Tumori, 95: 597-609, 2009

Cancer prevention and population-based screening

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

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Abstract

Cancer prevention, screening and early detection can provide some of the greatest public health benefits for cancer control. In low resource settings, where cancer control is challenged by limited human, financial and technical resources, cancer prevention and screening are of utmost importance and can provide significant impacts on the cancer burden. Public policies, social, environmental and individual level interventions which promote and support healthy eating and physical activity can lower cancer risks. Tobacco use, a significant cancer risk factor, can be reduced through the application of key mandates of the World Health Organization Framework Convention on Tobacco Control. In addition, cancer screening programs, namely for cervical and breast cancers, can have a significant impact on reducing cancer mortality, including in low resource settings. Comprehensive cancer control programs require interventions for cancer prevention, screening and early detection, and involve sectors outside of health to create supportive environments for healthy ways of life. Sharing experiences in implementing cancer control programs in different settings can create opportunities for interchanging ideas and forming international alliances.

1. Introduction

Cancer prevention, screening and early detection can provide some of the greatest public health benefits for cancer control. Evidence suggests that 40% of cancers can be prevented, through risk factor reduction and a further 30% of cancers can be cured if detected early, through screening and early diagnosis and appropriate treatment[1]. Known cancer risk factors include tobacco use, low fruit and vegetable intake, physical inactivity, obesity, alcohol, and exposure to physical and chemical carcinogens such as ultraviolet radiation, asbestos, formaldehyde, benzoic acid, and cancer causing infections such as Human Papilloma Virus (HPV), *Helicobacter pylori*, and hepatitis B (HBV) and C (HCV) viruses. Interventions aimed at reducing the population exposure and individual level of these risk factors can greatly reduce cancer risks. In low resource settings, where cancer control is challenged by limited human, financial and technical resources, cancer prevention and screening are of utmost importance and can provide significant impacts on the cancer burden.

1.1. Cancer risk factors

Tobacco is the single most important cancer risk factor. It is a causal factor for lung cancer and a co-factor for oral, laryngeal and pharyngeal, bladder, cervical, kidney, stomach and pancreatic cancers. It is estimated that more than 20% of cancer mortality is caused by tobacco use[2]. Public policies, such as tobacco taxation, restrictions on tobacco marketing and sponsorship, packaging and labeling of tobacco products, and smoking restrictions in public places can effectively reduce tobacco use. In an effort to regulate and reduce tobacco use globally, the World Health Organization (WHO) Framework Convention on Tobacco Control (FCTC) was developed and entered into force in 2005[3]. The treaty has some 164 Parties and includes mandates on policies and legislation that will reduce tobacco from both a demand and supply side. Some of the key mandates of the FCTC involve raising tobacco taxes, tobacco advertising bans, protection of non smokers and promotion of smoking cessation.

The relationship between cancer and diet, physical activity and obesity has been well established, namely for colorectal, breast, and endometrial cancers[1,4,5]. Diets rich in fruit and vegetables, along with physically active ways of life and healthy weights have been associated with lower cancer risk. New analysis recently undertaken for the World Cancer Research Fund indicates that policies and actions by governments, industries, communities, and individuals can positively influence healthy patterns of diet and physical activity and have the potential to prevent significant numbers of cancer cases[4,5]. Many of these risk factors are shared with other chronic diseases such as cardiovascular diseases and diabetes, thus interventions aimed at risk factor reduction have the added value of reducing overall chronic disease risk. Global initiatives including the WHO Global Strategy for Diet and Physical Activity and the WHO Non-Communicable Disease Action Plan propose intersectoral policies and interventions that promote healthy ways of life and consumption of fruit and vegetables.

The most common environmental and occupational cancers due to chemical agents are lung, skin, bladder cancers and leukemia. Ultraviolet (sun) exposure is an important occupational risk factor for skin cancer. It is estimated that 1%-2% and 5%-10% of cancers can be attributed to exposure to carcinogens in the environment and workplace, respectively, in industrialized countries[1]. Environmental and occupational exposure to pesticides, tobacco smoke, sun, asbestos, benzene, and crystalline silica, among many other compounds, are well-documented causes of cancer.

In developing countries, cancer causing infections are much more of a significant risk factor. Chronic infection with HBV is a causal factor for liver cancer, which has a high incidence in many developing countries. Stomach cancer is among the leading cause of cancer incidence and mortality in most of South and Central America, and is caused by infection with Helicobacter pylori. Furthermore, persistent infection with oncogenic types of HPV is the main cause of cervical cancer, which remains among the leading causes of cancer in women in developing countries despite its preventable nature. The

availability of HBV vaccines and HPV vaccines is an important contribution to prevent liver and cervical cancers respectively through immunization, although the cost of HPV vaccines remain a principal barrier to its widespread use in developing countries.

1.2. Screening and early detection

Screening asymptomatic individuals for precancerous lesions or to detect early stages of cancer has been successfully demonstrated to reduce cancer mortality for cancers of the cervix, breast and colo-rectum[1,6,7]. Screening and early detection of cancer are integral components of a cancer control program. Screening requires an effective and accurate screening test, public education to ensure participation of the target population and follow-up care for those detected with pre-cancer and cancer. Early diagnosis can be improved by public and health provider education, and can result in substantial improvement in the outcome of persons detected with cancer, provided there is no delay in diagnosis and effective treatment.

Effective screening programs have often been associated with the use of sophisticated technology and high level of infrastructure and resources. Yet, organized screening programs can be effectively implemented in limited resources settings without relying on sophisticated or costly technologies. For example, cervical cancer screening has been effectively conducted in many low resource settings using the conventional Papanicolaou (Pap) screening test; and in areas with no access to the Pap test, an alternative approach has been successfully applied using visual inspection with acetic acid (VIA) to screen for cervical precancerous lesions, followed by cryotherapy to treat the pre-cancers in primary care settings. The critical factors for effective screening programs, regardless of resource level, are having an organized system that allows for achieving a high screening coverage, using an effective screening test, and ensuring treatment for all those detected with disease.

2. Experiences in cancer prevention and screening

Given the substantial and growing evidence on the role of diet, physical activity and the importance of primary and secondary prevention in the control of cancer, it is important for public health professionals to further understand the current scientific evidence and to examine successful programmatic interventions for primary cancer prevention and risk factor reduction. These include individual and population-based interventions, such as public policy, social and environmental interventions, as well as screening and early detection for cervix and breast cancers, and they need to be examined in the context of high, middle and low resource settings. In doing so, awareness of evidence-based policy, public health, community and individual actions which can reduce cancer risk and prevent cancer can be raised, lessons can be learned, and opportunities for the interchange of technical assistance and networking between countries in the areas of primary cancer prevention and screening programs can be created.

2.1. Cancer control and prevention in a public health framework: social, economic and environmental as well as biological and personal factors

Geoffrey Cannon

Control and prevention of cancer is conventionally seen as a medical and a personal matter. Cancer surveillance, screening, early detection, treatment and palliation will remain central and essential. Also, as shown by the 2007 World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR) Diet and Cancer Report[4], there is much that people as members of communities, families and households, and as individuals, can do to reduce their risk of many common cancers. However, on a population basis, treatment of cancer is not the most rational approach to its control, if only because of the cost of treatment, and the fact that cancer is usually diagnosed at a late stage. Also, there is a limit even to what privileged people can do to protect themselves against cancer. The 2009 WCRF/AICR Policy Report examines the physical environmental, economic and social as well as the behavioral and biological determinants of cancer risk. Its recommendations, the responsibility of an expert panel from all the main continents, supported by observers from UN and other international bodies, are derived from the most systematic examination of the literature so far attempted. It is published at a time of unusual international economic and other disturbance, and takes into account climate change, economic globalization, the impact of trans-national corporations on food systems, and other big issues. The Report concludes that concerted collaboration between all relevant actors is required, in a broad public health context. This all implies that the whole concept of cancer control needs to become broader. Seen in this light, the prevention of cancer is as great a global challenge and opportunity as that faced in Europe by the public health pioneers of the mid 19th century.

2.2. Does screening have any impact on cancer outcomes?

Eduardo Franco

Screening for precancerous lesions and early cancer via opportunistic or organized activities is the main component of secondary cancer prevention. The fundamental assumption is that early detection can prompt treatment to arrest further neoplastic development, thus

preventing the onset of invasive or advanced lesions and consequently reducing the cause-specific mortality rate. It is essential that the natural history of the pre-clinical phase of the target cancer be reasonably long and well understood so that lesion detection and treatment interventions can be efficacious in improving the prognosis. Evaluating the impact of screening on cancer outcomes is a multistep process that requires vigorous multidisciplinary collaboration in studies that take many years to be completed. It begins with the demonstration that a candidate technology has adequate sensitivity and specificity for the target lesion, and can be affordably deployed in a population in which prevalence of the earliest grade of the malignancy to be detected is sufficiently high for screening to be cost-effective.

Once a candidate technology satisfies these requirements the next step is to demonstrate efficacy in improving cancer outcomes. Today's health technology assessment standards require stringent evidence-based criteria to judge efficacy, coupled with sensible health economic analyses of any new screening strategy. For efficacy, the highest level of evidence comes from demonstrating via a randomized controlled trial (RCT) that implementation of a new screening technology reduces cancer-specific mortality relative to the existing standard of practice. However, RCTs typically take many years to complete and are not always feasible, either because of ethical reasons (e.g., when discovery of the intermediate endpoint is already an accepted basis for treatment) or because studies would have to be extremely large to the point of being impractical (e.g., rare cancers such as neuroblastoma). Interventions that have focused on pre-malignant or early cancerous lesions that can be treated or excised, with consequent arrest of neoplastic development, include those for high grade dysplasia of the uterine cervix, oral leukoplasias, and colonic adenomas.

Historically, the stepwise process to bring a screening technology to become accepted public health practice has varied across cancer sites. Papanicolaou (Pap) cytology screening for cervical cancer is unequivocally accepted as a standard of practice; yet this technology has never been evaluated in RCTs. Widespread adoption of Pap screening in the 1960s in Western countries, first as opportunistic activity, as part of professional guidelines, and later on as organized programs in Canada and in Nordic countries, led to an acceleration of the decline in cervical cancer incidence and mortality. Such ecologic-level evidence was further complemented by numerous case-control and cohort studies that demonstrated that women who had deficient screening histories had much higher risks of cervical cancer than those who complied with screening, as defined in the respective populations. The collective evidence from ecologic and observational studies, judged to be highly sufficient, is the reason why RCTs of Pap screening were never required. On the other hand, the new molecular methods for detecting cervical precancerous lesions, such as HPV DNA testing, must be evaluated via RCTs that can suitably compare the effectiveness of these technologies against Pap cytology, as the standard of practice. Such studies are presently ongoing in several countries.

For other diseases, such as breast and colorectal cancers, there is now ample evidence from RCTs that specific technologies (e.g., mammography and fecal occult blood, respectively) coupled with treatment interventions in average risk populations can reduce mortality from these malignancies when deployed at appropriate intervals and age groups. The RCT-level evidence is beginning to emerge for prostate-specific antigen (PSA) testing in prostate cancer but early results from these trials have not been entirely consistent. For lung cancer screening, sputum cytology and chest X-rays, have been shown to increase survival rates but with little or no impact on mortality. The advent of more sensitive techniques, such as spiral computerized tomography, has shown promising results in cohort studies but RCT-level evidence is not yet available. Proper evaluation of the collective evidence for or against a screening intervention requires understanding the many issues and sources of biases that affect the interpretation of all types of study designs used in evaluating the efficacy of screening. Some are easy to predict and understand mechanistically, which facilitates the epidemiologist's work in advising clinicians and policymakers with respect to their impact and the means to avoid them. These include self-selection (volunteer or referral) and length-biased sampling, lead time bias, and over-diagnosis bias. These problems affect all types of study designs, including ecologic, case-control, cohort, and even RCTs. Other biases are more insidious and complex; and as such, they are seldom considered in health technology assessment. Verification bias, false sensitivity gains due to test combinations, and sticky diagnosis and slippery linkage biases are important issues that must be considered for specific screening methods or their combinations. Overcoming these biases at the study design or data analysis stages poses substantial challenges that incur increased research costs, population-specific ethical concerns, and the need to resort to statistical methodology that is difficult to communicate to clinicians and public heath practitioners.

Juxtaposing the findings from a variety of study designs and sensibly interpreting them are major challenges in health technology assessment and meta-analyses of screening interventions. Several agencies and consortia of investigators have produced informative reports based on uniform criteria for judging and grading evidence for efficacy against different endpoints for various cancer screening interventions. Unfortunately, such systematic overviews of evidence do not always reach the same conclusions, which forces policymakers and clinicians to rely on expert professional opinions based on subjective judgment.

Research on secondary cancer prevention is a rapidly evolving field. New technologies based on molecular methods and genetic testing to identify individuals for targeted screening interventions have the potential to become accepted practice in the future. Some of the new screening methods incur high costs due to requirements of sophisticated equipment, laboratory infrastructure, and specialized personnel training, all of which will contribute to further inequities in cancer control. Low-technology strategies are urgently needed in developing countries, which bear the heaviest burden from many forms of screening-preventable cancers.

3. Food, nutrition, physical activity and cancer prevention: the policy implications of the report from the World Cancer Research Fund

The relationships between diet, physical activity and cancer risk, and how best to prevent cancer, were recently reviewed in the World Cancer Research Fund/American Institute for Cancer Research reports with recommendations for policies and actions to reduce the impact of these factors on cancer risk at both the level of the individual and population. With the release of the recommendations, countries will have to decide whether diet and physical activity should be a priority in their cancer control program, how to effectively educate the public and implement initiatives to promote healthy environments, healthy ways of life and healthy eating, and what is feasible in their setting with the resources that they have at their disposal.

3.1. Counseling for cancer prevention in Peru

Abel Limache-García, Mercedes Quesquen-Puente

Background Cancer in the world and in the Andean Region constitutes a public health problem, due to high levels of morbidity and mortality, as well as personal, familial, social, and economic costs. Advances in science and technology have allowed the development of highly sophisticated equipment and techniques for early detection, diagnosis and treatment of cancer; however, many developing countries do not have access to these technologies[8].

Methodology Three years ago, the Health Promotion and Cancer Control Department and the Nursing Department of the Peru National Cancer Institute (Instituto Nacional de Enfermedades Neoplásicas - INEN) developed the Preventive Counsel of Cancer, a new methodology for interpersonal communication. The purpose was to motivate people to adopt a healthy way of life that leads to cancer prevention.

Results As part of the learning methodology, we developed role playing games that can be utilized in counseling the users of the services of our institution or in health campaigns in the community. To date, 180 nurses have been trained by professionals on the theoretical aspects of the disease and the methodology of the Preventive Counsel, and have provided customized and specialized information to 18,500 people.

Conclusion Considering that in Peru 80% of cancer cases are diagnosed in advanced stages and 75% of them can be prevented, as well as the relationship between cancer and modifiable risk factors, such as tobacco use, physical inactivity, obesity, long exposure to sun radiation, and some types of infections, the Preventive Counsel is a strategy to consider that gives the activities for primary prevention of cancer an integral character and an educational dimension.

3.2. Reducing overweight/obesity and increasing fruit and vegetable consumption in the workplace: effectiveness of an intervention study in Brazil

Fabio da Silva Gomes, Sueli Gonçalves Couto, Carla Fernandez dos Santos, Ísis Zeferino Botelho, Ana Paula Melo Petermann

Background It is evident that the relationship between healthy eating practices, weight control and the prevention of cancer is mediated by the settings in which life is happening[4,5]. The workplace is one of these settings, where at the same time we find barriers and catalysts for change.

Objectives To assess the effectiveness of a workplace intervention to promote fruit and vegetable (FV) consumption and to reduce the prevalence of overweight/obesity (OW/OB) among employees of the National Cancer Institute of Brazil (INCA).

Methods Anthropometric measures and data regarding the habits of FV consumption were collected before and after the intervention (2007-2008). The intervention consisted of the daily delivery of a 100g portion of fruit to all INCA employees, as well as individual nutritional follow-up for workers who were OW/OB. From the 157 workers in total, 78% were interviewed in 2007 and 54% in 2008.

Results The proportion of workers that consume fruit 7 days per week increased significantly from 39.2% to 62.7% (PR: 1.6; 95% CI: 1.1 - 2.1). Additionally, the proportion of workers that consume fruit 2 or more times per day increased by 50%, and the proportion of workers that consume vegetables in at least one of the main meals (i.e. lunch or dinner) increased by 27%.

Conclusion The intervention has achieved its objective by reducing the body mass index (BMI) of workers who were overweight or obese. More than one third of the workers that were overweight or obese in 2007 changed to a better nutritional status in 2008 (40% from obesity to overweight; 35% from overweight to adequate BMI). An increase in the fruit and vegetable consumption was also achieved, highlighting the importance of

facilitating the consumption of fruit and vegetables in the workplace.

4. HPV vaccines and cervical cancer prevention in middle and low income countries

Globally, cervical cancer is the second leading cause of cancer deaths in women and continues to be a significant public health problem despite the availability of effective interventions to screen for and prevent cervical cancer. There are now new technologies such as HPV vaccines, HPV DNA screening tests and visual inspection screening[9], which provide opportunities to reduce cervical cancer mortality. Within each setting, there will be different opportunities and barriers to the introduction of these new technologies into public health programs and different reactions by the professional community and the public. Guidance will be needed on when and how to introduce these new technologies and integrate them into public health programs.

4.1. New tools for comprehensive cervical cancer prevention planning: striking a balance between screening/treatment and vaccination

Scott Wittet

Exciting new tools for prevention of cervical cancer include HPV vaccines, HPV DNA screening tests, and the use of simple, visual inspection methods for screening[10]. Once broadly implemented, new strategies for screening and treatment, coupled with vaccination of those not yet infected with HPV, could reduce cervical cancer mortality in low-resource settings to the low rates common in wealthy countries.

The most rapid and extensive health benefits will result when national programs are able to offer vaccine to girls and affordable and effective screening and treatment to adult women. Unfortunately policy makers, who for the most part have only recently learned about cervical cancer, lack experience to guide design of comprehensive cervical cancer prevention programs. Guidance also is needed relating to evaluating cost-effectiveness, assessing affordability and planning for sustainable programs.

Recognizing this gap, PATH and its partners in the Cervical Cancer Action coalition[11] decided that providing decision-making assistance related to comprehensive programs would become a top priority for 2009-2011. The strategy is two-pronged and includes: 1) outreach to top level influential planners (such as African Parliamentarians, Ministers of Health and their advisors, and donor agencies, among others); and 2) technical assistance for mid-level program planners. The first strategy is being implemented through regional meetings, along with direct contact with key individuals in select countries. The second strategy involves in-depth work with multidisciplinary teams, the focus being those responsible for immunization and those working on women's health.

New tools are available to help with planning comprehensive programs, including an interactive, web-based tool called the "Cervical Cancer Prevention Action Planner." Demonstrations will stimulate discussion about how the tools could benefit cancer prevention planning now and how they might be improved in future.

5. Environmental and occupational issues in cancer prevention

There are well-established cancer risks associated with exposure to environmental and occupational carcinogens. However, exposures to these different carcinogens differ within and between countries, and therefore prevention strategies need to be tailored to the specific context. Examples of effective strategies which can be applied to eliminate, prevent and control exposure to these carcinogens are available, along with the multi-sectoral approaches that are required for policy development across the environmental, health and labor sectors.

5.1. Public health policies on environmental prevention of cancer: Bulgarian perspectives

Lyubomir Ivanov, Ekaterina Mirkova

A national public health policy to advance the primary prevention and control of environmental causes of cancer has been worked out and incorporated in the national cancer action plan submitted for consideration to the Bulgarian Ministry of Health. The integrated environmental cancer preventive strategy for reducing the national cancer burden focuses on prevention and lowering environmental exposures, such as occupational mutagens and carcinogens through environmental tobacco smoke, diet, air pollution, water and soil contamination, electromagnetic fields and other non-ionising radiation, and workplace exposures. The priority actions elaborated to reduce workplace-related cancer risk factors focus on prevention and reduction of occupational carcinogenic exposures, and proposes the application of contemporary genomics cancer risk biomarkers in cancer risk assessment and control.

Biomarkers of chromosome damage (lymphocyte chromosomal aberrations and micronuclei) are established cancer risk predictors[12,13]. The National Center of Public Health Protection in Sofia, Bulgaria has been internationally recognized for their contribution to the validation of cytogenetic cancer risk biomarkers, and has extensive national experience in their application for occupational cancer risk assessment, prevention

and control purposes in the bio-monitoring of chronic low level occupational exposures to complex genotoxic mixtures carried out in the petroleum refinery and rubber manufacturing industries. Legislative initiatives for using cytogenetic cancer risk biomarkers for surveillance of high-risk workers, occupational cancer risk assessment and monitoring of workplace carcinogenic exposures have all been proposed as priority occupational cancer prevention and control actions in the national environmental cancer preventive strategy.

6. The good and the bad: lessons from screening programs in developed countries and what other countries can learn from the experiences

There are numerous evidence-based approaches to screening and early detection programs, ranging from a Western approach which is highly technological to a less technology based approach used in other countries. In examining the experiences of countries in different settings and with different approaches, it is possible to explore whether effective screening and early detection programs are feasible in low resource settings, or whether they are dependent on availability of resources and sophisticated technology; whether opportunistic screening is effective or whether personal invitations to participate in screening programs lead to improved program outcomes; the importance of screening test sensitivity and specificity; and the usefulness of screening program indicators, such as screening coverage, information and participation.

6.1. A collaboration between Italy and Bosnia Herzegovina to disseminate cervical cancer screening

Livia Giordano, Margherita Granero, Vasvija Sahinovic, Bojana Stanic, Sahaudina Avdukic, Gioia Montanari, Sergio Arnaud, Nereo Segnan

Aims The aims of the project are as follows: 1) to plan and evaluate a cervical cancer pilot screening project in Breza, Bosnia Herzegovina; 2) to build capacity of Bosnian health professionals; and 3) to increase the level of preventive health care in a post war setting[14].

Methods From September 2003 to May 2006, all women 25-64 years of age in Breza were contacted to undergo a completely free Pap smear. The recruitment strategy was based both on personal invitation letters and on women's sensitization by specifically trained midwives.

Results Out of 5609 women in the target population, 1576 were contacted personally by the screening unit to arrange an appointment, while the remaining 4033 received an invitation letter. Of the women who received an invitation letter, 795 women scheduled an appointment, for a compliance of 19.7%. The overall participation rate was 42.3%. A total of 2169 Pap smears were performed with a referral rate for colposcopy of 10.1%. The positive predictive value for cervical intraepithelial neoplasia (CIN) 2+ was 28.5%, and the detection rate was 1.8%, 17.5% and 1.3% for CIN 1, CIN 2-3 and invasive lesions, respectively. A satisfactory agreement with international protocols has been estimated for high-grade squamous intraepithelial lesions, inadequate slides and invasive cancer, but it was substandard for low-grade squamous intraepithelial lesions.

Conclusion The participation rate achieved by invitation letters did not reach high performance levels while the staff engagement in proactive recruitment was far more effective. One third of women with a positive cytology did not need further assessments. The detection rate of intraepithelial and invasive lesions was higher compared with corresponding rates in Western European programs[15].

6.2. Colorectal screening in Canada: a national collaboration of provincial initiatives

Heather Bryant, Candice Anderson, Verna Mai, Susan Fekete

The National Colorectal Cancer Screening Network was initiated by the Canadian Partnership Against Cancer in December 2007. At the time, one province (of ten provinces and three territories in Canada) had initiated screening program activities, and two other provincial programs were announced and under development, and guidelines had been established nationally[16]. Since then, another five provinces and one territory have announced programs. All programs are dedicated to the basic principles of reduction in colorectal cancer mortality through the provision of high quality screening and higher population participation rates[17]. However, the route each province has chosen to reach these goals varies considerably. For recruitment, for example, some programs are sending tests to potential participants by direct mail, others are implementing financial incentives to encourage primary care physicians to refer patients for tests, and others are using public and professional awareness programs to encourage uptake. The initial screening test is a fecal test in all cases, but some have chosen a guaiac-based test, others an immunochemical tests, and others are piloting both alternatives. However, the programs have united through this initiative in order to learn from one another's experiences, and to develop a set of quality indicators that all are committed to collecting so that program performance can be assessed in the future. These variables include indicators of population participation, screening test performance, and key follow-up steps, and will eventually include such markers as interval cancer rates. Another initiative of this group is a national survey on attitudes to colorectal cancer screening, the results of which will be used to develop a national awareness program that could be adopted by any province that choos-

es to do so. Through this initiative, important synergies will accelerate the impact of colorectal cancer screening on population outcomes in Canada.

6.3. Screening history of invasive cervical cancer cases in Friuli Venezia Giulia region, Italy

Antonella Zucchetto, Elena Clagnan, Diego Serraino, Ornella Forgiarini, Emilia De Santis, Tiziana Angelin, Margherita de Dottori, Loris Zanier, Antonella Franzo

Background In Friuli Venezia Giulia region in the north east of Italy, an organized cervical cancer screening program (OCSP), covering the whole resident population, was implemented in 1999[18]. Women aged 25-64 years are invited to undergo a free Pap-smear every 3 years. In 2005, OCSP coverage was 90%, with 55% compliance[19]. However, despite OCSP and a widespread use of opportunistic screening, several hundred cases of invasive cervical cancer (ICC) have been diagnosed in recent years in FVG[20].

Objective To evaluate the screening history of women who developed ICC in Friuli Venezia Giulia region, in order to identify flaws undermining prevention.

Methods Using the Friuli Venezia Giulia region Cancer Registry, 438 ICC cases diagnosed between 1999 and 2005 were identified. Computerized databases allowed us to track the cytological and histopathological histories of these women. ICC cases were classified according to history of Pap-smear (ever/never screened), OCSP invitation and compliance, and last Pap-smear results.

Results There were 273 (62%) cases of women screened inside or outside OCSP: 72 (26%) women had a previous negative Pap-smear (53% less than 3 years before diagnosis), whereas 201 (74%) cases of ICC were detected at screening. The other 165 (38%) women had no information about previous Pap-smear results (i.e., never screened). Among these, 71 (43%) were not compliant to OCSP, 69 (42%) were not invited by OCSP because they were above 64 years of age, and 25 (15%) had been diagnosed before the first OCSP invitation. Never screened ICC cases were older and had higher tumor stages compared to ever screened cases.

Conclusion Among women in the target population, nonattendance primarily limits the effectiveness of OCSP.

6.4. Prevalence of positive family history of colorectal cancer in the Iranian general population

Bijan Moghimi-Dehkordi, Azadeh Safaee, Mohamad Amin Pourhoseingholi, Manijeh Habibi, Asma Pourhoseingholi, Mohammad Reza Zali

Background Subjects with a positive family history of colorectal cancer have an increased risk of developing this type of cancer[21-25]. The risk depends on the number of affected relatives and the age at diagnosis.

Aim The aim of this study was to assess the prevalence of a positive family history of colorectal cancer, within a random sample of the Iranian general population.

Methods A total of 5500 subjects aged ≥20 years were invited to participate in an interview about the occurrence of colorectal cancer in their first- or second-degree relatives.

Results Of all responders, 162 (2.9%) subjects reported a positive family history of colorectal cancer. 71 (1.24%) responders reported having one first-degree relative with colorectal cancer diagnosed before the age of 50, or two or more first-degree relatives with colorectal cancer. In addition, 83 (1.51%) and 14 (0.25%) subjects reported having one and two or more second-degree relatives with colorectal cancer, respectively.

Conclusion The prevalence of a positive family history of colorectal cancer in Iran is lower than America and European countries. Identification of a high-risk population for colorectal cancer and encouraging them to participate in screening programs is the first step in targeting preventive measures.

7. Breast cancer early detection guidelines and experiences in middle and low income countries

Breast cancer is the most common cause of cancer death in women worldwide, with case fatality rates higher in low resource areas. Early breast cancer detection improves outcome, provided treatment is provided, but requires organized programs. The Breast Health Global Initiative (BHGI) has developed evidence-based guidelines appropriate for limited resource settings to improve breast cancer outcomes[26]. Experiences of middle and low income countries in addressing breast cancer screening and early detection can be helpful in determining which strategy is best for population-based breast cancer screening and early detection in middle and low income countries, including age to initiate population screening; the use of clinical breast evaluation (CBE) as a screening tool and whether it can effectively improve breast cancer outcomes; and the role for breast ultrasound in middle and low resource settings.

7.1. A proposal for breast cancer prevention in the shantytowns of Nairobi, Kenya

Claudia Allemani, Pamela Minicozzi, Milena Sant, Gianfranco Morino

Data from the Nairobi Cancer Registry (NCR) and verbal report from physicians indicate that cancer incidence is increasing in Kenya; it now numbers among the top 10 causes of mortality[27]. In women, breast cancer is the most common neoplasm and most patients present with advanced stage at diagnosis, when the cost

of treatment is high and the chances of survival are limited. This situation is mostly due to the lack of information or misinformation on breast cancer among Kenyan women, although a Breast Health Program (KBHP)[28] was founded in 1999. In Nairobi, about 500,000 women do not have access to the hospital for diagnosis and treatment and are not captured by the NCR. The KBHP alone could not cover all women living in the shantytowns of Nairobi.

In the framework of a possible collaboration between the Istituto Nazionale dei Tumori of Milan and the World Friends non-governmental organization[29] operating in Nairobi, we propose a breast cancer prevention program for scholars attending the school of the main shantytowns of Nairobi (Baba Dogo, Korogocho, Kariobangi, Soweto, Kahawa), where a Safe-Motherhood program is ongoing and students are already inclined to public health notions. Our target population is young women attending these schools and their teachers and mothers. The program includes an initial survey to assess the baseline knowledge, several seminars on breast cancer prevention and a final survey to evaluate the program. To collect this information we will prepare an English questionnaire for the scholars and a questionnaire translated in Kiswahili, with explicative pictures, for their mothers.

The main themes of the seminars will be: 1) basic disease description; 2) definition of "prevention"; 3) self-examination; 4) the importance of breast-feeding; and 5) essential information on healthy nutritional behavior. Informative videos and educational leaflets will be produced and distributed. In addition, we will promote initiatives to support the creation of diagnostic-therapeutic centers within the reach of less affluent women.

7.2. Assessment of the utility of ultrasound guided biopsy of the breast for diagnosis of breast cancer in countries with limited resources

Annina N Wilkes, Barbara Cavanaugh, Barry B Goldberg, Juan Palazzo

Proposed project To evaluate the current capability of radiologists who work in countries with limited resources to perform standard of care ultrasound guided core biopsy of the breast. Evaluation would include assessment of: 1. training and skill of radiologists in performing ultrasound and ultrasound guided percutaneous procedures; 2. supportive technology, equipment, and facilities; 3. pathology lab standard of performance and technology; 4. current standard of care in breast cancer diagnosis and treatment; 5. the current state and potential for outreach, recruitment and follow up of patients; 6. how the ability to perform ultrasound guided breast biopsy could favorably affect the current status of breast cancer diagnosis and treatment in their country or region.

The goal of this evaluation would be to establish a program for teaching and maintaining ultrasound guided breast biopsy as a method of diagnosis of breast cancer, which is well suited for countries with limited resources.

Method We will survey radiologists who have participated in recent ultrasound training programs sponsored by the Jefferson Ultrasound Research and Education Institute. We will survey radiologists from Central and Eastern Europe, Sub-Saharan Africa, the Caribbean and Central and South America who have participated in the "Teaching the Teachers" Ultrasound Physician Training Program [the "Teach the Teachers" program is a Radiological Society of North America (RSNA) Research and Education Foundation grant supported program of the Jefferson Ultrasound Research and Education Institute].

Discussion In many countries with limited resources priority is placed on control of infectious diseases and environmental sanitation. Cancer diagnosis and treatment receives a small percentage of the available funding. Breast cancer is the most common cause of cancer related deaths in women around the world[30,31]. In these countries, breast cancer rates are rising and mortality rates are high as many present for treatment at an advanced stage. The technology and recourses for early diagnosis is unavailable, and for many of these women, treatment is not aggressive. In Sub-Saharan Africa, higher mortality rates fall within women age 45-59, which is a major workforce group, and in addition to the devastating effect that these deaths have on the family structure, there is a direct effect on the country's economy[32]. These deaths add to those from HIV/AIDS and other communicable diseases.

Breast cancer mortality can be reduced with early diagnosis and treatment. In countries with limited recourses, this can only be accomplished through the development of cost- effective methods that are tailored to the specific population[33,34]. Ultrasound is used for diagnostic imaging for most parts of the body and is relied upon heavily in countries with limited resources. More expensive modalities such as computed tomography (CT) and magnetic resonance imaging (MRI) which are used for the same diagnostic purposes in wealthier nations are not as widely available. Ultrasound scanners are portable, relatively inexpensive and are more durable in comparison with other imaging modalities. The cost of supplies and maintenance are lower. It has been my experience that because of these factors, radiologists become very skilled in its use.

Advances in ultrasound technology have expanded its ability beyond diagnostics and in the US, ultrasound is commonly used to guide core biopsy and aspiration of breast masses[35,36]. Current and future applications also include ultrasound guided breast cancer ablation and extraction. In the hands of trained operators, ultrasound guided breast biopsy is an accurate, and many times preferable alternative to surgical biopsy, cutting the cost

of operating room time and anesthesia. The biopsy can be performed within an hour, has a low complication rate and has very few post procedure restrictions to activity. Most patients tolerate the procedure very well[37,38]. Newer biopsy guns are easier to use and require less storage and electricity. These factors make ultrasound guided breast biopsy a good cost effective method to cutting breast cancer death rates through earlier diagnosis and treatment in countries with limited resources.

For more than 2/3 of the world's population, radiology equipment and services such as those described above are unavailable[33]. These services are provided for a small percentage of the population in large city hospitals by a few highly skilled but overworked radiologists who work with outdated and poorly maintained equipment. The World Health Organization, non-profits, and individual radiologists have worked to address this problem. In collaboration with equipment manufacturers and non profits, Dr. Goldberg has developed a program which trains doctors and instructs these doctors to train others, and works to provide donations of ultrasound equipment for training centers. There are currently 75 affiliate centers around the world in Africa, Central and South America and the Caribbean[39-43].

The goal of this project is to establish a train the trainers program for ultrasound guided breast biopsy in countries that would best utilize and benefit from this technique.

8. Tobacco control

With growing numbers of smokers in developing countries, there is an urgent need to take action at a national and global level to reduce the risks for cancer, and other chronic diseases, due to tobacco smoke. Several countries in high, middle and low income settings have successfully implemented strategies to reduce tobacco exposure at the population level, and they can provide valuable insight on how tobacco control programs can be effectively implemented; the necessary components and partners for a multi-sectoral approach; how the cancer control agenda can be integrated with the tobacco control agenda; the challenges to implementing tobacco control programs in lower income countries given different social, cultural, and economic factors affecting smoking and trends in tobacco use[44,45]; and the experiences and application of the WHO Framework Convention on Tobacco Control in different settings.

8.1. Tobacco prevalence in Brazil: a systematic review of population-based surveys

Leticia Casado, Luiz Claudio Santos Thuler

Background Brazil is a significant market for tobacco companies since its large young population is an attractive consumers' pool. Brazil has world leadership in the implementation of measures regulating the tobacco industry.

Methodology The objective of this systematic review is to estimate the differences in tobacco use prevalence and their relationship to the tobacco control actions from the 1980's.

Results There are many studies on the prevalence of tobacco use in Brazil; however, most were conducted in the big cities of the South and Southeast regions of the country. In addition, little methodological standardization exists in the sampling and profile of the investigated population, making comparisons among them difficult. The four studies[46-49] conducted in the 1980's and 1990's reported prevalences of 16.7% to 34.9% (median 31.4%), while five surveys[46,50-53] carried out from 2001 to 2004 reported values ranging from 12.9% to 25.2% (median 22.3%) and six studies[46-48,52,54,55] conducted between 2005 and 2008 reported results between 11.1% and 18.0% (median 15.7%). Methodological differences may have contributed to the great variability found in the prevalence. However, in spite of all of the methodological problems, a trend in time series reduction was observed in the percentage of actual tobacco users.

Conclusion The median prevalence of tobacco use was reduced by 50.0% from the first to the last period analyzed. There seems to be a major reduction in the prevalence of smoking in Brazil which may be related to the comprehensive tobacco control programs implemented in the 1980's in the country. The timing of the public health actions related to smoking suggests that the declines were the result of the restriction and ban on advertisements of tobacco products, the effects of cigarette package warning labels, and the restriction on environmental tobacco smoke exposure in public places.

8.2. Control of cancer - promotion of smoke free environments in Brazil

Vera Lucia Silvia Colombo

Introduction Tobacco control represents an important strategic component for reducing the morbidity and mortality from cancer and other chronic diseases. In Brazil, the National Program of Tobacco Control has been developed and coordinated by the National Institute of Cancer. Important challenges need to be faced; among them the need to enlarge the actions taken to control cancer by promoting smoke free environments and overcoming the barriers presented by the federal legislation that are hindering its execution. Under the Bloomberg Foundation's auspices, national actions have begun to be developed for the promotion of smoke free environments and to improve the federal legislation.

Objective To inform the population and to promote governmental and non-governmental activities regarding: 1) the harms and damages from exposure to second hand smoke; 2) the creation of local legislation specific

for the banishment of environmental tobacco smoke in closed environments, which will serve as incentive and an important action that will influence the improvement of the federal legislation; 3) the alteration of the Federal Law 9.294/96, which has lagged behind in relation to the guidelines extolled by the Framework Convention of Tobacco Control.

Methodology We provide technical and financial support, and participate in seminars or forums of debates, discussions and change of experiences, trainings, strategic meetings and workshops of planning of activities of the states of the federation with the goal to assist local actions promoting atmospheres free from environmental tobacco smoke.

Results Through the National Program of Tobacco Control, we have: 1) created local legislation in many states of the country; 2) created adhesion of the Brazilian population to the alteration of the Federal Law, such that 85% of the population and 79% of smokers support the prohibition of tobacco in closed environments; 3) attended and supported events about the theme in many states.

8.3. Global battle against cancer through tobacco control: a global campaign by youth, for youth, of youth

Venkatachalam Pillai Regunathan

Objective To create an indelible awareness on the ill effects of tobacco among the global youth and school aged children, through a novel signature campaign. The project is named "Global Battle Against Tobacco - with 10 Million Signatures – with 10 Thousand Banners".

Methodology The project envisages: a) to sensitize a minimum of 10 million global youth and school aged children, across all countries of the globe about the ill effects of tobacco; b) to collect 10 million "Signatures-against-Tobacco" from them on 10 thousand cloth banners, each measuring 2 meters in length and 1 meter in width, as a token of their moral commitment to be free from tobacco during their life-time; c) to display signature-banners-against-tobacco at an international venue to a distance of 25 kilometers, creating the World's longest signature wall against tobacco with a mosaic of millions of voices in all languages from all countries and inviting the attention of the print and electronic media of all countries across the globe to highlight the importance of creating a tobacco-free global society; d) to hand-over finally all the signature panels to the Secretary General of United Nations (through the Director-General of WHO) and forming the world's biggest ever and longest ever "Human-Chain-against-Tobacco" by global youth representing all countries, urging the United Nations to protect the youth from tobacco.

Result To date, more than 1000 banners have already been collected from various countries, including Taiwan, Thailand, the United States, Canada, and India. The project is currently under implementation in various countries, including Singapore, Japan and several South American countries.

9. Conclusions

Comprehensive cancer control programs require interventions for cancer prevention, screening and early detection. This involves actions, both inside and outside of the health sector, to create healthy public policies and physical and social environments which support healthy choices and healthy ways of life, limit exposure to environmental and occupational carcinogens and offer opportunities for cancer screening that will ultimately reduce risk and prevent cancer. Tobacco control, promotion of fruit and vegetable consumption, limiting red meat and processed meat, regular physical activity, healthy body weights and limiting alcohol consumption are among the general recommendations for primary cancer prevention. Because many of these cancer risk factors are shared with other chronic diseases, cancer control would benefit from an integrated approach to chronic disease prevention. Screening for early stages of cancer or pre-cancerous lesions is another way to reduce the cancer burden, assuming that infrastructure is in place to provide treatment when cancer is detected. In developing countries and low resource areas, the challenge remains to have cancer prevention and screening a high public health priority, given the many competing public health priorities and limited financial and technical resources.

Acknowledgments

This work was supported by: Lombardy Region; Fondazione IRCCS "Istituto Nazionale dei Tumori" under the patronage of the Italian Ministry of Work, Health and Welfare; Public Health Agency of Canada; Canadian Partnership against Cancer; Alleanza contro il Cancro (ACC); International Atomic Energy Agency; Dr Borras organization - Institute Catala d'Oncologia; Livestrong; European School of Oncology (ESO); National Cancer Institute; Lega Italiana per la Lotta contro i Tumori, Milano (LILT); Associazione Italiana di Epidemiologia (AIE); Istituto Superiore di Sanità; IRCCS Oncological Hospital "Giovanni Paolo II", Bari; National Cancer Institute "Regina Elena", Rome; Italian Federation of the Volunteer Associations in Oncology (FAVO).

The authors wish to thank Catherine Sutcliffe for her assistance in preparing this manuscript.

Acknowledgments to the ICCC-3 Session C group: *paragraph 2.1:* G. Cannon (American Institute for Cancer Research, Minas Gerais, Brazil); *paragraph 2.2:* E. Franco

(McGill University, Montreal, Canada); *paragraph 3.1:* A. Limache-García, M. Quesquen-Puente (National Cancer Institute of Peru, Lima, Peru); *paragraph 3.2:* FS. Gomes, SG. Couto, CF. Dos Santos, IZ. Botelho, APM. Petermann (National Cancer Institute of Brazil, Rio de Janeiro, Brazil); *paragraph 4.1:* S. Wittet (PATH, Seattle, USA); *paragraph 5.1:* L. Ivanov, E. Mirkova (National Center of Public Health Protection, Sofia, Bulgaria); *paragraph 6.1:* L. Giordano, G. Montanari, S. Arnaud, N. Segnan (CPO Piedmont, Turin, Italy), M. Granero (Associazione Alma Terra, Turin, Italy), V. Sahinovic (Visoko Hospital, Visoko, Bosnia), B. Stanic, S. Avdukic (Centar za zene Breza, Breza, Bosnia); *paragraph 6.2:* H. Bryant, C. Anderson, V. Mai, S. Fekete (Canadian Partnership Against Cancer, Toronto, Canada); *paragraph 6.3:* A. Zucchetto, D. Serraino (Centro di Riferimento Oncologico, Aviano, Italy), E. Clagnan, L. Zanier, A. Franzo (Regional Health Agency of Friuli Venezia Giulia, Udine, Italy), O. Forgiarini, E. De Santis, T. Angelin (Friuli Venezia Giulia Cancer Registry, Italy), M. de Dottori (INSIEL Spa, Italy); *paragraph 6.4:* B. Moghimi-Dehkordi, A. Safaee, MA. Pourhoseingholi, M. Habibi, A. Pourhoseingholi, MR. Zali (Shahid Beheshti University M.C., Tehran, Iran); *paragraph 7.1:* C. Allemani, P. Minicozzi, M. Sant (Fondazione IRCSS "Istituto Nazionale dei Tumori", Milan, Italy), G. Morino (World Friends Medical Coordinator, Ruaraka Neema Hospital, Nairobi, Kenya); *paragraph 7.2:* AN. Wilkes, B. Cavanaugh, BB. Goldberg, J. Palazzo (Thomas Jefferson University Hospital, Philadelphia, USA); *paragraph 8.1:* L. Casado, LCS. Thuler (National Cancer Institute of Brazil, Rio de Janeiro, Brazil); *paragraph 8.2:* VLS. Colombo (National Cancer Institute of Brazil, Rio de Janeiro, Brazil); *paragraph 8.3:* VP. Regunathan (Volunteers Against Smoking and Tobacco, Tiruchirapalli, India); *ICCC-3 Working Group:* SB. Sutcliffe, K. Sarwal, H. Torrance (International Cancer Control Congress, Vancouver, Canada), CG. Sutcliffe (Bloomberg School of Public Health, Johns Hopkins University, Baltimore, USA), P. Baili, C. Amati, F. Di Salvo, C. Frazzingaro, N. Sanz, A. Micheli (Fondazione IRCCS "Istituto Nazionale dei Tumori", Milan, Italy).

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