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Opportunities for Cancer Epidemiology and Control in Low- and Middle-Income Countries: A Report from the American Society for Preventive Oncology International Cancer Prevention Interest Group

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Introduction

Despite steady decreases in the cancer burden in industrialized countries, its rapid increase in the developing world means that the number of cancer cases and deaths will likely more than double worldwide over the next two decades (1). Already a leading cause of death around the globe, cancer—grouped as all types of the disease—was associated with 7.4 million deaths in 2004 and is projected to lead to 12 million deaths in 2030 (2). Notably, more than 70% of all cancer deaths occur in low- and middle-income countries (2).

The key drivers of these epidemiologic trends are the increasing numbers of older individuals in developing countries coupled with the rising prevalence of behavioral risk factors. Specifically, the trends toward increased cigarette smoking, physical inactivity, and obesity are not offset by projected declines in infection-related cancers (3). Despite the dramatic increase in the cancer burden in the low- and middle-income countries, international awareness of the problem is low, as reflected by the omission of cancer from the United Nations Millennium Development Goals.

In a major report released in 2007 that was entitled *Cancer Control Opportunities in Low- and Middle-Income Countries*, the Institute of Medicine called “for governments, health professionals, nongovernmental organizations, and others in low- and middle-income countries, with the help of the global health community, to achieve a better understanding of the current and future burden of cancer in low- and middle-income countries and take appropriate and feasible next steps in cancer control” (1).

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In response to the rising cancer burden in resource-poor settings, the American Society for Preventive Oncology established the International Cancer Prevention Interest Group in 2007, under the direction of Dr. Frank Meyskens, as a means of reversing that trend and serving as a worldwide cancer prevention resource. At its 34th annual meeting in Bethesda, MD in 2010, the American Society for Preventive Oncology convened a symposium that focused on cancer epidemiology and prevention issues in the Middle East, Russia, and Latin America. Foremost among these are: (a) improved cancer surveillance, (b) strengthened efforts in tobacco control and obesity prevention, and (c) increased availability of vaccines against cancers of infectious etiology in developing countries. The purpose of this report is to summarize the group's key discussion points for dissemination to the cancer prevention and control community.

Case Study 1: Setting Up the Middle East Cancer Consortium

Dr. Hoda Anton-Culver of the University of California at Irvine reported on her work in The Middle East Cancer Consortium (MECC), which was established in 1996 between the Ministers of Health of Egypt, Israel, Jordan, Cyprus, the Palestinian Authority, and eventually, Turkey. Contributing to the justification to establish cancer registries in these countries was increased cancer awareness in the Middle East and non-Hodgkins lymphoma diagnoses and deaths of several prominent figures, including Golda Meir, King Hussein, and the Shah of Iran. MECC is supported by funds from the Office of International Affairs at the National Cancer Institute (<http://mecc.cancer.gov/>).

Population characteristics

The wide variety of lifestyle, environmental, and genetic factors in MECC provide an opportunity to expand our knowledge of risk factors that contribute to cancer. As Dr. Anton-Culver pointed out, risk factors vary in their contribution to cancer in different settings. Compared with developed countries, cancer mortality is higher in the MECC due to the late stage at diagnosis and lack of

availability of the latest treatment modalities in some of these countries. Some implications of late presentation of cancer in MECC include lower cure rates, more suffering and stigma, and a greater need for palliative care and public health education. Although the age-adjusted incidence rates are lower in the MECC, the age-specific incidence rates for most cancer sites are similar to those in developed countries. However, there is much variation across specific sites. For example, there is a ~10-fold difference in liver cancer incidence between men in Egypt and Jordan from 1999 to 2001.

Notably, since the inception of cancer registries, cancer incidence rates in MECC have increased mainly due to better ascertainment and reporting because proper cancer registration eliminates the underestimation of cancer incidence rates. Common cancer risk factors, such as tobacco use, unhealthy diet, and obesity contribute most to the cancer burden in MECC, as they do around the globe (4). The prevalence of obesity is expanding in MECC populations; in Egypt, for example, more than 50% of the adult population is obese or overweight.

Key components of the MECC

Recognizing that registries require sustained commitment and trained personnel, the MECC has the following key components: (a) development and maintenance of standards of operation for the MECC consortium and individual MECC registry operations manual, data use files and security, confidentiality, Institutional Review Board (IRB), and disaster recovery; (b) resolution of software issues through the IARC; (c) regular communication with members of MECC registries; (d) a plan for adding new required data items (e.g., cause of death, tumor markers, and detailed treatment); (e) development of a research agenda and plan to promote research efforts using MECC data and resources; (f) engagement with data analysis and publications and identification of mentors for the working groups to help develop competitive research applications; (g) associate membership to the MECC; (h) development of a process by which mentors could communicate with investigators within the MECC; and (i) engagement with academic institutions in close proximity to MECC registries to participate in cancer control research projects.

One of the major strengths of the MECC is its training program for junior researchers from participating countries. To date, more than 26 fellows from participating countries have received 3 to 6 months of additional training in cancer surveillance, epidemiology, and biostatistics at the University of California, Irvine, CA. As a mark of strengthened capabilities and infrastructure in MECC, at least three fellows to date are leading Ministers of Health within their home countries.

Case Study 2: Tobacco Control in Russia

Tobacco smoking is one of the most important global cancer risk factors (4), with 80% of the world's 1.1 billion

smokers residing in low- and middle-income countries (5). Extensive evidence is available on the broader global determinants of tobacco consumption such as trade liberalization and global marketing, which have led to a comprehensive response from the global public health community and culminated in the Framework Convention on Tobacco Control (3). Dr. Paul Engstrom of the Fox Chase Cancer Center placed the spotlight on the need for research and action on global tobacco control and used his studies in Russian oncology settings to illustrate the point.

Population characteristics

Tobacco use among cancer patients in Russia is higher than in the United States (41% versus 30%, respectively); the rates are particularly high among patients with cancers of the lung, colon, and head and neck. Further compounding the public health problem of tobacco use in Russia is the fact that about two thirds of Russian physicians lack training in tobacco cessation counseling. However, almost a half of them are interested in acquiring such skills. Hence, Dr. Engstrom argued that it was important to develop interventions that go beyond traditional smoking cessation counseling and incorporate a biobehavioral approach. There is a consensus that such an approach would lead to a more comprehensive and effective response to the tobacco problem.

Key components of the research program

Dr. Engstrom described three tobacco control studies that are part of the American-Russian Cancer Alliance: (a) tobacco survey of Russian cancer patients ($n = 750$ patients with lung, head and neck, or colorectal cancer); (b) tobacco survey of Russian oncologists; and (c) biobehavioral model of smoking cessation among Russian cancer patients. This action-oriented translational research incorporates the fact that >50% of the variation in smoking cessation is due to genetic factors related to nicotine dependence (e.g., DRD2, DRD4, and CB1 TAG haplotype; ref. 6). On the basis of these findings, Dr. Engstrom emphasized the need for both biological and behavioral approaches to smoking cessation.

Case Study 3: Stomach Cancer in Latin America

The third case study focused on stomach cancer as an example of infection-related cancers, which together account for more than 20% of tumors in developing regions (7). Specifically, *Helicobacter pylori* (*H. pylori*) infection is the main cause of stomach cancer, which is the second leading cause of cancer death worldwide (8). Dr. Greenberg of the Fred Hutchinson Cancer Research Center discussed a randomized clinical trial of *H. pylori* eradication in Latin America that is organized and coordinated through the Southwest Oncology Group.

Population characteristics

Participating clinical sites are located in Santiago, Chile; Guanacaste, Costa Rica; Sonora and Chiapas, Mexico; Nariño, Colombia; Santa Rosa de Copan, Honduras; and Leon, Nicaragua. Participants were 1,500 adult men and women who were drawn from the general population of these sites and are infected with *H. pylori*, as shown by a positive C13 urea breath test.

Key components of the research program

The trial compares the effectiveness of three regimens for *H. pylori* eradication: (a) a standard 14-day regimen of a proton pump inhibitor, amoxicillin, and clarithromycin; (b) a 5-day concomitant regimen of proton pump inhibitor, amoxicillin, and clarithromycin plus metronidazole; and (c) a 10-day sequential regimen of proton pump inhibitor plus amoxicillin for 5 days followed by proton pump inhibitor plus clarithromycin and metronidazole for 5 days. Eradication was assessed by urea breath test 6 weeks after randomization, and reinfection was assessed by urea breath test after 1 year. The Southwest Oncology Group statistical center in Seattle manages data entry and quality through a web-based system. This multi-site clinical trial highlights the rich opportunities for conducting cancer prevention clinical trials in Latin America, but there are also challenges posed by the complex and unique regulatory environments in different countries.

Challenges in conducting epidemiologic and cancer control research in developing countries

The three case studies illustrate specific challenges that arise in conducting cancer epidemiologic and control research in regions with limited capacity. The top three challenges in strengthening research in cancer epidemiology and control in developing countries include:

Infrastructure and regulatory issues. Although bureaucracy is often necessary to implement large-scale cancer epidemiologic and intervention studies, this is not without its downsides. One of the challenges of conducting multi-country trials is that each country has its own regulatory requirements, as articulated by Dr. Greenberg. The process of maneuvering medical devices, reagents, or biological samples across countries can

be daunting. Data, particularly those from Web-based sources, could also be subject to limited connectivity, particularly when operating in rural regions.

Effective collaborations. Assembling investigators and ensuring equitable credit is critical for maintaining successful collaborations between investigators from developed and developing countries. It is also important to promote the learning and use of technologies in developing countries; these include devices, reagents, and software. Cooperation and trust-building are critical building blocks of thriving international research programs.

Training. As the three case studies illustrate, scientists in developing countries need to strengthen their training capabilities to develop sustainable research programs. Collaborative relationships could facilitate this capability not only by allowing scientists in developing countries to learn new skills but also by enabling their counterparts from developed countries to acquire knowledge of local practices and customs.

Conclusions and Future Directions

In summary, studying cancer epidemiology in developing countries is an important approach to uncovering possible factors that could be applied to cancer prevention worldwide. Preventive interventions and policies have the potential to slow the global increase in cancer incidence and its disproportionate effect on lower income countries. The case studies illustrate the promise of strengthening tobacco control and vaccination against infections related to cancer in averting these trends. Collaboration among stakeholders from developed and developing countries is critical to successful cancer prevention efforts. The American Society for Preventive Oncology International Cancer Prevention Group will focus on facilitating such efforts and establishing itself as a worldwide cancer prevention resource.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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