

NCI Center for Global Health Global Priorities

Introduction

This White Paper is intended to guide discussion at the March, 2012 workshop organized by NCI's new Center for Global Health (CGH) to assist with the planning of the Center's research mission to help control cancer—and its causes and its consequences—throughout the world. The essay outlines categories of research activities among which NCI leadership will have to make difficult decisions in hopes of spending limited public resources with maximal impact.

The NCI CGH was founded last year with the recognition that mortality rates for many cancers are higher in the lower income than in the rich areas of the world and that the prominence of cancer as a cause of morbidity and mortality will continue to rise with the aging of populations in the developing world, thanks to better control of infectious diseases and others. As the world's largest funder of cancer research, the NCI appreciates the important role that it can play in efforts to control cancer globally; but it also understands the difficulty of choosing how to invest its resources in a large array of potentially fruitful studies and research-related activities, especially in view of competition for funds in an era of stagnant budgets.

To focus discussion on the several large domains in which the CGH expects to be engaged, this brief essay is organized to address some of the research opportunities that might be pursued by the NCI under the guidance of the new Center. The workshop program is also organized in accord with these domains. The Center's work plan will ultimately likely be described within that framework, ranging from basic cancer research and training to epidemiology, tests of prevention, diagnosis, treatment, and palliation strategies, and implementation science.

Cancer control planning and implementation

There is general agreement that countries that assemble a national cancer plan are more likely to succeed in reducing the burdens of cancer through public health measures and research. Yet the assembly of such blueprints is not a simple matter, and each country requires its own plan, tailored to local conditions.

One of the first steps to national cancer control planning is determining the burden of cancer across a population, as well as the prevalence of known risk factors for cancer. Robust health surveillance systems, which can capture incidence of different types of cancers, the causes of death, and risk factors for chronic diseases, must be in place in order to design effective national cancer control plans. A variety of approaches to tele-pathology have the potential to make an accurate pathologic diagnosis, which is necessary for these systems and registries to be useful, part of routine care in low- and middle-income countries. The NCI has played a key role in providing technical expertise to other countries as they work to strengthen cancer registries and health surveillance systems.

Ongoing efforts include close collaboration with the International Agency for Research on Cancer (IARC), the US Centers for Disease Control and Prevention (CDC), and the new Global Initiative for Cancer Registry.

The US NCI has worked closely with the CDC and American Cancer Society (ACS) to help the 50 US states, Native American tribes, and Pacific Island territories develop cancer control plans. In addition, NCI, ACS, and CDC have also worked with 5 countries in Latin America to help them develop national cancer control plans. Current opportunities for consideration include building trans-divisional NCI teams to work with countries on the development of cancer control plans, to provide technical assistance on implementation of those plans, to develop epidemiological tools and surveys, and to design research studies evaluating the effectiveness of different strategies in cancer control plans.

Whether at the national, state, or district level, thoughtful cancer control planning permits policy makers to intervene effectively to reduce the burden of cancer. NCI research in cancer prevention, screening, diagnosis, treatment, and symptom management has helped build the evidence base on which to plan such interventions. In addition, NCI's support of implementation science, in studying the diffusion of innovation and effective cancer care delivery, can help develop a cadre of investigators with expertise in health care policy related to cancer.

Knowing effective, inexpensive interventions that can prevent, screen for, or treat cancer and its symptoms cannot control cancer, unless it is known how best to make these interventions available to as many people as possible and how to integrate the interventions into routine public health practice. Developments in mobile health offer the potential to foster compliance and to disseminate accurate information on cancer more widely than ever before.

Common risk factors for non-communicable diseases

Low- and middle-income countries face a growing burden of non-communicable diseases (NCDs), such as cardiovascular disease, chronic lung disease, diabetes mellitus, and cancer. There has been growing awareness that several of these conditions have common risk factors, most notably tobacco use—the most important risk factor in oncology—and obesity. Research related to tobacco control and obesity, therefore, has the potential to help us develop effective interventions to prevent and control multiple NCDs. The Global Alliance for Chronic Disease has now demonstrated a model for coordinated and parallel national research funding initiatives. Their first initiative targeted one key risk factor for heart disease, namely hypertension. The Centers of Excellence set up by the National Heart, Lung, and Blood Institute to promote global health research in cardiovascular disease also provide potential settings for collaborative work.

Cancers associated with chronic infection

In the developing world more than 20% of cancers are associated with chronic infection. Carcinogenic infectious agents include the hepatitis viruses, human papillomavirus (HPV),

helicobacter pylori, Epstein Barr Virus (EBV), and trematodes, such as those causing bladder and bile duct cancers. In addition, chronic immunosuppression associated with HIV infection increases the risk of certain cancers.

The progress made to date for some of these cancers underscores the importance of a comprehensive research strategy, including classical and molecular epidemiology, translational research, vaccine development, improvements in screening and treatment, and implementation science. Reducing the burden of liver cancer associated with hepatitis B, for example, required the development of an effective vaccine, the availability of that vaccine at a price appropriate for low-resource settings, and widespread implementation of infant vaccination against hepatitis B as part of routine public health practice. The identification of aflatoxin as a co-factor for the development of liver cancer has documented the need for better storage of grains and nuts to complement vaccine use. There is also an urgent need for developing an effective vaccine against Hepatitis C virus, which causes around 200,000 cases of liver cancer each year, as well as serious non-malignant liver disease.

Chronic HPV infection causes 99% of cervical cancers, as well as 50% of anal, vulvar, and penile cancers, and about 25% of oropharyngeal cancers. Cervical cancer is the third most common cancer in women, with an estimated 530,000 new cases and 275,000 deaths in 2008. More than 85% of the global burden of cervical cancer occurs in developing countries, where it accounts for 13% of all female cancers. Widespread uptake of those vaccines has been hindered by price, issues of social acceptability, and the challenges of delivering vaccines to a population (adolescent girls) for whom, until recently, no vaccines were recommended. Current opportunities for further research include the development of prophylactic vaccines covering more oncogenic types, therapeutic HPV vaccines (and combined prophylactic/therapeutic vaccine strategies), development and validation of low-cost screening strategies for cervical neoplasia, as well as implementation science questions regarding roll-out of screening and improved access to care for both preinvasive and invasive cervical neoplasia.

EBV is a potential target for vaccine development; in addition, strategies have been proposed and tested on a small scale to reduce chronic infection with *Helicobacter pylori* infection. These and other infection control measures are potential “low hanging fruit” in the realm of cancer prevention.

Ecological-niche cancers

Cancer research in resource-limited settings is often difficult, but when certain cancers are found to occur at especially high incidence in certain geographical regions, their analysis may accelerate progress towards understanding and controlling cancers that occur at lower rates in many other places. Very high rates of gallbladder cancer, for example, occur in Chile, particularly among people of Native American descent. This situation offers an opportunity to work with colleagues in Chile to elucidate the molecular epidemiology of gallbladder cancer, as well as to carry out screening, prevention, and treatment trials. Similar opportunities exist in Africa and Latin America to elucidate the association between

Burkitt lymphoma and malaria, as well as to improve treatment for patients with Burkitt lymphoma. Other cancers for consideration include nasopharyngeal, esophageal, and stomach cancers, all of which are common in East Asia.

Building the infrastructure for global cancer research and training

As we have learned in the US, inadequate resources for research hamper progress in disease control, and this may represent an even greater limitation in other countries unless research capacity is developed.

First on the list for capacity building is human capital, namely the doctors, nurses, laboratory investigators, biostatisticians, data managers, and other professionals who understand research and how it should be conducted. NIH has undertaken considerable efforts in training such professionals, mainly through the Fogarty International Center, but the categorical institutes, such as the NCI, could identify disease-specific niches, such as cancer pathology, in which investments in training could be critical for supporting research efforts. In addition, further consideration might be given to programs that train American personnel who are interested in careers that include the performance of research in less affluent settings.

Other key elements that may require support are components of institutional research infrastructure, including the capacity for ethical review and oversight of clinical studies, effective grants administration, bio-banking, and commitment to appropriate staffing levels to permit research as well as clinical care. Multi-institutional, multi-national networks that can collaborate on prospective clinical studies include epidemiologic, prevention, screening, and treatment trials, could be helpful in this regard. Existing ties between research institutions in the US, such as NCI-designated cancer centers, and those in the developing world may be useful points of departure for these efforts.

International science at the NCI

The NCI has traditionally supported a wide array of international research activities, some of which are conducted in developing countries or directed at cancers and cancer risk factors that are prevalent in such countries. These projects are conducted by a variety of NCI divisions, centers, and offices, and by both intra- and extramural scientists. (A full inventory of current projects has been developed and can be made available to workshop participants upon request.) The Center for Global Health has been created with the expectation that these many elements of the Institute will continue to be engaged in research related to the mission of the Center, and that the Center's role will primarily be one that involves leadership, encouragement, and coordination of the NCI's efforts to control cancer more effectively in the developing world through the work of its various components.

The Center also has its own resources to sustain its personnel, administrative costs, and the support of a few existing programs that are directly managed by the Center. In an era of flat budgets, the Center's budget can grow only at the expense of other components of the

NCI; part of the goal of the March workshop is to identify critical projects that might fit best or only within the Center's research portfolio.

Partnerships

Although new funds are limited, it is encouraging that many potential partners are already active in the pursuit of cancer control in the developing world. Wherever possible, the Center will attempt to potentiate the NCI's research program in global health through partnerships with WHO, other US government entities, non-governmental organizations, other funders of global health research, professional societies, the pharmaceutical, biotechnology, and medical equipment industries, and academic programs committed to global health.

For example, partners in efforts to develop national health plans would likely include the CDC and USAID, the American Cancer Society, WHO and its regional offices, the International Agency for Research on Cancer, the International Atomic Energy Agency (IAEA) and its Program of Action for Cancer Treatment (PACT), and the International Union for Cancer Control. Potential national partners include Mexico, with whom discussions about cancer control planning are already underway, those countries selected for the first wave of IAEA/PACT partnership (Albania, Nicaragua, Sri Lanka, Tanzania, Vietnam, Yemen), as well as those countries in Latin America with whom NCI, ACS, and CDC worked in the past. The Center envisions other collaborative activities in most of the research domains discussed in this prospectus.

Conclusions

This is an opportune time scientifically to develop a strategy for reducing the burden of cancer in the developing world. The broad categories of global health research on cancer described here are intended to frame the discussion at the forthcoming inaugural workshop and to assist the drafting of recommendations for future research at the NCI's new Center for Global Health. Suggestions from all workshop participants will be welcomed as a plan for the Center is developed.

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