

## Cancer Prevention for Global Health: A Report from the ASPO International Cancer Prevention Interest Group

Dejana Braithwaite<sup>1</sup>, Paolo Boffetta<sup>2</sup>, Timothy R. Rebbeck<sup>3</sup>, and Frank Meyskens<sup>4</sup>

### Abstract

As cancer incidence and mortality rates increase in low- and middle-income countries, the need for cancer prevention and control research directed to these countries becomes increasingly important. The American Society of Preventive Oncology (ASPO) is a community of professionals in cancer prevention and control whose mission is to "foster the continuing development of investigators and the exchange and translation of scientific information to reduce the cancer burden."

In the session presented at the ASPO 36th Annual Meeting in Washington, DC in March 2012, chaired by Drs. Frank Meyskens and Dejana Braithwaite, Dr. Paolo Boffetta discussed some of the achievements in global cancer prevention and suggested that future efforts focus on three major causes of cancer: tobacco-use, infections, and overweight/obesity. Dr. Timothy Rebbeck presented an overview of prostate cancer research in sub-Saharan Africa and highlighted how the complex nature of prostate cancer etiology and outcomes can be addressed through capacity-building research partnerships.

Cancer is an emerging public health challenge in developing countries because of the aging and expansion of the population and increased prevalence of cancer risk factors such as smoking, obesity, physical inactivity, and reproductive factors. There are opportunities to reduce the growing cancer burden through the development of research capacity and the application of resource-appropriate interventions. *Cancer Epidemiol Biomarkers Prev*; 21(9); 1606–10. ©2012 AACR.

### Introduction

Cancer is a growing cause of death worldwide. The cancer burden in low- and middle-income countries (LMIC) has been disproportionately increasing with 60% of new cases and 70% of all cancer deaths occurring in LMIC (1). Survival is closely and positively related to country income for several cancers, including cervical, breast, and prostate (2). In September 2011, a high-level meeting of the UN General Assembly on Noncommunicable Disease Prevention and Control included the development of a plan to address cancer's role in the global health agenda, alongside other noncommunicable diseases (3). In response to the rising cancer burden in resource-poor settings, American Society of Preventive Oncology (ASPO) established the International Cancer Prevention Special Interest Group (SIG) in 2007, under

the direction of Dr. Frank Meyskens, as a means of reversing that trend and serving as a worldwide cancer prevention resource (4). The SIG's mission is to facilitate new scientific collaborations and interactions, and to serve as a resource for global health research in cancer prevention.

At its 36th annual meeting in Washington, DC in 2012, ASPO convened a session focusing on cancer prevention in developing countries. This session, chaired by Drs. Frank Meyskens and Dejana Braithwaite, presented 2 case studies that addressed cancer prevention for global health. The first speaker, Dr. Paolo Boffetta from the Mount Sinai School of Medicine in New York City, highlighted past achievements and future research priorities in global cancer prevention. The second speaker, Dr. Timothy Rebbeck presented his research program on prostate cancer in sub-Saharan Africa and highlighted how the complex nature of prostate cancer etiology and outcomes can be addressed through capacity-building research partnerships. Below we provide an overview of Dr. Boffetta's presentation followed by that from Dr. Rebbeck.

### Dr. Boffetta: Global Cancer Prevention—What Has Been Achieved and What Could Be Achieved?

Dr. Boffetta began his presentation by highlighting that LMIC suffer from a heavier burden of cancer incidence and mortality than high-income countries (HIC). Figure 1 shows the trends for key cancer risk factors across the

**Authors' Affiliation:** <sup>1</sup>Department of Epidemiology and Biostatistics, Helen Diller Family Comprehensive Cancer Center, University of California, San Francisco, California; <sup>2</sup>Mount Sinai School of Medicine, New York; <sup>3</sup>University of Pennsylvania, Philadelphia, Pennsylvania; <sup>4</sup>Chao Family Comprehensive Cancer Center, University of California, Irvine

**Corresponding Author:** Dejana Braithwaite, Department of Epidemiology and Biostatistics, Helen Diller Family Comprehensive Cancer Center, University of California, San Francisco 185 Berry Street, Suite 5700, San Francisco, CA 94107. Phone: 415-514-8019; Fax: 415-514-8150; E-mail: DBraithwaite@epi.ucsf.edu

doi: 10.1158/1055-9965.EPI-12-0848

©2012 American Association for Cancer Research.

|            | HIC   | LMIC  |
|------------|-------|-------|
| Tobacco    | +++ ↓ | +++ ↑ |
| Infection  | + ↓   | +++ ↓ |
| Nutrition  | ++ ↑  | + ↑   |
| Alcohol    | + ↓   | + ↑   |
| Hormones   | ++ ↑  | + ↑   |
| Occupation | + ↓   | (+) ↑ |
| Radiation  | + ↔   | (+) ↔ |

Figure 1. Main causes of human cancer, their impact (and trend) in HIC and LMIC.

globe (5). Among the main causes of cancer, tobacco has the largest impact in both LMIC and HIC but the trend is decreasing in HIC and increasing in LMIC. Infection has a large impact in LMIC but only a modest impact in HIC and the trend is decreasing in both LMIC and HIC. Nutrition has a modest impact in LMIC and a moderate impact in HIC, with an increasing trend in both. The impact of alcohol use is modest in both LMIC and HIC although the trend is downward in HIC and upward in LMIC. The impact of hormones (endocrine disruptors) is modest in LMIC and moderate in HIC but the trend is upward in both. The effect of occupational exposures is modest in both LMIC and HIC but the trend is downward in HIC and upward in LMIC. Finally, the effect of radiation exposures is modest in both LMIC and HIC.

Dr. Boffetta was recently involved in estimating the proportion of cancer deaths occurring in France in 2000 that were attributable to known risk factors based on data on the frequency of exposure around 1985 (6). He highlighted France because it is similar to other developed countries in terms of the prevalence of cancer risk factors. Dr. Boffetta and colleagues found that tobacco smoking was responsible for 23.9% of cancer deaths, alcohol drinking for 6.9%, and chronic infections for 3.7%. Occupation was responsible for 3.7% of cancer deaths in men; and the lack of physical activity, overweight/obesity, and use of exogenous hormones were responsible for 2% to 3% of cancer deaths in women. Thus, known risk factors explained 35.0% of overall cancer deaths, and 15.0% among never smokers. Dr. Boffetta pointed out that, like in the United States, tobacco smoking was one of the key cancer risk factors, particularly in relation to lung cancer.

The precise contribution of nutritional factors to the cancer burden remains elusive. Dr. Boffetta referred to his article on fruit and vegetable intake in relation to cancer risk (7). In this prospective analysis of the European Prospective Investigation into Cancer and Nutrition cohort, he and his colleagues showed that associations between reduced cancer risk and increased intake of total fruits and vegetables combined and total vegetables for

the entire cohort were similar [200 g/d increased intake of fruits and vegetables combined, HR = 0.97, 95% confidence interval (CI) = 0.96–0.99; 100 g/d increased intake of total vegetables, HR = 0.98, 95% CI = 0.97–0.99]; intake of fruits showed a weaker inverse association (100 g/d increased intake of total fruits, HR = 0.99, 95% CI = 0.98–1.00). This study also showed a very small inverse association between intake of total fruits and vegetables and cancer risk.

Dr. Boffetta then went on to mention a similar project in China that focused on estimating cancer incidence and mortality attributable to tobacco smoking, infection, overweight, obesity, physical inactivity, and alcohol drinking (8–11). China serves as an illustrative example because it has much better epidemiologic data compared with other developing countries. These studies showed that major preventable causes of cancer in China were infection, tobacco smoking, and alcohol use. Dr. Boffetta stated that the distribution of risk factors between China and developed countries is comparable. Low fruit/vegetable intake also emerged as an important risk factor in China, because the rural population has a relatively low intake but the contribution of nutrition-related factors was relatively small compared with developed countries.

Dr. Boffetta outlined 4 examples of successful primary prevention initiatives in developing countries: (i) chronic infections, (ii) tobacco control, (iii) nutrition, and (iv) occupational exposures.

### Chronic infections

Dr. Boffetta highlighted a nationwide hepatitis B vaccination program that was implemented in Taiwan in 1984 represents the simplest most successful story (12). Since the institution of this program, the incidence of hepatocellular carcinoma in children has declined. Specifically, the average annual incidence of hepatocellular carcinoma in children 6 to 14 years of age declined from 0.70 per 100,000 children between 1981 and 1986 to 0.57 between 1986 and 1990, and to 0.36 between 1990 and 1994 ( $P < 0.01$ ). The incidence of hepatocellular carcinoma in children 6 to 9 years of age declined from 0.52 for those born between 1974 and 1984 to 0.13 for those born between 1984 and 1986 ( $P < 0.001$ ; 12).

### Tobacco

Dr. Boffetta highlighted tobacco control as another major accomplishment for cancer prevention. He provided descriptive data on the United States and China (8) showing the parallels between the 2 countries. Whereas approximately 10% of total deaths in the 1950s was due to tobacco smoking among U.S. adults, tobacco smoking was responsible for approximately 10% of total death in 1990 in Chinese men. By 1990, approximately 30% of total mortality was attributable to smoking among U.S. adults; the identical estimate, approximately 30%, is the projected total proportion of smoking-related deaths among Chinese men by 2030. As Dr. Boffetta pointed out, it is

remarkable how the United States experience is getting repeated in China. Tobacco consumption has markedly declined in the United States and other developed countries and it is hoped that China and other LMIC will learn from this example by averting this global pandemic. Toward this end, it will be important to implement the World Health Organization (WHO) Framework Convention on Tobacco Control and commit adequate resources for public health interventions based on the science of epidemiology, economic burden, and tracking the tobacco industry(13).

### Nutrition

Dr. Boffetta also discussed some of his work in France about alcohol use and cancer. Notably, there has been a decrease in mortality in France from alcohol-related cancers such as oral cancer and those of esophagus, pharynx, and larynx (6). Spirits were widely used in France up to 1970s but following increased alcohol taxation in this country, this trend started to change around that time period. This example shows the major impact that policy can play in cancer prevention. Another example is stomach cancer, whose incidence is decreasing in low-risk countries such as the United States, in intermediate-risk countries such as China as well as in high-risk countries such as Japan (14). There is no consistent answer as to what is responsible for this downward trend.

### Occupational exposures

A decline in asbestos exposure has contributed to a decline in mortality, particularly in developed countries (15). Trends by age group in men show decline in the incidence of mesothelioma and lung cancer, particularly in younger cohorts, with similarly decreased rates observed in the United States. Yet, exposure is still widespread in developing countries for many important occupational carcinogens, including asbestos. Although estimates of the global burden of occupational and environmental cancers result in approximately 2% and <1%, respectively, these cancers concentrate in population subgroups. In addition, exposure is involuntary and can, to a large extent, be avoided (15).

### Lessons Learned and Conclusions

In sum, there are examples where prevention has worked but this is not the case for all cancers. For example, there has been an increase in the incidence of breast cancer in countries such as India, Hong Kong and Colombia (16), which is likely due to changes in reproductive history in women, including reduced parity and earlier age at menarche. In conclusion, Dr. Boffetta pointed out that up to 50% of human cancer can be prevented if the right strategies were implemented. Whereas some accomplishments in cancer prevention were planned, others have been a consequence of policy and other societal changes. Moving forward, Dr.

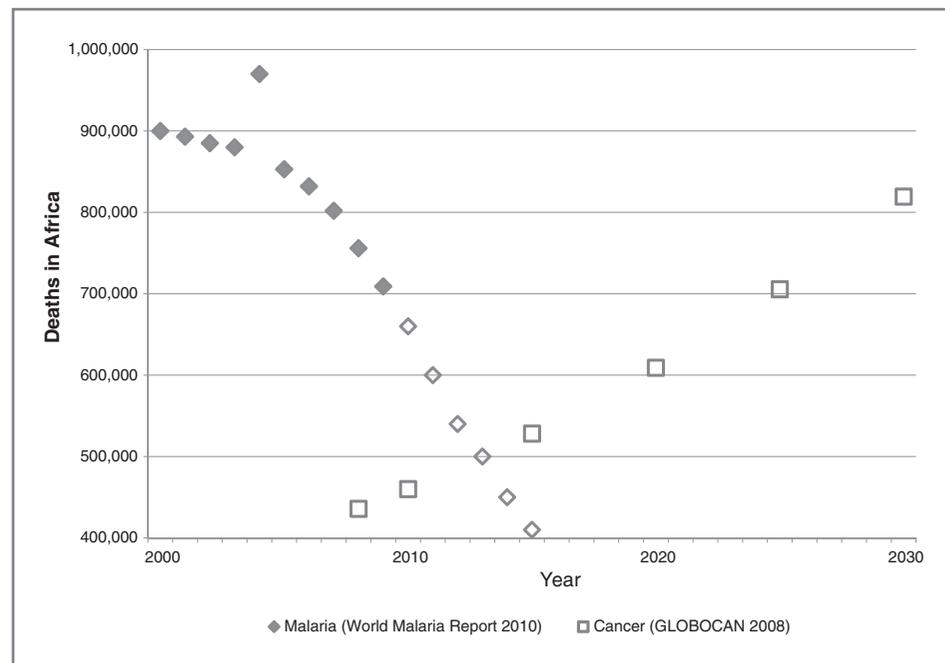
Boffetta recommended that global cancer prevention efforts focus on the 3 major cancer causes: tobacco, infections, and overweight/obesity.

### Dr. Rebbeck: Capacity Building Research Partnerships in Sub-Saharan Africa

Africa presents both challenges and unique opportunities in terms of building research and translational capacity. Dr. Rebbeck pointed out that although infectious disease remains an important issue in sub-Saharan Africa, cancer is also an increasingly important issue. Furthermore, Africans may have unique exposure and risk factor patterns as well as a unique natural history of the disease that can help generate novel insights about cancer. Whereas some common cancers in the United States are identified at an early stage because of the availability of screening, cancer in Africa tends to be diagnosed at late stage and, hence, there is an opportunity to study the full natural history of cancer in Africa. Studying the course of the disease in Africa could also contribute to the understanding of cancer in the African descent populations worldwide. Cancer is also an underappreciated disease in Africa and, hence, there is a need to improve its detection and prevention as well as to develop Africa-specific interventions that can directly benefit the African population. Dr. Rebbeck mentioned that the philosophy he endeavors to follow is encapsulated in the following statement by Julio Frenk, Dean of the Harvard School of Public Health: "*The creation of knowledge has been central to advancement of health in the 20<sup>th</sup> century and is critical for improved global health.*" By raising our awareness of cancer prevention, treatment, and detection in Africa, there is great potential for new knowledge to be generated to improve the health of all populations.

Dr. Rebbeck explained that prostate cancer is the most commonly occurring of all cancers among men of African descent, including African, Caribbean, and African American, and is also the leading cause of cancer mortality among African and Caribbean populations (17). Prostate cancer is clearly an important public health problem, with approximately 28,000 men in Africa and 5,000 in the United States dying each year. Approximately 70% of men diagnosed with prostate cancer in Africa die compared with 40% in the Caribbean and 15% in the United States. In addition, prostate cancer incidence is predicted to increase from 2010 to 2030 with an 87% increase in the United States, 71% in the Caribbean, and 104% in Africa (17). Notably, Dr. Rebbeck showed that cancer rates are increasing although malaria is declining. A number of factors may explain the growing cancer rates in sub-Saharan Africa. First, there is a paucity of cancer funding and research in sub-Saharan Africa (refs. 17, 18; Fig. 2). The populations of sub-Saharan Africa and other developing countries are aging, such that the demographic composition of developing countries may resemble the developed world by 2050 (14). Cancer risk factors are also

Figure 2. Malaria and cancer death trends in Africa.



changing. For example, the prevalence of obesity is on the increase in Africa. Between 2002 and 2010, data from the WHO Global InfoBase show that the percentage of African men with body mass index  $>25$  kg/m<sup>2</sup> is growing in many parts of Africa (19). In addition to increased cancer incidence, cancer deaths are growing because facilities for clinical care are inadequate in most of sub-Saharan Africa. Data from International Atomic Energy Agency indicate that there is insufficient access to radiotherapy in Africa, with only 24 of 53 countries reporting the availability of radiation treatment centers. The supply of radiotherapy in Africa in 2002 was only 18% of the total needed (20). In addition, only 11% of the African population is covered by population-based cancer registries, and only about 1% of the population by registries that meet the International Agency for Research on Cancer's criteria for high-quality incidence (21).

The mission of Dr. Rebbeck's research program, the Men of African Descent and Carcinoma of the Prostate (MADCaP) consortium is to develop and translate knowledge through high-quality research and training in sub-Saharan Africa. This and other initiatives intend to minimize the loss of domestic professionals and facilitate local capacity building. Strategic planning has been conducted to identify partners and establish Centers of Excellence in multiple regions of sub-Saharan Africa. The MADCaP has developed a number of academic and network partnerships, and is coordinated by the African Organization for Research and Training in Cancer. The MADCaP consortium brings together groups from Africa, North America, and the Caribbean that contribute resources to facilitate high-quality

cancer research, including biobanking, laboratory science, epidemiology, and hospitals for patient accrual. MADCaP also includes common databases and common research questions. After spending almost a decade developing the infrastructure, MADCaP now has begun to have the critical mass of researchers and resources to address relevant cancer questions in Africa. Of note, pathology services are also available within MADCaP Centers through a partnership with the American Society for Clinical Pathology, which is fundamental to improving clinical care and research (22).

### Lessons Learned and Conclusions

In noting the lessons he has learned in Africa, Dr. Rebbeck mentioned some of the key limitations of research in sub-Saharan Africa. First and foremost, limited knowledge about cancer rates in sub-Saharan Africa limits our ability to understand the magnitude of the problem. There is also limited research culture in sub-Saharan Africa, including among physicians: the lack of academic/tenure-track and the lack of protected time limits the ability to create sustainable research. In addition, research, education, and funding are also inadequate.

Creating high-level partnerships and trust among researchers is paramount. Moving forward, Dr. Rebbeck hopes that other key institutions will be engaged in cancer research in sub-Saharan Africa, including the African Union and the new Global Health Center at the National Cancer Institute. In addition, investigators seeking to develop research projects in Africa need a dedicated local

principal investigator and senior investigators who are willing to foster holistic training and promote junior researchers. Finally, there is a need for a Cancer Plan by the Ministries of Health to make the cancer research enterprise sustainable.

### Summary

In conclusion, cancer is an emerging public health challenge in developing countries because of the aging and expansion of the population and increased prevalence of cancer risk factors such as smoking, obesity, physical inactivity, and reproductive factors. There are opportunities, however, to reduce the grow-

ing cancer burden through the development of research capacity and the application of resource-appropriate interventions.

### Acknowledgments

D. Braithwaite is supported by the Mentored Research Scholar Award (121891-MRSG-12-007-01-CPHPS) from the American Cancer Society. Research by T. Rebbeck supported by the 2011 Landon Foundation-AACR INNOVATOR Award for International Collaboration in Cancer Research, grant number 11-60-27-REBB. Authors are grateful to Electra Paskett, PhD, for helpful comments.

Received July 17, 2012; accepted July 20, 2012; published OnlineFirst July 31, 2012.

### References

1. Thun MJ, DeLancey JO, Center MM, Jemal A, Ward EM. The global burden of cancer: priorities for prevention. *Carcinogenesis* 2010;31:100–10.
2. Farmer P, Frenk J, Knaul FM, Shulman LN, Alleyne G, Armstrong L, et al. Expansion of cancer care and control in countries of low and middle income: a call to action. *Lancet* 2010;376:1186–93.
3. General Assembly of the United Nations: President of the 65th session. High level meeting on non-communicable diseases, September 19–20, 2011 [accessed June 6, 2012]. Available from: <http://www.un.org/en/ga/president/65/issues/ncdiseases.shtml>.
4. Braithwaite D, Wernli KJ, Anton-Culver H, Engstrom P, Greenberg ER, Meyskens F. 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. *Cancer Epidemiol Biomarkers Prev* 2010;19:1665–7.
5. Sankaranarayanan R, Boffetta P. Research on cancer prevention, detection and management in low- and medium-income countries. *Ann Oncol* 2010;21:1935–43.
6. Boffetta P, Tubiana M, Hill C, Boniol M, Aurengo A, Masse R, et al. The causes of cancer in France. *Ann Oncol* 2009;20:550–5.
7. Boffetta P, Couto E, Wichmann J, Ferrari P, Trichopoulos D, Bueno-de-Mesquita HB, et al. Fruit and vegetable intake and overall cancer risk in the European Prospective Investigation into Cancer and Nutrition (EPIC). *J Natl Cancer Inst* 2010;102:529–37.
8. Wang JB, Jiang Y, Wei WQ, Yang GH, Qiao YL, Boffetta P. Estimation of cancer incidence and mortality attributable to smoking in China. *Cancer Causes Control* 2010;21:959–65.
9. Xiang W, Shi JF, Li P, Wang JB, Xu LN, Wei WQ, et al. Estimation of cancer cases and deaths attributable to infection in China. *Cancer Causes Control* 2011;22:1153–61.
10. Wang D, Zheng W, Wang SM, Wang JB, Wei WQ, Liang H, et al. Estimation of cancer incidence and mortality attributable to overweight, obesity, and physical inactivity in China. *Nutr Cancer* 2012;64:48–56.
11. Liang H, Wang J, Xiao H, Wang D, Wei W, Qiao Y, et al. Estimation of cancer incidence and mortality attributable to alcohol drinking in China. *BMC Public Health* 2010;10:730.
12. Chang MH, Chen CJ, Lai MS, Hsu HM, Wu TC, Kong MS, et al. Universal hepatitis B vaccination in Taiwan and the incidence of hepatocellular carcinoma in children. Taiwan Childhood Hepatoma Study Group. *N Engl J Med* 1997;336:1855–9.
13. Mackay J. Implementing tobacco control policies. *Br Med Bull* 2012;102:5–16.
14. WHO. International Agency for Research on Cancer: World Cancer Report. In Stuart BW, Kleihues P, editors. Geneva, Switzerland: WHO; 2008.
15. Boffetta P. Epidemiology of environmental and occupational cancer. *Oncogene* 2004;23:6392–403.
16. International Agency for Research on Cancer: Cancer Incidence in Five Continents (CICF) 8th edition. 2002 [accessed June 6, 2012]. Available from: <http://globocan.iarc.fr/>.
17. WHO. World Malaria Report. International Agency for Research on Cancer. Globocan; 2008 [accessed June 6, 2012]. Available from: <http://globocan.iarc.fr/>.
18. World Health Organization. The World Malaria Report. 2010 [accessed June 6, 2012]. Available from: [http://www.who.int/malaria/world\\_malaria\\_report\\_2010/en/index.html](http://www.who.int/malaria/world_malaria_report_2010/en/index.html).
19. WHO Global InfoBase. 2011 [accessed June 6, 2012]. Available from: <https://apps.who.int/infobase/>.
20. Barton MB, Frommer M, Shafiq J. Role of radiotherapy in cancer control in low-income and middle-income countries. *Lancet Oncol* 2006;7:584–95.
21. Jemal A, Bray F, Forman D, O'Brien M, Ferlay J, Center M, et al. Cancer burden in Africa and opportunities for prevention. *Cancer* 2012. [Epub ahead of print].
22. Roberts DJ, Wilson ML, Nelson AM, Adesina AM, Fleming KA, Milner D, et al. The good news about cancer in developing countries—pathology answers the call. *Lancet* 2012;379:712.