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Comprehensive cancer control-research & development: knowing what we do and doing what we know

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Contents

Key words: ICCC-3, cancer control, international collaboration.

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Abstract

Comprehensive cancer control is defined as an integrated and coordinated approach to reducing cancer incidence, morbidity, and mortality across the cancer control continuum from primary prevention to end-of-life care. This approach assumes that when the public sector, non-governmental organizations, academia, and the private sector share with each other their skills, knowledge, and resources, a country can take advantage of all its talents and resources to more quickly reduce the burden of cancer for all its population. One critical issue for comprehensive cancer control is the extent to which the private sector can contribute to cancer prevention and control programs and policies that have historically been lead by the public health sector, and similarly how can the public sector increase its investment and involvement in clinical research and practice issues that are largely driven by the private sector worldwide?

In addition, building capacity to integrate research that is appropriate to the culture and context of the population will be important in different settings, in particular research related to cancer control interventions that have the capacity to influence outcomes. To whatever extent cancer control research is ultimately funded through the private and public sectors, if investments in research discoveries are ultimately to benefit the populations that bear the greatest burden of disease, then new approaches to integrating the lessons learned from science with the lessons learned from service (public health, clinical, and public policy) must be found to close the gap between what we know and what we do. Communities of practice for international cancer control, like the ones fostered by the first three International Cancer Control Congresses, represent an important forum for knowledge exchange opportunities to accelerate the translation of new knowledge into action to reduce the burden of cancer worldwide.

1. Introduction

Comprehensive cancer control has been defined by the US Centers for Disease Control and the International Union Against Cancer as an integrated and coordinated approach to reducing cancer incidence, morbidity, and mortality across the cancer control continuum from primary prevention to end-of-life care. The comprehensive cancer control approach assumes that when the public sector, non-governmental organizations (NGOs), academia, and the private sector share with each other their skills, knowledge, and resources a country can take advantage of all its talents and resources to more quickly reduce the burden of cancer for all its population.

The world distribution of new cancer patients shows that approximately 60% are outside the United States, Europe and Japan. Latin America has 10% of new patients, 28% are in China, and 30% are in other regions of Asia[1]. Thus, while high income countries invest substantial resources in cancer control programs, low and middle income countries, with far fewer resources, bear the greatest burden of disease and presumably would benefit most from adopting a comprehensive cancer control approach.

High income countries are replete with both academic institutions and NGOs, which can contribute substantially to comprehensive cancer control plans and programs, whereas the principal resources in low and middle income countries come from the public and private sectors. Thus, a critical issue is the extent to which the private sector can contribute to cancer prevention and control programs and policies that have historically been lead by the public health sector, and similarly how can the public sector increase its investment and involvement in clinical research and practice issues that are largely driven by the private sector worldwide?

In addition, in all settings it will be important to build capacity to integrate research that is appropriate to the culture and context of the population; in particular research related to cancer control interventions that have the capacity to influence outcomes. This paper was prepared to highlight the experiences of countries in high, middle and low income settings in conducting research to improve knowledge on effective practices and interventions to prevent and control cancer. The areas of research that are important for cancer control programs, regardless of the setting, and that are the focus of this paper, include 1) Tumor Tissue Bio-repositories, 2) Clinical Trials, 3) Registries and Cancer Survival, 4) Health services and health economics, 5) Translating research into practice, and 6) Palliative Care.

2. The role of the private and public sectors in cancer control

2.1. Global cancer control: a corporate view

Derek Yach

With the workplace so fundamental to our lives, corporations have taken a leading role in helping employees (and their families) manage and reduce the pervasiveness of cancer in our society. They do this individu-

ally and through a World Health Organization (WHO) - World Economic Forum Workplace Wellness initiative. This expanding corporate effort includes providing workplace wellness and cancer control programs and management, tobacco control and smoke-free initiatives, obesity and physical activity programs, cancer screenings, the reduction of occupational exposures to carcinogens, and the promotion of healthful eating. Corporations recognize the need to ensure that best practices in cancer control are applied globally and adapted to the needs of low and middle income companies.

Most corporations also respond to the needs of the global community by joining forces with government agencies, research organizations, NGOs and non-profit organizations around the world, providing resources, technologies, and skilled personnel to improve access to cancer treatment and medicines in countries and regions where health resources are lacking or non-existent. Further, biomedical research companies are the leading source of all available medicines and vaccines, including cancer treatments, offering hope and the potential of good health for people all over the globe. These companies need to work with the newly announced Global Alliance for Non-communicable Disease Research (that includes major public health agencies from the United States, United Kingdom, Canada, Australia, India and China) to define unique and supportive roles for the private sector.

2.2. The public sector's role in clinical research

Eduardo Cazap

Clinical research is vital to the development and improvement of methods to prevent, detect and treat cancer. Institutional participation in clinical trials improves quality of care for all patients treated at that site. Doctors and nurses who participate in clinical trials are more likely to adopt effective innovations into routine practice, as well as to practice cancer care more rigorously[2].

The majority of clinical trials take place in the developed world through sponsored pharmaceutical company research. The American Cancer Society highlights the disproportionate amount of cancer clinical research performed in the US and the rest of the world (roughly 2 times more). Less than 15% of the clinical trials are conducted in resource-challenged countries[3-5]. The corresponding lack of research in resource-challenged countries results in two unmet needs related to cancer treatment in those regions.

First, recommended treatments do not reflect ethnic (genetic), cultural and resource differences between resource-rich and resource-challenged countries that are not subject to clinical research. Second, there is little research conducted on those cancers that are primarily found in resource-challenged countries. Thus, the ability to diagnose and treat these diseases is impaired.

Health care systems vary from country to country. National populations vary by age structure, co-morbidity, and genetic background. Particularly with the newer generation of biological agents, we need to establish whether treatment effect or toxicity varies by population genetics.

Given that this general picture reflects today's situation globally, it is critical to promote clinical research in resource-challenged countries mainly with training of all levels of research professionals (data managers, research nurses, etc.) in a local context, and training on identifying resources to fund research outside of pharmaceutical company sponsorship. Thus, publicly funded trials will determine whether interventions found to be effective in other countries are also effective in one's own country.

Another potential benefit from publicly funded trials networks is the addition of translational research components to cancer trials. These additional components may include epidemiology, evaluation of biologic mechanisms, development and validation of prognostic markers, evaluation of novel imaging, evaluation of cost-effectiveness, and evaluation of the intervention in select populations. All these additional components have the potential to add great value to an individual trial. In many cases, companies may be unwilling or unable to support these critical components. Publicly funded cancer trials networks facilitate the translation of research discoveries from academia into clinical practice.

Finally, the presence of a national publicly supported clinical trials network may attract interest from the international pharmaceutical companies both in potential collaboration as well as in the potential market for their new agents. Companies are attracted by the existence of a clinical trials network with proven capability and expertise.

3. Tumor tissue bio-repositories

Human bio-samples can provide a bridge between laboratory research and clinical information about actual patients. Annotated bio-samples enable researchers to study the characteristics of a cancer, and to link those with what is known about the clinical behavior of the cancer. Specifically, human bio-samples can be used to identify and test new drugs; identify how cancers develop; identify and test new ways to screen for or diagnose specific types of cancer; identify groups of patients likely to respond to new drugs or experience side-effects from drugs; and identify groups of patients and predict which type of treatment is right for them.

Issues that need to be considered in the development, maintenance and use of bio-banks include the relevance and impact of bio-banks on cancer control in low and middle income countries; collaboration between bio-banks due to the small number of samples; harmonization of approaches through the use of a commonly accepted quality management standard; the collection of medical information; the management and technology requirements; the impact of privacy laws in different countries on research; and economic analyses of research bio-banks in different countries.

The following experiences highlight situations where bio-banking could facilitate research on the intersection between diseases and the development of a successful bio-bank network in Canada.

3.1. HIV serology of pediatric cancers in Africa: Ocean Road Cancer Institute (ORCI) 2008 study

Jane Kokwakila Kaijage, Patricia A Scanlan

Background Over eighty percent of two million children infected with human immunodeficiency virus (HIV) are from Africa. HIV greatly increases the risk of cancer[6,7]. We aimed to survey HIV status in pediatric cancer patients presenting at a large cancer center in Tanzania. We documented the clinical profile and spectrum of incident cancers in children in 2008 and compared the overall profile of pediatric cancers with the profile of pediatric cancers among children who were HIV-seropositive.

Procedure A retrospective chart study of the spectrum and clinical presentation of cancers among children (<18 years) referred to the Ocean Road Cancer Institute (ORCI) in 2008 was conducted.

Results In 2008, 248 children were referred to ORCI. HIV sero-status was available for 172 (approximately 70%) children. Of these 16 (9%) were infected with HIV. A comparison of malignancy in children tested for HIV with children not tested suggested some bias in the HIV testing. Testing was more likely to be performed for children with Kaposi's sarcoma (KS) and Non Hodgkin's Lymphoma (NHL) (84% tested) than for other diagnoses (61% tested). Of 16 HIV-positive children, 7 had KS and 7 had NHL. HIV-associated KS represented 54% and HIV-associated NHL represented 10% of all patients. No difference in the clinical presentation of HIV-positive and negative KS was noted.

Conclusions The majority of the HIV-positive children referred to ORCI had a diagnosis (KS and NHL) that indicated progression to AIDS. Cancer constitutes a significant co-morbidity of HIV infection in children. Efforts are necessary to integrate HIV care centers with cancer centers, thus allowing for timely diagnosis and treatment. There is also a critical need to study the burden of HIV-associated cancers in children in Africa.

3.2. CTRNet: facilitating translational cancer research through a national tumor bank network

Brent Schacter, Peter Geary, Spencer Gibson, Anne-Marie Mes-Masson, Michael Sawyer, Lois Shepherd, Peter Watson, Brent Zanke

The Canadian Tumor Repository Network (CTRNet) was formed in 2004 with funding from Canadian Institutes of Health Research Institute of Cancer Research to foster translational research on such topics as the determinants of cancer, predicting drug response and identifying new targets. CTRNet is a not-for-profit consortium of leading provincial tumor banks as well as the biorepository from the National Cancer Institute of Canada Clinical Trials Group (NCIC-CTG).The partners are bound by formal agreement and policies dealing with ethics/consent, training, documentation, consent, material handling/release, and privacy.

Canada functions within a universal health care system under provincial jurisdiction which results in differences in clinical administrative practices and in the level of the legal framework surrounding the use of biological material. A major endeavor of CTRNet has focused on the harmonization of bio-banking practices across the five participating provinces and the NCIC-CTG in order to respond to the growing need for human biological material in biomedical research. Key to the success of CTRNet has been the development and adoption of national standard operating procedures (SOP's) that cover topics ranging from consent, privacy, specimen handling/access, quality control and materials request/release among others. These SOP's have undergone independent international review and are freely available to the research community at large (www.ctrnet.ca). CTRNet also provides a unique portal for material requests from all participating bio-banks with a streamlined unique application process. Another major activity of CTRNet has been the development and implementation of tumor bank software with functionalities related to clinical annotation, consent, specimen handling, derivative products, storing and shipping.

The presentation will address issues around the availability of human biological materials for research, challenges bio-banks face in supporting translational research, needs to structure bio-banking to support the growing trend towards large population-based cohorts and efforts to resolve these issues in Canada through CTRNet.

4. Clinical trials

In economically "emerging countries" like China, India, Brazil or Egypt, the amount of clinical cancer research, as measured by the number of trials, the number of patients enrolled in trials and the amount of research funding, has increased dramatically in the past

decade. A great majority of this research has funding originating from the private sector, and, generally, there is little support from governments or public funds for clinical research.

Discussions on this issue by the cancer control community should focus on how to promote public investment in clinical trials at the international level, how to define objectives useful for the different patient populations and how to integrate clinical and epidemiological research in proactive actions towards global cancer control.

4.1. Implementation of a framework for data management, monitoring and analysis to support cancer control studies at the Instituto Nacional de Câncer of Brazil (INCA)

Isabele Avila Small, Daniele Blasquez Olmedo, Marisa Dreyer Breitenbach, Luiz Antonio Santini, Luis Augusto Maltoni, Daniela Ramalho, Carlos Gil Ferreira

INCA is the Brazilian Ministry of Health (BMH) branch in charge of cancer policies. In addition, INCA integrates the Brazilian Network for Clinical Research. This is a BMH initiative to foster clinical trials addressing key public health issues. In order to cope with those tasks a tool for data management, monitoring and analysis has been developed supporting cancer control studies of risk or prognosis, in addition to local and multicenter clinical trials run by INCA.

The strategy has been two-fold: intramural (institutional) and extramural (network-based) support for studies of interest to the BMH. The framework is based upon a data management and analysis routine developed by INCA's health professionals using statistical and database management software and is integrated with another network project of INCA: the National Tumor Bank. The implementation at INCA was based upon two pillars: a) a multi-step routine that includes meetings with investigators and data collection training; establishment of clinical report forms; a real-time distance monitoring of data collection and oral presentations either pre-planned or upon request in a manner that the data manager is able to check data consistency as they arrive and acknowledge and request investigators to correct data and clarify possible doubts; b) a central relational database customized for each study with an easy-to-use interface and several tools to reduce data entry errors.

Currently, several institutional and network-based research projects coordinated by INCA are supported by this framework involving cervical, lung, breast and colon cancer, in line with BMH priorities. An effective framework for cancer control studies has been implemented, minimizing the costs, simplifying the conduct of institutional and network-based studies and improving quality assurance. Thus, it increases the capability of cancer investigators at INCA and throughout Brazil to conduct studies to support the decision making process in cancer care.

4.2. Is a single HPV DNA test effective in triaging women with low-grade abnormal cytology to cytological surveillance or colposcopy? Results from the UK TOMBOLA trial

Linda Sharp, Seonaidh Cotton, Julian Little, Margaret Cruickshank, Louise Smart, Rashmi Seth, Ian Duncan, Kirsten Harrild, Keith Neal, Norman Waugh

Background There has been prolonged debate about the value of testing women with low-grade abnormal cytological smears for high-risk HPV (hrHPV) types in order to optimize management[8-11]. HPV testing might help decide which women should be referred for colposcopy and which could safely be returned to routine smears. We undertook a multi-center individually-randomized controlled trial, nested within the UK Cervical Screening Programs, to investigate the value of hrHPV DNA testing in determining the most effective management.

Methods 4031 women aged 20-59 years with low-grade smears were randomized to cytological surveillance (6-monthly smears in primary care) or referral for colposcopy. hrHPV status was determined at recruitment using a polymerase chain reaction enzyme immunoassay (PCR-EIA) and GP5+/6+ primers. Women were followed for three years concluding with a colposcopy. The primary endpoint was cumulative incidence of CIN2 (Cervical intraepithelial neoplasia) or more severe disease (CIN2+) at 3 years. CIN3+ was considered as a secondary outcome. We compared clinical effectiveness of the policies in detecting CIN2+ in (1) hrHPV+ve and (2) hrHPV-ve women by testing for interactions between hrHPV status and management.

Results The cumulative incidence of CIN2+ was three times higher in hrHPV+ve women (114 per 1,000 person-years) than in hrHPV-ve women (36 per 1,000 person-years). This pattern was seen in both the cytological surveillance and the initial colposcopy arms, and there was no significant interaction between management policy and hrHPV status (p(interaction) = 0.756). In addition, almost 30% of women who had CIN2+ during the three year follow-up were hrHPV-ve at recruitment. Conversely, almost 70% who were hrHPV+ve at recruitment did not have CIN2+ during follow-up. Findings were similar when the outcome of CIN3+ was considered.

Conclusions The findings of this large, population-based, randomized controlled trial suggest that a single hrHPV DNA test is not useful in determining the most effective management for women with low-grade cytological abnormalities.

5. Registries and Cancer survival - the EUROCARE study, population-based cancer registries and international collaboration

Cancer registries provide a method for monitoring trends in cancer incidence, distribution, care and survival, as well as inequalities in cancer outcomes across various groups within and between populations. The EUROCARE study (EUROpean CAncer REgistry-based project on survival and Care of cancer patients), as well as national (e.g., SEER-US, FRANCIM-France) and international (CONCORD) projects, provide examples from high income countries of how registries can be used to inform cancer control programs. The role of registries and the most appropriate methodology for monitoring survival and patterns of cancer care in low and middle income countries are issues that need to be further considered.

5.1. Cancer control monitoring with cancer incidence, mortality and survival trends in Osaka, Japan

Akiko Ioka, Yuri Ito, Naomi Sato, Hideaki Tsukuma

Background Among the leading cancer sites in Japan, stomach, colorectal, breast and cervical cancers are good candidates for secondary prevention because efficient screening modalities are available. Every cancer screening program, however, was carried out as an opportunistic screening program, and the coverage was less than 20% in Osaka, 2004. We compared incidence and mortality trends for these cancers to evaluate the effectiveness of cancer control, especially early detection.

Methods Age-adjusted (Japanese Model population of 1985) mortality rates for Osaka were calculated from vital statistics. Age-adjusted incidence rates were obtained from the Osaka Cancer Registry. Annual Percent Change with a Joinpoint regression model was estimated[12].

Results For stomach/colorectal cancer, both mortality and incidence showed decreasing trends, but the decrease in mortality was smaller than in incidence. For female breast, both incidence and mortality increased, with more increase in the incidence, however, gaps between them leveled off in the last few decades. For uterus, the decreasing trend in mortality was parallel to the decrease in the incidence. The proportion of localized stage was less than 50% in stomach/colorectal, and less than 65% in female breast/uterus. Relative 5-year survival for stomach/colorectal increased steadily, and the survival for female breast/uterus remained stable since the 1980's.

Conclusions Increasing breast cancer mortality seems to be related to the delay in introduction of screening with mammography, which only started in 2004 in Japan. Effective secondary prevention is very important, especially in Osaka, where the gap between incidence and mortality for each cancer remained small or decreased, the proportion of localized stage was very low with the very low coverage of the cancer screening program, and survival increased slightly over the last decade.

5.2. A pilot study of the Chinese breast cancer multi-center clinical epidemiologic study

Jing Li, Bao-Ning Zhang, Jin-Hu Fan, Hui-Yun Zhong, You-Lin Qiao

Background Incidence and mortality of breast cancer in China is thought to be increasing especially in the metropolitan areas according to very limited data from the cancer registry. As primary prevention has its limits, screening and appropriate treatment are regarded as effective in reducing breast cancer mortality[13]. China is dedicated to the control of breast cancer.

Objective To explore the breast cancer clinical trend over the past ten years and to estimate the breast cancer burden in China for the first time, thus providing scientific data for policy makers to develop a breast cancer control strategy in China. The purpose of this pilot study was to examine the feasibility of conducting this project nationwide.

Method This was a hospital-based, multi-center retrospective study of female primary breast cancer. One hospital from one of the 7 geographic regions was selected. One month was randomly selected for each year from 1999 to 2008. All cases within the selected month were reviewed and the designated information was collected. The cancer hospital/institute, Chinese Academy of Medical Sciences (CICAMS) was the selected hospital from north China and was the pilot hospital. 50% of cases (n = 283) in CICAMS were reviewed.

Result and conclusion Breast cancer peaked among women aged 40-49 yrs (36.04%) and 50-59 yrs (30.04%). The most common cancer was infiltrating ductal carcinoma (84.04%). Clinical stage I and IIA accounted for 31.32% and 37.01% of cases, respectively. 280 cases had ER (estrogen-receptor) and PR (progesterone receptor) tests; among them, 53.93% were positive for both. 281 cases had Her-2 test; 47.69% of them were Her-2 positive and 44.48% were negative. The number of cases also showed a trend over time. The study demonstrated that the required information can be collected by medical case review and is reliable. The randomly selected month reflected the trend from that year. This study was determined to be feasible to conduct nationwide.

5.3. The burden of cancer in adolescents and young adults

Maria Paula Curado, Thais JS Pontes

The aim of this study is to report the ten most common cancer diagnoses for adolescents and young adults (AYA)[14-20] aged 15 to 24 years-old by gender in all five continents (Africa, America, Asia, Europe and Oceania) in

the period between 1998 to 2002. Data is derived from the IARC (International Agency for Research on Cancer) / WHO (World Health Organization) database on cancer in five continents, volume IX[21-23]. In Europe and the United States, increasing incidence of malignancies among AYA 15-19 years of age have been found. Nearly 280,000 new cases of cancer were registered in the world for that age group in the five-year period studied. The types of cancer that occur in AYA were heterogeneously distributed around the world. In Africa, HIV-related cancers had the highest rates, with Kaposi sarcoma being the major cancer diagnosed for both sexes. In females in all five continents, the two major cancer diagnoses noted were thyroid and ovary. Males had an elevated rate for testis cancer worldwide. For Oceania, melanoma of the skin was a major oncological problem in that area, with significantly higher rates when compared to all other regions of the world, especially among women. European females also presented this diagnosis as the major incident cancer. Hematological neoplasms (such as Hodgkin's disease, Myeloid Leukemia and Lymphoid leukemia), along with bone cancer, also repeatedly ranked among the ten most common cancers for both genders worldwide. The data presented indicate the major cancer diagnoses worldwide for AYA and provide information for further investigation and public health policies.

6. Health services and health economics

In view of limited resources in low, middle, and high income countries, it is important to consider the way in which "cancer control packages" should be determined. In deciding what should be included in a control program, some important factors to consider are disease burden, cost-effectiveness of interventions and the wealth of the country, as well as how to promote wide and equal access to cancer services. By examining the experiences from countries in different settings, it will be possible to determine whether it is only relatively cheap primary prevention efforts and palliative care that can be implemented in low income countries, or whether there is also ample room for secondary prevention and treatment. There is a need in the cancer control community to consider how to establish which cancer control interventions should be implemented, and what the role of international research, practice and policy collaborations could be.

6.1. Addressing research and development needs with a National Centre for Health Economics, Services, Policy and Ethics (HESPE)

Stuart Peacock, Jeffrey Hoch, Zahra Musa, Kimberly van der Hoek

Background Cancer control research agendas and priorities should be driven by the needs of policy-makers and practitioners, and should take into account the values of patients and the public. The complex cancer control problems identified through stakeholder consultation often require a team of professionals from a variety of backgrounds and disciplines to work together to address these issues. In addition, effective knowledge translation is needed to affect policy change, enhance cancer control programs, and improve patient and population health outcomes.

Objective To develop a research model that is responsive to the needs of the cancer control community, employs an interdisciplinary approach and allows for effective knowledge translation.

Research model The newly established National Centre for Health Economics, Services, Policy and Ethics (HESPE) in Cancer Control will employ a novel research model to achieve the stated objective. Investigators of the HESPE Centre include researchers, senior decision-makers from the Canadian cancer care system, and practicing clinicians. In addition to eliciting the views of the investigators, HESPE will administer surveys and host stakeholder consultations to determine its national research priorities. Once research directions are confirmed, projects will be carried out by experts from cancer control and HESPE disciplines. HESPE's research approach is not only interdisciplinary and inter-professional, but is also inter-provincial, with collaborators drawn from across Canada. Lastly, HESPE uses an integrated knowledge translation model: consumers of research results – the cancer control community – will be engaged in developing the research agenda, undertaking projects, disseminating results, and the early adoption of novel approaches.

Conclusion The HESPE research model has been well received by researchers, policy-makers, and practitioners, and a number of policy-relevant research projects have already been identified. Other early results from the integrated knowledge translation model will also be discussed.

6.2. Building a state-based infrastructure for data driven, evidenced based cancer control in the United States

Hannah K Weir, Carol Friedman, Robert German

The US CDC administers the National Program of Cancer Registries (NPCR) and the National Comprehensive Cancer Control Program (NCCCP), which helps support cancer control programs in all 50 states. With the US cancer burden expected to double between 2000 and 2050[24], addressing this increasing burden will require a coordinated, sustained effort between cancer registries and cancer control programs.

The CONCORD study revealed 5-year survival rates for black men and women diagnosed 1990 to 1994 with breast, colorectal or prostate cancer were substantially lower than for white men and women. The study also

included a patterns-of-care component in which 8 NPCR registries collected clinical and socio-economic information on a sample of patients (4,844 breast, 4,332 prostate, and 4,422 colorectal) diagnosed in 1997 and followed through 2000+.

Analyses of the patterns of care studies found that black women were less likely to receive radiation therapy following breast conserving surgery or hormonal treatment for hormone receptor-positive tumors. Racial differences in survival diminished when adjusted for socio-economic status (SES) and clinical variables. SES was found to be an underlying risk factor for racial disparities in survival for all 3 cancers, with low SES associated with more advanced disease stage and less aggressive treatment.

This presentation will update information on the US POC studies, discuss how cancer coalitions can implement interventions aimed at reducing disparities, and discuss CDC's strategies for building a state-based infrastructure for data driven and evidenced based cancer control throughout the United States.

6.3. Screening for colorectal cancer in Ireland: would it be cost-effective and what screening test should be used?

Linda Sharp, Lesley Tilson, Sophie Whyte, Alan O Ceilleachair, Cathal Walsh, Cara Usher, Paul Tappenden, Jim Chilcott, Anthony Staines, Michael Barry, Harry Comber

Background More than one million new cases of colorectal cancer are diagnosed worldwide annually[25]. In Ireland, incidence rates are among the highest in western Europe, survival is lower than the European average, and mortality in men exceeds that in other western European countries[26]. We evaluated the cost-effectiveness of a population-based colorectal cancer screening program in Ireland.

Methods Three screening scenarios were assessed: (1) biennial guaiac-based fecal occult blood testing (gFOBT) in those aged 55-74; (2) biennial fecal immunochemical testing (FIT) in those aged 55-74; and (3) once-only flexible sigmoidoscopy (FSIG) at age 60. A Markov model was used to follow a cohort of 55-year-old individuals over their lifetime. Model parameters were obtained from local data, literature review and expert clinical opinion. Costs included screening and diagnostic tests, cancer treatment, complications, and surveillance of screen-detected adenomas. Health outcomes were assessed in quality-adjusted life years (QALYs). Costs and outcomes were discounted at 4% per annum. Screening scenarios were compared with the status quo ("no screening"). Probabilistic sensitivity analyses were undertaken.

Results All three screening scenarios were highly cost-effective compared to no screening. In the base-case analysis, FSIG had the lowest incremental cost-effectiveness ratio (ICER = € 589 per QALY gained), followed by FIT (€ 1,696 per QALY gained), and gFOBT (€ 4,428 per QALY gained). gFOBT was the least cost-effective. Compared to FSIG, FIT was associated with a greater health gain, and greater lifetime reductions in colorectal cancer incidence (15%) and mortality (36%). However, it was more costly than FSIG, required more colonoscopies, and would result in more complications. The ICER for FIT *versus* FSIG was € 2,058 per QALY gained. Results were robust to variations in parameter estimates.

Conclusions Introducing a population-based screening program in Ireland would be a highly cost-effective healthcare intervention. The optimal screening test would be FIT, as it is associated with the greatest health gain.

7. Translating research into practice

Tens of billions are spent on research discovery and thousands of billions on health service delivery worldwide, by both the public and private sectors[27]. Yet what is spent to connect the two? Relative to the investments in discovery and delivery, the answer may be viewed as "decimal dust". If science is about parsimony and simplicity, the challenge of moving science into practice and policy is not all that scientific, as yet. It is based more on anecdote than data and more on tacit knowledge from experience than explicit knowledge from knowledge translation research.

This may be particularly challenging in low and middle income countries. In order to determine how best to reach vulnerable populations who bear the highest burden of cancer in these regions, it will be important not only to consider examples of knowledge translation research and different models of knowledge exchange practice, but also to combine the lessons learned from science, largely funded in high income countries, and the lessons learned from policies and practices prevalent in low and middle income.

7.1. Creating a knowledge management culture in a virtual, Pan-Canadian cancer organization

Anna Greenberg, Lee Fairclough, Wayne Roberts

The Canadian Partnership Against Cancer's (CPAC) mandate is to accelerate the use of existing knowledge in cancer control. A major impetus for a national cancer control strategy is the potential to reduce duplication of effort and resources across provincial and territorial cancer systems in Canada through effective knowledge management. This case study describes the development of CPAC's Knowledge Management Strategy to support knowledge to action[28] in cancer control nationally.

It highlights: 1) the development of a web-based portal as a knowledge management platform to serve the Canadian cancer control community, including social networking technology to support virtual communities of practice; 2) how, much more than deploying technology, fostering a culture of knowledge management is pivotal to the success of this endeavour[29]; 3) the approaches CPAC is taking to build such a culture across geographic jurisdictions and organizational sectors by pairing technology solutions with human interaction using concepts such as community engagement, training, mentorship, and the tailoring of and embedding of novel processes into existing work patterns and behaviors; 4) a particular challenge is reaching and serving the needs of many different communities within Canada, including aboriginal and multi-ethnic groups, as well as a wide range of age groups; 5) the challenge and necessity of adapting and applying traditional knowledge management concepts beyond a single organization to virtual, pan-Canadian networks; and 6) how CPAC, as a new organization leveraged existing and extensive networks to accelerate strategy implementation in established cancer systems.

7.2. Virtual healthcare library for cancer control: an approach to data integration and knowledge diffusion

Daniele Masterson Tavares Pereira Ferreira, Eliana Rosa da Fonseca, Letícia Casado

INCA plays a pivotal role in coordination and development of cancer control strategies through actions in the areas of teaching, research, prevention, surveillance, early detection, information and oncologic assistance[30]. It has been developing the Thematic Area of Cancer Control in the Virtual Healthcare Library (BVS), through a partnership with the General Documentation and Information Control Unit (CGDI) in the Brazilian Ministry of Health[31,32]. Its implementation is designed to ensure ongoing enhancement and expansion of information services, while projecting an open, horizontal, technical, and scientific data dissemination policy offering free access to citizens, healthcare practitioners, researchers, managers, and administrators of the Brazilian National Health System (SUS).

Implementation of the Thematic Area provides improved data management services according to actions developed for dissemination of technical, scientific and normative information. This task consists of collection, selection, description, indexation, and generation of a database informed by data sources in the oncology field[33], with the goal of composing thematic representation axes for widespread and comprehensive dissemination of cancer control literature, both published and non-published, technical and scientific, as well as information of public interest, such as Healthcare Hints[34].

INCA offers different communication channels targeted towards several distinct public audiences, such as the main homepage, specialized libraries, information bulletins and even one LILACS-indexed institutional scientific journal, the "Revista Brasileira de Cancerologia", directed to all Brazilian healthcare professionals dealing with cancer control. The development of a Thematic Area is in itself a main integration instrument to fulfill the information needs of all these audiences. By blending information and communication technologies, this approach ensures a steady supply of integrated products and services[35], offering an excellent example of how to ensure dynamic access and integration of many different sources focused on a core topic, while enhancing the visibility and representativeness of institutional outputs.

8. Palliative care

Palliative care is an important component of a cancer control program in any setting, but may be even more critical in middle and low income countries where the infrastructure and resources for screening, early detection, and treatment are limited, such that cancer patients access services at an advanced stage of disease when available treatments may be less effective. The research and development necessary to advance population-based palliative care will be different depending on the setting and resources. These must be considered in order to determine what research is most meaningful for subject content advance, health systems performance and integration, and optimal clinical practice, as well as what mechanisms are best suited to advance palliative care research within and across national environments. The following examples of palliative care research provide a starting point for examining the practical opportunities and challenges for conducting palliative care/end-of-life/supportive care research in different settings, and how these challenges can be addressed.

8.1. A research program for cancer survivor care and control

Mary L McBride, Anne-Marie Broemeling, Victor Glickman, Karen Goddard, Maria Lorenzi, Sheila Pritchard, Sam Sheps, Linda Siegel, John J Spinelli, Paul C Rogers

The majority of cancer patients in Western countries now survive their cancer. Quality of life and late effects are emerging issues for survivors. Research to identify problems and inform guidelines for survivor care is needed.

A population-based research program is examining outcomes among survivors of cancer diagnosed in British Columbia before age 25 who survived at least

five years. A retrospective cohort of 3,483 survivors, and representative comparison groups, have been identified from registries, and linked to administrative databases of risk factors and outcomes. Survivors of childhood and adolescent cancer had over nine times the mortality rate of the general population[36], five times the risk of a second cancer[37], and almost four times the risk of severe late morbidity[38]. Survivors had similar educational achievement to their peers (except survivors of brain tumors). Income and employment were also examined. Survivors utilized more health care than their peers. They had three times the odds of being hospitalized, and were approximately twice as likely to visit a general practitioner and specialist over a 3-year period. There was decreased primary provider continuity of care as survivors transitioned from pediatric to adult care. Brain tumor survivors, and those who received radiotherapy treatment, were at higher risk of nearly all poor health and educational outcomes, and had elevated health care utilization when compared to other survivors. Socio-demographic factors had little to no effect on outcomes.

This program identifies long term risks, health care utilization, and quality of care among long-term cancer survivors. This research will not only inform future health care policy and practice, but also generate hypotheses for further research. Survivorship is an aspect of cancer control that requires ongoing surveillance and research.

8.2. Neuropsychology in cancer survivorship: preliminary results

Maria Antonietta Annunziata, Lorena Giovannini, Katia Bianchet, Barbara Muzzatti, Massimiliano Berretta, Arben Lleshi, Umberto Tirelli

Previous studies on cancer patients have found the presence of cognitive impairments after chemotherapy even for diagnoses other than brain cancer[39,40]. Moreover, anecdotal reports of cognitive deficits during and after exposure to chemotherapy are increasing. The aim of this study is to provide objective (neuropsychological tests) and subjective (self-assessment questionnaire) measures of cognitive functioning in long-term cancer survivors.

The National Cancer Institute (Aviano, Italy) has implemented the first Italian "Medical and psychosocial rehabilitation program for long-term cancer survivors". All patients attending the service, as inclusion criteria, had been out of illness and treatment for at least five years. Patients were individually administered a self-report questionnaire and neuropsychological tests. Memory, attention, and executive functions were assessed.

Preliminary results from this particular sample of patients (N = 40) show that, although all participants do not suffer from brain injuries and are in remission, many of them self-report moderate levels of difficulty in remembering recent information and frequently exhibit the tip-of-the-tongue phenomenon. Therefore, they complain of difficulties with their memory and planning abilities.

On standardized neuropsychological tests, cancer survivors exhibit average cognitive profiles. Nevertheless, poorer performance emerged in attention and memory measures in comparison with normative data.

Although cancer survivors exhibit average neuropsychological profiles, when deficits are present they can make it difficult to work effectively in cognitively challenging situations. Although more studies are needed to comprehensively describe the cognitive profile of cancer survivors, particularly long-term after treatment, a specific and highly sensitive neuropsychological assessment could be useful, in order to recognize deficits and undergo specific compensative training.

8.3. Survival patterns of patients after enrollment in Island Hospice Service's Palliative Care Program

Chenjerai Naboth Sisimayi

Introduction It is generally acknowledged amongst palliative care researchers that most patients are referred to palliative care services rather late in their illnesses[41-43]. In Zimbabwe, it is common for patients to be referred for palliative care service when they are no longer responsive to curative treatment and have already been discharged for home based care, rather than at diagnosis or early stages of disease progression. As palliative care services aim to attain the best quality of life for patients, a programming issue that arises from the prevailing and current scenario is whether days in care are adequate for the attainment of this goal. Target groups and settings to which findings of previous studies are inferable are, however, distinct from Zimbabwe's scenario where the palliative care burden has been compounded by the severity of the HIV/AIDS pandemic. This study therefore aimed to investigate the survival of patients after enrollment into Island Hospice Service, a Zimbabwean palliative care program established as the first hospice in Africa.

Methodology The study took the form of a retrospective cohort design with data obtained from a computerized database. Patients enrolled in the program between January 1, 2006 and December 31, 2007 were included and followed up with respect to mortality from their respective dates of enrollment to the study end-date December 31, 2008. Observations were censored on the study end-date or date of transfer/relocation.

Results The study established a higher median survival time for the cohort relative to the range of 11 to 54 days obtained from other studies. Similar to these studies however, associations between survival time and factors like age, gender, referral source and diagnosis

were established. Patients with HIV-related cancers had lower median survival times than those with cancer or HIV/AIDS only.

9. Conclusions

The private and public sectors can both play a role in supporting cancer prevention and control research and practice. Corporations can support international cancer control research with a public health and clinical focus. Thus, in addition to providing wellness and cancer screening programs for their employees worldwide, there are opportunities for corporations to use their considerable marketing expertise to aid in the development of culturally appropriate health promotion messages for diverse populations in different countries to promote, for example, increased physical activity and healthier eating habits to help address the growing obesity epidemic.

Beyond access to improved treatments and medicines in countries and regions where health resources are lacking or non-existent, corporations may choose to play a role in supporting primary prevention and early detection initiatives in low and middle income countries. While these parts of the cancer control continuum are usually left only to the public sector, there may be an important role for the private sector as well. Finally, a key question for all corporations who market products in the global economy is how do corporations view their "societal" responsibilities with respect to the impact of their product marketing on cancer control specifically and public health in general?

There is a critical need for the public sector to invest more in clinical trials research, which internationally has been largely dominated by the private sector. Too often, investigators at publicly funded research institutes and universities are not able to bring new discoveries into clinical evaluation, because they do not have easy access into clinical trials networks and may not be able to stimulate interest from pharmaceutical and biotechnology companies in partnership. Publicly funded cancer clinical research networks can expand the opportunities for evaluation of novel interventions from industry.

Often, companies may only be able to underwrite evaluation of their novel agents in the most common cancers. By collaborating with a publicly funded network, companies can facilitate the evaluation of their new agent in less common cancers, as well as in age groups which are more difficult to study, such as children and the elderly.

Publicly funded cancer clinical research networks can encourage the evaluation of novel agents from several different companies in combination. Frequently, companies will see other companies as rivals and not consider combinatorial strategies. A national cancer clinical research network can foster collaboration between companies. Thus, public sector investment in clinical research may be able to better address those cancers where vulnerable populations in low and middle income countries bear the greatest burden of disease.

Irrespective of whether cancer control research is ultimately funded publicly or privately, if investments in research discoveries are to benefit the populations that bear the greatest burden of disease, then new approaches to integrating the lessons learned from science with the lessons learned from service (public health, clinical, and public policy) must be found to close the gap between what we know and what we do. To make this happen, scientists, public health and clinical practitioners, policy makers, patients and their families, and the public at large all need to work together to expand their understanding of the meaning of evidence from the context of research and the context of the real world[27].

New knowledge translation and integration approaches must be made that recognize the differences between the research context in which most cancer control science is produced (e.g., in the academy, biomedical industries) and communicated (e.g., peer-reviewed publication, scientific conferences), and the public health practice, clinical practice, and policymaking contexts in which innovations that emerge from cancer control science are first observed and evaluated by potential practice and policy users, before adaptation and implementation are even, if ever, considered.

Thus, new models for research/practice/policy partnerships need to be supported so that approaches that are shown to increase knowledge exchange and the adoption of evidence-based cancer prevention and control strategies can be sustained both within and among countries. Communities of practice for international cancer control, like the ones fostered by the first three International Cancer Control Congresses, support knowledge exchange forums among researchers, practitioners, and policymakers, and provide important exemplars for efforts within countries to increase the integration of science and service, and to accelerate the translation of new knowledge into action to reduce the burden of cancer worldwide.

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