Addressing the Growing International Challenge of Cancer: A Multinational Perspective

Harold Varmus1* and Harpal S. Kumar2*

Leaders in cancer research and policy from 15 economically diverse countries met at the U.S. National Institutes of Health in November 2012 to discuss opportunities to reduce cancer incidence and mortality, improve cancer care, and increase our understanding of disease pathophysiology. Here, we present recommendations that the participants believe will enable faster progress in addressing the growing international challenge of cancer.

INTRODUCTION

The diseases grouped together as cancers are among the major liabilities of human life. The global burden of cancer includes 12.7 million newly diagnosed cases per year, of which more than half occur in less developed regions of the world (1). Cancers now account for more than 15% of the world’s annual deaths (>7.5 million per year), and that number is rising, especially in less affluent countries (2). Moreover, cancers are among the most feared medical conditions, often causing prolonged periods of suffering, requiring substantial health-care expenditures for advanced care, and being fought with medical tools that are relatively ineffective and themselves frequently disabling. [In this Commentary, the authors represent the views of participants at an international meeting of leaders in cancer research (complete list shown in Table 1).]

Leaders of institutions and organizations that fund and perform cancer research came from 15 countries to the U.S. National Institutes of Health (NIH) in November 2012 to discuss opportunities to reduce cancer incidence and mortality, improve cancer care, and increase our understanding of the many forms of the disease. Here, we present recommendations supported by the meeting participants, who represented more than half of the world’s population, including citizens in low- and middle-income countries. We address several areas that the group believes to be of great importance, such as development of cancer registries and national cancer-control plans; implementation of better methods to prevent, detect, and treat cancers; and ways to expand and improve research on a wide range of cancer-relevant topics.

AN EXPANDING PERSPECTIVE

Until recently, efforts to improve the world’s capacity to combat cancers have not often been addressed in a globally coordinated way. Notwithstanding critical work by professional societies and by many international and national nongovernmental organizations (NGOs) to improve care, increase awareness of cancer, and provide basic infrastructure and equipment, most countries—and those responsible for the support and conduct of cancer care and research within them—have focused on cancers that most commonly afflict their own citizens, using a variety of approaches and resources.

There are several possible explanations for this heterogeneity. First, countries differ substantially with respect to the kinds of cancers that are prevalent locally and the underlying environmental, behavioral, and genetic factors that predispose to those cancers. Second, countries have different fiscal, professional, and political capacities to confront disease. Efforts in each national context may also be influenced by competing health concerns, such as infectious diseases (for example, HIV/AIDS or malaria) or chronic conditions (such as diabetes or cardiovascular diseases), and by varying abilities to help address the plights of citizens of other nations. Finally, countries have distinct traditions—and individual citizens have different perspectives—that affect the way their governments approach cancers. These views may date to a time when malignant diseases were relatively rare and tools for controlling them and their complications were usually ineffective.

The signatories to this article are individuals with influential positions at agencies and institutions that perform or support research on various kinds of cancer in several countries. The November 2012 meeting followed an initial gathering of a similar group at Cancer Research UK in London in 2011. Participants at the two meetings discussed how we can augment our individual efforts: (i) by promoting the application and expansion of existing knowledge to prevent, detect, and treat cancers in many nations, and (ii) by seeking opportunities to foster pioneering research in laboratories and clinics on all aspects of these diseases, including cancers that take their greatest toll in the developing world.

We have been encouraged in our deliberations by a variety of factors. These include a greater appreciation of epidemiological evidence for the large and growing burden of cancers, especially in developing countries; major advances in the understanding of can-
Table 1. Consensus statement. All participants at the November 2012 meeting at NIH are co-signatories to this article. They are listed alphabetically by country, with title and institutional affiliation(s). The views expressed here are endorsed by the signatories as individuals and do not necessarily represent the views or policies of their organizations or nations.

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Cancers made possible by technologies that include genomics, cell and molecular biology, microbiology, and informatics; and the development, over the past few decades, of more effective methods to prevent and treat certain types of cancers and their symptoms. We also note and welcome the inclusion of cancer in the 2011 United Nations Declaration on Non-Communicable Diseases (www.un.org/ga/search/view_doc.asp?symbol=A/66/L.1), with a commitment to reduce preventable deaths by 25% by the year 2025.

We write this article to make a larger audience aware of these features of cancer and to share our aspirations to control cancer more effectively and globally through joint activities. Our statements are directed toward two general goals: to improve implementation of those aspects of cancer control that research has already validated and to promote new research efforts that promise broad benefits over the short and long terms.

Although most of us are primarily responsible for cancer research, not necessarily for medical care or public health policies, we have a broad interest in controlling cancer with all of the methods now available—most of which have been developed and confirmed through the kinds of research we support—and in finding better ways, through research, to diminish cancer incidence and mortality. It is from this perspective that we make recommendations directed at policy-makers, the general public, and our own research communities in the areas of registries, prevention, screening, treatment, and research.

CANCER REGISTRIES AND PATHOLOGY

Reliable, population-based registries that define the incidence, mortality, and survival rates of different types of cancers are fundamental to the design of local, regional, and national plans for improving cancer prevention and treatment and for investing in research. Yet, in many parts of the world, accurate assessments of the burden of cancer and the distribution of its various types are unavailable or inaccurate (3). For example, the worldwide cancer estimates made by the International Agency for Research Against Cancer (IARC) depend on data from only about one-third of 184 countries (4).

Support for infrastructure for population-based cancer registries and for training of specialized personnel to build and maintain these resources is vital for a better accounting of cancer. Another crucial need is adequate cancer registries and for training of about one-third of 184 countries (4).
that range from conventional microscopy to those enabling molecular classification of cancer subtypes. We encourage governments and other organizations to support efforts that would increase the coverage and reliability of cancer registries by investing in necessary infrastructure and personnel and by training and recruiting skilled pathologists. Systems of triage and use of telepathology to ascertain difficult diagnoses could help make more effective use of scarce pathology resources.

CANCER PREVENTION

The most sensible and usually the most cost-effective means to reduce the burden of cancer is through prevention. Yet, implementation of measures to mitigate factors now known to promote cancer—tobacco, certain infectious agents, ultraviolet radiation, alcohol, obesity, lack of exercise, and diet—is often inadequate, even when methods that lower such risks are scientifically well-established, as in the case of tobacco control (5, 6). Sometimes these failures result from the difficulty or cost of using preventive strategies (such as expensive vaccines), while at other times cancer prevention may be at odds with financial interests (such as revenues generated from the production and sale of tobacco).

Furthermore, as gauged by responses around our own conference table, funding organizations often spend too little on prevention research. Those funders among us intend to explore ways in which we can increase the proportion of our activity on this critical aspect of cancer control. Areas of high interest include identifying clearer risk factors with public health implications, developing and testing new interventions, determining how to increase the effectiveness or uptake of those interventions, and testing means to limit exposure to carcinogens.

Tobacco use. With respect to modifiable lifestyle risk factors for cancer, there is a consensus that tobacco use remains, by far, the most important at a global level. Governments play a critical role in the adoption of measures that can prevent cancer, and we urge them to recognize the health of their citizens as a more important priority than global trade agreements or the national economic benefits of tobacco farming and trade. Measures we recommend include exemption of tobacco products, which are both addictive and harmful to health, from trade agreements, and the imposition of higher taxes on the sale of tobacco products, a well-established means to both lower tobacco use and raise revenues. These are important steps in country-wide adoption of broader sets of tobacco-control policies, such as those embodied in the Framework Convention for Tobacco Control—policies that are known to reduce the incidence of cancers of the lung and other organs (7).

Governments can also act preemptively to ensure that tobacco use does not rise among those populations with currently low rates of use—such as women in countries with cultural or religious prohibitions against smoking and people living in Sub-Saharan Africa—by protecting them from expected efforts by the tobacco industry to expand into new markets. Use of tobacco products by health professionals remains a barrier to public recognition of its harms and should be reduced. Efforts to de glamourize and decrease the social acceptability of tobacco use should also be enhanced.

Because many strategies for tobacco control have been proposed but not carefully evaluated, some of the meeting participants intend to establish a global consortium to coordinate such research efforts. The consortium should supplement work of the World Health Organization and others and address the design and value of tobacco-control measures in the general population, in different parts of the world, and in highly vulnerable populations (such as people with mental illnesses or members of economically deprived communities).

Vaccines. Successful programs to administer human hepatitis B virus (HBV) vaccines to large segments of exposed populations, including those in areas of Africa and Asia with high endemic rates of transmission, are reducing the incidence of HBV infection and virus-induced hepatoma (8–10). However, with some exceptions, efforts to use the human papilloma virus (HPV) vaccines to protect populations against HPV-induced cancer of the cervix—the leading cause of cancer mortality among women in many countries—have yet to be similarly successful (11).

In Australia, where uptake of the HPV vaccine is high (~80% in adolescent females), researchers have already observed population-wide reductions in HPV prevalence and associated disease with short incubation times (12). But use of HPV vaccines has fallen below expectations in most other countries, even in economically developed countries such as the United States, where sociocultural sensitivities have limited vaccine uptake to about one-third of adolescent girls and fewer than 5% of boys (13).

A few economically underdeveloped countries, such as Rwanda, are vaccinating girls against HPV with the support of the GAVI Alliance (www.gavi.org). However, in most developing nations, no HPV vaccination programs have been initiated. This situation reflects, in large part, the high costs of the vaccine—which can be up to $360 for a full course of immunization—but also the programmatic challenges of vaccinating the at-risk population and the unusual age (early adolescence) at which the vaccine is best administered (14).

We urge governments and other organizations to consider ways to increase the production and distribution of low-cost versions of HPV vaccines. Such efforts could also encourage research to develop prophylactic vaccines against other cancer-causing infectious agents, such as hepatitis C and Epstein-Barr viruses (15).

Chemoprevention. Efforts to employ medication to lower the risk of cancer have historically proven ineffective. However, recent studies provide compelling evidence that the use of daily, low-dose aspirin can reduce the incidence of and mortality from a variety of cancers (16, 17). The benefits of aspirin need to be promulgated more widely along with an assessment of its risks and optimal strategy for use. In addition, public health authorities should state, more clearly, the cases for use of other cancer-preventing agents, such as hormone inhibitors that can reduce breast cancer incidence. We encourage and intend to undertake further research to define the optimal dose and duration of use of such chemopreventive agents. Other objectives include better means to identify individuals who will gain the greatest benefits from the use of chemopreventive agents, because of a high risk for certain cancers, and those who should avoid their use, because of an increased risk of harmful consequences.

CANCER SCREENING

The importance of screening individuals for certain cancers (of the cervix, breast, prostate, and colorectum, in particular) has been emphasized in some countries and influenced by resource availability and public health priorities. While such practices can substantially lower the risk of cancer incidence and mortality, as documented especially well for cervical and colorectal cancers (18, 19), they also have the potential to promote “overreatment” of indolent lesions that would not have become lethal cancers even
if left undetected. This potential for harmful consequences from screening has been recognized increasingly over the past few years (20) and warrants enhanced efforts to provide more balanced information to the public on benefits and risks and to learn how to discriminate between lesions that are inherently indolent and those that are likely to behave aggressively. Moreover, the existence of reliable means to distinguish between clinically benign and malignant lesions would encourage researchers to develop new strategies for early detection, which will in turn improve the cost-effectiveness of screening.

CANCER TREATMENT

Optimal cancer treatment is a complex process, requiring accurate and timely histological diagnosis and staging of tumors as well as evidence-based choices among the many available methods of care—including surgery, radiation therapy, anticancer drugs, and several means to control the symptoms of disease and the complications of often debilitating therapies. With the advent of molecularly targeted therapies—both drugs and monoclonal antibodies (21)—therapeutic decisions often also depend on complex tests for mutations and gene expression.

Although appropriate cancer therapies are often successful in curing disease, especially when it is diagnosed at relatively early stages, or are able to hold disease at bay for many years, we recognize that current treatments are far from perfect. First, the care of cancer patients is an expensive proposition, and the costs have continued to rise, limiting the capacity of countries across the entire economic spectrum to deliver the best modern cancer therapies to all patients. Second, there are major global disparities in the availability, affordability, and access to modern multidisciplinary cancer care, especially in poorer countries. Third, while some disseminated cancers, such as testicular carcinomas and several leukemias and lymphomas, are now curable, current treatments generally fail to eliminate most metastatic cancers and often control them briefly or not at all.

We envision several measures that could be taken to improve this situation. All countries, especially those relatively poor countries that offer very limited cancer therapy at present, should create or strengthen national cancer plans to enable more judicious use of available resources and, thereby, improve the availability of relatively low-cost cancer care (22). Second, medical and scientific communities should strive to develop strategies that can deliver the benefits of new forms of cancer therapy more swiftly and economically to all countries. Cancer research organizations should continue to expand translational and clinical investigations with the goal of improving the repertoire and effectiveness of therapeutic options.

Development of new therapies will require greater enrollment of cancer patients in clinical trials, and those trials will increasingly be international in scope. If expensive and difficult clinical research is to be pursued with maximum effect, sharing of information and harmonization of practices are essential. Funding agencies will need to mandate the use of online registries for clinical trials and require that the results of all trials, whether with negative or positive outcomes, be made available to the scientific community through publication or entries in trial registries.

We also encourage efforts to reduce obstacles to the design and conduct of international trials by making the practices of the major regulators of drug testing and production as uniform as possible, such as the U.S. Food and Drug Administration, the European Medicines Agency, Japan’s Pharmaceuticals and Medical Devices Agency, and others, as exemplified by the International Conference on Harmonisation guidelines (www.ich.org/products/guidelines.html).

To take full advantage of new opportunities for improved therapies as well as preventive strategies, funding agencies—including those listed in Table 1—must provide greater financial support for trials that are sponsored by academic institutions, especially when the work includes expensive procedures (such as multiple biopsies and molecular tests), addresses rare cancer types, or involves surgery, radiotherapy, or the repurposing of existing drugs. We also encourage pharmaceutical companies to cooperate with each other and with funding organizations in the design and conduct of clinical trials that use multiple agents produced by more than one company, a situation that preclinical studies suggest will be increasingly required to achieve maximal benefits from targeted therapies.

EXPANDING THE REACH OF CANCER RESEARCH

Basic and preclinical cancer research has entered a phase in which advances are emerging at an increasing pace through the use of new molecular technologies, such as DNA sequencing and cell-based high-throughput genetic and chemical screening, and through the development of highly informative models of many cancer types in both tissue-culture systems and animals, largely mice (23). Furthermore, research results from academic laboratories are becoming increasingly relevant to epidemiological and clinical issues (causation, prevention, and classification and treatment of tumors). Under these circumstances, international collaboration, sharing of data, and adoption of global standards for biomedical research becomes particularly important to foster work that is more reproducible and has worldwide significance.

We urge the international cancer research community to give greater attention to principles that promote the best scientific practices and productive collaborations within and across national boundaries. We stress several measures that would encourage movement in these directions and that we intend to adopt:

- Support of internet-based infrastructures and the adoption of practices that allow the open exchange of information. These include public electronic libraries that house scientific articles and books, open access journals, Web sites that contain reliable and accessible cancer-related information, and the means for transmitting “negative” as well as “positive” results and for storing and using full sets of research data.

- Development of well-characterized cell- and animal-based models of cancers that can be relied upon for preclinical studies because they have been validated by internationally agreed-upon processes.

- Construction of standardized, interoperable, and internationally accessible databases that house information about cancer genomes and other biological features related to cancers, incorporate clinical and epidemiological information in accord with ethical precepts, and operate under internationally accepted procedures.

- Opposition to patenting of genes or gene mutations, thereby removing obstacles to cancer research and to the design and reasonable pricing of improved means to classify and treat cancers based on genetic information.

CONCLUSIONS

As leaders of institutions that fund and perform cancer research in many countries, we
have prepared this joint statement to highlight opportunities to make greater and faster progress against cancer by recognizing common concerns. As efforts to improve public health and achieve sustainable development shift their emphasis from infectious and childhood diseases to chronic conditions of adults, cancer will be among the disorders that receive increasing attention. Successful campaigns to control cancers with existing methods and to improve current strategies through research will increasingly depend on a multinational consensus and collaborative work. In that spirit, we intend to take the lead in areas that are within our remits. We also call upon governments and NGOs to consider our recommendations.

REFERENCES AND NOTES

27. From “Andrea Del Sarto” by Robert Browning.

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