Costs, affordability, and feasibility of an essential package of cancer control interventions in low-income and middle-income countries: key messages from *Disease Control Priorities*, 3rd edition

*Hellen Gelband, Rengaswamy Sankaranarayanan, Cindy L Gauvreau, Susan Horton, Benjamin O Anderson, Freddie Bray, James Cleary, Anna J Dare, Lynette Denny, Mary K Gospodarowicz, Sumit Gupta, Scott C Howard, David A Jaffray, Felicia Knaul, Carol Levin, Linda Rabeneck, Preetha Rajaraman, Terrence Sullivan, Edward L Trimble, Prabhat Jha, for the Disease Control Priorities-3 Cancer Author Group**

Investments in cancer control—prevention, detection, diagnosis, surgery, other treatment, and palliative care—are increasingly needed in low-income and particularly in middle-income countries, where most of the world's cancer deaths occur without treatment or palliation. To help countries expand locally appropriate services, *Cancer* (the third volume of nine in *Disease Control Priorities*, 3rd edition) developed an essential package of potentially cost-effective measures for countries to consider and adapt. Interventions included in the package are: prevention of tobacco-related cancer and virus-related liver and cervical cancers; diagnosis and treatment of early breast cancer, cervical cancer, and selected childhood cancers; and widespread availability of palliative care, including opioids. These interventions would cost an additional US$20 billion per year worldwide, constituting 3% of total public spending on health in low-income and middle-income countries. With implementation of an appropriately tailored package, most countries could substantially reduce suffering and premature death from cancer before 2030, with even greater improvements in later decades.

Published **Online**
November 11, 2015
http://dx.doi.org/10.1016/S0140-6736(15)00755-2

*Members listed at end of Review

Center for Disease Dynamics, Economics & Policy, Washington, DC, USA (H Gelband MHS); **International Agency for Research on Cancer, Lyon, France**

Introduction

The UN's Sustainable Development Goals (SDGs) for 2030 (announced on Sept 25, 2015) call for reducing premature mortality from non-communicable diseases (NCDs) by a third through prevention and treatment.[1] Accelerated reductions in cancer mortality are essential to meeting that goal.[2] This Review summarises the analyses and recommendations of the *Disease Control Priorities*, 3rd edition (DCP-3) volume about cancer (third of nine in total),[3] which will focus on a set of interventions that could be effective, cost-effective, affordable, and feasible in many low-income and middle-income countries (LMICs), and could help countries meet the NCD goals.

The intent is to help governments of LMICs commit to locally appropriate, national cancer control strategies that include a range of cost-effective interventions (customised to local epidemiological patterns and available funding), and to convey this commitment to their populations. In regions where affordable treatment can be provided, conveying this information to the public can motivate people to seek treatment while their cancers are at earlier, more curable stages. The full costs of cancer treatment are unaffordable as out-of-pocket payments for most patients in LMICs, so cancer services deemed appropriate in national packages should be included in any plans to expand universal health coverage.[4]

The DCP-3 essential package includes some prevention strategies, but many cancers cannot be prevented to any great extent by available methods. However, some can be treated cost-effectively with curative intent (eg, early breast cancer, other resectable cancers, and various childhood cancers), and the availability of effective treatment bolsters public

Key messages

- Cancer is a major cause of death in low-income and particularly in middle-income countries (LMICs), and will continue to increase as a percentage of deaths in LMICs, being driven by population ageing and substantial decreases in mortality from other causes.
- In most populations, helping current tobacco users to quit and preventing young people from starting smoking are the most urgent priorities to prevent cancer (and other non-communicable diseases [NCDs]), along with vaccination against the cancer-causing hepatitis B virus and human papillomavirus (HPV). Increased tobacco taxation will help to reduce cancer incidence and generate substantial extra revenues for governments.
- Excluding tobacco-related and virus-related cancers, most other common cancers are not preventable, but many cases can be effectively treated—eg, breast cancer and colorectal cancer are common and curable if treated early. Additionally, in the next few decades, until the protective effects of HPV vaccination are widespread, cervical precancerous changes and early cancers will remain common and are treatable. Interventions supported by the analyses in *Disease Control Priorities,* 3rd edition (DCP-3) go further than WHO's best buys (most beneficial interventions at the lowest cost), which are limited to interventions deliverable without hospital facilities.
- DCP-3's essential package of cost-effective and feasible interventions would, if fully implemented, cost an additional US$20 billion per year, or 3% of total public spending on health in LMICs (2·6% in upper-middle-income, 5% in lower-middle-income, but 13% in low-income countries). In terms of annual expenditure per capita, this amounts to $5·7 in upper-middle-income countries, $1·7 in lower-middle-income countries, and $1·7 in low-income countries. Such increases are potentially feasible in all but the low-income countries, which would need external support.
- Some cancer services should be considered for inclusion in universal health coverage, focusing on ensuring their availability and affordability.
- Global initiatives for cancer control in LMICs are needed to reduce the costs of key inputs for the essential package, including large-scale commodity purchases; to expand technical assistance and dissemination of skills; and to promote cancer research.

	Annual deaths at ages 0–69 years					5-year survival† (%)	
	Low-income countries* (n=0·8)‡	Lower-middle-income countries* (n=2·4)‡	Upper-middle-income countries* (n=2·3)‡	High-income countries* (n=1·2)‡	World (total; n=6·7)‡	LMICs	High-income countries
Cancer site							
Lung, mouth, or oesophagus	70 000	260 000	560 000	300 000	1 200 000	10%	20%
Liver	30 000	90 000	270 000	60 000	440 000	10%	20%
Breast	30 000	140 000	110 000	80 000	360 000	75%	90%
Stomach	20 000	80 000	210 000	50 000	360 000	20%	40%
Colon or rectum	20 000	80 000	120 000	100 000	310 000	50%	60%
Cervix	40 000	90 000	60 000	20 000	200 000	55%	65%
Ovary	8000	30 000	30 000	30 000	100 000	25%	40%
Prostate	4000	10 000	20 000	20 000	60 000	70%	90%
Other or unknown site	110 000	330 000	470 000	310 000	1 220 000	NA	NA
Leukaemia							
Age 0–14 years	3000	10 000	10 000	2000	30 000	65%	90%
Age 15–69 years	10 000	40 000	60 000	30 000	140 000	30%	50%
All non-communicable diseases	1 660 000	6 300 000	5 950 000	2 200 000	16 070 000	NA	NA
Communicable or external causes	4 100 000	7 380 000	2 650 000	500 000	14 660 000	NA	NA
All causes	5 760 000	13 680 000	8 600 000	2 700 000	30 730 000	NA	NA
All cancers (% of all causes)	350 000 (6%)	1 170 000 (9%)	1 920 000 (22%)	1 000 000 (37%)	4 400 000 (14%)	NA	NA

Population and mortality data are from WHO's Global Health Observatory[9] and the UN Population Division.[10] Number of deaths greater than 10 000 are rounded to the nearest 10 000, so totals might differ. LMICs=low-income and middle-income countries. NA=not applicable. *By World Bank income grouping of countries.[11] †Estimated 5-year survival from Allemani and colleagues,[12] rounded to the nearest 5%. ‡n is the 2012 population (in billions) at ages 0–69 years only, excluding people aged 70 years or older; including all ages, the total world population in 2012 was 7 billion.

Table 1: **Worldwide cancer deaths in 2012 in patients aged 0–69 years by cancer site and country income grouping, and 5-year survival rates in LMICs and high-income countries**

(R Sankaranarayanan MD, F Bray DPhil); **Centre for Global Health Research, St Michael's Hospital, Dalla Lana School of Public Health** (C L Gauvreau PhD, A J Dare PhD, Prof P Jha DPhil), **and Institute of Health Policy Management and Evaluation** (T Sullivan PhD), **University of Toronto, Toronto, ON, Canada; University of Waterloo, Waterloo, ON, Canada** (Prof S Horton PhD); **Fred Hutchinson Cancer Research Center, Seattle, WA, USA** (B O Anderson MD); **University of Wisconsin, Madison, WI, USA** (J Cleary MD); **University of Cape Town, Cape Town, South Africa** (L Denny MD); **Princess Margaret Cancer Centre, Toronto, ON, Canada** (M K Gospodarowicz MD, D A Jaffray PhD); **Hospital for Sick Children, Toronto, ON, Canada** (S Gupta MD); **Health Sciences Center, University of Tennessee, Memphis, TN, USA** (Prof S C Howard MD); **Harvard University, Cambridge, MA, USA** (F Knaul PhD); **University of Washington, Seattle, WA, USA** (C Levin PhD); **Cancer Care Ontario, Toronto, ON, Canada** (L Rabeneck MD); **and National**

confidence in the overall programme.[5–7] Cancer control programmes can mobilise broad political support, as occurred in Mexico with the addition of breast and childhood cancer treatment in the 2012 expansion of national health insurance.[8]

In high-income countries most patients who develop cancer survive, although survival depends strongly on the type of cancer (table 1). In LMICs, less than a third of people survive, and in some populations the proportion is much smaller.[13] These differences in survival are partly due to differences in the patterns of cancer incidence; some cancer types that are common in many LMICs—such as lung cancer, oesophagus cancer, stomach cancer, and liver cancer—have a poor prognosis even in high-income countries.[14] Another major contributor to poor outcomes is that a smaller proportion of those with cancer in LMICs present for treatment with early, curable stages of cancer than in high-income countries, partly because effective and affordable treatment is not available.[12,13]

The aim of DCP-3 is to identify potentially cost-effective, feasible, and affordable interventions that address large disease burdens in LMICs (appendix). Accordingly, we have examined the avoidable burden of premature death (defined as before age 70 years, the estimated global life expectancy[2]) from cancer in LMICs (table 1); the main cost-effective interventions for the prevention, early detection, treatment, and palliation of cancer; and the costs and feasibility of developing, in an appropriate timescale, health-system infrastructures that could deliver progressively wider coverage of a set of cost-effective cancer services.

We define an essential package of cost-effective interventions for cancer and discuss their affordability and feasibility, which greatly differs between low-income, lower-middle-income, and upper-middle-income countries. Even in the same income category, countries might differ in epidemiological patterns and health systems, resulting in country-specific essential packages. Hence, this Review is not intended to lead to a common cancer plan for all LMICs, but to spur dialogue within countries about rational cancer control planning and implementation that will result in national cancer plans tailored to local conditions, retaining the characteristics of effectiveness, cost-effectiveness, feasibility, and affordability. Finally, we assess ways in which global initiatives—particularly for supplies, training and professional development—could help LMICs reduce the costs of expanded cancer control.

Changes in cancer burden

WHO's International Agency for Research on Cancer (IARC) estimated 14 million new cases of cancer and 8 million deaths from cancer in 2012, with more than half of the deaths in people aged younger than 70 years (table 1).[13] Of the 4·4 million cancer deaths in people aged younger than 70 years, 3·4 million were in LMICs

 www.thelancet.com **Published online November 11, 2015 http://dx.doi.org/10.1016/S0140-6736(15)00755-2**

(0·3 million in low-income, 1·2 million in lower-middle-income, and 1·9 million in upper-middle-income countries). Two-thirds of these deaths were from cancers of the lung, mouth, or oesophagus (0·9 million; many caused by tobacco); liver (0·4 million, many caused by vaccine-preventable hepatitis B virus [HBV] infection); stomach (0·3 million); breast (0·3 million); cervix (0·2 million, many caused by vaccine-preventable human papillomavirus [HPV] infection); and colon or rectum (0·2 million; table 1, figure 1).[9,13,14]

Worldwide, cancer death rates in people of a specific age are slowly decreasing (table 2). Between 2000 and 2010, age-standardised cancer death rates in people aged younger than 70 years fell by about 1% per year, bolstered by worldwide decreases in cervical cancer and stomach cancer (for reasons which are not fully understood). Male lung cancer mortality rates decreased in some countries between 2000 and 2010, but tobacco-associated cancer death rates rose slightly in lower-middle-income countries.

Absolute numbers of cancer deaths and cancer as a proportion of all deaths will, however, continue to rise because of three factors: world population is increasing (particularly in people aged older than 50 years), mortality from diseases other than cancer is decreasing quicker than decreases in cancers, and in some major populations the effects of tobacco are increasing.[15]

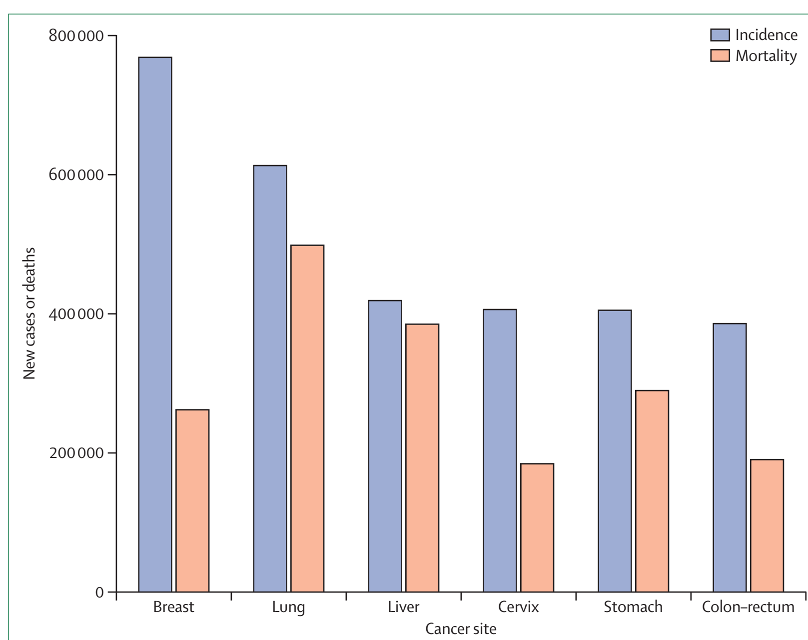

Figure 1: **Incidence and mortality of some cancer types in people aged younger than 70 years in low-income and middle-income countries in 2012**
Data are from Ferlay and colleagues.[13]

Effect of cancer on households and poverty

By contrast with common perceptions, cancer death rates are often higher in the poor than in the rich. For example, in India, the age-standardised death rate from cancer at ages 30–69 years was double in illiterate compared with educated populations.[16] Moreover, cancer, similar to other NCDs, is an important cause of catastrophic health expenditures that can push households into poverty.[17–20] In many LMICs, cancer surgery, radiotherapy, and chemotherapy are largely paid for out-of-pocket. In Bangladesh[17] and Cameroon,[19] high user fees increase the likelihood that patients will not return for cancer surgery. Conversely, however, in India some standard types of cancer surgery (eg, mastectomy) are supposed to be provided at a low affordable cost in public hospitals; likewise, in China the national health insurance scheme now offers standard types of cancer surgery at prices most can afford. Nevertheless, even in China and India cancer can impose a major financial burden on families, especially on those in the lowest income groups, and in India access is limited to some large cities.[21]

An essential package of interventions

Criteria for essential interventions

DCP-3 seeks to develop essential packages of cost-effective interventions to be considered and modified as appropriate by countries for all health conditions in the nine volumes. Both the specific interventions and the criteria used to choose them (ie, effectiveness, cost-effectiveness,[22] feasibility, and affordability) are intended to help LMICs decide what to support and what not to.[3] For middle-income countries that already have many cancer treatment centres and clinics, the DCP-3 approach could be used to help assess additional interventions now or in the future, or to reassess current activities. In all LMICs, it could help ensure due consideration about how interventions regarded as locally appropriate can achieve high population coverage.

WHO has already formulated its own list of NCD best buys (most beneficial interventions at the lowest cost) for LMICs, which are feasible without hospital facilities.[23] Those most relevant to cancer are three preventive measures: tobacco control interventions, HBV vaccination to prevent liver cancer, and some form of screening and treatment for precancerous cervical lesions.[23] The DCP-3 *Cancer* essential package adds HPV vaccination to prevent cervical cancer in addition to treatment of early stage cervical cancer (and, by implication, other resectable cancers; table 3); diagnosis and treatment for early breast cancer;[24] diagnosis and treatment for selected highly curable childhood cancers;[25] and palliative care,[26] including, at a minimum, opioid drugs for severe pain control. This package is organised according to different delivery platforms, classified as national level policy, regulation or community information, primary health clinics or mobile outreach, first-level hospitals (district hospitals), or specialised cancer centres.

Cancer Institute, Bethesda, MD, USA (P Rajaraman PhD, E L Trimble MD)

Correspondence to:
Ms Hellen Gelband, Center for Disease Dynamics, Economics & Policy, Washington, DC 20005, USA
gelband@cddep.org

or

Prof Prabhat Jha, University of Toronto, Toronto, ON M5B2C5, Canada
prabhat.jha@utoronto.ca

See **Online** for appendix

	Percentage change in mortality rates				
	Low-income countries	Lower-middle-income countries	Upper-middle-income countries	High-income countries	World
All cancers	−6%	−2%	−12%	−13%	−10%
Lung, mouth, oesophagus (mainly tobacco related)	−6%	+1%	−11%	−12%	−9%
Cervix, liver, stomach (mainly infection related)	−13%	−2%	−18%	−24%	−15%
Other cancers	−4%	−3%	−9%	−12%	−8%
All causes	−21%	−15%	−23%	−17%	−19%

Data are from International Agency for Research on Cancer's GLOBOCAN[13] and WHO's Global Health Observatory.[9]

Table 2: **Percentage change in mortality rates for cancer deaths and all causes by country income group, from 2000 to 2010 in people aged 0–69 years**

	Number of deaths (in 2012) of people aged <70 years	Interventions	Level of delivery
All cancers*	3 230 000	Education on tobacco hazards, value of HPV and HBV vaccination and importance of seeking early treatment for common cancers; palliative care including, at a minimum, opioids for pain relief	National policies, regulation, or information
Tobacco-related cancers (oral, lung, and oesophagus)	900 000	Taxation, warning labels or plain packaging, and bans on public smoking, advertising, and promotions, and monitoring of tobacco use and its effects; cessation advice and services (mostly without pharmacological therapies)	National policies, regulation, or information; primary health clinic or mobile outreach
Liver cancer	380 000	HBV vaccination (including birth dose)	Primary health clinic or mobile outreach
Breast cancer	280 000	Treat early-stage cancer†	Specialised cancer centre or unit‡
Colorectal cancer	210 000	Emergency surgery for obstruction	First-level hospital§
Cervical cancer	180 000	School-based HPV immunisation; opportunistic screening¶ (visual inspection or HPV DNA testing); treat precancerous lesions; treat early-stage cancer	National policies, regulation, or information; primary health clinic or mobile outreach; first-level hospital§; specialised cancer centre or unit
Childhood cancers‖	80 000	Treat selected cancers in paediatric cancer units or hospitals	Specialised cancer centre or unit

Cancer totals are rounded to nearest 10 000. DCP-3=*Disease Control Priorities,* 3rd edition. HPV=human papillomavirus. HBV=hepatitis B virus. *Education and basic palliative care are relevant for cancers at all ages. †Early-stage cancer generally refers to stages I and II. ‡Some interventions might take place at first-level hospitals (eg, by a specialised surgeon visiting once per month). §First-level hospitals are referred to as district hospitals in some countries. ¶Opportunistic screening focuses on existing available populations, and differs from organised screening which is a well defined process including formal invitations to participate, recalls, reminders, tracking results, ensuring follow-up, and monitoring of and reporting of programme performance results; however, it could include some outreach. ‖Includes some solid tumours.

Table 3: **Essential cancer intervention package recommended by DCP-3**

Assessment of the feasibility of these interventions follows the model of resource-level appropriate interventions developed for breast cancer by the Breast Health Global Initiative.[27] This classification recognises that different generations of effective breast cancer treatments are available with different resource costs and infrastructure requirements.

The cost of the essential package is for the entire population, not just those aged younger than 70 years. We estimated the global and per capita costs of every intervention in the package separately for low-income, lower-middle-income, and upper-middle-income countries (figure 2). Most LMICs should be able to implement a locally customised essential package that includes most of their population by 2030, in view of anticipated increases in public spending on health.[4] The schedule of implementation will vary, however, as some interventions, particularly increased tobacco taxes and widespread pain palliation, can begin now in many countries.[7,28] By contrast, affordable availability of treatments that need substantial infrastructure development might take many years to be fully achieved, even if a start is made immediately.

Prevention

Most countries (183 worldwide) vaccinate infants against HBV, with 81% global coverage in 2013. This will prevent many liver cancers in future decades, but a birth dose (important in countries with high mother-to-child transmission) reached only 26% of newborns in 2011.[29]

75 countries (including high-income countries) have started national HPV vaccination programmes and others are developing experience with the vaccine.[30] Additionally, Gavi is supporting pilot programmes in several low-income countries in sub-Saharan Africa. The delivery cost of giving adolescent girls three doses is the major barrier, because the Gavi-subsidised vaccine costs only US$0·60–1·20 for the recommended three doses, whereas programme costs range between $4 and $13 per fully immunised girl.[30,31] HBV and HPV vaccinations will have their main effect on mortality during the second half of this century, when the cohorts of immunised children reach middle age and these cancers would have become more common.

Tobacco control consists of increased taxes on cigarettes and other tobacco products, counter-

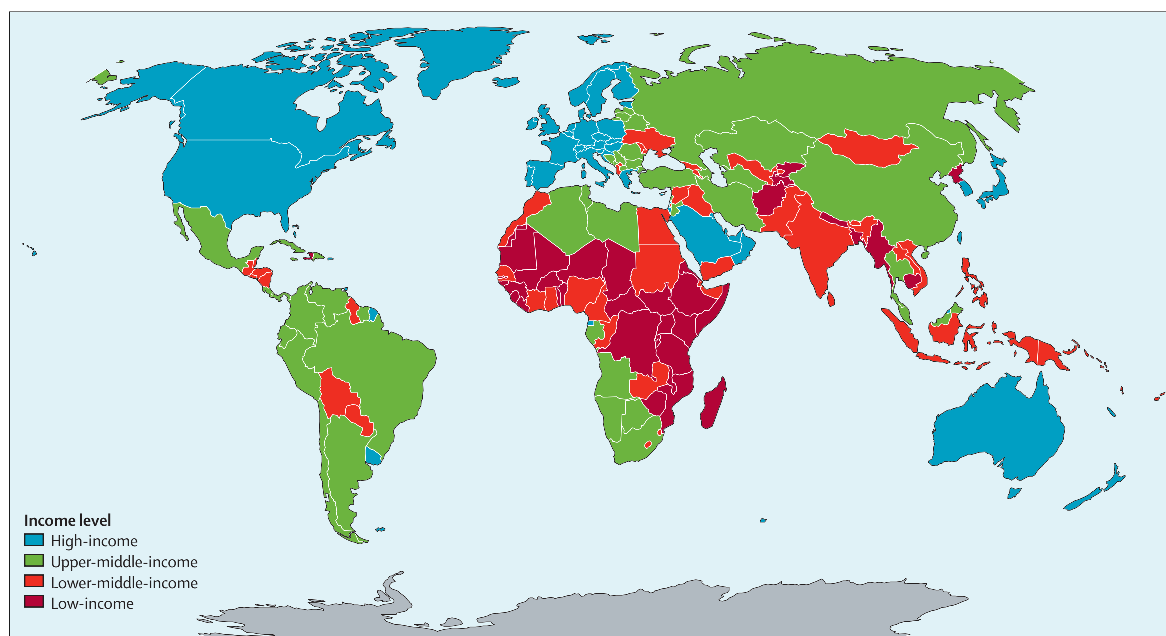

Figure 2: **Country income groupings in 2013**
Data are based on World Bank income groupings.

advertising, warning labels and other packaging requirements, bans on advertising, bans on smoking in public places, cessation support for smokers, and anti-smuggling technologies[32] and can achieve quick health gains. People who quit smoking before age 40 years avoid more than 90% of the risk they would have incurred had they continued to smoke.[32] Therefore, a substantial saving of lives could start in 5–10 years after tobacco control measures are introduced, with increasing gains thereafter. The most effective tobacco control intervention is increased excise taxes, which increases adult cessation and discourages youth initiation.[15,32] However, unlike in many high-income countries, cessation is uncommon in most LMICs, with adults quitting only after developing cancer (or some other major disease) and not while healthy to avoid disease.[33]

Only 28 countries are undertaking comprehensive tobacco control programmes with high taxes as a major strategy,[34] with some notable successes. France and South Africa used large tax increases in the 1990s to triple the price of cigarettes and by 2005, consumption had halved but real government revenues from tobacco had doubled.[32,35,36] Brazil has also greatly reduced smoking prevalence.[37] Despite severe industry opposition, in the past 5 years Mexico, the Philippines, and India substantially increased cigarette taxes, and Mexican cigarette sales have already started to decrease.[34,38] WHO's Framework Convention on Tobacco Control has been adopted by more than 180 countries and is an important enabler of country action for comprehensive tobacco control measures.[39]

Screening

The emphasis on diagnosis and treatment of cancers at an early stage (or in a precancerous stage for cervical cancer screening) might suggest the appropriateness of many cancer screening programmes,[40] but population screening is expensive and needs considerable infrastructure. Only opportunistic cervical screening (with or without some added outreach) meets the DCP-3 criteria and is therefore suggested for consideration in the essential package. Cervical screening with visual inspection (with acetic acid to stain abnormalities) can detect precancerous changes that can be treated inexpensively and often during the same visit.[41] When convenient rapid diagnostic tests for the main carcinogenic types of HPV infection become affordable they could further increase cervical screening effectiveness and reliability.[42] Two or three such screenings every 5–10 years in women aged 30–35 years at first screening should halve the lifetime risk of cervical cancer.[43]

The DCP-3 essential package does not include any type of screening for prostate or breast cancer. Both have attracted much controversy in high-income countries, albeit for different reasons. The most widespread means of prostate cancer screening is through a blood test for prostate-specific antigen (PSA; a protein from cancerous prostate cells), with or without physical examination. Although simple, PSA testing can lead to overdiagnosis and overtreatment, with many more patients being harmed by treatment side-effects than are saved from cancer. The US Preventive Services Task Force discourages PSA testing.[44] By contrast, screening mammography for breast cancer is supported by most high-income countries

For more about **WHO's Framework Convention on Tobacco Control** see http://www.who.int/fctc/about/en/

Panel: Possible strategies for treatment of early breast cancer in low-income and middle-income countries

By definition, in early breast cancer (stage I, II, and IIIA) all detectable disease can be removed surgically, but micrometastases might remain that later cause recurrence and death, and adjuvant treatments might be given after surgery to reduce this risk. In high-income countries, most women receiving appropriate treatment for early breast cancer survive their disease.[48] The success of breast-conserving surgery (lumpectomy) plus radiotherapy to the conserved breast is about the same as for mastectomy (removal of the entire breast, plus perhaps some local lymph nodes). Either treatment can be offered to patients if safe radiotherapy is available. The most basic surgical procedure for early breast cancer is some form of mastectomy.[24] For women in low-income and middle-income countries (LMICs) with early breast cancer, the first requirement is good quality, safe surgery. Particularly in low-income countries, timely access to safe surgery is a major barrier. In middle-income countries in which population access to surgical services is generally better, surgical quality is the major concern, particularly for adequate resection of a tumour.[49] After technically successful surgery, treatments can be based on oestrogen-receptor status, estimated recurrence risk, and general health.[24]

Oestrogen-receptor status of surgically removed breast cancers can be determined at a reasonable cost (about US$10 in India). For patients with cancer that is oestrogen-receptor positive, about 5 years of endocrine drug therapy substantially reduces the 15-year recurrence risk and is relatively non-toxic. Endocrine drugs such as tamoxifen or, for postmenopausal women, an aromatase inhibitor[50] can be dispensed safely to outpatients and are available as low-cost generics (generic tamoxifen costs about $15 per year in India, and generic aromatase inhibitors cost about $50 per year). Chemotherapy also reduces recurrence, but has more toxic side-effects and needs more careful medical supervision to ensure safety and efficacy than do endocrine treatments. New drugs (eg, trastuzumab) that target other breast cancer receptors are not cost-effective in LMICs.

Basic regimens of generic cytotoxic drugs (eg, four cycles of daunorubicin and cyclophosphamide with drug costs of about $200 in India) should be used wherever surgery is practicable,[24] and could be offered to women who are otherwise in good health but whose disease has already spread from the breast to the local lymph nodes.[48] More effective cytotoxic regimens (eg, with taxanes) would increase toxic effects, drug costs, and supervision costs.

Finally, global initiatives might help to reduce the cost of cancer drugs and other commodities, and develop and disseminate standardised, resource-appropriate treatment protocols (such as those developed by the Breast Health Global Initiative). The successful global initiatives to aid the diagnosis and treatment of HIV/AIDS could be used as a model for cancer.[51]

as an expensive but moderately effective measure, although the optimum age range for screening and screening frequency are still debated. Clinical breast examination might be a viable option in LMICs, but its effectiveness is uncertain.[24] Other common cancers with detectable precancerous stages are colorectal cancer (precancerous polyps)[45] and oral cancer (visible lesions).[46] Eventually, cancer screening might be widened, but a greater priority in LMICs now is to provide appropriate treatment for the cancers already being found.

Diagnosis and treatment

Accurate diagnosis is needed for cancer treatment, but a scarcity of trained pathologists and other laboratory technologists and scarce facilities and supplies crucially restrict diagnostic capacity in many LMICs.[47] In addition to an initial diagnosis of cancer (which might be based on biopsy specimens) that can help assess the success of surgery, diagnostic services can help determine treatment strategies after surgery. Simple tumour, node, metastasis staging has long been clinically useful. Other tests on the tumour itself can determine post-surgical management, particularly, breast cancer surgical specimens that should be tested for oestrogen receptor positivity; only if results are oestrogen receptor positive will endocrine treatment substantially reduce the chances of cancer recurrence and death (panel).

Treatment for early breast cancer and cervical cancer involves surgery, radiotherapy, chemotherapy, and targeted (eg, endocrine) therapy; although a patient might not need every modality.[5,27] For early cervical cancer, surgery is the primary treatment and radiotherapy is an adjunct. For whatever method is regarded as complete treatment in a specific country context, all components of care should be accessible by patients once treatment is started. Incomplete treatment can cause side-effects with little clinical benefit.

Childhood cancer is rare, causing only 1% of cancer deaths in high-income countries. It represents the smallest burden of the cancers targeted by the essential package. Although these types of cancer cannot generally be prevented, many types of childhood cancer do have a high cure rate in high-income countries, making them feasible targets in other countries.[52] Cure rates in most LMICs are lower, but reasonably good outcomes have been achieved in specialised childhood cancer centres and through national referral plans, particularly for acute lymphoid leukaemia, Burkitt lymphoma, and Wilms' tumour.[53]

Palliative care

Many incurable cancers cause intractable pain. Opioid medications can generally relieve this pain, greatly improving the quality of life in the last few weeks or months for both patients and families. The simplest and

 www.thelancet.com **Published online November 11, 2015 http://dx.doi.org/10.1016/S0140-6736(15)00755-2**

least expensive preparation is oral morphine, which works for an estimated 90% of patients with severe terminal cancer pain.[28] It is also used by patients with HIV/AIDS and other chronic conditions. At present, reasonably good palliative care is widely available only in high-income countries, but it could be made available in LMICs quite rapidly even before other types of treatment become available. Although palliative care includes more than pain control and is relevant throughout the course of illness, pain control is at its core.

With appropriate organisation and cooperation from government and health-care sectors, opioids can be provided even in rural areas, at home, and at a low cost. However, the reality is that few people have access to effective pain medicines because of unnecessary country restrictions. In 2006, 66% of the world's population lived in countries that had virtually no consumption of prescribed opioids, 13% in countries with low consumption, and 4% in countries with moderate consumption.[54]

Local priority conditions

Any essential package of cancer control should be customised and augmented with locally appropriate and feasible interventions. These interventions might include storage of grain and other foods to avoid fungal contamination, which can cause liver cancer in parts of Africa and Asia;[55,56] opportunistic screening (especially of high-risk tobacco users) and treatment for precancerous lesions and early-stage oral cancer in India and other countries with high oral cancer burdens;[16,46] screening and treatment for colorectal cancer in Argentina and Uruguay;[41,45] elimination of liver flukes (by 1 day of inexpensive praziquantel) to prevent bile duct cancer in the few areas where flukes are common; or treatment of schistosomiasis to prevent bladder or intestinal cancer in parts of Africa, the Middle East, and Asia.[57]

Finally, occupational and environmental cancer hazards (eg, use of power tools on asbestos roofing or insulation, heavy smoke pollution in houses, and heavy fungal contamination of stored carbohydrate foodstuff) should be monitored and mitigated where appropriate.[58]

Costs of interventions

For most types of cancer, reported literature about cost-effectiveness in LMICs is small:[59] nine studies were identified for breast cancer, two (plus four from high-income Asian countries) for colorectal cancer, one for liver cancer prevention, and none for paediatric cancer. 17 studies were sourced from an expert search for cervical cancer, and in 2012 a systematic review[60] for vaccines identified three studies for HBV vaccination. A useful benchmark was to exclude from the essential package those interventions that are not clearly cost-effective in high-income countries. Most new drug treatments for advanced cancer fall into this category, such as bevacizumab (a monoclonal antibody) for metastatic breast cancer, which, at current prices, does not meet cost-effectiveness criteria even in high-income countries.[61–63] Similarly, cetuximab (a monoclonal antibody for metastatic colon and lung cancers) and irinotecan (for colon cancer) are not judged to be cost-effective in the UK.[64] Radiotherapy is one of the interventions included in curative treatments for early cervical and breast cancer and, where available, it is considered cost-effective.[65]

Excise taxes on tobacco, opportunistic cervical cancer screening and treatment of precancerous lesions, and HBV vaccination are cost-effective in LMICs. HPV vaccination cost-effectiveness depends on the vaccine price and programme costs, and some aspects of the treatment for early breast cancer are cost-effective irrespective of which country the breast cancer surgery is done in. The perspective of tobacco control is of health gains compared with the minimal costs of the interventions. Various reviews of the broader welfare perspective on taxation have reached similar conclusions about the desirability of increased tobacco taxes.[20,32,38] In China, raising tobacco taxes provides substantial financial protection to those in low-income groups.[66]

Costs of national packages

To illustrate per-capita cost estimates for an essential package, we combined information about costs and demography from Nigeria, India, and Brazil (although Nigeria is a lower-middle-income country, we use its demographic structure and scarce facilities and human resources to represent low-income countries, mainly in sub-Saharan Africa). To account for training, pathology services, and other system costs, we used a multiplier equal to 50% of the intervention-based costs, a figure used in similar costing studies for nutrition[67] and for health systems.[68] However, we do not include the one-time investment costs for construction of hospitals, clinics, and other infrastructure that would be needed to support cancer and other clinical services in the long term.[7,47]

The DCP-3 essential package of cancer control interventions would cost roughly an additional \$1·7 per capita in low-income and lower-middle-income countries, and \$5·7 per capita in upper-middle-income countries (table 4), for total costs of about \$1·4 billion, \$4·4 billion, and \$13·8 billion, respectively.[4] There are obvious uncertainties about current and future costs. Importantly, drug costs can fall substantially as their patents expire, and global initiatives could further reduce prices of key generic versions.

Affordability and domestic financing of essential cancer services

The total estimated annual cost of the essential package of cancer interventions for all LMICs is about \$20 billion (table 5). As a proportion of current total public spending on health, this is about 3% in upper-middle-income and 5% in lower-middle-income countries, but 13% in low-income countries.[11] As a broad benchmark,

	Low-income countries (US$)	Lower-middle-income countries (US$)	Upper-middle-income countries (US$)
Comprehensive tobacco control measures	0·05	0·07	1·06
Palliative care and pain control	0·05	0·06	0·06
Hepatitis B virus vaccination	0·08	0·04	0·04
Promote early diagnosis and treat early-stage breast cancer	0·43	0·43	1·29
Human papillomavirus vaccination	0·23	0·23	0·40
Screen and treat precancerous lesions and early-stage cervical cancer	0·26	0·29	0·87
Treat selected childhood cancers	0·03	0·03	0·09
Subtotal costs	1·13	1·15	3·81
Ancillary services (50% of subtotal)	0·57	0·58	1·91
Total costs	1·70	1·73	5·72

Calculations based on *Cancer* volume of *Disease Control Priorities,* 3rd edition (DCP-3), and Horton and Gauvreau.[59] Demographic and epidemiological information from Nigeria, India, and Brazil is used to model costs for low-income (mainly in sub-Saharan Africa), lower-middle-income, and upper-middle-income countries, respectively.[59] However, country-specific planning will need country-specific estimates.

Table 4: **Estimated marginal costs of essential interventions from the DCP-3 cancer package for low-income, lower-middle-income, and upper-middle-income countries per capita in 2012**

	Low-income countries	Lower-middle-income countries	Upper-middle-income countries	Total LMIC
Public spending on health (% of country GDP in 2013)	2·0%	1·8%	3·1%	3·0%
Total public spending on health in 2013 (billions; US$)	$11	$89	$534	$634
Cost of cancer interventions in 2013 (billions; US$)	$1·4	$4·4	$13·8	$19·6
Cancer package as percentage of total public spending on health in 2013*	13·0%	4·9%	2·6%	3·1%

LMIC=low-income and middle-income countries. GDP=gross domestic product. *Calculations are based on spending data from the World Bank.[11]

Table 5: **Annual resource requirements for essential cancer intervention package for LMICs**

high-income countries devote 3–7% of total health spending to cancer control.[69] Most LMICs allocate far less: cancer accounts for about 1% of health spending (public and private) in Brazil and India, and only 2% in China and Mexico.[6,41,70]

Financing of cancer control will have to come mainly from national health-care budgets, particularly in middle-income countries where rising incomes are enabling expansion of public financing for health.[4,71] South Africa has assessed which interventions it might include in an expanded national health insurance package[72] and similar work is underway in India.[68,73] In low-income countries, it would be inappropriate for governments to shift to allocating 13% of their health-care expenditures to cancer. External assistance will be needed in those countries to establish an expansion path for cancer control. A clear principle to use is the eventual goal of coverage for every person (even if coverage expands gradually), but not coverage of everything,[74] since poorly conceived plans might provide expensive ineffective treatments for a few, while missing the opportunity to expand cost-effective population coverage. However, public finance is not necessarily synonymous with public delivery.[75] Properly regulated private hospitals, facilities, and providers can be contracted to deliver cancer control interventions. For both public and private hospitals, alignment of payment incentives to good quality and outcomes is essential.[73]

Several Latin American countries are already expanding their health insurance systems from coverage restricted to occupational groups or selected susceptible groups, to more comprehensive coverage (using general taxation).[41] However, for some lower-middle-income countries and most low-income countries, substantial increases in public finance for health, paired with economic growth or external assistance, would be needed to finance a full package of interventions.[4] Even those countries, however, could benefit from considering the future cancer burden, costs, and financing to project a future cancer control plan. Higher tobacco taxes are the most important single cancer prevention intervention at a practical level, and a tripling of the excise tax on tobacco (thereby almost doubling prices) could mobilise an extra $100 billion worldwide in annual revenue.[32] For all LMICs, the epidemiological dividend that accrues from a decreased burden of infectious disease should generate revenue that can be spent on NCD control.[76]

Implementation challenges for an essential package

In the essential package, some interventions can be implemented reasonably quickly, such as tobacco control measures that include taxation and regulation,[38] and policy changes to increase access to narcotics (although to establish nationwide programmes and train a full cadre of providers might take years).[26] Some interventions can be scaled to reasonably large coverage quickly with existing infrastructure, such as school-based HPV vaccination in adolescent girls, or HBV vaccination in newborn babies. By contrast, other interventions will need expanded clinical access—most notably surgical treatment of early stage breast cancer and cervical cancer.[49] To increase a country's surgical capacity is expensive but feasible from an organisational perspective, especially if existing district hospitals can be strengthened[77,78] (eg, by being paired with central cancer clinical expertise), whereas expansion of chemotherapy treatment needs an extensive network of laboratories and follow-up, which in low-income and lower-middle-income countries is feasible in only urban areas. Scaling up radiotherapy needs large capital expenditures, and substantial attention to guidelines, treatment protocols, and monitoring of safety precautions.[79,80]

 www.thelancet.com Published online November 11, 2015 http://dx.doi.org/10.1016/S0140-6736(15)00755-2

Particularly for low-income countries in which minimal cancer services exist in the public sector, the needed expertise and resources for cancer treatment will take years of steady investment in physical and human infrastructure. Elements missing or in short supply in LMICs[16,47,81] include: trained professionals in oncology and relevant disciplines; appropriately equipped facilities for surgery, radiotherapy, pathology, and other laboratory testing services (eg, breast cancer oestrogen receptor testing; panel); supplies (eg, chemotherapy drugs); geographical access to facilities with affordable cancer services, including surgery; public awareness of the availability and effectiveness of cancer control interventions; and cancer incidence and cause-of-death data.

As more people are successfully treated and live for many years, survivorship services (eg, rehabilitation, remedies for physical deficits caused by treatment, restriction of the social stigma of having had cancer, and follow-up for recurrence) will increase in importance, but costs for survivorship programmes are not included in the recommended package.[82]

The DCP-3 package emphasises treatment for early stage cervical and breast cancers, and similarly for other cancers included in specific country plans, because cure rates are substantially higher than for more advanced cancers. Locally appropriate opportunistic cervix screening is included, but organised population-wide screening programmes are not. Even without screening, however, LMICs might be able to achieve a somewhat earlier stage of presentation of common cancers by making affordable treatment available and communicating this to patients. Historical evidence from high-income countries (eg, stage-shifting cervix cancer in Sweden before organised screening began about 1960) supports this approach.[83]

Cancer treatment can be organised through existing medical facilities (particularly district hospitals) or through specialised centres. However, good links between facilities, with a centralised locus of monitoring and guidance, are needed.[7,47] For example, all children with cancer in Honduras (population 8 million) are treated in two centres that collaborate and communicate closely.[84] By contrast, children with cancer in Colombia (population 48 million) can be treated in more than 150 health-care institutions of varying size, with little communication between centres,[25] adversely affecting patient outcomes and costs. India has a population of 1·3 billion, and is building a National Cancer Grid[85] to link non-specialist hospitals with specialist cancer centres and to standardise treatment protocols.

Building and improving cancer control capacity needs attention to the quality of services, from pathology and diagnosis to surgery, chemotherapy, radiotherapy, and palliative care.[47] Additionally, hospitals need upgrading to provide basic cancer surgical services,[77] develop cancer referral networks, track service performance, integrate the delivery of different types of services, and ensure that financial flows accompany services.

Global initiatives for cancer control

Only 1% of the $30 billion development assistance for health in 2010 was for NCDs, of which very little was for cancer.[86] Funding for NCDs will increase with increasing global recognition of their importance, but it is unlikely that substantial global funds will be allocated to national health systems to deal with cancer. As additional funding becomes available, we suggest three priorities for international support. First, we suggest lowering the costs of key inputs for the essential package and other cost-effective interventions, such as HPV and other vaccines, cancer drugs (including generics), pathology tests, radiotherapy machines, and other relevant goods. The Global Fund to Fight AIDS, Tuberculosis and Malaria, Gavi, the Clinton Health Access Initiative, and other international partnerships have developed mechanisms to reduce prices of infectious disease control commodities by using economies of scale. Similar efforts for cancer are possible with subsidies for reputable and affordable medicines, advanced market commitments, and bulk purchases of drugs or radiotherapy machines.[79]

For more about **The Global Fund to Fight AIDS, Tuberculosis and Malaria** see http://www.theglobalfund.org/en/

For more about **Gavi** see http://www.gavi.org/

For more about the **Clinton Health Access Initiative** see http://www.clintonhealthaccess.org/

Second would be to expand technical assistance in cancer control. International and regional networks exist for many aspects of cancer care (eg, treatment guidelines, networks on cervical screening, childhood cancer treatment and research, and palliative care). Other support modalities (eg, institutional twinning) typically include institutions in high-income and low-income countries (north–south collaborations), but opportunities should grow to add south–south collaborations (LMICs with other LMICs). Within countries, peer-based professional standards of cancer care and reporting of outcome and performance for various facilities can improve patient quality of care.[87,88]

Finally, support for research might be the best use of scarce overseas developmental assistance. Research could include tracking of national cancer burdens, clinical trials, implementation science (including research into delivery systems and economics, notably local economic analyses to define appropriate essential packages of services), cancer epidemiology and biology, and development of widely practicable low-cost technologies.[89]

Conclusions: benefits of expanded cancer control

Despite substantial challenges in most LMICs, appreciable reductions in the cancer burden might be possible by 2030 (with even greater reductions by 2050 and later[2]), particularly through treating common cancers that are detected early, tobacco control that encourages widespread adult smoking cessation, and vaccination against HBV and HPV. Age-standardised cancer death rates at ages 0–69 years were decreasing worldwide at 10% per decade from 2000 to 2010. If this rate of decrease continues, then from 2010 to 2030 death rates will fall by about 20%. To achieve the UN's 2030 goals of a third reduction in NCDs, tobacco cessation in LMICs must accelerate to approach the rates in high-income countries, where at about age

50 years, there are now more ex-smokers than current smokers.[2,32] WHO estimates that tobacco control, HPV and HBV vaccination, and opportunistic cervical cancer screening could avoid about 6% of cancer deaths by 2030 (about 200 000 deaths annually before age 70 years)[23] and the DCP-3 essential package could help to achieve greater reductions. If, as expected, the availability of treatment shifts diagnoses for common treatable cancers to earlier stages, additional lives could be saved. The benefits of pain relief are not measured in lives saved, but are important to patients and their families. Increases to provision of cancer services might also help shrink the health gap between rich and poor, because many cancers and risk factors suggested for targeting are more prevalent in patients at the lower end of the economic ladder. Cancer control is often approached with pessimism, but practicable, deliberate, cost-effective steps can enable many countries to substantially reduce the suffering and premature death from cancer by 2030, with much greater improvements by 2050.

Contributors

HG and PJ generated the plan for this study. HG prepared the first draft with input and revisions from all authors. SH and PJ developed the costs of the essential package. All authors approved the final draft. HG and PJ had responsibility for submitting for publication.

Members of the DCP-3 Cancer Author Group

Issac Adewole, Hemantha Amarasinghe, Benjamin O Anderson, Federico G Antillon, Samira Asma, Rifat Atun, Rajendra A Badwe, Freddie Bray, Frank J Chaloupka, Ann Chao, Chien-Jen Chen, Wendong Chen, James Cleary, Anna J Dare, Anil D'Cruz, Lynette Denny, Craig Earle, Silvia Franceschi, Cindy L Gauvreau, Hellen Gelband, Ophira M Ginsburg, Mary K Gospodarowicz, Thomas Gross, Prakash C Gupta, Sumit Gupta, Andrew Hall, Mhamed Harif, Rolando Herrero, Susan Horton, Scott C Howard, Stephen P Hunger, Andre Ilbawi, Trijn Israels, David A Jaffray, Dean T Jamison, Prabhat Jha, Newell Johnson, Jamal Khader, Jane J Kim, Felicia Knaul, Carol Levin, Joseph Lipscomb, W Thomas London, Mary MacLennan, Katherine A McGlynn, Monika L Metzger, Raul Murillo, Zachary Olson, Sherif Omar, Krishna Palipudi, C S Pramesh, You-Lin Qiao, Linda Rabeneck, Preetha Rajaraman, Kunnambath Ramadas, Chintanie Ramasundarahettige, Timothy Rebbeck, Carlos Rodriguez-Galindo, Rengaswamy Sankaranarayanan, Monisha Sharma, Ju-Fang Shi, Isabelle Soerjomataram, Lisa Stevens, Sujha Subramanian, Richard Sullivan, Terrence Sullivan, David Thomas, Edward L Trimble, Joann Trypuc, Stéphane Verguet, Judith Wagner, Shao-Ming Wang, Christopher P Wild, Pooja Yerramilli, Cheng-Har Yip, Ayda Yurekli, Witold Zatonski, Ann G Zauber, and Fang-Hui Zhao.

Declaration of interests

FK reports grants from GlaxoSmithKline, Avon Mexico, Pfizer, Susan G Komen for the Cure, NADRO, Chinoin Pharmaceutical Products, Sanofi, and Roche; and reports non-financial support from PISA and Grunenthal. All other authors declare no competing interests.

Acknowledgments

We thank George Alleyne for helpful comments on an earlier draft. The Bill & Melinda Gates Foundation provides financial support for the Disease Control Priorities Network project, of which this volume is a part. We received funding from the US National Cancer Institute, Canadian Institutes of Health Research (grant 126347), and Centre for Global Health Research.

References

1. UN Department of Economics and Social Affairs. Transforming our world: the 2030 Agenda for Sustainable Development. https://sustainabledevelopment.un.org/post2015/transformingourworld (accessed Oct 31, 2015).
2. Norheim OF, Jha P, Admasu K, et al. Avoiding 40% of the premature deaths in each country, 2010–30: review of national mortality trends to help quantify the UN Sustainable Development Goal for health. *Lancet* 2015; **385:** 239–52.
3. Jamison DT. *Disease Control Priorities*, 3rd edition: improving health and reducing poverty. *Lancet* 2015; published online Feb 4. http://dx.doi.org/10.1016/S0140-6736(15)60097-6.
4. Jamison DT, Summers LH, Alleyne G, et al. Global health 2035: a world converging within a generation. *Lancet* 2013; **382:** 1898–955.
5. Brown ML, Goldie SJ, Draisma G, et al. Health service interventions for cancer control in developing countries. In: Jamison DT, Breman J, Measham AR, et al, eds. Disease control priorities in developing countries, 2nd edn. New York: Oxford University Press, 2006: 569–89.
6. Knaul FM, Gralow JR, Atun R, et al. Closing the cancer divide: an equity imperative. Cambridge, MA: Harvard Global Equity Initiative and Harvard University Press, 2011.
7. Sloan FA, Gelband H. Cancer control opportunities in low- and middle-income countries. Washington, DC: National Academy Press, 2007.
8. Knaul FM, González-Pier E, Gómez-Dantés O, et al. The quest for universal health coverage: achieving social protection for all in Mexico. *Lancet* 2012; **380:** 1259–79.
9. WHO. Health statistics and information systems: global health estimates, 2012. http://www.who.int/gho/mortality_burden_disease/en/ (accessed Oct 31, 2015).
10. UNPD. World population prospects: the 2012 revision. New York: UN Population Division, 2012.
11. World Bank. World Bank development indicators 2014: table 2.15 health systems. http://wdi.worldbank.org/table/2.15 (accessed May 31, 2015).
12. Allemani C, Weir HK, Carreira H, et al, and the CONCORD Working Group. Global surveillance of cancer survival 1995–2009: analysis of individual data for 25 676 887 patients from 279 population-based registries in 67 countries (CONCORD-2). *Lancet* 2015; **385:** 977–1010.
13. Ferlay J, Soerjomataram I, Dikshit R, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. *Int J Cancer* 2015; **136:** e359–86.
14. Bray F, Soerjomataram I. Chapter 2. The changing global burden of cancer. In: Gelband H, Jha P, Sankaranarayanan R, Horton S, eds. Disease control priorities, 3rd edn. Volume 3: cancer. Washington, DC: World Bank, 2015 (in press).
15. Jha P. Avoidable global cancer deaths and total deaths from smoking. *Nat Rev Cancer* 2009; **9:** 655–64.
16. Dikshit R, Gupta PC, Ramasundarahettige C, et al, and the million Death Study Collaborators. Cancer mortality in India: a nationally representative survey. *Lancet* 2012; **379:** 1807–16.
17. Hamid SA, Ahsan SM, Begum A. Disease-specific impoverishment impact of out-of-pocket payments for health care: evidence from rural Bangladesh. *Appl Health Econ Health Policy* 2014; **12:** 421–33.
18. Hoang Lan N, Laohasiriwong W, Stewart JF, Tung ND, Coyte PC. Cost of treatment for breast cancer in central Vietnam. *Glob Health Act* 2013; **6:** 18872.
19. Ilbawi AM, Einterz EM, Nkusu D. Obstacles to surgical services in a rural Cameroonian district hospital. *World J Surg* 2013; **37:** 1208–15.
20. John RM, Sung HY, Max WB, Ross H. Counting 15 million more poor in India, thanks to tobacco. *Tob Control* 2011; **20:** 349–52.
21. Mallath MK, Taylor DG, Badwe RA, et al. The growing burden of cancer in India: epidemiology and social context. *Lancet Oncol* 2014; **15:** e205–12.
22. WHO. Macroeconomics and health: investing in health for economic development. Geneva: World Health Organization, 2001.
23. WHO. Scaling up action against non-communicable diseases: how much will it cost? Geneva: World Health Organization, 2011.
24. Anderson BO, Lipscomb J, Murillo RH, et al. Chapter 3. Breast cancer. In: Gelband H, Jha P, Sankaranarayanan R, Horton S, eds. Disease control priorities, 3rd edn. Volume 3: cancer. Washington, DC: World Bank, 2015 (in press).
25. Gupta S, Howard SC, Hunger SP, et al. Chapter 7. Childhood cancers. In: Gelband H, Jha P, Sankaranarayanan R, Horton S, eds. Disease control priorities, 3rd edn. Volume 3: cancer. Washington, DC: World Bank, 2015 (in press).

26 Cleary J, Gelband H. Wagner J. Chapter 9. Cancer pain relief. In: Gelband H, Jha P, Sankaranarayanan R, Horton S, eds. Disease control priorities, 3rd edn. Volume 3: cancer. Washington, DC: World Bank, 2015 (in press).

27 Anderson BO, Cazap E, El Saghir NS, et al. Optimisation of breast cancer management in low-resource and middle-resource countries: executive summary of the Breast Health Global Initiative consensus, 2010. *Lancet Oncol* 2011; **12:** 387–98.

28 Foley KM, Wagner JL, Joranson DE, Gelband H. Pain control for people with cancer and AIDS. In: Jamison DT, Breman J, Measham AR, et al, eds. Disease control priorities in developing countries, 2nd edn. Washington, DC: World Bank, 2006: 981–93.

29 WHO Immunization Practices Advisory Committee. Final meeting report and recommendations, 12–13 April, 2011. http://www.who.int/immunization/policy/committees/IPAC_2011_April_report.pdf?ua=1 (accessed May 31, 2015).

30 Gavi, the vaccine alliance. Millions of girls in developing countries to be protected against cervical cancer thanks to new HPV vaccine deals, 2013. http://www.gavi.org/library/news/press-releases/2013/hpv-price-announcement/ (accessed May 31, 2015).

31 Denny L, Herrero R, Levin C, et al. Cervical cancer. Chapter 4. In: Gelband H, Jha P, Sankaranarayanan R, Horton S, eds. Disease control priorities, 3rd edn. Volume 3: cancer. Washington, DC: World Bank, 2015 (in press).

32 Jha P, Peto R. Global effects of smoking, of quitting, and of taxing tobacco. *N Engl J Med* 2014; **370:** 60–68.

33 Chen Z, Peto R, Zhou M, et al, for the China Kadoorie Biobank (CKB) collaborative group. Contrasting male and female trends in tobacco-attributed mortality in China: evidence from successive nationwide prospective cohort studies. *Lancet* 2015; **386:** 1447–56.

34 WHO. WHO report on the global tobacco epidemic 2013. Geneva: World Health Organization, 2013.

35 Van Walbeek C. Tobacco control in South Africa. *Promot Educ* 2005; **12** (suppl 4): 25–28 (in French).

36 Hill C. Impact de l'augmentation des prix sur la consummation de tabac. Paris: Institut Gustave Roussy, 2013. http://www.igr.fr/doc/cancer/pdf/prevention/prixtab2013.pdf (acessed May 31, 2015).

37 Monteiro CA, Cavalcante TM, Moura EC, Claro RM, Szwarcwald CL. Population-based evidence of a strong decline in the prevalence of smokers in Brazil (1989-2003). *Bull World Health Organ* 2007; **85:** 527–34.

38 Jha P, MacLennan M, Yurekli A, et al. Chapter 10. Global hazards of tobacco, benefits of cessation and of taxation of tobacco. In: Gelband H, Jha P, Sankaranarayanan R, Horton S, eds. Disease control priorities, 3rd edn. Volume 3: cancer. Washington, DC: World Bank, 2015 (in press).

39 Jha P. Deaths and taxes: stronger global tobacco control by 2025. *Lancet* 2015; **385:** 918–20.

40 Sullivan T, Sullivan R, Ginsburg OM. Chapter 12. Screening for cancer: considerations for LMICs. In: Gelband H, Jha P, Sankaranarayanan R, Horton S, eds. Disease control priorities. 3rd edn. Volume 3: cancer. Washington, DC: World Bank, 2015 (in press).

41 Goss PE, Lee BL, Badovinac-Crnjevic T, et al. Planning cancer control in Latin America and the Caribbean. *Lancet Oncol* 2013; **14:** 391–436.

42 Sankaranarayanan R, Nene BM, Shastri SS, et al. HPV screening for cervical cancer in rural India. *N Engl J Med* 2009; **360:** 1385–94.

43 Goldie SJ, Gaffikin L, Goldhaber-Fiebert JD, et al, and the Alliance for Cervical Cancer Prevention Cost Working Group. Cost-effectiveness of cervical-cancer screening in five developing countries. *N Engl J Med* 2005; **353:** 2158–68.

44 US Preventive Services Task Force. Final recommendation statement. Prostate cancer: screening, May 2012. http://www.uspreventiveservicestaskforce.org/Page/Document/RecommendationStatementFinal/prostate-cancer-screening (accessed May 31, 2015).

45 Rabeneck L, Horton S, Zauber AG, et al. Chapter 6. Colorectal cancer. In: Gelband H, Jha P, Sankaranarayanan R, Horton S, eds. Disease control priorities, 3rd edn. Volume 3: cancer. Washington, DC: World Bank, 2015 (in press).

46 Sankaranarayanan R, Ramadas K, Amarasinghe H, et al. Chapter 5. Oral cancer. In: Gelband H, Jha P, Sankaranarayanan R, Horton S, eds. Disease control priorities, 3rd edn. Volume 3: cancer. Washington, DC: World Bank, 2015 (in press).

47 Gospodarowicz MK, Trypuc J, D'Cruz A, et al. Chapter 11. Cancer services and the comprehensive cancer care center. In: Gelband H, Jha P, Sankaranarayanan R, Horton S, eds. Disease control priorities, 3rd edn. Volume 3: cancer. Washington, DC: World Bank, 2015 (in press).

48 Early Breast Cancer Trialists' Collaborative Group (EBCTCG), Peto R, Davies C, Godwin J, et al. Comparisons between different polychemotherapy regimens for early breast cancer: meta-analyses of long-term outcome among 100 000 women in 123 randomised trials. *Lancet* 2012; **379:** 432–44.

49 Dare AJ, Anderson BO, Sullivan R, et al. Chapter 13. Surgical services for cancer care. In: Gelband H, Jha P, Sankaranarayanan R, Horton S, eds. Disease control priorities, 3rd edn. Volume 3: cancer. Washington, DC: World Bank, 2015 (in press).

50 Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Aromatase inhibitors versus tamoxifen in early breast cancer: patient-level meta-analysis of the randomised trials. *Lancet* 2015; **386:** 1341–52.

51 Piot P, Quinn TC. Response to the AIDS pandemic—a global health model. *N Engl J Med* 2013; **368:** 2210–18.

52 Smith MA, Seibel NL, Altekruse SF, et al. Outcomes for children and adolescents with cancer: challenges for the twenty-first century. *J Clin Oncol* 2010; **28:** 2625–34.

53 Gupta S, Rivera-Luna R, Ribeiro RC, Howard SC. Pediatric oncology as the next global child health priority: the need for national childhood cancer strategies in low- and middle-income countries. *PLoS Med* 2014; **11:** e1001656.

54 Seya MJ, Gelders SF, Achara OU, Milani B, Scholten WK. A first comparison between the consumption of and the need for opioid analgesics at country, regional, and global levels. *J Pain Palliat Care Pharmacother* 2011; **25:** 6–18.

55 Groopman JD, Kensler TW, Wild CP. Protective interventions to prevent aflatoxin-induced carcinogenesis in developing countries. *Annu Rev Public Health* 2008; **29:** 187–203.

56 Gelband H, Chen C-J, Chen W, et al. Chapter 8. Liver cancer. In: Gelband H, Jha P, Sankaranarayanan R, Horton S, eds. Disease control priorities, 3rd edn. Volume 3: cancer. Washington, DC: World Bank, 2015 (in press).

57 IARC. IARC mongraphs on the evaluation of carcinogenic risks to humans: volume 61, Schistosomes, liver flukes and *Helicobacter pylori*. Lyon: International Agency for Research on Cancer, 1994.

58 IARC. IARC Mongraphs on the evaluation of carcinogenic risks to humans: volume 100. Lyon, International Agency for Research on Cancer, 2012.

59 Horton S, Gauvreau CL. Chapter 16. Cancer in low- and middle-income countries: an economic overview. In: Gelband H, Jha P, Sankaranarayanan R, Horton S, eds. Disease control priorities, 3rd edn. Volume 3: cancer. Washington, DC: World Bank, 2015 (in press).

60 Ozawa S, Mirelman A, Stack ML, Walker DG, Levine OS. Cost-effectiveness and economic benefits of vaccines in low- and middle-income countries: a systematic review. *Vaccine* 2012; **31:** 96–108.

61 Rodgers M, Soares M, Epstein D, Yang H, Fox D, Eastwood A. Bevacizumab in combination with a taxane for the first-line treatment of HER2-negative metastatic breast cancer. *Health Technol Assess* 2011; **15** (suppl 1): 1–12.

62 Dedes KJ, Matter-Walstra K, Schwenkglenks M, et al. Bevacizumab in combination with paclitaxel for HER-2 negative metastatic breast cancer: an economic evaluation. *Eur J Cancer* 2009; **45:** 1397–406.

63 Montero AJ, Avancha K, Glück S, Lopes G. A cost-benefit analysis of bevacizumab in combination with paclitaxel in the first-line treatment of patients with metastatic breast cancer. *Breast Cancer Res Treat* 2012; **132:** 747–51.

64 Tappenden P, Jones R, Paisley S, Carroll C. Systematic review and economic evaluation of bevacizumab and cetuximab for the treatment of metastatic colorectal cancer. *Health Technol Assess* 2007; **11:** 1–128.

65 Ringborg U, Bergqvist D, Brorsson B, et al. The Swedish Council on Technology Assessment in Health Care (SBU) systematic overview of radiotherapy for cancer including a prospective survey of radiotherapy practice in Sweden 2001—summary and conclusions. *Acta Oncol* 2003; **42:** 357–65.

66 Verguet S, Gauvreau CL, Mishra S, et al. The consequences of tobacco tax on household health and finances in rich and poor smokers in China: an extended cost-effectiveness analysis. *Lancet Glob Health* 2015; **3:** e206–16.

67 Bhutta ZA, Das JK, Rizvi A, et al, and the Lancet Nutrition Interventions Review Group, and the Maternal and Child Nutrition Study Group. Evidence-based interventions for improvement of maternal and child nutrition: what can be done and at what cost? *Lancet* 2013; **382:** 452–77.

68 Rao Seshadri S, Jha P, Sati P, et al. Karnataka's roadmap to improved health: cost effective solutions to address priority diseases, reduce poverty and increase economic growth. Bangalore: Azim Premji University, 2015.

69 OECD. OECD health policy studies. Cancer care: assuring quality to improve survival. Paris: Organization for Economic Co-operation and Development (OECD) Publishing, 2013.

70 IARC. World cancer report 2014. In: Stewart BW, Wild CP, eds. World Cancer Report. Geneva: International Agency for Research on Cancer, 2014.

71 Knaul F, Horton S, Yerramilli P, et al. Chapter 17. Financing cancer care in low-resource settings. In: Gelband H, Jha P, Sankaranarayanan R, Horton S, eds. Disease control priorities, 3rd edn. Volume 3: cancer. Washington, DC: World Bank, 2015 (in press).

72 Shisana O, Rehle T, Louw J, Zungu-Dirwayi N, Dana P, Rispel L. Public perceptions on national health insurance: moving towards universal health coverage in South Africa. *S Afr Med J* 2006; **96:** 814–18.

73 Jha P, Laxminarayan R. Choosing health: an entitlement for all Indians. Delhi and Toronto: Centre for Global Health Research, 2009.

74 WHO. The world health report 2000—health systems: improving performance. Geneva: World Health Organization, 2000.

75 Musgrove P. Public and private roles in health: theory and financing patterns. Health, nutrition and population (hnp) discussion paper. Washington, DC: World Bank, 1996.

76 Jamison DT, Jha P, Malhotra V, et al. The 20th century transformation of human health: its magnitude and value. In: Lomborg B, ed. how much have global problems cost the world? A scorecard from 1900–2050. Cambridge, UK: Cambridge University Press, 2011: 207–46.

77 Mock CN, Donkor P, Gawande A, Jamison DT, Kruk ME, Debas HT, for the DCP3 Essential Surgery Author Group. Essential surgery: key messages from *Disease Control Priorities*, 3rd edition. *Lancet* 2015; **385:** 2209–19.

78 Dare AJ, Ng-Kamstra JS, Patra J, et al, and the million Death Study Collaborators. Deaths from acute abdominal conditions and geographical access to surgical care in India: a nationally representative spatial analysis. *Lancet Glob Health* 2015; **3:** e646–53.

79 Union for International Cancer Control (UICC). Global task force on radiotherapy for cancer control: secondary global task force on radiotherapy for cancer control. http://gtfrcc.org/global-radio-therapy/ (accessed May 31, 2015).

80 Jaffray DA, Gospodarowicz MK. Chapter 14. Radiation therapy for cancer. In: Gelband H, Jha P, Sankaranarayanan R, Horton S, eds. Disease control priorities, 3rd edn. Volume 3: cancer. Washington, DC: World Bank, 2015 (in press).

81 Bray F, Znaor A, Cueva P, et al. Planning and developing population-based cancer registration in low- and middle-income settings. Geneva: International Agency for Research on Cancer (IARC) Technical Publications, 2014.

82 Hewitt M, Greenfield S, Stovall E. From cancer patient to cancer survivor: lost in transition. Washington, DC: Institute of Medicine and National Research Council, 2005.

83 Pontén J, Adami H-O, Bergstrom R, et al. Strategies for global control of cervical cancer. *Int J Cancer* 1995; **60**: 1–26.

84 Metzger ML, Howard SC, Fu LC, et al. Outcome of childhood acute lymphoblastic leukaemia in resource-poor countries. *Lancet* 2003; **362:** 706–08.

85 Pramesh CS, Badwe RA, Sinha RK. The national cancer grid of India. *Indian J Med Paediatr Oncol* 2014; **35:** 226–27.

86 Institute for Health Metrics and Evaluation. Financing global health 2012: the end of the golden age? Seattle: Institute for Health Metrics and Evaluation, 2012.

87 Peabody JW, Taguiwalo MM, Robalino DA, Frenk J. Improving the quality of care in developing countries. In: Jamison DT, Breman J, Measham AR, et al, eds. Disease control priorities in developing countries, 2nd edn. Washington, DC: World Bank, 2006: 1293–307.

88 Varmus H, Trimble EL. Integrating cancer control into global health. *Sci Transl Med* 2011; **3:** 101–28.

89 Trimble EL, Rajaraman P, Chao A, et al. Chapter 15. Cancer research: the need for national commitment. In: Gelband H, Jha P, Sankaranarayanan R, Horton S, eds. Disease control priorities, 3rd edn. Volume 3: cancer. Washington, DC: World Bank, 2015 (in press).