "there is a fair measure of stability in the site pattern. The cancers predominant in the first decade are prominent in the sixth, and on the whole there is a fairly close concordance with the findings in the Kampala Cancer Survey". Cancer did not appear to be a disease imported by westerners.

Denis Burkitt was an Irish Surgeon who, in 1957, observed a child with swellings in the angles of the jaw. He made further enquiries and established that jaw tumours were common in children in Uganda. In 1958, he published 'A sarcoma involving the jaws of African children'. (Burkitt, 1958) This newly identified cancer became known as Burkitt's Lymphoma and was subsequently shown to have unique pathological characteristics. (Burkitt et al, 1961; O'Conor, 1961)

A second major contribution of Burkitt was in regard to the potential effect of diets high in fibre reducing the risk of cancer of the large bowel. Burkitt (1971) noted the close relationship between bowel cancer and other non-infective diseases of the bowel, such as benign tumours, diverticular disease, and appendicitis, indicating to him that these conditions may have a common or related aetiology. Their close association with the refined diet characteristic of economic development suggested to him that the reduction of dietary fibre may be a causative factor. This hypothesis was popular for some period of time but subsequent research has demonstrated that this association does not hold. However, the role of fibre in the causation of diabetes and cardiovascular disease is still a promising subject of research.

John Higginson, an Irish Pathologist, led some important work in geographic pathology in South Africa. He published extensively on Liver Cancer (Higginson et al, 1956, 1957a), Oesophageal cancer (Higginson et al, 1958), gastrointestinal cancer (Higginson et al, 1961), bladder cancer (Higginson et al, 1962), as well as examining the general pattern of cancer among the Bantu (Higginson et al, 1957b) and the Bantu and Cape Coloureds (Higginson et al, 1960).

There are several more examples. Dodge et al. (1963) noted an association between circumcision and cancer of the penis in a study of men in Kenya and Uganda. Guy de Thé studied the association between Epstein-Barr Virus and Nasopharyngeal cancer in North Africa. Outstanding contributions to cancer epidemiology and pathology come from the work of fine researchers such as Denis Burkitt, Albert Cook, Anton Geser, John Higginson, Alan Linsell, Greg O'Conor and Guy de Thé among others.

Current Situation

The current situation of cancer in Africa is described in this volume in the words of African cancer specialists: the overall situation is shocking and deplorable. There is, however hope that a better future will comes from some high-quality, sustainable projects such as in Eldoret (AMPATH Oncology) (Strother et al, 2013), the work of Hospice Africa Uganda, the collaborations between Crumlin Children's Hospital (Dublin, Ireland) and Tanzania, the development by UNC-Zambian colleagues of scalable surgical services for women with cancer (Parham et al, 2015) and the Breast Health Global Initiative (BHGI).

These projects, and others, contribute positively to the control of cancer on the Continent. Another major source of hope is the remarkable dedication of the doctors, nurses and ancillary staff who work in Africa in conditions that would not be tolerated in high income countries. Progress against cancer needs to be made through strengthening general health systems, the attainment of Universal Healthcare Coverage and delivery of the sustainable development goals. These are huge challenges against a backdrop of significant social, economic and political fragility. Indeed, other serious health problems are competing. The battle against the ravages of infectious diseases continues.

The Globalisation of Cancer

The continued growth and ageing of the world's population will greatly affect the future cancer burden and it is widely expected that the global cancer burden will double by 2030. (Boyle et al, 2008) The greatest impact will be on the rapid increase in prevalent cases of cancer and the greatest effect of the increase will fall on low-resource and medium resource countries where, already in 2001, almost half of the disease burden was from non-communicable disease. (Boyle, 2006)

Africa and other lower-resource regions are, arguably, harder hit by cancer than the high-resource countries. Such countries often have a limited health budget and a high background level of communicable disease. Cancer treatment facilities are not universally available and life extending therapies are often unavailable for economic reasons. Cancer and other chronic diseases, which are becoming more common, can cause devastating damage to entire families in several circumstances—including when the head of household and the only source of income for a frequently extended family succumbs to cancer or when death of the mother results in girls stopping their education to look after the household. (Boyle, 2006)

A major challenge for African countries is how to find sufficient funds to treat the large numbers of cancers which will be diagnosed in the coming years. Effective prevention will reduce the risk of cancer and effective screening will allow many others to be successfully treated for their disease. Preventive action can be implemented today to reduce the burden of major cancer killers: tobacco control against lung cancer and other forms of cancer and vaccination against cancers of the cervix and liver.

Although many African countries assign high priority in their national health strategies to chronic diseases, including cancer, the donor community and most bilateral development agencies do not as yet consider cancer control a high priority. If cancer is not given higher priority through focused global efforts, health-care systems in low-income and middle-income countries will encounter further problems as the number of cancer cases increase. More and more people will die prematurely and needlessly from cancer, with devastating social and economic consequences for households, communities, and countries. Cancer will become a major impediment to socioeconomic development in low income and economically emerging nations.

The Challenge: What Could be Done?

Despite the absence of accurate, population-based data from the majority of countries, all estimates indicate that the global cancer burden has doubled over the last 25 years and is set to double again before 2030 (Boyle et al, 2008). Not only have the incidence and the mortality increased, but the prevalence of cancer survivors has been growing at an even faster rate. This is of substantial economic importance, as a significant proportion of cancer survivors are receiving active treatment and intense follow-up.

Simultaneously, there has been remarkable improvement in many aspects of Oncology. Over the past several decades we have better understanding of the causes of cancer, both the changeable lifestyle and environmental factors and the immutable biological. There has also been enormous progress in developing more effective treatments for many forms of cancer. Progress has been made in each of the four Pillars of Oncology (table 1) although, tragically, disparities exist at many levels of society and not every cancer patient has access to these modern advances. Even less of these advances have been implemented for the benefit of patients across the African continent.

Table 1: The Four Pillars of Oncology

The Four Pillars of Oncology:

1. Prevent all cancers that can be prevented
2. Treat all cancers that can be treated
3. Cure all cancers that can be cured
4. Provide Palliation whenever palliation is required

The above four points represents a global Charter for populations, cancer patients, governments, industry and society in every part of the world.

The Charter outlines in a simple manner the Rights of every patient with cancer today and for the future.
Compliance with this Charter in the case of individual patients, industry and individual countries should be used as a measure of the success of Oncology.

What is needed in Africa bears striking similarities to that needed elsewhere but it must to be modified to cope with the challenges presented by the unique situation in every country across Africa. This is a continent of extraordinary diversity and richness, culturally, linguistically (there are around 2510 languages spoken across the continent) and from socio-economic perspectives.

Prevent all Cancers That can be Prevented

Avoidable causes are known for about one half of cancers in high-resource countries (such as France (Boffetta et al, 2007)) although this preventable fraction is declining, as the rates of cancers caused by tobacco use, especially cigarette smoking, continue to fall. In high-resource countries, important in cancer prevention is avoiding tobacco use, reducing alcohol consumption, avoiding excessive exposure to natural or artificial sunlight, taking all precautions to reduce exposure to carcinogenic chemicals and adopting a healthier lifestyle, including increasing physical activity and maintaining a healthy body weight, all contribute to cancer prevention. (Boyle et al, 2003)

This preventable fraction is probably higher in Africa as a large number of cancers (especially lymphoma, cancers of liver and cervix and Kaposi's Sarcoma) are caused by infections. Many are theoretically avoidable through prevention of infection and by the development and delivery of effective vaccines. Key actions whose implementation would lead to a reduction in cases of cancer in Africa are listed in Table 2.

Table 2: Cancer Code for Africa

You can reduce the risk of cancer by following the guide below:

1. Do not use any tobacco product, particularly when smoked, and do not stay in the presence of others who smoke
2. Drinking alcohol only in moderation
3. Avoid eating mouldy and poorly stored foods
4. Walk, jog, run or take part in sports for at least 30 minutes every day
5. Do not put on weight as an adult
6. Breast feed your children for 2 years
7. Avoid handling chemicals without adequate protective equipment
8. Practice safe sex – limit number of sexual partners and men should wear a condom during intercourse
9. Making sure your baby is vaccinated against Hepatitis B
10. Make sure that young girls are vaccinated against Human Papilloma Virus (HPV)
11. Be screened for cervical cancer at least once in your life or every three years if possible

Do not use any tobacco product, particularly when smoked, and do not stay in the presence of others who smoke. Tobacco use is the major cause of cancer in high-resource countries (Boyle et al, 2010) and the increasing uptake of the habit in Africa is certain to contribute to the evolving epidemic of cancer in Africa. It is essential to avoid the use of any tobacco product, particularly when smoked, and individuals should not remain in the presence of others who smoke as environmental exposure does cause cancer.

Drink alcohol only in moderation. Drinking of alcohol, even in small amounts, increases the risk of several types of cancer (Boyle et al, 2013). Alcohol should be avoided or at the least consumed in moderation. Moderation in western society is usually defined as a maximum of two units of alcohol per day for men and one for women. Recommendations are lower for women in view of the increased risk of breast cancer associated with even low levels of regular alcohol consumption. A unit of alcohol is generally considered as a glass of beer, a glass of wine or a glass of spirits, each corresponding to approximately 10 gm of alcohol. However, in Africa, there is a lack of a generally accepted unit of alcohol consumption. One bottle of beer in Africa generally contains at least 2 units of alcohol, as defined by western standards.

Avoid eating mouldy and poorly stored foods. The main causes of liver cancer in Africa are chronic infection with hepatitis B virus (HBV) and, to a lesser extent, hepatitis C virus (HCV), compounded by exposure to aflatoxins, a class of carcinogenic mycotoxins that contaminate food commodities in western and Central African countries (Hainaut, 2016). Aflatoxins grow on poorly stored foodstuffs. It is imperative to avoid eating mouldy or poorly stored foods.

Walk, jog, run or take part in sports for at least 30 minutes every day. Regular physical activity is associated with a reduction in the risk of a number of cancers, especially colon cancer, cancer of the breast (at post-menopausal ages) (Pizot et al, 2016), and cancer of the endometrium. The protective effect of physical activity on cancer risk increases with increasing levels of activity though such a recommendation should

be moderated in individuals with cardiovascular disease in the absence of medical advice. Everyone should walk, jog, run or take part in sports for at least 30 minutes every day.

Do not put on weight as an adult. It is important to avoid weight gain and to maintain a normal body weight. Obesity is an established and major cause of morbidity and mortality and most countries have seen the prevalence of obesity increasing rapidly over the years. Overweight and obesity have been recognized as cancer risk factors, mainly for the colorectal, (postmenopausal) breast, endometrial, and renal cancer, and for adenocarcinoma of the oesophagus.

Breast feed your children for 2 years. The longer women breast feed, the more they are protected against breast cancer. Therefore, mothers should breast feed for the longest duration feasible. Indeed, the cumulative incidence of breast cancer in high-income countries would be reduced by more than half if women had the average number of births and lifetime duration of breastfeeding that has been prevalent in low-income countries. Breastfeeding could account for almost two-thirds of the estimated reduction in breast cancer incidence. Ironically, promotion of infant formula in low resource countries is now impeding breast cancer prevention.

Avoid handling chemicals without adequate protective equipment. The prevention of exposure to occupational and environmental carcinogens is best brought about if:

1. legislators and regulators adapt scientific consensus evaluations into law, and control compliance with these regulations;
2. managers, hygienists and doctors in industry comply with those laws and regulations and encourage others to do so; and
3. every citizen protects their own health and the health of others, by paying heed to the presence of carcinogenic pollutants and follow instructions and regulations aimed at mitigating or preventing exposure to carcinogens.

Practice safe sex – limit number of sexual partners and men should wear a condom during intercourse. Risk of cervix cancer and HIV infection increases with the number of sexual partners and the practice of unprotected sexual intercourse. Individuals with HIV/AIDS are at increased risk of several forms of cancer including Kaposi's Sarcoma, Lymphoma and Cervix cancer.

Make sure your baby is vaccinated against Hepatitis B. Hepatitis B virus (HBV) infection is a major public health problem. Approximately two billion people are infected worldwide, and more than 400 million are chronic (lifelong) carriers. The fraction of hepatocellular cancer attributable to HBV has been estimated as 23% in developed countries and 59% in developing countries. The virus also causes a large number of deaths from non-cancerous liver diseases. Hepatitis B is clearly a public health problem in Africa (Hainaut, 2016). Widespread hepatitis B vaccination of babies in Taiwan has been shown highly effective in reducing the prevalence of hepatitis.

Make sure that young girls are vaccinated against Human Papilloma Virus (HPV). Chronic infection with Human Papilloma Virus (HPV) is the cause of a large proportion of cervix cancer. It is recommended that routine HPV vaccination be initiated at age 11 or 12 years. The vaccination series can be started beginning at age 9 years. Vaccination is also recommended for girls aged 13 through 26 years.

Be screened for cervical cancer at least once in your life or every three years if possible. Cervix cancer is one of the most common forms of cancer in Africa (Brawley et al, 2016; Arbyn et al, 2016), comprising about 25% of all cancers in women. Risk of cervix cancer and HIV infection increases with the number of sexual partners and the practice of unprotected sexual intercourse. Cervix cancer is one of the most common forms of cancer in Africa (Brawley et al, 2016; Arbyn et al, 2016), comprising about 25% of all cancers in women. The basic principle of cervical cancer screening is the detection of precursor dysplastic lesions and cancer intraepithelial neoplasia (CIN) which may develop into invasive cancer if infection of the cervix by the papilloma virus (HPV) remains persistent during adult life. A vast amount of descriptive epidemiological

data provides evidence of the efficacy of screening using a cervical smear (Pap) test performed every 3-5 years. Women in Africa, and other lower resource countries, should be screened for cervical cancer at least once in their lifetime and every three years if possible.

Randomized trials have evaluated the influence of visual inspection with acetic acid, cytology screening and HPV testing on the risk of cervical cancer death. (Sankaranarayanan et al, 2007; Sankaranarayanan et al, 2009) In addition, novel strategies such as a single visit 'see and treat' involving treatment of identified lesions with cryotherapy or cold coagulation in screen-positive women without evidence of cervix cancer have proven effective.

There is now strong evidence that implementation of Visual Inspection Screening (VIA) is effective and can be widely implemented in lower resource settings such as Africa. When rapid HPV testing becomes available at an affordable price it will be adopted widely. The combination of HPV vaccination and screening for chronic HPV infection has the potential to prevent the majority of cases of cervix cancer.

Implementing screening for other cancers in Africa is not straightforward. One of the criteria for screening as laid down by Wilson and Jungner (196) is that facilities for further diagnosis and treatment should be available. Sadly, this is not the case throughout Africa at the moment. Breast cancer screening with mammography, currently the subject of some debate in high-resource countries, is expensive and resource intense. The introduction of clinical breast examination screening should wait for evidence from ongoing trials. Improving breast awareness and access to early diagnosis and treatment in health services is a valuable breast cancer control option.

Kaposi's Sarcoma is endemic and its incidence has increased substantially with the advent of the AIDS epidemic in sub-Saharan Africa. For decades, the aetiology and pathogenesis of Kaposi's Sarcoma was unknown until Chang et al. (1994) reported the discovery of the Kaposi's sarcoma-associated herpes virus (KSHV), also known as human herpes virus-8 (HHV-8), and demonstrated an aetiological link between the virus and Kaposi's sarcoma. Today, it is appreciated that there are four clinical variants of Kaposi's Sarcoma (Orem, 2016). Endemic Kaposi's Sarcoma is a variant of the disease effecting primarily older men who are not infected with the human immunodeficiency virus (HIV).

Treat all Cancers that can be Treated

Scientific knowledge and understanding regarding cancer treatment has grown significantly. With each new therapy demonstrated to have efficacy in treating malignant disease, the overall survival time of the group of patients with the disease in question improves. One of the great challenges is still the treatment of advanced or metastatic disease. Despite great progress in developing cancer treatments in the past decades, many cancers remain difficult to manage and frequently still carry a poor prognosis. The development of resistance to chemotherapy constitutes one of the major challenges of treatment and results in the incurability of mainly advanced disease.

Alas, such scenarios apply to countries at the highest resource level since each new treatment is expensive and frequently requires specialist facilities to identify suitable patients for the treatments and to deliver and monitor the treatment. In high-resource countries, two out of three people live at least five years after a cancer diagnosis. In lower-resource settings, cancer survival rates are much poorer although demonstrating wide variations. (Sankaranarayanan et al, 2011)

Effective therapy requires quality surgery, radiotherapy and the medical oncology and palliative care skills. The manpower to support the entire system needs to be trained in place and adequately funded. The residents of many African countries have yet to see and/or benefit from the recent, significant advances in surgery, radiotherapy and chemotherapy. (Ngoma, 2013)

Even if these interventions were available many would not benefit. Most patients in Africa present with advanced stage disease, conservative surgery, which is now the norm for many cancers (such as breast) in high-income countries, is not an option. Furthermore the lack of surgeons, lack of hospitals equipped with operating theatres and patients inability to access and pay for surgical services pose real problems in Africa. In Africa, large advanced, inoperable cancers for which the only realistic option is palliation are still a common occurrence.

In most African countries radiotherapy is either not available or in short supply. Exemplifying the stark difference between poor and rich nations regarding radiotherapy facilities is Austria, which houses the International Atomic Energy Agency headquarters. Austria possesses ONE radiotherapy machine for every 200,000 people or fewer while many low-resource countries like Tanzania have only ONE radiotherapy machine for up to ten million people or more. Some of the world's poorest nations have no radiotherapy facilities whatsoever (Salminen et al, 2011) and those that have a facility frequently find that the machine is broken and in a poor state of repair (figure 1).

Figure 1: Uganda's radiotherapy machine for cancer treatment breaks

Source: BBC, 2016 (http://www.bbc.com/news/world-africa-35997075)

Abdel-Wahab et al. (2013) made a longitudinal assessment of the status of radiation oncology resources in Africa to measure the extent of the problem and the effects of programmes designed to enhance radiation services in the continent. Radiation Oncology departments in Africa were surveyed through the Directory of Radiotherapy Centres, and this information was supplemented by that available from International Atomic Energy Agency Regional African and Interregional project reports for 2010. Of 52 African countries included, only 23 are known to have external beam radiation therapy. These facilities are concentrated in the southern and northern states of the continent. Brachytherapy resources (high-dose rate or low-dose rate) were only available in 20 of the 52 African countries. Although progress has been made in the establishment of radiation oncology services in some countries, a large need still exists for basic radiation services, and much resource mobilisation is needed for services to keep pace with the burgeoning populations of many countries.

Furthermore even the radiotherapy treatment machines in low-income countries are usually the older cobalt 60 machines that are frequently out of order. Most of these countries have no linear accelerators capable of generating electron beam therapy or Multi Leaf Collimators. (Johnstone et al, 2016). With only Cobalt 60 machines available, it makes it impossible to implement radiotherapy protocols to the standards available in high-income countries. Lack of radiotherapy facilities in low-income countries is a challenge which needs to be solved in order to improve the care of cancer patients (Ngoma et al, 2016).

The important role of chemotherapy in the treatment of many forms of cancer is undisputed. However, the cancer chemotherapy drugs widely available in high-income countries are often not available in Africa. Most countries do not have many of the oncology drugs listed on the WHO Essential Medicines List. When available, these drugs are usually unaffordable to most patients and difficult to administer. Prescribing and delivering chemotherapy is frequently complex and is not as simple as writing a prescription for anti retrovirals, anti-hypertensives or statins. Cancer chemotherapy rarely comprises pills that can be administered by the patient in their home. In addition, there needs to be continual monitoring and assessment of patients receiving chemotherapy.

The delivery of cancer chemotherapy in Africa is hindered by widespread lack of healthcare professionals skilled in administering chemotherapeutic agents, access to laboratories for blood count analyses and effective antiemetic and supportive treatments. It is also important to note that most chemotherapeutic regimens have been field tested in clinical trials in high-income countries and that there is a possibility that treatment results from high-income countries are not generalizable to Africa, where the infrastructure, supportive care, patient and tumour characteristics differ markedly. (Magrath, 2003) In a situation like this, local clinical trials to establish what works best in low-income countries are highly recommended rather than embracing the one size fits all notion and the dangerous assumption that more expensive and newer drugs are better.

Personalised medicine and the consequent development of targeted therapy are major advances in cancer therapy. These technologies require adequate laboratory diagnostic facilities to determine tumour histology and identify the presence of therapeutic targets.

There must also be adequate staging and treatment facilities.

There is an acute absence of laboratories capable of measuring molecular targets for therapy in Africa where the routine collection of biological samples and their storage in adequate facilities is not a common feature (Vaught, 2016). The absence of these laboratories means little is known about the prevalence or frequency of many molecular targets for therapy patients in Africa. This includes lack of the necessary equipment, biological reagents and laboratory skills to measure markers and to exert quality control standards.

One way of dealing with the current disparities in treatment of cancer is to view cancer treatment and cancer control in general as a human rights issue. In so doing all world leaders and organizations have to work together to defend the human right of access to cancer care just like the way they defend democracy. African countries must set their own national cancer control agenda with the high-income countries and international organizations serving in a supporting role. Every cancer patient, no matter their situation, has a right to the most appropriate treatment for their condition at the right time.

Cure all Cancers That Can be Cured

There are many cancer patients now living longer and longer even with advanced stage disease and who maintain a good quality of life. Previously defining cure to be five-year survival is not appropriate today when life expectancy has increased substantially in many countries. Cure means much more than 5-year survival and should be taken to mean that a treated patient has a life expectancy similar to the population of the same age. While there are some outstanding examples of cures, curative therapies have proven elusive for many common forms of cancer.

Recent developments in understanding of cancer's biological mechanisms has started to produce drugs targeted at specific biological or genetic features of certain cancers with some highly encouraging success. This provides substantial hope for the near future. However, there are many hurdles which will limit the introduction of such therapies into all but the highest resource settings: in Africa there is a lack of high-quality laboratories and trained staff capable of performing the companion diagnostic assay, lack of biobanks to better understand the mutational profiles of populations and major infrastructure and financial issues to overcome.

The net result is that cancer patients in Africa who could benefit from new therapies are missing out.

Provide Palliation Whenever Palliation is Needed

There have been major improvements in all aspects of Palliative, Supportive and Terminal Care in the past decades although these improvements have been slowly introduced in many high-resource countries. It is also disquieting that the little that is known about the quality-of-life of cancer patients comes from a remarkably small number of well-designed trials. Palliation is needed not only for pain control at the end of life, but should be available at every part of the cancer pathway: at the time of surgery, radiotherapy and during chemotherapy. In Africa the situation is frankly appalling. There are very few trained in palliative care. Radiation therapy is very useful for pain control but approximately 30 African countries do not have a single radiotherapy machine. More than two dozen African countries have outlawed the importation of opioid medications. Where opioids are available, the average defined daily dose varied several hundred-fold. Paracetamol is not an effective medication for the control of severe cancer pain, but that is all that is available in too many countries.

There are nearly 30 countries without both opioid medications and radiotherapy. In these countries, hopes of a pain-free, dignified death from cancer is a priority that needs to be urgently addressed.

Patients living with and dying from cancer have the fundamental right to do so with dignity and comfort irrespective of their disease or where they live. The contrast between high-income and low-income countries in terms of supportive, palliative care and terminal care is even greater than for cancer treatment services. This year, more than 8,000,000 people internationally will die as a direct result of cancer, many of whom will have had their lives substantially shortened. This will rise to 17 million people by 2030. (Boyle et al, 2009) The predictable effects of advancing cancer challenge health systems to plan for and resource the relief of the suffering experienced by people and their caregivers as the disease progresses within a public health framework.

The continuing improvements in cancer prevention, early detection and treatment are still overshadowed by premature mortality as a result of cancer. In resource-rich countries, two out of every five people diagnosed with cancer will die prematurely. This can rise to nine out of ten people in resource-poor countries where late presentations and limited resources deliver poor survival rates and, frequently, deaths in atrocious circumstances.

The control of pain and suffering is central to health, and the right to health is stipulated in several International declarations. The Korean Declaration (2005) states that *"Every individual has the right to pain relief".* The Cape Town Declaration (Mpanga Sebuyira et al, 2003) states that the control of pain and symptoms is a human right. Appropriate drugs for pain control should be available in every country in sub-Saharan Africa as part of the essential drug list. This includes opioids such as morphine. Sadly, this is not the case in Africa.

Palliative care is an important aspect of treatment that is needed but poorly provided in Africa, and in many other low-income countries around the world. There is a lack of health care professionals skilled in palliative care. The few skilled palliative care workers are often restricted in their ability to provide comfort care and pain relief for cancer patients, especially as part of end-of-life care because many common and effective pain medications, such as morphine, are not readily available (World Health Organization, 1996).

The Practical: What Must be Done

There is a wide variety of statistics available regarding cancer in Africa although most, at best, provide estimates of the situation. However, statistics are patients with the tears wiped away. It is bad to have cancer and worse to have cancer if you are poor and disconnected from the public health system. Alarmingly, the gap between rich and poor, highly educated and less educated and the North-South divide is substantial and continuing to grow. Radical solutions to improve the situation in the poor countries are urgently needed: the status quo is not an appropriate response to the current situation. Recognising that no single government or source of philanthropy has the means to solve this problem, new models are needed to cope with and improve this situation.

It is bad to have cancer and worse to have cancer if you are poor. The gap between rich and poor, highly educated and less educated and the North-South divide is substantial and continuing to grow. Radical solutions are urgently needed: the status quo is not an appropriate response to the current situation. Recognising that no single Government or source of philanthropy has the means to solve this problem, new models are needed to cope with and improve this situation. It is impossible to avoid the conclusion that there is a need for major increases in expenditure on public health, wider application of health structural funds from ODA to include NCDs and creative approaches to Private-Public partnership, involving a number of sources from different areas, to make the necessary progress with the briefest delay. The partnership needs the commitment of the pharmaceutical industry and the wide span of industries involved in the technology for diagnosis and treatment. It needs the commitment of Governments and Non-Governmental Organisations to be effective. Effective will be measured against the Right of every patient with cancer to have the most appropriate treatment and care for their disease.

Working to improve health must cease to be viewed as a competition. Public and Private organisations have an underlying suspicion of each other that must be overcome in the interests of improving cancer care and outcome worldwide. The situation as portrayed in this Report is dramatic and urgent and it behoves all parties to put this frequently deep-rooted suspicion behind them and develop an effective collaboration to improve this key aspect of Public Health throughout the world.

There is no need for new Resolutions from major international organisations to bring about the changes necessary. Such already exists in the shape of the International Covenant on Economic Social and Cultural Rights (ICESCR), which was voted by the United Nations General Assembly

in 1966 and came into force in 1976. This multilateral treaty provides that State Parties to the Covenant recognize the right of everyone to the enjoyment of the highest attainable standard of physical and mental health. Article 12.2 contains important determinants of the right to health such as prevention and treatment of diseases essential for the enjoyment of the right. There are 164 parties to the treaty and this gives a strong justification to make changes to improve the health of the global population.

Reading through this report, particularly in the country chapters, the reader will find almost monotonously, phrases along the lines of 'lack of funds' and frequently used in the situation when patients with cancer cannot afford their treatment since they have to pay themselves. Within the context of the International Covenant on Economic Social and Cultural Rights (ICESCR), the phrase the right to health such as prevention and treatment of diseases is of crucial importance and a strong incentive for all countries, especially those African countries and others with significant poverty, to introduce Universal Health Coverage. This should also be viewed as a human right and its widespread implementation throughout Africa would make a significant difference to patients' lives.

While progress in Oncology has been remarkable in the recent decades, and the future looks very encouraging, not every cancer patient is benefitting from the advances made in treating their disease. This is true even in the high-resource countries where there are substantial differences in outcome according to the individual's deprivation status. The contrast in diagnosis, treatment and its outcome between the high-resource and low-resource countries is dramatic.

This is a particularly important issue since the pattern of cancer globally in the foreseeable future will be heavily dependent on what happens in China, India and Africa, where one half of the world's population currently live and the populations of each are ageing quickly and have developed lifestyle habits conducive to increasing cancer risk. India has a long tradition in Cancer Care but faces the challenge of extending that care to their growing population. China faces similar challenges to India and has been making solid investment in training and infrastructure to cope with the huge problem the country is facing. Life expectancy has increased from 55 in the 1960's to 75 today and with it has come a rapidly increasing burden of cancer and other chronic diseases linked to ageing. Africa presents the biggest challenge with population growth and life expectancy increasing in many countries as the toll of AIDS declines. However, there has been little investment in capacity of any sort to deal with the current cancer problem never mind the rapid increased in incidence which is underway. This is a critical area for investment and not only of a purely financial nature.

The current situation regarding Cancer in Africa is quite deplorable. Many patients do not seek medical advice. Those who do, do so when the cancer is at an advanced stage when cure is no longer possible. There is a lack of oncologists of all kinds, nurses and the necessary health professionals and technicians to support their work. There is a lack of treatment centres. There is a lack of treatments. Most countries do not have any Radiotherapy equipment. Most countries do not have access to opioid drugs for palliative care and pain control.

The situation is bound to get worse as the population grows and ages and cancer risk factors imported from high-resource countries begin to have their effect. The evidence is clear. Over the next decades, cancer will cause Africans to suffer and die in greater numbers; much greater numbers.

It is essential to move from a passive position to an active voice. We can turn our heads and walk away from this situation and betray all those wonderful clinicians, nurses and other personnel grasping with the overwhelming problem of cancer on the Continent. Or, we can do something.

There is an overwhelming and urgent need for international leadership and coordination in the area of Oncology. Compared with other global health communities, the global cancer control community is diffuse and often ineffective. It needs to be relaunched and to acquire focus and

priorities. Such priorities must be realistic and achievable, and include a focus on low-resource and medium-resource countries and the identification, delivery, and assessment of effective cancer control measures. These should emphasise strengthening the roles of surgery, medical oncology, radiation oncology, pathology and all related diagnosis and treatment specialities. The time has come to give more consideration to developing effective patient organisations in low-resource settings and to give conservation to care givers, whose work can be physically and emotionally draining.

As with cancers everywhere, cancer in Africans deserve to be prevented, to be treated, to be cured and to be palliated. If we don't do it now, starting immediately, it will be too late and Africa's cancer crisis will continue to grow out of control. The cancer situation in Africa is critical.

Call for Action

Radical solutions are necessary: the status quo is not an option. There is hope in the sense that there are outstanding examples where effective and efficient oncological services function. There are clearly identified needs. Global Society cannot, once again, react too slowly to an African health crisis.

Along with a long list of distinguished cancer specialists, we call on African governments, foreign governments and international organizations to address this challenge with specific, coordinated actions (table 3).

Table 3: Call for Action

This is a call to African governments, foreign governments and international organizations to address the challenge posed by Cancer in Africa with specific, coordinated actions:

1. There is a need to train more oncologists and health professionals in cancer care and provide the necessary infrastructure which is urgently needed to identify and treat patients. More general and specialist surgical capacity is critical as are concomitant enhancements in imaging and pathology.

2. The drugs and equipment necessary to treat patients with cancer must be made available. As a minimum each country should ensure the supply of all cancer drugs on the WHO Essential Medicines List. We need to deliver, install and maintain adequate numbers of resource appropriate Radiotherapy machines. It should be the right of cancer patients, no matter where they are to have access to the appropriate treatment of their disease.

3. Opioids must be available for controlling the pain of patients with terminal cancers (and other diseases). International Agencies should make this a priority activity and come to agreements with Governments of countries where these are not available.

4. Since half of cancer in Africa is currently caused by chronic infection, relevant infection control and vaccination programmes must be funded and implemented continent-wide.

5. Information and education campaigns to wipe out stigma and misinformation must be conceived and disseminated.

6. Making Universal Health Coverage globally available and strengthening health systems is critical for improving cancer care. This is also a critical area for the corporate and social responsibility agendas for the private industries including all trans-African corporations.

7. High quality cancer institutions, all over the world, should establish collaboration ventures with cancer centres and institutes in every African country, as well as with public health services.

8. International philanthropy is vital to help fund these efforts.

9. The International Covenant on Economic Social and Cultural Rights (ICESCR) should be invoked as the basis for action. This multilateral treaty provides that State Parties to the Covenant recognize the right of everyone to the enjoyment of the highest attainable standard of physical and mental health. Article 12.2 contains important determinants of the right to health such as prevention and treatment of diseases essential for the enjoyment of the right.

First of all, there is a need to train more oncologists and health professionals in cancer care and provide the necessary infrastructure which is urgently needed to identify and treat patients. More general and specialist surgical capacity is critical as are concomitant enhancements in imaging and pathology.

Two, the drugs and equipment necessary to treat patients with cancer must be made available. As a minimum each country should ensure the supply of all cancer drugs on the WHO Essential Medicines List. We need to deliver, install and maintain adequate numbers of resource appropriate Radiotherapy machines. It should be the **right** of cancer patients, no matter where they are to have access to the appropriate treatment of their disease.

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Finally, the International Covenant on Economic Social and Cultural Rights (ICESCR) should be invoked as the basis for action. This multilateral treaty provides that State Parties to the Covenant recognize the right of everyone to the enjoyment of the highest attainable standard of physical and mental health. Article 12.2 contains important determinants of the right to health such as prevention and treatment of diseases essential for the enjoyment of the right.

This is a call to African governments but also to the many foreign governments and international organizations who are distancing themselves from the crisis. Reports with idealised solutions are very well but that time has passed. The necessity now is for coordinated and sustainable action, the large part of which is affordable.

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The State of Oncology in Africa 2015

'The State of Oncology in Africa, 2015' is a unique report about cancer in Africa, written by health professionals working in Africa or international colleagues working closely with Africa.

Overall, despite painting a depressing and deplorable picture of the current situation regarding cancer, it reflects reality. It demonstrates how too many patients do not seek, or cannot access, professional medical services. Those who do, do so when the cancer is at an advanced stage, when cure is no longer possible.

Africa suffers from a lack of oncologists from all disciplines, oncology nurses and the other necessary health professionals and technicians to support their work. There is a lack of treatment centres. There is a lack of treatments. Most countries do not have any radiotherapy equipment at all. Most countries do not have access to opioid drugs for palliative care and pain control.

The crisis is bound to get worse as the population grows and ages and cancer risk factors imported from high-resource countries begin to have their effect, adding to the local risk factors, with infections still top of the list.

Global Society cannot, once again, react too slowly to an African health crisis.

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