Expansion of cancer care and control in countries of low and middle income: a call to action


Substantial inequalities exist in cancer survival rates across countries. In addition to prevention of new cancers by reduction of risk factors, strategies are needed to close the gap between developed and developing countries in cancer survival and the effects of the disease on human suffering. We challenge the public health community’s assumption that cancers will remain untreated in poor countries, and note the analogy to similarly unfounded arguments from more than a decade ago against provision of HIV treatment. In resource-constrained countries without specialised services, experience has shown that much can be done to prevent and treat cancer by deployment of primary and secondary caregivers, use of off-patent drugs, and application of regional and local mechanisms for financing and procurement. Furthermore, several middle-income countries have included cancer treatment in national health insurance coverage with a focus on people living in poverty. These strategies can reduce costs, increase access to health services, and strengthen health systems to meet the challenge of cancer and other diseases. In 2009, we formed the Global Task Force on Expanded Access to Cancer Care and Control in Developing Countries, which is composed of leaders from the global health and cancer care communities, and is dedicated to proposal, implementation, and evaluation of strategies to advance this agenda.

Introduction

Once thought to be a problem almost exclusive to the developed world, cancer is now a leading cause of death and disability, and thus a health priority, in poor countries. Low-income and middle-income countries now bear a majority share of the burden of cancer, but their health systems are particularly ill prepared to meet this challenge. The rising proportion of cases in these countries is caused by population growth and ageing, combined with reduced mortality from infectious disease. In 1970, 15% of newly reported cancers were in developing countries, compared with 56% in 2008. By 2030, the proportion is expected to be 70%.

Low survival rates in poor countries and improved survival in developed countries contribute to the disparity in the burden of cancer deaths. Overall, case fatality from cancer (calculated as an approximation from the ratio of incidence to mortality in a specific year) is estimated to be 75% in countries of low income, 72% in countries of low-middle income, 64% in countries of high-middle income, and 46% in countries of high income. Survival is closely and positively related to country income for certain cancers—such as cervical, breast, and testicular cancer, and acute lymphoblastic leukaemia in children—and hence the scope for these diseases to act on survival in high income countries is particularly large (figure).

Wealthy countries have made major strides in the fight against certain cancers, particularly in the past three decades. In the USA, both cancer incidence and mortality have declined since peaks in the early 1990s because of heightened awareness, prevention, earlier detection, and the availability of new and more effective treatment regimes. Although little progress has been made in the treatment of some cancers, such as pancreatic and lung cancer, low-cost and effective treatment options are available for several malignancies, including cervical, breast, and testicular cancer, and childhood leukaemia. Unfortunately, these interventions for early detection and treatment remain inaccessible for many people in developing countries.

For many cancers, future changes in incidence, survival, and mortality rates will greatly depend on whether key risk factors can be controlled in low-income and middle-income countries. In these countries, major risk factors such as smoking continue to rise, awareness of the importance of screening and early detection is low, and stigma associated with cancer and the financial barriers of poverty prevent many people from seeking preventive services or care at early stages. Without substantially increased prevention, through strong antitobacco campaigns and vaccination against human papillomavirus (HPV) and hepatitis B virus, and a focus on early detection, growth of the cancer burden in these countries could make treatment virtually unaffordable in the long term.

Thus, the world faces a huge and largely unperceived cost of inaction around cancer in developing regions, which merits an immediate and large-scale global response. Yet, only a small proportion of global resources for cancer are spent in countries of low and middle income: several studies have reported an estimate of 5% (see webappendix for further details). By contrast, these countries together account for almost
80% of the disability-adjusted life-years lost worldwide to cancer. Cancer is an underfunded health problem and an important cause of premature death in resource-poor settings, resulting in this staggering "5/80 cancer disequilibrium".12

International attention and financial resources to resource-poor settings have increased especially in the past 10 years, resulting in an impressive expansion in the availability of treatment for patients with certain infectious diseases, most notably AIDS. However, cancer remains sorely neglected. Public, private, and multilateral donors spend relatively little on efforts to expand cancer prevention, diagnosis, and treatment in these countries compared with other diseases. Furthermore, cancer is notably absent from the global health agenda, including key global health targets such as the Millennium Development Goals (MDGs).

A global call to action for cancer in low-income and middle-income countries is beginning to emerge, led by international agencies, academic institutions, and non-governmental organisations and associations.14–17 However, concerted action is needed from the global health community, together with the participation of local governments and extensive primary health-care networks to achieve an effective response. The agenda for action should catalyse expansion of cancer care, control, and prevention with strategies that are appropriate to the health systems of low-income and middle-income countries, accessible to patients with low incomes, and integrated into national health insurance systems. This agenda must include increasing access to drugs for treatment and palliation, expansion of coverage for preventive and diagnostic services, including vaccines, and development and implementation of innovative health-care delivery options to support rapid scale-up.

The Global Task Force on Expanded Access to Cancer Care and Control in Developing Countries

To push forward this agenda, the Dana-Farber Cancer Institute, Harvard Global Equity Initiative, Harvard Medical School, and Harvard School of Public Health convened the Global Task Force on Expanded Access to Cancer Care and Control in Developing Countries (GTF.CCC). Announced in November, 2009, the mandate of GTF.CCC is to design and implement global and regional initiatives for the financing and procurement, and strengthening of coverage for preventive and diagnostic services, including vaccines, and development and implementation of innovative health-care delivery options to support rapid scale-up.

GTF.CCC’s strategy is to collaborate with and support existing initiatives. GTF.CCC will base much of its work on the lessons learned from previous initiatives, including those designed to address AIDS, tuberculosis (including multidrug-resistant [MDR] tuberculosis), maternal and child health, maternal mortality, sexual and reproductive health, and mental health. Furthermore, the strategy calls for identification and exploitation of opportunities for synergy between these initiatives and cancer care and control, particularly in the context of health-system strengthening, and the wide network of services devoted to the health of women and children.

GTF.CCC also seeks to build on, work with, and support international calls, initiatives, and recommendations, including the UN 2011 General Assembly summit on non-communicable diseases,18 the World Cancer Declaration of the International Union Against Cancer;19 the 2005 World Health Assembly resolution on cancer prevention and control,20 the 2007 report on cancer in low-income and middle-income countries produced by the Institute of Medicine of the National Academies,21 the findings of the World Cancer Report 2008 by the International Agency on Cancer Control and WHO, and other work by academic institutions and grassroots associations and alliances in developed and developing countries.

Through collaborations with these initiatives and institutions, GTF.CCC will support existing efforts, particularly those on tobacco control, such as the WHO Framework Convention on Tobacco Control. GTF.CCC will also support continuing global and national efforts to improve diet and nutrition, reduce environmental risks, promote healthy lifestyles, increase screening and vaccination against cancer-causing infections (HPV and hepatitis B virus),22 and educate the public to combat existing misconceptions and stigma associated with cancer.

To contribute effectively to the global movement, GTF.CCC will focus on health-system strengthening, implementation of regional and global mechanisms for financing and procurement, and strengthening of primary and secondary care to allow innovative delivery

Figure: Ratio of mortality to incidence in a specific year by cancer type and country income

Case fatality (calculated by approximation from the ratio of mortality to incidence in a specific year) is much lower in high-income countries than in low-income countries for cancers that are treatable, such as childhood leukaemia (0·26 vs 0·78) and testicular cancer (0·05 vs 0·47), treatable if detected early, such as breast cancer (0·24 vs 0·48), or preventable, such as cervical cancer (0·37 vs 0·63). Estimates are based on International Agency for Research on Cancer GLOBOCAN data for 2002 and 2008 (http://globocan.iarc.fr).23
Panel 1: Reasons for rapid scale-up of cancer treatment

Address the immense and immediate need for treatment to save and extend the lives of millions of people with cancer

The humanitarian rationale is clear: many of the 4 million deaths from cancer every year in low-income and middle-income countries can be averted through early detection and treatment. Millions of people with advanced or untreatable cancer, but without access to true palliation, will die with great and preventable suffering, impoverished from attempting to meet even the most basic treatment costs.

Strengthen health systems, particularly primary health care

A diagonal approach—in which resources are distributed in ways that strengthen entire health systems—can be applied to cancer. Strategies include: awareness building and services for prevention; management of infections and adverse drug reactions; community-based care and support; education to combat stigma; provision of pathological testing for accurate and timely diagnoses; and surgical support where indicated. This approach should help to identify synergies and link cancer care and control with many services associated with a broad range of medical disorders, and reinforce human resources and physical infrastructure in health systems and avoid creation of a parallel structure for service delivery.

Unacceptable inequity in the distribution of resources for cancer care and control

The inequity in the distribution of resources for cancer is evident: almost 80% of the disability-adjusted life-years lost worldwide to cancer are in countries of low and middle income, but these countries have only a very small share of global resources for cancer—an estimated 5% or less (see webappendix for details). This inequity is even worse in certain parts of the developing world. For example, the African region accounts for only 0.2% of global cancer medical costs compared with just over 1% of global spending on health, 6-4% of new cancer cases, and 15% of the global population.

Some contend that restricted international resources for global health should not be spent on expensive treatments for malignancies or costly vaccines. Furthermore, the prevailing belief is that safe and effective cancer treatment is rendered impossible in many poor countries by the shortage or absence of oncology specialists and facilities, treatment guidelines, and regulatory mechanisms.

Policy barriers are equally limiting and often among the most difficult to surmount. Restrictions on importation of drugs, especially for palliation, non-existent cancer treatment budgets, and failure to recognise cancer as a health priority will have to be overcome to effectively address prevention, detection, and treatment. The evidence presented in panel 2 challenges the assumption that cancer control and care is not feasible or effective in countries of low and middle income, and supports global and national policy change. In several middle-income countries, pioneering national programmes have been implemented throughout health systems, including health insurance coverage for people living in poverty and application of protocols to guide delivery of cancer treatment.

Lowering of costs and generation of effective financing and delivery mechanisms

Increased access to primary care combined with well designed and affordable disease-control programmes can greatly improve cancer care and control in low-income and middle-income countries. Primary health—as the first locus of care—must increasingly embrace a chronic care model, especially because diseases such as AIDS become chronic and require long-term management.

Opportunities exist for cancers that are amenable to prevention, and education and strengthening of networks in primary and community care can be important for early at the local level. Thus, in addition to strong support for efforts to prevent future cancers by reduction of risk factors, especially tobacco, GTF.CCC calls for immediate action in the face of existing needs. Specifically, GTF.CCC focuses on development and implementation of pathways and public policies to expand coverage of existing vaccines, early detection and treatment of cancers for which cure or major improvements in life expectancy can be achieved, and palliation to reduce suffering and pain. The work of GTF.CCC is predicated on the conviction that barriers to access can be removed, and that the reasons for rapid scale-up of cancer treatment merit an invigorated global response (panel 1).

Scepticism about scale-up of access to an integrated system of early detection, diagnosis, treatment, and palliation in poor countries is concentrated on the scarcity of funds and perceived obstacles to treatment.
detection of other cancers, which then offers substantial opportunities for cure when treatment options are made available (panel 3). Although surgical needs will continue to challenge treatment of cancers, important examples of initiatives show that low-cost techniques that are generally applicable can improve surgical services and help to strengthen health systems.30

Many of the cancers that pose the greatest burden in developing countries are amenable to treatment with drugs of proven effectiveness that are off-patent and can be manufactured generically at affordable prices. These drugs should be a focus of cancer treatment programmes, rather than expensive on-patent drugs. In the case of breast cancer for example, the USA achieved important improvements in outcomes before 1975 with surgery and early detection through awareness building, before the widespread use of mammography, adjuvant chemotherapy, and hormonal therapy.31,32 Additionally, in the past decade, tamoxifen—a low-cost drug for hormone-receptor-positive breast cancer—has substantially improved survival (Shulman LN, Willett WC, Knaul FM, unpublished data). Some forms of cancer are curable with systemic treatment even when diagnosed at a late stage, although surgery might sometimes also be needed (panel 3). For example, Hesseling and colleagues33 report that in Malawi, Cameroon, and Ghana, the total cost of a generic first-line chemotherapy drug with a 50% cure rate for Burkitt’s lymphoma is less than US$50 per patient.

For several cancers, life can be substantially extended with fairly low-cost systemic drug treatment (panel 3). In settings, cases, and cancers (pancreatic, lung, and advanced cancer) where treatment is not an option, palliation to relieve pain and reduce human suffering is a human right. Pain control is typically low cost and easily delivered, and the barriers to delivery are mostly caused by substance controls, which block health-care providers from supporting urgent needs in oncology and many other specialties.34,35

Delivery of education, diagnostics, surgery, drugs, and services to poor people is challenging, but innovation in developing regions has improved the design, implementation, and financing of effective delivery models. Many of these initiatives, adapted to the constraints of resource-poor environments, seek to upgrade the role of the community, non-specialised health professionals (eg, health promoters), nurses and primary care physicians, and clinics and non-specialty hospitals. Although special training is required, this approach can be effective for provision of high-quality care in many settings and should be considered as an option even for developed countries.36 Partners In Health—an institution that addresses seemingly untreatable health problems in especially challenging circumstances—is an example of innovation in and implementation of such models.37 Another is Mexico’s conditional cash transfer programme, Oportunidades, which covers more than 95% of the poorest families, and provides cash transfer incentives to promote health education and use of health-care resources.38,39

The cost of drugs is often a specific and substantial barrier to prevention and treatment of cancer in poor countries, and opportunities to reduce price and expand absorptive capacity should be identified and implemented. Many chemotherapeutic interventions remain cost-prohibitive for national ministries of health in poor countries. One of the most promising recent innovations for prevention, vaccination against HPV, continues to be too costly for widespread use in these countries.40 Global and regional negotiation strategies for pricing and procurement can provide opportunities to reduce prices. Nevertheless, the costs of care and control are prohibitive for the vast majority of families in developing countries. Prevention and early detection of cancer should be incorporated into basic health-care packages and financed as entitlements. Cancer care must be free of charge to prevent further impoverishment.

Approaches to overcome challenges

Many challenges to widespread and comprehensive cancer control resemble those cited a decade ago, during debates about the feasibility of treatment for HIV infection and tuberculosis, especially MDR disease.41 Critics asserted that complex care could not be scaled up
within weak health systems, particularly in sub-Saharan Africa. They thought that antiretroviral treatment and, especially, second-line tuberculosis therapy were not sufficiently cost effective to merit international funding, and were too impractical to effectively administer in countries of low and middle income. Some argued that prevention, palliation, and gradual implementation of the least expensive treatment interventions were the only possible steps.

However, for HIV infection, MDR tuberculosis, and tuberculosis in general, effective therapy has quickly become a successful and integral component of control. Complex and (at least initially) expensive treatment became possible when accompanied by innovative treatment models and new investments. Coordination of financing and procurement strategies helped to lower prices and streamline supply chains for therapeutics and diagnostics. Through concerted global action and new sources of funding, the number of people receiving antiretroviral treatment for HIV infection in developing countries has increased by more than ten times since 2003, and is now close to 4 million. This achievement is impressive since the poorest countries have very few physicians and virtually no infectious disease specialists. As part of this revolution in treatment, AIDS is fast becoming a chronic illness requiring survivorship care.

One of the strategies that made the scale-up of HIV treatment successful was the inclusion of actors both within and outside of international institutions such as WHO, allowing many players to come to the table with innovative ideas. The early work of the Clinton Health Access Initiative substantially increased access to generic HIV drugs. The Global Fund to Fight AIDS, Tuberculosis and Malaria relied on normative and technical support from organisations like WHO, but channelled its funds directly to governments and non-governmental organisations. The US President’s Emergency Plan for AIDS Relief, announced in 2003, greatly increased the funding available worldwide to combat HIV infection. UNITAID, launched in 2006, established a novel financing mechanism for the purchase of commodities to treat HIV infection, malaria, and tuberculosis, and is now working to establish a patent pool for HIV drugs. Thus, a lesson for scale-up of cancer care is not to centralise or generate innovation-stifling central nodes of control.

Advocates should not assume that global health resources for cancer care and control are limited to present levels. Efforts to control HIV infection, tuberculosis, and malaria have shown that substantial, life-saving investments can feasibly be raised from public and private sources for research in and implementation of global health interventions, saving millions of lives. The world has witnessed an unprecedented success in mobilisation of resources to increase awareness and access to vaccines and drugs in poor countries. UNITAID, the Pan American Health Organization Revolving Fund for Vaccine Procurement, the Global Alliance for Vaccines and Immunisation, the Global Fund to Fight AIDS, Tuberculosis and Malaria, and non-profit organisations, such as the Bill & Melinda Gates Foundation and the Clinton Health Access Initiative, have pioneered financing and procurement schemes to guarantee access to much needed vaccines, drugs, and laboratory tests.

The experience with HIV provides an important lesson: neither care nor prevention can be neglected. In fact, some evidence suggests that global efforts to prevent HIV infections have waned, increasing the risk of a major increase in the need for antiretrovirals that cannot be met. In the case of both cancer and AIDS, neglect of care leads to unnecessary death and suffering, and neglect of prevention leads to unaffordable treatment.

Successful treatment of cancer in extremely resource-poor settings: Malawi, Rwanda, and Haiti

A frequently cited barrier to cancer treatment in resource-poor settings is the absence of specialists and specialty centres. An international partnership of Partners In Health and the Dana-Farber Cancer Institute, Harvard Medical School, and Brigham and Women’s Hospital, working in rural Malawi, Rwanda, and Haiti, is proving that this barrier can be surmounted even in the poorest settings. In partnership with national ministries of health, Partners In Health helps to operate health centres and hospitals in rural districts, serving catchment areas of 1 200 000 in Haiti, 800 000 in Rwanda, and 175 000 in Malawi. Because no oncologists are available, care is provided by local physicians and nurse teams. With support and training from the Harvard-based facilities, these centres and hospitals have begun to deliver chemotherapy to patients with a variety of treatable malignancies including breast, cervical, rectal, and squamous head and neck cancers, Hodgkin’s and non-Hodgkin lymphoma, and Kaposi’s sarcoma.

Despite important success with the programme—patients have received treatments safely and with good outcomes—the reach of these pilot initiatives is dwarfed by the burden of disease. Treatment needs to be delivered free of charge, but scale-up is severely constrained by lack of funding, especially for the cost of drugs. Furthermore, late detection lowers the effectiveness of most treatments. Still, these pilot programmes in Malawi, Rwanda, and Haiti show that the absence of oncological specialists need not delay the implementation of mutually reinforcing efforts to prevent, screen, treat, and palliate cancer. Much can be accomplished in the short term, even in extremely resource-poor settings, by use of local clinicians and community health workers, supported by remote
Inclusion of cancer treatment in national health insurance programmes: Mexico and Colombia

A key aspect of scale-up of cancer treatment that will help to strengthen health systems is development of explicit entitlements to health care and financial protection. Cancer is a catastrophic illness in both financial and personal terms. Mexico and Colombia are examples of a handful of countries in which cancer care and control is an entitlement and is incorporated into health insurance programmes targeted to poor people.

In Mexico, recognition of the growing burden of cancer and the opportunity for treatment has been transformed into action as part of continuing efforts to strengthen the health system. Through Popular Health Insurance, Seguro Popular de Salud—which was introduced in 2004 and now covers almost 37 million individuals, with a focus on low-income populations—the range of entitlements to cancer treatment has been steadily expanded. Comprehensive treatment regimes for cervical and breast cancer, and a range of childhood and adolescent malignancies are covered for all Mexicans. Although Mexico is a country of high-middle income, almost 20% of the population lives below the national food poverty line, and these are the families targeted by Popular Health Insurance. Furthermore, in view of the legal basis of the reform, the population and package of services continue to be covered despite the present economic crisis. The delivery of cancer services, though, is suboptimum and creative initiatives to reach more patients and detect disease earlier are needed.

In Colombia, universal social health insurance has been in place since 1993, with a subsidised scheme providing specific entitlements for the poor. The mandatory health plan has included treatment for cancers since 1994. The package is being updated to account for developments in medical technology, and to ensure equal access for subsidised populations. In the meantime, patients have been able to sue for the right to treatment that is not included in the package. Yet, and as in Mexico, delivery is suboptimum and financial sustainability is a challenge.

These examples show that entitlements for cancer treatment can be increased in middle-income countries by use of local funding. However, in most low-income and middle-income countries, national insurance is far from universal or entitlements are much more restricted than in Mexico or Colombia. Often, only the small proportion of people who can afford the most expensive, local private hospitals are able to access cancer diagnostics and treatments. These examples also show that insurance for treatment should be combined with additional investment in early detection and prevention. Delivery options need to be improved to guarantee effective access to both prevention and treatment.

Expansion of access to treatment through a national centre of excellence: Jordan

Jordan provides a replicable example of a country of low-middle income that, despite few resources, has been able to establish a specialised centre of excellence. The King Hussein Cancer Center—the only cancer centre in a developing region that has been accredited by the Joint Commission—is legally governed by the King Hussein Cancer Foundation, and operates the Foundation’s medical arm. Founded in 1997, the Foundation is an independent, non-governmental, and non-profit organisation. The Center offers high-quality cancer treatment, professional training, and awareness building, and focuses on reaching internationally recognised standards of care. Both the Foundation and Center provide care to patients who have no means to cover the costs of their treatment, while simultaneously providing services under contract with the government and private sectors, and operating as a regional hub. In the case of breast cancer, the Foundation and Center treat about 60% of new cases in Jordan, and also lead the Jordan Breast Cancer Program focusing on awareness building, early detection, and establishment of national guidelines for screening and diagnosis.

National shortages of human resources and infrastructure are evident in the face of the projected increase in the cancer burden and the increasing demand for services. In response, the King Hussein Cancer Center is undertaking training and upgrading of other centres in Jordan and surrounding regions, but financing mechanisms for these projects will need to be identified. In addition to service provision, key national and regional functions of the Center are to: provide proof of concept to drive policy around the provision of high-quality care to all population groups; serve as a model and catalyst to scale up delivery; promote dialogue between sectors and steer the course for policy change; and support the expansion of key instruments such as the national cancer registry and guidelines for increased access in a resource-poor setting.

Conclusions

The time has come to challenge and disprove the widespread assumption that cancer will remain untreated in poor countries. We, as participants in GTF.CCC, believe that compelling evidence of the feasibility and effectiveness of comprehensive cancer control merits a renewed global effort to expand cancer prevention, diagnosis, treatment, and palliation in countries of low and middle income, including provision of affordable and reliable drug supplies and vaccines. Achievement of this aim will require additional resources that can be derived from innovative global, regional, and national financing and procurement mechanisms.

We propose that cancer care and control become rapidly and broadly available as quickly as possible, with the focus on cancers that can be prevented or cured, or, for
cases in which neither is possible, palliated. More immediately, we propose three changes. First, simultaneous implementation of large-scale demonstration programmes in the next few years to define and build new infrastructure, train health professionals and paraprofessionals, and harness the opportunities of technology and especially telecommunications to overcome many on-site limitations in resources. Carefully designed evaluation and monitoring will enable identification of the most effective measures to alleviate the burden of cancer and expand the volume of health services in developing countries, and will provide lessons for all health systems, including those in the developed world. Second, design and implementation of regional and global pricing and procurement mechanisms to offer individual countries the opportunity to participate in collective, multicountry negotiation to secure reduced prices for essential services, drugs, and vaccines. Third, identification and implementation of innovative financing mechanisms, which should decisively expand the financial resources available for prevention, treatment, and palliation of cancer in the developing world.

A recalibrated global response could transform cancer care and control, but will need coordinated efforts and synergy among international organisations, such as WHO, the World Bank and regional development banks, bilateral donors, national research funding bodies, non-governmental agencies, governments, and local, regional, and global civil society organisations. New funding from private, bilateral, and multilateral donors should be used to strengthen entire health systems. Both advocates and experts should use evidence to convert zero-sum debates about which life-saving interventions to deny poor patients into alternatives to mobilise resources, identify synergies between disease-specific interventions, and recognise that saving a patient from one disease does not eliminate the risk that they can develop another.

We can no longer differentiate between diseases of the poor and the rich. Furthermore, restriction of health systems in poor countries to treatment of infectious diseases is a response to a false dichotomy. Even in the most severe of crises, exemplified by Haiti after the earthquake in January, 2010, suffering from chronic illness, especially cancer, intensifies alongside most other health needs. Poor people endure a double burden of communicable and non-communicable chronic illness, requiring a response that is well integrated into the health systems of low-income and middle-income countries. Extension of cancer prevention, diagnosis, and treatment to millions of people with or at risk of cancer is an urgent health and ethical priority. A bold research, financing, and implementation agenda is essential for the international community to fill the gaping voids in cancer care and control worldwide.

Contributors
All authors contributed to the framework and theoretical design. PF, JF, FMK, and LNS contributed to analysis. PF, JF, FMK, and LNS wrote the text with comments and contributions from GA, RA, DB, LC, RF, MG, JG, AL, AM, DM, PP, KSR, JDS, MS, and JRS. FMK coordinated the submission.

Conflicts of interest
PF, JF, LNS, GA, LA, DW, LC, RF, AL, CN, AM, DM, PP, KSR, JDS, MS, and JRS declare that they have no conflicts of interest. FMK is associated with a non-profit programme in Mexico (Gomatez o Pecho) to promote early detection of breast cancer; receives honoraria from the Mexican Health Foundation, which has submitted research grant applications to GlaxoSmithKline and Roche; and has been nominated to become a board member (unpaid) for the International Union Against Cancer. MG serves as a board member (unpaid) for the International Union Against Cancer. JG’s institution has received grants from Genentech, Sanofi-Aventis, Roche, Amgen, and Novartis. SG is a board member of non-profit organisation LIVESTRONG, a staff member of Emory Clinic Department of Neurosurgery, chief medical correspondent for CNN, and a medical contributor to CBS and Time Magazine.

Acknowledgments
We thank Harold Varmus for his comments and recommendations; Amanda Berger, Hector Arreola-Ornelas, Oscar Méndez Carniado, and Javier Dorantes Aguilar for their excellent research assistance; Mounica Vallurupalli for careful review of the text; Cassia van der Hoof Holstein for insightful comments and review of the text; Ramiro Guererro, Afsan Bhadelia, Rebecca Firestone, and Salmaan Keshavjee for comments on an initial draft; Luke Messac and Amy Sievers for their excellent work in preparation of the first draft of the background paper for this report; Patricia Hernández for input into the analysis of global spending; and the four anonymous reviewers whose comments enriched the paper. The research in this paper had no outside funding. Support in-kind came from each of the authors, and especially Harvard Global Equity Initiative, the Department of Global Health and Social Medicine of Harvard Medical School, the Dana-Farber Cancer Institute, the Division of Global Health Equity of Brigham and Women’s Hospital, and Harvard School of Public Health.

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