

Affordable cancer care 2



Evidence-informed frameworks for cost-effective cancer care and prevention in low, middle, and high-income countries

Kalipso Chalkidou, Patricio Marquez, Preet K Dhillon, Yot Teerawattananon, Thunyarat Anothaisintawee, Carlos Augusto Graboys Gadelha, Richard Sullivan

Evidence-informed frameworks for cost-effective cancer prevention and management are essential for delivering equitable outcomes and tackling the growing burden of cancer in all resource settings. Evidence can help address the demand side pressures (ie, pressures exerted by people who need care) faced by economies with high, middle, and low incomes, particularly in the context of transitioning towards (or sustaining) universal health-care coverage. Strong systems, as opposed to technology-based solutions, can drive the development and implementation of evidence-informed frameworks for prevention and management of cancer in an equitable and affordable way. For this to succeed, different stakeholders—including national governments, global donors, the commercial sector, and service delivery institutions—must work together to address the growing burden of cancer across economies of low, middle, and high income.

Introduction

Cancer is one of the most important and expensive non-communicable diseases facing health-care systems globally. However, in high-income countries, major gains in some cancers (eg, breast and bowel) are offset by increasingly divergent outcomes between affluent and deprived populations.¹ Ample evidence shows that the cost of cancer is becoming, or has already become, unaffordable in many countries.² The claim that increased expenditure leads to better outcomes is not substantiated by data³ and, in some cases, there is an inverse relation between spending and outcomes. Structural, organisational, and cultural issues are equally important factors—if not more so—in the delivery of effective cancer treatment than expenditure alone.⁴ The requirement for priority-setting and cost-effectiveness as a core part of cancer systems is now clear, particularly in view of the cost of cancer's growing disease burden.⁵

In high-income settings, the increasingly unaffordable care model for cancer focuses on specialist treatment (typically at the expense of primary care), and expensive technologies and medicines. Scant attention is paid to cancer prevention and the structural issues in the treatment care model (eg, duplication of pathways), with few or no options for transition across providers and care settings (eg, referral between primary and secondary care). However, with more than 70% of the global cancer burden falling in middle-to-low-income settings, most people with malignant disease do not have access to the resources and systems available in high-income countries. As a result, the high-income care model is unlikely to be a solution for patients with cancer in resource-limited settings as progress is made towards some form of universal health-care coverage. The challenges of access to cancer care, and its quality and affordability, are shared between high-income countries and poorer nations,

despite their very different starting points in terms of infrastructure and levels of wealth. Shared challenges point to shared solutions. Less well-embedded commercial and professional vested interests, particularly in low-income settings, might make restructuring the health-care system easier and gear it towards tackling the challenge of cancer.

Many evidence-based guidelines have been published about improvement of practice, including for cancer care.⁶ Implementation issues are equally important, and guidelines must be linked to regulation, providers' accreditation, professionals' and patients' education, and payment reform. However, evidence-based medicine in high-income countries has almost always steered away from issues of payment, affordability, and value for money. In the UK, the National Institute for Health and Care Excellence (NICE) is unique in that it explicitly considers costs and cost-effectiveness when developing guideline recommendations. In the context of guidelines, trade-offs must be made and priorities for cost-effective resource allocation set—ideally in an open manner and based on evidence—between diseases, for prevention and treatment of the same disease, and for different technologies. Further downstream, comparative evidence of clinical and cost-effectiveness can (and increasingly does) affect technology procurement, pricing decisions, and provider payment mechanisms, including pay-for-performance initiatives. For example, NICE has developed a set of indicators for the world's largest pay-for-performance scheme in primary care—namely, the UK's Quality and Outcomes Framework.

Here, we discuss how evidence-informed frameworks apply to different stages of cancer management and prevention, from purchasing to provision of care. Furthermore, we look at how we can improve the effectiveness, equity, efficiency, and affordability of cancer care systems globally, using case studies from a selection of countries across the Human Development Index.

Lancet Oncol 2014

Published Online
February 14, 2014
[http://dx.doi.org/10.1016/S1470-2045\(13\)70547-3](http://dx.doi.org/10.1016/S1470-2045(13)70547-3)

See Online/Comment
[http://dx.doi.org/10.1016/S1470-2045\(14\)70062-2](http://dx.doi.org/10.1016/S1470-2045(14)70062-2)

This is the second in a **Series** of three papers on affordable cancer care

NICE International, London, UK (K Chalkidou PhD); World Bank, Accra, Ghana (P Marquez MD); South Asia Network for Chronic Disease, Public Health Foundation of India, New Delhi, India (P K Dhillon PhD); Health Intervention and Technology Assessment Program (HITAP), Ministry of Public Health, Nonthaburi, Thailand (Y Teerawattananon MD); Department of Family Medicine, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand (T Anothaisintawee PhD); Ministry of Health, and the National School of Public Health, Oswaldo Cruz Foundation, Brasilia, Brazil (Prof C A G Gadelha PhD); and Kings Health Partners Cancer Centre and Institute of Cancer Policy, Kings College, London, UK (Prof R Sullivan MD)

Correspondence to:
Dr Kalipso Chalkidou,
NICE International, London
SW1 2BU, UK
kalipso.chalkidou@gmail.com

For more on the **Quality and Outcomes Framework** see
<http://www.nice.org.uk/aboutnice/qof>

High-income countries

The modern approach to dealing with the burden of cancer in high-income countries is becoming financially unsustainable. The focus on hospital-based specialist care, expensive therapeutic technologies (eg, proton-beam therapy), and patent-protected drugs that typically have marginal effects on survival or quality of life, coupled with very few examples of national or system-level primary care and prevention truly embedded within the system, has made it difficult to address escalating costs. In an unusual move, in April 2013, more than 100 experts in leukaemia stated their concerns about the unsustainable nature of drug prices in the USA,⁷ suggesting the high costs could compromise some patients' access to treatment and harm national health-care systems. Disparities in cancer incidence, mortality, and spending also exist across Europe (figures 1 and 2).^{8,9}

For more on PCORI see <http://www.pcori.org/pfaawards/>

USA

The USA has a privatised health system—albeit one that absorbs substantial amounts of public resources—that features high out-of-pocket payments, strong private insurance and provider sectors, and vocal professional and pharmaceutical lobbies. Furthermore, the discussion around the US health system suffers from an ideological (or perhaps political) aversion to openly talking about difficult choices related to costs and cost-effectiveness. The affordability challenge is prominent: parts of the population can be faced with substantial costs for treatment that can drive them into bankruptcy,¹⁰ or force an individual to delay or forego necessary care.¹¹

Moreover, other patients, even those with generous insurance coverage (eg, the Medicare scheme), can either encounter out-of-pocket costs^{12,13} or be exposed to harm from overtreatment¹⁴ when suffering from cancer. Cancer is now a substantial burden for patients and their families, and for the health-care system and the broader US economy, costing more than US\$120 billion in 2010; charges are projected to reach almost US\$160 billion by 2020.¹⁵

In response, attempts have been made to manage escalating costs and treatment overuse by generating evidence about real-world best practice and making this information public for use by patients, payers, and providers. The Patient-Centered Outcomes Research Institute (PCORI), which is spearheading US President Obama's Comparative Effectiveness Research movement, has (since its launch in 2011) made available tens of millions of dollars for research into the comparative effectiveness of technologies and services for management of priority diseases, including cancer.

Historically, agencies of the US Government (eg, the Agency for Healthcare Research and Quality) and US professional associations (eg, the American Society for Clinical Oncology) have produced clinical guidelines. However, efforts to develop guidelines, particularly when led by specialists, have sometimes been unobjective.^{16,17} Further upstream, generation of evidence and its selective publication¹⁸ can be subject to bias and affected by professional and commercial interests. The existence of evidence or guidelines without the support of institutional and legal frameworks, or unlinked with payment, education, and other means of ensuring their implementation, is likely to have little effect on the efficiency and quality of cancer care in the USA.

Indeed, current payment mechanisms make controlling expenditure based on the most effective treatment methods almost impossible for Medicare, the largest single payer in the US health-care system.¹⁹ Medicare's recent decision to pay for sipuleucel-T (US\$93 000 per course), an expensive prostate cancer vaccine, is a case in point.²⁰ While private insurers are experimenting with ways to get guidelines into practice through provider payment,²¹ as long as comparative cost-effectiveness remains outlawed,²² clinical guidelines are unlikely to inform decisions by payers (individual patients and insurance companies).

England and Wales

By contrast with the USA, the UK has the National Health Service (NHS), a universal social health system. Within this organisation, NICE has been working with professional associations, patient groups, and economists since 1999 to produce clinical guidelines that are based on both clinical and economic evidence, using a process that aims to protect against bias and vested interests.²³ Somewhat disproportionately to the country's disease burden, cancer is by far the most frequent guideline

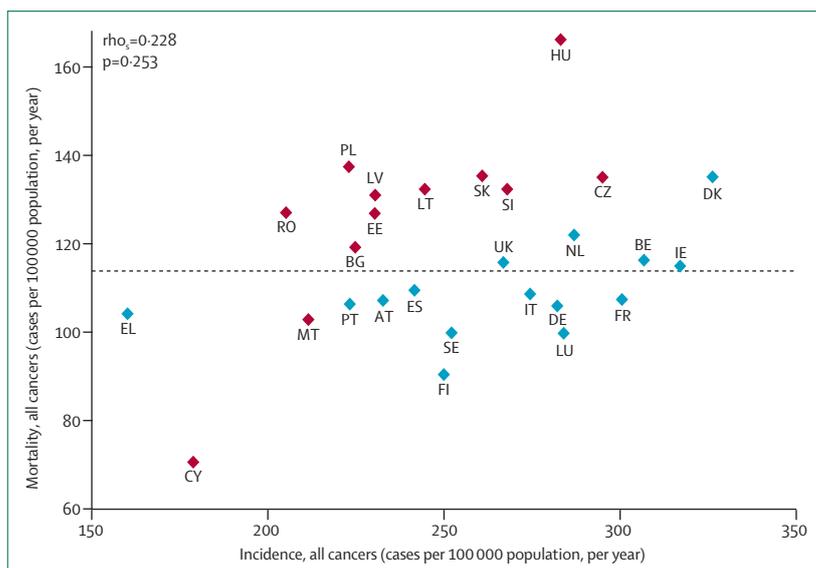


Figure 1: Disparities in cancer incidence and mortality across Europe

Data obtained from reference 8. Affluent UN member states (mainly from western Europe) are depicted in blue and more deprived areas (typically from eastern Europe) are shown in red. AT=Austria. BE=Belgium. BG=Bulgaria. CY=Cyprus. CZ=Czech Republic. DE=Germany. DK=Denmark. EE=Estonia. EL=Greece. ES=Spain. FI=Finland. FR=France. HU=Hungary. IE=Republic of Ireland. IT=Italy. LT=Lithuania. LU=Luxembourg. LV=Latvia. MT=Malta. NL=Netherlands. PL=Poland. PT=Portugal. RO=Romania. SE=Sweden. SK=Slovakia. SI=Slovenia. UK=United Kingdom.

topic.²⁴ NICE also considers whether cancer drugs should be available through the NHS and occasionally negotiates price deals for the NHS based on evidence of value. Increasingly, companies are making (confidential) price concessions. Most importantly, although less well known, is NICE's role in informing national policy on prevention (eg, prevention of skin and lung cancer).²⁵

However, the highly political nature of cancer in the UK, by which some politicians use the disease to garner support, means that mechanisms have been developed to bypass the NICE process, working against evidence of clinical, economic, and even societal values.²⁶ For example, the cancer drugs fund—introduced by the UK Government after unfavourable public reactions to NICE decisions on a number of cancer drugs—is a means of paying for drugs deemed by NICE not to be cost effective, and the end-of-life premium instructs NICE's committees to be more generous when assessing life-extending drugs used towards the end of life—so far being applied to cancer drugs alone.²⁷ Support for treatment versus prevention is also reflected in government funding, which only applies to drugs and other technologies, disregarding prevention interventions. This ethos is further reinforced through the NHS constitution. Empirical evidence²⁸ shows that such preferential consideration of cancer drugs results in distortions and crowding out of other diseases, with a real and measurable cost on human lives. Through its insistence on evidence and due process, NICE is likely to have made a contribution to improving quality and efficiency in the English NHS. Although we cannot attribute the observed improvement in cancer mortality outcomes, such as in breast cancer mortality,²⁹ to NICE's activities, NICE offers an integrated evidence-informed and implementable framework for consideration of costs and effects of treatment and services across the board, from prevention to treatment and from primary care services to tertiary care and drug pricing. The NICE framework is generating interest in countries around the world, including the USA, as shown by the work of NICE International.

Middle-income countries

The World Bank's definition of middle-income countries covers a very wide range of nations at different stages of economic development and with very different health-care systems. India belongs in the lower group of middle-income countries (income of about US\$1000–4000 per person per year) whereas Brazil and Thailand are in the upper level (annual incomes roughly US\$4000–12 500). Although the incidence of all types of cancer is highest in high-income countries, mortality is higher in all middle-income countries.³⁰ In most middle-income countries, cancer control programmes remain under-resourced, with inadequate infrastructure and weak systems (ie, policy decisions regarding health priorities are based on little evidence, with scant quality assurance mechanisms and inadequate

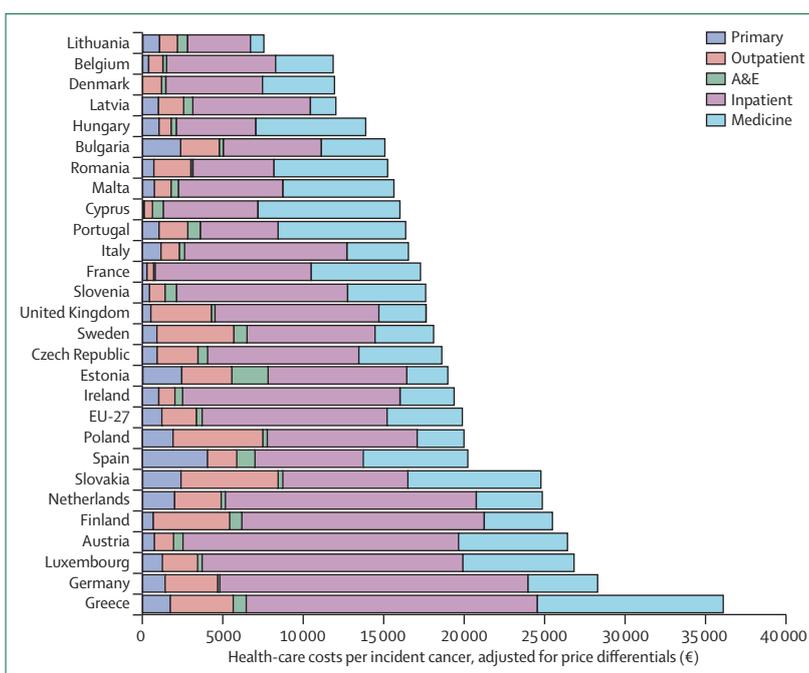


Figure 2: Health-care costs per incident cancer across Europe

Data obtained from reference 9. A&E=accident and emergency department.

monitoring and evaluation of investment). Timely and equitable access is compromised further by continued reliance on out-of-pocket contributions. Health-care expenditure in middle-income countries ranges from US\$30 per person in Pakistan to US\$1121 per person in Brazil, with publicly funded universal health coverage so far achieved in only 22 middle-income countries.

Due to the rising incidence of non-communicable diseases, including cancer, issues of quality, affordability, and access to evidence-based cost-effective treatments should become important issues for public policy. The trend, however, is for investment in high-cost technologies of marginal benefit, concentrated in urban tertiary hospitals (ie, specialist centres such as university hospitals), while across the broader system there is limited institutional infrastructure for development, dissemination, and implementation of evidence-based guidelines for provision and for purchasing of care. Furthermore, social obstacles such as cancer fatalism (ie, the belief that death is inevitable when cancer is present) and social discrimination against patients, which often contribute to late diagnosis and presentation, are the least likely to be addressed through investments in tertiary care clinics.

India

As India strives to meet the Millennium Development Goals by 2015, it must simultaneously address its growing burden of non-communicable diseases, which accounts for 54% of the country's mortality.³¹ Cancer is the third most common cause of death from non-communicable

For more on the NHS constitution see <http://www.gov.uk/government/publications/the-nhs-constitution-for-england>

For more on NICE International see <http://www.nice.org.uk/niceinternational>

diseases in India, where people with little education and women from rural populations have higher mortality rates than urban residents.³¹ National policies exist for primary prevention, early detection, and increased capacity for the building of cancer institutions and hospitals (table 1), but these initiatives have not yielded higher levels of cancer awareness, led to a rise in earlier-stage cancer diagnosis,³² provided enough sufficiently trained personnel,³³ or resulted in better survival (table 2).³⁴ This situation reflects a public health system with poor financing, access, availability, and quality of care.³⁵

Although equity has been a guiding principle for India's health care since independence,³⁶ most urban and rural populations have been seeking care from a rapidly growing, unregulated, and more expensive private sector (in 1947, the private sector accounted for 8% of all hospitals; in 2011, it accounted for 93% of hospital, 80% of outpatient visits, and 57% of inpatient visits).³⁷ Despite an overall growth of 7% since 2005, India's public spending on health is among the lowest in the world (1% of gross domestic product [GDP] in 2008–09),³⁵ leaving

its citizens to pay out-of-pocket expenses for most health care.³⁶ The disadvantaged (based on caste, education, income, and place of residence) face the highest cancer mortality rates³⁸ along with the largest proportion of out-of-pocket expenditure and the greatest risk of catastrophic health spending, which accounts for more than half of Indian households that fall into poverty.³⁶ National insurance schemes that target the most vulnerable populations (eg, Rashtriya Swasthya Bima Yojana [RSBY]), and state-level schemes that either increase health-care coverage (eg, Aarogyasri in Andhra Pradesh) or select patients with cancer (eg, in the Punjab and Tamil Nadu states), all provide important contributions but fall short of substantially reducing the financial burden for many cancers. For example, in 2013, RSBY provided US\$461·50 per family per year. In a study of cancer patients at government hospitals in five Indian states, the average cost of investigations and treatment was estimated at US\$967·50; costs at private institutes would be much higher.³⁹

Cancer has the highest out-of-pocket expenses for admissions, outpatient visits, and risk of catastrophic

For more on RSBY see
<http://www.rsby.gov.in/>

For more on Aarogyasri see
<http://www.aarogyasri.gov.in/>

	Years	Objectives	Cancer activities
National Cancer Control Programme	1975, 1984–85	Primary prevention of tobacco-related cancers; secondary prevention of cancers of the cervix, mouth, breast, etc; tertiary prevention includes extension and strengthening of therapeutic services, including pain relief on a national scale, through regional cancer centres and medical colleges (including dental colleges)	Establishment of 17 regional cancer control centres; provision of diagnostic facilities at the level of primary and secondary care; opportunistic screening; filling gaps in radiotherapy units; information, education, and communication activities on tobacco, lifestyle changes, and symptom awareness
National Programme for Prevention and Control of Cancer, Diabetes, Cardiovascular Diseases and Stroke	2010	Prevention and control of common non-communicable diseases through behaviour and lifestyle changes; early diagnosis and management of common non-communicable diseases; to build capacity at various levels of health care for prevention, diagnosis, and treatment of common non-communicable diseases; training of human resources within the public health setup—ie, doctors, paramedics, and nursing staff—to cope with the increasing burden of non-communicable diseases; establishment and development of capacity for palliative and rehabilitative care	Community awareness through information, education, and communication (prevention and early symptoms); capacity building of district hospitals (to provide common diagnostic services, chemotherapy, and palliative care) and tertiary care facilities (for training); cancer research and surveillance; monitoring and evaluation
Rashtriya Swasthya Bima Yojana	2007	Provision of cashless inpatient coverage (Rs30 000 [US\$500] per family per year) for people living below the poverty line; beneficiaries pay a Rs30 (\$0.50) registration fee, whereas central and state governments pay a premium to the insurer on basis of competitive bidding; expansion of beneficiaries to include building and other construction workers, Mahatma Gandhi National Rural Employment Guarantee Act (MGNREGA) beneficiaries, street vendors, tobacco beedi workers, and domestic workers	Covers costs related to admissions for cancer; does not cover early detection, diagnostic, or treatment costs for outpatient visits
National Rural Health Mission	2005	To provide accessible, affordable, and quality health care to the rural population, particularly vulnerable communities, to reduce maternal mortality (from 407 deaths per 100 000 livebirths to 100 deaths per 100 000 livebirths), infant mortality (60 deaths per 1000 livebirths to 30 deaths per 1000 livebirths), and total fertility (from 3.0 births per lifetime to 2.1 births per lifetime) by 2012; improvement of manpower through provision of accredited social health activists (ASHAs), who are trained voluntary community health workers with links to the community (one ASHA per 1000 in every village); increased financing for health; capacity building for subcentres, primary health centres, community health centres, district hospitals, first referral units, and mobile medical units for outreach; monitoring and accountability	Preventive and promotional health educational services on tobacco, alcohol, diet, obesity, and physical activity; screening for common cancers; strengthening of teaching at tertiary care institutions for leadership in research and practice—cancer is identified as a priority condition; policy interventions through tobacco control
12th Five Year Plan on Health	2012–17	Expansion of health care towards the long-term objective of universal health-care coverage in India; reduction of maternal mortality (to 100 deaths per 100 000 livebirths), infant mortality (to 25 deaths per 1000 livebirths), and total fertility (to 2.1 births per lifetime) by 2017; prevention and reduction of under-nutrition in children younger than 3 years, to half the level in the National Family Health Survey 3; prevention and reduction of anaemia among women aged 15–49 years, to 28%; raising of the child sex ratio in children age 0–6 years, from 914 girls per 1000 boys to 950 girls per 1000 boys; prevention and reduction of the burden of communicable and non-communicable diseases (including mental illness) and injuries; reduction of out-of-pocket expenditure for poor households	Preventive and promotional health educational services on tobacco, alcohol, diet, obesity, and physical activity; screening for cervical, breast, and oral cancer; strengthening of teaching at tertiary care institutions for leadership in research and practice—cancer is identified as a priority condition; policy interventions through tobacco control, including raising taxes, enforcing bans on consumption in electronic media, counselling to quit, and clean indoor air legislation

Table 1: National programmes, policies, and objectives that affect cancer control in India

	Total (per 100 000)	Communicable, maternal, neonatal, and nutritional disorders	HIV /AIDS and tuberculosis	Maternal disorders	Nutritional deficiencies	Non-communicable diseases	Cancer	Injuries
Mortality (n=9 938 490)								
Proportion of total	..	35.0%	6.0%	0.6%	1.7%	53.5%	6.7%	11.5%
Rate per 100 000	811.2	284.3	49.0	5.19	13.6	433.7	54.1	93.2
Morbidity (DALYs; n=518 879 000)								
Proportion of total	..	42.7%	4.8%	0.8%	4.6%	45.4%	8.1%	11.8%
Rate per 100 000	42352.3	18105.3	2025.2	323.1	1943.7	19232.7	1558.5	5014.2

DALYs=disability-adjusted life-years.

Table 2: Mortality and morbidity (DALYs) for communicable diseases, non-communicable diseases, and injuries that receive high international priority and funding in India

health spending among non-communicable diseases in India: 51% of Indian households with cancer borrowed money or sold assets to finance inpatient care.⁴⁰ Most costs are accounted for by deregulated and increasing drug prices.³⁶ Some relate to India's essential medicines, such as fluorouracil, for which the price variation between bulk and retail differs by 1166%,⁴¹ and trastuzumab, a course of which costs more than ten times India's per-capita income. Perhaps as a result of the high cost and pressures from the Indian Government, Roche recently gave up its patent for trastuzumab in India. The high-level expert group on universal health coverage for India³⁷ proposes universal access to what it deems essential drugs, of which 15.1% are anti-cancer treatments. The group aims to bring about universal access by increasing public procurements, curtailing irrational use, pricing drugs on the basis of supply-induced demand, and safeguarding them from so-called evergreen patents (ie, a strategy to extend the life of a patent by making small changes to a drug), and through use of an autonomous council to generate evidence on cost-effective practices and to monitor their implementation.³⁷

Thailand

Thailand established a tax-based universal health-care system in 2002, although its rapidly ageing population and continued introduction of high-cost technologies for cancer care are increasing the pressure on this system. Inability to ensure access to essential cancer treatments for the Thai population led the Thai Ministry of Public Health to grant compulsory licences for four patented cancer drugs in January, 2008: letrozole for breast cancer, docetaxel for breast and lung cancer, erlotinib for lung cancer, and imatinib for gastrointestinal stromal tumour (GIST) and leukaemia. Although the decision was contentious, findings of an evaluation by local scholars of the health and economic impact of the policy show that the public health benefits were generally positive, particularly with respect to access and affordability.⁴²

The Thai benefit package comprises the national list of essential medicines and the universal health-care package for other interventions—eg, high-cost investiga-

tions, surgical procedures, and rehabilitation. All relevant stakeholders (public health managers, health professionals, academics, civil society, patients' representatives, the general population, and industry representatives) play a part in setting the research agenda for development of the universal health coverage benefit package. In recent years, comprehensive assessment of population-based cancer prevention, and screening and provision of several cancer treatments, have led to the adoption of new technologies or to the revision of the previous benefit package for cancer prevention and control (table 3).

Data for cost-effectiveness and the effect of the health-care budget on introduction of new health technologies are used to guide Thai development of cancer prevention and control programmes. Preventive interventions are more likely to represent greater value for money than are cancer treatments. Having gained strong political support from Thai decision makers, interventions with cost-savings or good cost/benefit ratios have been included in the benefit package. However, because cost-effectiveness results depend largely on epidemiology, health, and the economic infrastructure, interventions judged cost effective in other countries with universal health-care systems might not be in another. For example, although mammography screening for breast cancer is cost effective in Europe and North America, it is unlikely to be good value in Thailand, even for once-in-a-lifetime screening, because of the much lower prevalence of breast cancer and relatively higher cost of mammography screening in Thailand compared with high-income settings.⁴³ Thus, country-specific intervention selection and assessment are important, and such geopolitical factors must be taken into account by decision makers.

Brazil

Brazil is the only country in the world with a population of more than 100 million people to have a constitutional right to health on a universal, comprehensive, and equitable basis. Its experience in cancer reflects a major transformation of an emerging economy committed to building a welfare state while catching up economically and technologically with developed economies. In the

	Strategy	Intervention	Comparator	Incremental cost-effectiveness ratio (Baht per quality-adjusted life-year)	Budget effect (million Baht per year)	Inclusion in universal health-care coverage benefit package
Hepatocellular carcinoma	Prevention	Population-based HBsAg screening for people age 31–40 years	No screening	Cost saving	NA	Yes
Hepatocellular carcinoma	Prevention	Lamivudine in HBsAg-positive individuals, and administration of tenofovir after development of lamivudine resistance	Do nothing	Cost saving	NA	Yes
Alcohol-associated malignant disease	Prevention	Screening for an alcohol-use disorder with the Alcohol, Smoking, and Substance Involvement Screening Test (ASSIST), followed by brief intervention in people age 15–59 years	No screening	Cost saving	NA	Under consideration
Smoking-associated malignant disease	Prevention	Application of a community pharmacist-based smoking cessation programme	Usual care	Cost saving	NA	Under consideration
Cervical cancer	Screening	Visual inspection with acetic acid every 5 years for women aged 30–45 years, followed by Papanicolaou smear every 5 years for women aged 50–60 years	No screening	Cost saving	NA	Yes
Chronic myeloid leukaemia resistant to standard-dose imatinib	Treatment	Dasatinib	High-dose imatinib (800 mg/day)	Cost saving	NA	Under consideration
Chronic myeloid leukaemia resistant to standard-dose imatinib	Treatment	Nilotinib	High-dose imatinib (800 mg/day)	72 908	..	Under consideration
Cervical cancer	Prevention	HPV vaccine for girls aged 15 years	Papanicolaou smear for women aged 35–60 years, every 5 years	181 000	6000	No
Breast cancer	Screening	Once-in-a-lifetime population-based mammographic screening for women aged 40–49 years	No screening	1 847 481	2086	No
Breast cancer	Screening	Once-in-a-lifetime population-based mammographic screening for women aged 50–59 years	No screening	1 368 764	1579	No
Advanced-stage gastrointestinal stromal tumour	Treatment	Imatinib 400 mg/day, followed by sunitinib 50 mg/day if disease cannot be controlled	Imatinib 400 mg/day, followed by palliative care if disease cannot be controlled	2 273 414	695	No
Advanced-stage clear-cell renal-cell carcinoma	Treatment	Interferon α , followed by palliative care	Palliative care	478 486	19	No
Advanced-stage clear-cell renal-cell carcinoma	Treatment	Sunitinib, followed by palliative care	Palliative care	1 887 373	131	No
Advanced-stage clear-cell renal-cell carcinoma	Treatment	Bevacizumab plus interferon α , followed by palliative care	Palliative care	3 825 307	216	No
Cancer patients with anaemia induced by chemotherapy	Palliative	Recombinant human erythropoietin	Blood transfusion	3 700 000	NA	No

Data obtained from the Health Intervention and Technology Assessment Program (HITAP), 2013.

Table 3: Cost-effectiveness league table on cancer prevention and control in Thailand

For more on HITAP see <http://www.hitap.net/splash>

past 10 years, about 50 million people came out of poverty to join the middle classes, and the country has advanced 26 positions in the UNICEF index of infant mortality over the past two decades.

At the same time, a shift has taken place in the epidemiological profile of major diseases in Brazil, with chronic conditions becoming increasingly prominent.⁴⁴ Cancer is the second leading cause of death behind cardiovascular disease. Deaths from cancer—along with violence—have shown the most pronounced growth, increasing more than five times since the 1930s across the country.

In the new economic and sociopolitical environment of democracy, Brazil has shaped an institutional framework

for the incorporation of technology.⁴⁵ In 2011, a legal framework created the National Commission for the Incorporation of Technologies in the National Health System (CONITEC), to advise the Brazilian Ministry of Health. CONITEC—accountable to the Secretariat of Science, Technology, and Strategic Products—is transparent and participatory. It operates with standardised criteria, legislated timelines, and through an institutional network of 44 universities and hospitals for carrying out health technology assessment.⁵

Technology adoption in Brazil has to be compatible with objective universal access; oncology is the flagship of this policy, aiming to couple innovation with sustainability through three components. First, the

Brazilian Government is attempting to bring together different national policy priorities through the Health Economic Industrial Complex.⁴⁶ In the context of the Health Economic Industrial Complex, the Ministry of Health is involved in defining the research agenda and in bringing together technology adoption in line with the country's industrial, clinical research, and innovation policies. Second, a proactive approach is needed with respect to technology incorporation. Figure 3 shows the current trend, with the Ministry of Health driving the agenda for health technology assessment. Third, the Brazilian Government is working to adopt new technologies, with several drugs incorporated into the health system only in the past 2 years—eg, trastuzumab, interferon alfa, rituximab, erlotinib, gefitinib, and HPV vaccination. Furthermore, Brazil has established clinical cancer research networks, public-private partnerships for both product development and transfer of practical knowledge (eg, in relation to HPV vaccination), and an innovation network in oncology products, which all accord with the principle of sustainable universal access.

The Brazilian experience in oncology emphasises the importance of systemic actions towards technology incorporation, research, and innovation. Such a perspective empowers the Brazilian Government to address the problem of judicial challenges driving technology adoption decisions, by presenting the legal system with scientific evidence and with due process underpinning decisions—positive and negative—on new technologies.

Low-income countries

Several projects promote use of evidence in clinical practice in low-income countries, through primary research, systematic reviews (eg, the Cochrane collaboration and WHO's evidence-informed policy network [EVIPnet]), and economic evaluation (eg, the Disease Control Priorities Project and WHO's CHOICE programme). Several consulting initiatives have also been undertaken to develop formularies and design basic packages of services and technologies, typically in the context of Development Bank projects, or as part of WHO's essential drugs list.⁴⁷ However, few (if any) instances exist whereby guidelines have been developed, adjusted, applied locally, and updated regularly by local experts in response to demand by local policy makers and using local evidence and data. In 2012, a working group from the Center for Global Development reported little or no demand from institutions for making decisions on health-care priorities, including services and technologies, in low-income countries.⁴⁸ Furthermore, in a later report from the Center for Global Development entitled *More Health for the Money*, evidence-informed priority-setting processes were found to be rare among global donors. Basic packages or essential drug lists—when not linked to clearly articulated local demand, local institutions, and explicit decision-making processes—might not be of much use, particularly in the context of externally funded

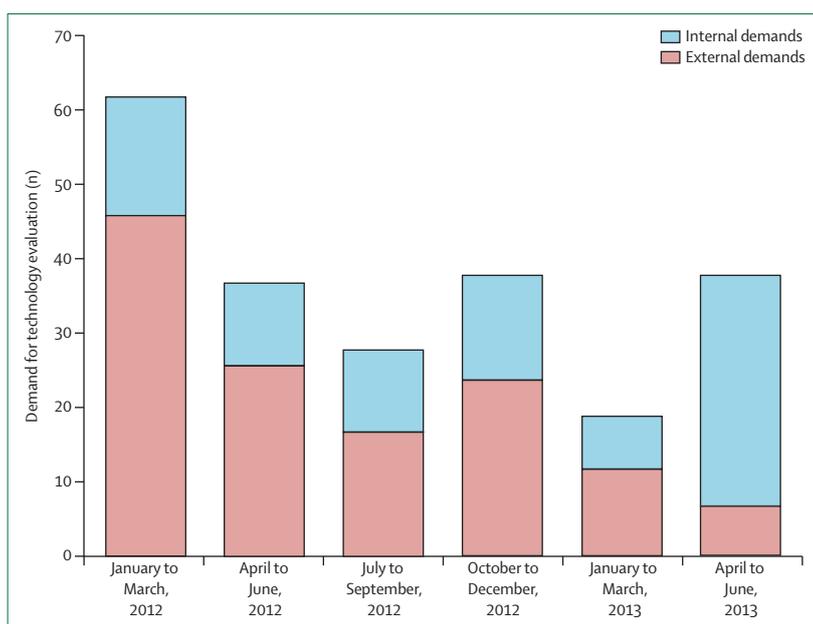


Figure 3: Demands for technology evaluations in Brazil, 2012–13

Data are absolute numbers of requests or demands for evaluation.

vertical programmes that focus on one specific infectious disease or technology rather than covering a range of diseases and interventions.

The WHO essential drugs list,⁴⁷ which is still influential, particularly among low-income countries, despite waning influence among emerging economies, is a case in point. Although the move to include more cancer drugs is understandable since about 47% of all cancer deaths globally occur in low-income countries, the latest proposal to add trastuzumab for breast cancer was initiated by three US-based groups (two universities and a development think-tank) and was supported by only the Rwandan Ministry of Health. The application for trastuzumab's inclusion includes scant consideration of local costs (including opportunity costs [ie, when making a choice precludes selection of alternatives in the future]), budgetary effect, and implementation challenges (eg, HER2 assays). These omissions are understandable perhaps, because such factors are fairly context-specific and hard to estimate by other countries. The proposal is under consideration by WHO's 19th Expert Committee.⁴⁹

Sub-Saharan Africa

In Africa, cancer burden is expected to more than double between 2008 and 2030. The number of new patients developing cancer is projected to rise from 681 000 to 1.6 million, and cancer-related deaths are projected to increase from 512 000 to 1.2 million.⁵⁰ Tellingly, while the lifetime risk of developing cancer in girls and women under the age of 64 in Africa is 30% lower than the risk in developed countries, the risk of dying is almost twice as high.⁵¹

For the Cochrane collaboration see <http://www.cochrane.org/>

For more on EVIPnet see <http://global.evipnet.org/>

For the Disease Control Priorities Project see <http://www.dcp2.org>

For more on CHOICE see <http://www.who.int/choice/en/>

For the report *More Health for the Money* see <http://www.morehealthforthemoney.org>

Cervical cancer—a preventable disease that usually results from sexual transmission of the human papillomavirus (HPV)—is one of the leading causes of premature death and ill health among women in sub-Saharan Africa.⁵² The global regions with the highest frequency of cervical cancer are western and eastern Africa,⁵³ where prevalence exceeds 50 cases per 100 000 population and age-standardised mortality is more than 40 deaths per 100 000 people. With scant screening services available for cervical cancer, a substantial number of patients are diagnosed with advanced-stage disease. In eastern and southern Africa, prevalence and prognosis are compounded by the high frequency of HIV, with HIV-positive women four to five times more likely to develop cervical cancer. A key problem in most cases is the limited health-system capacity to undertake widespread cytological screening. Of 20 countries reporting cervical cancer screening activities in 2009 in Africa, only 11 had ongoing country programmes; of 49 projects initiated, only six were funded by the domestic government.⁵⁴

Demonstration programmes in Botswana and Zambia⁵⁵ show how low-cost see-and-treat procedures (ie, immediate treatment after assessment or diagnosis) when adopted and integrated into existing service-delivery platforms—such as maternal and child health or HIV/AIDS programmes—can serve as equally effective alternatives to conventional diagnosis and management approaches, particularly for reaching women living in distant or underserved regions.

In view of the present high cost of HPV vaccines, countries need to use available evidence to decide the best strategies for their use to allocate resources efficiently and equitably. Although the GAVI Alliance has decided to support the introduction of HPV vaccines,⁵⁶ and public-private partnerships exist to make breast and cervical screening and HPV vaccination more available and affordable in sub-Saharan Africa, countries still need to consider the longer term budgetary implications for sustainable programmes, and they must ensure that effective treatment is available for detected malignant lesions.⁵⁷

Afghanistan

Afghanistan is one of the most fragile countries in the world. It has experienced almost uninterrupted conflict for the past 30 years, with the present conflict now lasting more than a decade. With no history of a functioning health-care system, creation of a basic package of health services, led by the International Security Assistance Force (ISAF/NATO), was a response to Afghanistan's dire health needs after decades of war.⁵⁸ The objective was to provide a bare minimum of essential health services that could be scaled up rapidly with the help of non-governmental organisations. The process of creating the basic package of health services took only 2 years, from 2001 to 2003.^{58,59} Disability and mental health have

now been added to the original priorities of maternal and child health and immunisation, nutrition, communicable diseases, disability, and supply of essential drugs.⁶⁰ Despite the immense challenges, this contracted care system has begun to develop structural mechanisms for delivery of affordable cancer care, and policy makers are keen to investigate institutional arrangements for development and application of evidence-informed pathways for non-communicable diseases—eg, through a recently signed memorandum of understanding between NICE and the Afghan Ministry of Health.⁶¹ In urban Afghanistan, non-communicable diseases still make up 45% of the burden of disability-adjusted life-years and 59% of deaths, and cancer risk-factor exposure (eg, smoking in men) continues to grow.⁶²

Moving beyond cancer treatment

Prevention, screening, early detection, and palliative care Table 4 presents summary comparative statistics on cancer epidemiology and cancer spending across the seven countries discussed—UK, USA, Brazil, India, Thailand, Afghanistan, and Botswana (taken as a representative sub-Saharan African country). Data from GLOBOCAN 2012 show that about 8·2 million deaths a year worldwide are attributable to cancer. Of these, more than 40% could be prevented by tackling key risk factors, including cancer-related infections (1·5 million deaths), smoking (1·5 million), alcohol use (0·35 million), and obesity (0·14 million).⁶⁴ With the global prevalence of obesity almost doubling in the past two decades, this risk factor is likely to cause even more cancer deaths in the future.

Reduction of risk factors can substantially lessen the risk of cancer and reduce cancer rates. For example, the cumulative risk of lung cancer for a 75-year-old smoker is 16%, compared with 10% for people quitting smoking at the age of 60 years, and 2% for those quitting at age 30 years.⁶⁵ In people who have stopped drinking alcohol, the risk of malignant disease of the larynx or pharynx falls by about 4% a year, and the risk of liver cancer diminishes by an average of 7% per year.⁶⁶ Giving up smoking and quitting or reducing alcohol consumption, vaccinating against hepatitis B, screening for cervical cancer, enhancing physical activity, and adopting healthier dietary habits are the most cost effective, if not always cost-saving, strategies for cancer prevention, yet they receive less attention (and less money) from payers and providers, compared with new drugs.

Of course, not all cancers are amenable to preventive interventions. For example, breast cancer prevention strategies, although important,⁶⁷ are unlikely to affect the proportion of incident cases and mortality. And whereas some cancers (eg, cervical cancer) can benefit from screening, others (eg, lymphoma and leukaemia) can only be managed by treatment.

In view of the frequency of advanced-stage cancer in countries of low and middle income, strategies for early

For GLOBOCAN 2012 data see
<http://globocan.iarc.fr>

	UK	USA	Brazil*	India	Thailand	Afghanistan†	Botswana‡§
Population (million)	63	314	201	1270	67	31	2.0
Proportion of population covered by public sector or public health insurance scheme	100%	31%	100% (75% use public system)	10–24%§	99%	6%	About 80%
Burden of disease (male/female DALYs lost to cancer, all ages [ASR per 100 000 population])¶	2487/2602	2473/2373	2381/2232	1606/1900	2294/2347	2080/2345	1846/1878
Cancers with highest incidence (based on ASRs)							
Men	Prostate; bowel; lung	Prostate; lung; bowel	Prostate; lung; bowel	Lung; lip and oral; stomach	Liver; lung; bowel	Stomach; oesophagus; lung	Oesophagus; prostate; lung
Women	Breast; lung; bowel	Breast; lung; bowel	Breast; cervix; bowel	Breast; cervix; bowel	Breast; cervix; lung	Breast; cervix; stomach	Cervix; breast; non-Hodgkin lymphoma
Health spending (% of GDP)	9.3%	17.9%	8.8%	3.9%	4.1%	9.6%	5.1%
Public/private split of health spending	83%/17%	46%/54%	49%/51%	31%/69%	70%/30%	6%/94%	61%/39%
Proportion of public health expenditure on cancer	18%	21%	2.42%	<1%	Not available	Not available	Not available

ASR=age-standardised rate. DALYs=disability-adjusted life-years. GDP=gross domestic product. *Data obtained from Instituto Brasileiro de Geografia e Estatística Português (IBGE), Instituto Nacional de Câncer José Alencar Gomes da Silva (INCA), and DataMonitor Healthcare. †All data extrapolated from urban hospital-based registries. ‡Data obtained from reference 63 and the World Bank. §Estimate based on coverage of Rashtriya Swasthya Bima Yojana in 2013; the scheme has not yet reached maximum coverage (currently reaching 21.2% of people living below poverty line, according to the Indian Government's Planning Commission). Other insurance schemes exist in India, which cover maternal and child health, and there are state-level insurance schemes, but neither of these are counted for the purpose of this estimate. ¶ASRs for DALYs are for all cancers (excluding non-melanoma skin cancers). ||Data taken from GLOBOCAN 2012 (<http://globocan.iarc.fr>; accessed Dec 26, 2013).

Table 4: Prevention, screening, early detection, and palliative care for cancer

detection have the potential to be both cost effective and more effective clinically, particularly as early-stage disease generally needs less extensive treatment with fewer side-effects. Breast cancer is a case in point, whereby raising awareness among women and increasing detection rates through clinical breast examination could lead to better health outcomes. No nationwide cancer screening programme exists in India, although a few states (eg, Tamil Nadu and Karnataka) have initiated population-level cervical screening and breast examination. Findings of an ongoing cluster-randomised trial in India⁶⁸ could provide valuable information about the role of clinical breast examination and visual inspection of the cervix for early cancer detection. Screening methods need to be low-cost, feasible, and acceptable for widespread adoption. In randomised controlled trials, both HPV screening (eg, a single HPV DNA test) and visual examinations have led to diminished mortality in cervical⁶⁹ and oral⁷⁰ cancer. Although visual examination or screening for oral cancer is being adopted for wider implementation, HPV testing will not replace visual inspection with either acetic acid or Lugol's iodine until it is cheaper, simpler, and faster than the current approach to screen and treat (with cryotherapy).^{69,71} The challenges of delayed diagnosis, advanced cancer stage, and low adherence to treatment in resource-constrained environments also present opportunities for cost-effective therapeutic innovation. India's rural trials on metronomics—the combination of repetitive, low-dose chemotherapy and drug repositioning—have created resurgent interest in a low-cost, low-dose, minimally toxic, acceptable, and clinically effective strategy for advanced or refractory cancer.⁷²

In primary prevention, India's biggest success in the fight against cancer could emerge from a different area.

The *12th Five-Year Plan* outlines plans to engage government, private, and non-governmental stakeholders in multisectoral efforts towards tobacco control, which could yield the most cost-effective prevention for up to a third of the world's cancer burden.

Although breast cancer is the second most common cancer among Thai women, Thailand has not yet established a national breast-cancer screening programme. With only 139 mammography machines in Thailand, every device serves about 74 000 women older than 45 years,⁷³ compared with one machine per 11 000 women in the USA.⁴ In view of this situation, research to develop a breast cancer risk-prediction model was initiated, with development of a screening questionnaire for all Thai women aged 40–59 years, to identify high-risk groups for mammography.⁷⁴ This approach could reduce the need for mammography from 7 601 145 women per year (based on universal screening) to 126 939 per year (for screen-identified high-risk groups). Although risk-stratified mammographic screening can result in missing a substantial proportion of breast cancer cases, since fewer than 10% of Thai women (mainly those of high socioeconomic status) have access to mammography services, targeting individuals at increased risk could save some women's lives and enhance equity and solidarity in Thailand's health-care system. A cluster-randomised trial of this screening approach is planned for 2014, before it is introduced nationwide.

Similar to the scant emphasis on prevention, palliative care is systematically underfunded, particularly in countries of low and middle income, despite the fact that 50% of cancer cases are not cured; therefore, an urgent need exists to relieve the pain of terminally ill patients and their caregivers.⁷⁵ Findings of systematic

For IBGE see <http://www.ibge.gov.br/english/>

For INCA see <http://www.inca.gov.br/estimativa/2012/>

For DataMonitor Healthcare see <http://www.datamonitorhealthcare.com>

For World Bank data see <http://datatopics.worldbank.org/hnp>

For the 12th Five-Year Plan see <http://12thplan.gov.in/>

reviews support the effectiveness of palliative care in different settings in terms of pain control, quality of life, and reduction of the overall cost of care, by decreasing the amount of time patients spend in acute hospital settings.⁷⁶ Although palliative care does not need high-cost technology and is widely applicable, the lack of access to palliative care in poor countries remains a major public health problem and a human rights issue.

For more on CENETEC see <http://www.cenetec.salud.gob.mx/>

For more on NCPAM see http://uhmis2.doh.gov.ph/doh_ncpam/

Recommendations for action

The need for well-coordinated national, and perhaps regional and global, cancer management policies that include prevention as part of their scope is vital. Without such policies, the cost for cancer care alone might compromise movement towards universal health-care coverage in countries of low or middle income and could potentially undermine the sustainability of universal care in high-income countries. WHO's Framework Convention on Tobacco Control (FCTC) is an example of when global mobilisation has resulted in a worldwide effect. We propose that evidence-informed frameworks—guidelines, technology appraisals, purchasing and provider payment, and general implementation policies—that are underpinned by the necessary information, technical and clinical capacity, and institutional mechanisms needed for their development and application locally can help address this challenge. To progress this agenda, several immediate actions or changes in policy are needed.

For more on FCTC see <http://www.who.int/fctc/en>

Empirical research

Economies of scale with respect to evidence-informed frameworks (ie, cost advantages gained from the size or throughput of an operation; eg, generating global evidence from local decision making) are a popular and sensible idea. However, further empirical research is needed to inform how we can build such economies of scale, from purchasing to delivery of high-quality affordable care. We need to better understand the aspects of evidence that are context-specific and generalisable, the best scientific methods for synthesis and interpretation of findings, and the process of translating research into policy and then implementing it locally. Such work needs to be practical and include policy makers from the outset; it does not need to repeat the development of complex toolkits and toolboxes, such as lists of essential services and technologies designed by institutes in developed regions, which are hard to implement in a local setting and tend to discourage policy makers.

National institutions

Governments, which are usually the main financial stakeholders in health-care services as systems move towards universal health-care coverage, need to invest in

their own national institutions for articulating research needs, guiding research commissioning, and synthesising research evidence, values, and practicalities of implementation through legitimate and accountable local processes. This work can then inform accreditation schemes, contracts and regulation, education, and payment reform. Mexico and the Philippines, for example, stand to benefit greatly from engaging their strong existing institutions responsible for making decisions on individual technologies—such as the National Centre for Health Technology Excellence (CENETEC) in Mexico and the National Centre for Pharmaceutical Access and Management (NCPAM) in the Philippines—in the design of pathways of care, performance measurement, and payment schemes. These can then be implemented through the major insurance schemes driving universal health-care coverage, such as Seguro Popular in Mexico and PhiHealth in the Philippines.

Donors

Multilateral and bilateral donors, particularly in low-income settings, can set an example by using scientific and context-specific evidence and due process during development of their own policies. For example, throughout production of WHO's essential drugs lists⁴⁷ and the World Bank's technical assistance projects, one-off clinical guidelines, drug formularies, and benefits packages were developed. Furthermore, during interactions with countries receiving aid, global donor agencies can help to set targets for tackling worldwide risk factors and for reducing the incidence of preventable malignant diseases such as lung and cervical cancer.

Industry

The commercial sector, particularly the health-care products industry, can contribute to evidence-informed policy-making by encouraging the establishment of, and cooperation with, national authorities keen to institutionalise purchasing and procurement practices. Such processes are a predictable means of negotiating with the increasingly concentrated and powerful purchasing power of insurance schemes, and with Ministries of Health in emerging markets that are moving towards universal health-care coverage. Low-price high-volume deals, price structures, and joint ventures might be the best alternative to the wave of intellectual property challenges.⁷⁷

Partnerships

Institutions and practitioners from developed and developing countries have a lot to gain from partnerships with each other, which can help to build capacity at purchasing, provision, and policy levels. For example, successful partnerships exist between: the Health Intervention and Technology Assessment Program (HITAP) and the Thai Ministry of Public Health; NICE and the Indian⁷⁸ and Chinese⁷⁹ Ministries of Health;

For more on HITAP see <http://www.hitap.net/splash>

King's Health Partners and Somaliland and Sierra Leone; and global paediatric cancer programmes led by the World Child Cancer and St Jude Children's Hospital.⁸⁰ Although only anecdotal evidence of benefit exists,⁸¹ additional research is needed to inform how such peer-to-peer partnerships can become more effective, and how to measure their effectiveness (including assessment of the effect on institution-strengthening).

Conclusions

As the examples of Thailand and Brazil show, implementation of comprehensive and sustainable cancer prevention and control programmes in middle-income countries needs systematic and evidence-informed frameworks for priority-setting. These frameworks need to go beyond particular technologies and instead must encompass all health-system components, including governance, financing, human resources, information technology, health products, service delivery, and effective mechanisms for evidence generation and translation. Guidelines and technology appraisals for cancer prevention and treatment need to be based on evidence of comparative clinical effectiveness and cost-effectiveness and social values: they must be adapted to the local context and the realities of implementation. Moreover, they need to be linked to taxation policy, providers' payment reform, audit and quality indicators and performance management, providers' and patients' education, and contractual agreements. Guidelines and technology appraisals should be priced realistically and linked to actual budgets, and they need to be updated regularly through a locally driven process. Only then can such evidence-informed frameworks be useful (and usable) policy methods.

But such evidence-informed frameworks need legitimate local institutions to develop or adapt guidelines and then to implement them, making explicit trade-offs in the context of a country's own budget and values.⁸² In low-income settings in particular, where well-funded donors can impose their own agendas on disease control,^{57,83} local institutions can help to wield the countervailing power of a country's government and service users against these externally imposed distorting priorities. Here is perhaps the point at which universal health-care coverage becomes a potentially powerful enabler of the necessary institutional, evidential, and technical capacity to develop or adapt and implement evidence-informed frameworks. The examples of Thailand and Brazil—and other major leaders in universal care such as Chile and Mexico—show that development and implementation of evidence informed frameworks within universal health-care coverage is possible in middle-income countries. However, nations with a low income may be adversely affected by global donors who provide most of the disposable funds for health care (beyond salaries and infrastructure) and so

Search strategy and selection criteria

We searched the Web of Science, PubMed, and LISTA with the following MESH terms: "affordability", "LMIC", "economics", "health systems development", and "priority setting". We also did a grey literature search (for reports not indexed in databases) using Google. All reports published in English were selected for review, covering the years 1990 to 2013. We chose case studies and comparative cross-country data that described how evidence can inform purchasing and provision and highlight opportunities for joint learning across countries at different stages of health system development and wealth (appendix pp 1–2).

For more on King's Health Partners see <http://www.kcl.ac.uk/aboutkings/worldwide/initiatives/global/global-health>

See Online for appendix

have a big role with respect to allocation of resources. Genuine commitment to universal health-care coverage on the part of governments is likely to force discussions about the governance and technical aspects of evidence-informed frameworks, including issues of appropriate care, benefits design and entitlements, and of deriving milestones and metrics for success, not only for cancer but also across diseases and conditions (rather than a new post-2015 Millennium Development Goal for cancer).⁸⁴ Funders and national governments, supported—in an ideal world—by advocates for one disease and one technology, and by patient and professional groups, have an opportunity to promote cost-effective population-level prevention and primary care for screening, early detection, and follow-up, through evidence-informed, participatory, and transparent policy-development processes.⁸⁵ This move can only be achieved by increasingly diagonal programmes that cut across diseases and technologies, going beyond isolated disease-specific decision making, for example, learning from the experiences and infrastructure of infectious disease networks. Only then can we effectively battle cancer and other chronic diseases.⁸⁶

Contributors

KC and RS were responsible for overall coordination of this paper, and for writing the discussion and recommendations sections and the UK and US sections. RS provided the section on Afghanistan. PM wrote the section on Botswana and sub-Saharan Africa. CAGG contributed to the section on Brazil. PD wrote about India. YT and TA provided the sections on Thailand and middle-income countries, and made general comments on the discussion and recommendations sections.

Conflicts of interest

We declare that we have no conflicts of interest.

Acknowledgments

We thank Sagri Negi for contributing to the India component of our report; Ana Raquel de Campos Dutra for help with the Brazilian section; and Klim McPherson for input on breast-cancer screening.

References

- 1 Albrecht T, McKee M, Alexe DM, Coleman MP, Martin-Moreno JM. Making progress against cancer in Europe in 2008. *Eur J Cancer* 2008; 44: 1451–56.
- 2 Meropol NJ, Schulman KA. Cost of cancer care: issues and implications. *J Clin Oncol* 2007; 25: 180–86.

- 3 Begley S. Is high spending on cancer care 'worth it'? April 9, 2012. <http://www.reuters.com/article/2012/04/09/us-cancercare-idUSBRE8380SA20120409> (accessed Nov 19, 2013).
- 4 Sullivan R, Peppercorn J, Sikora K, et al. Delivering affordable cancer care in high-income countries. *Lancet Oncol* 2011; **12**: 933–80.
- 5 Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. *PLoS Med* 2006; **3**: e442.
- 6 Smith TJ, Hillner BE. Ensuring quality cancer care by the use of clinical practice guidelines and critical pathways. *J Clin Oncol* 2001; **19**: 2886–97.
- 7 Experts in chronic myeloid leukemia. The price of drugs for chronic myeloid leukemia (CML) is a reflection of the unsustainable prices of cancer drugs: from the perspective of a large group of CML experts. *Blood* 2013; **121**: 4439–42.
- 8 Ades F, Senterre C, de Azambuja E, et al. Discrepancies in cancer incidence and mortality and its relationship to health expenditure in the 27 European Union member states. *Ann Oncol* 2013; **24**: 2897–902.
- 9 Luengo-Fernandez R, Leal J, Gray A, Sullivan R. Economic burden of cancer across the European Union: a population-based cost analysis. *Lancet Oncol* 2013; **14**: 1165–74.
- 10 Kantarjian HM, Fojo T, Mathisen M, Zwelling LA. Cancer drugs in the United States: *justum pretium*—the just price. *J Clin Oncol* 2013; **31**: 3600–04.
- 11 Banegas MP, Yabroff KR. Out of pocket, out of sight? An unmeasured component of the burden of cancer. *J Natl Cancer Inst* 2013; **105**: 252–53.
- 12 Davidoff AJ, Erten M, Shaffer T, et al. Out-of-pocket health care expenditure burden for Medicare beneficiaries with cancer. *Cancer* 2013; **119**: 1257–65.
- 13 Ubel PA, Abernethy AP, Zafar SY. Full disclosure: out-of-pocket costs as side effects. *N Engl J Med* 2013; **369**: 1484–86.
- 14 Chustecka Z. \$32 million: cost of overtreatment of prostate cancer. Feb 13, 2013. <http://www.medscape.com/viewarticle/779223> (accessed Nov 19, 2013).
- 15 Mariotto AB, Yabroff KR, Shao Y, Feuer EJ, Brown ML. Projections of the cost of cancer care in the United States: 2010–2020. *J Natl Cancer Inst* 2011; **103**: 117–28.
- 16 Institute of Medicine. Clinical practice guidelines we can trust. March 23, 2011. <http://www.iom.edu/Reports/2011/Clinical-Practice-Guidelines-We-Can-Trust.aspx> (accessed Nov 20, 2013).
- 17 Engelberg J, Parsons CA, Tefft N. First, do no harm: financial conflicts in medicine. Aug 13, 2013. http://papers.ssrn.com/sol3/papers.cfm?abstract_id=2297094 (accessed Nov 20, 2013).
- 18 Nguyen T-A-H, Dechartres A, Belgherbi S, Ravaud P. Public availability of results of trials assessing cancer drugs in the United States. *J Clin Oncol* 2013; **31**: 2998–3003.
- 19 Bach PB. Limits on Medicare's ability to control rising spending on cancer drugs. *N Engl J Med* 2009; **360**: 626–33.
- 20 Stein R. Review of prostate cancer drug Provenge renews medical cost-benefit debate. Nov 8, 2010. <http://www.washingtonpost.com/wp-dyn/content/article/2010/11/07/AR2010110705205.html> (accessed Nov 20, 2013).
- 21 Newcomer LN. Changing physician incentives for cancer care to reward better patient outcomes instead of use of more costly drugs. *Health Aff (Millwood)* 2012; **31**: 780–85.
- 22 Neumann PJ, Weinstein MC. Legislating against use of cost-effectiveness information. *N Engl J Med* 2010; **363**: 1495–97.
- 23 Bennett WL, Odelola OA, Wilson LM, et al. Evaluation of guideline recommendations on oral medications for type 2 diabetes mellitus: a systematic review. *Ann Intern Med* 2012; **156**: 27–36.
- 24 Chalkidou K, Culyer A, Littlejohns P, Doyle N, Hoy A. Imbalances in funding for clinical and public health research in the UK: can NICE research recommendations make a difference? *Evid Policy* 2008; **4**: 355–69.
- 25 National Institute for Health and Care Excellence. Skin cancer prevention: information, resources and environmental changes (PH32). January, 2011. <http://guidance.nice.org.uk/PH32> (accessed Nov 20, 2013).
- 26 Linley WG, Hughes DA. Societal views on NICE, cancer drugs fund and value-based pricing criteria for prioritising medicines: a cross-sectional survey of 4118 adults in Great Britain. *Health Econ* 2013; **22**: 948–64.
- 27 Faden RR, Chalkidou K, Appleby J, Waters HR, Leider JP. Expensive cancer drugs: a comparison between the United States and the United Kingdom. *Milbank Q* 2009; **87**: 789–819.
- 28 Claxton K, Martin S, Soares M, et al. Methods for the estimation of the NICE cost effectiveness threshold. November, 2013. [http://www.york.ac.uk/media/che/documents/papers/researchpapers/CHERP81_methods_estimation_NICE_costeffectiveness_threshold_\(Nov2013\).pdf](http://www.york.ac.uk/media/che/documents/papers/researchpapers/CHERP81_methods_estimation_NICE_costeffectiveness_threshold_(Nov2013).pdf) (accessed Nov 20, 2013).
- 29 Autier P, Boniol M, La Vecchia C, et al. Disparities in breast cancer mortality trends between 30 European countries: retrospective trend analysis of WHO mortality database. *BMJ* 2010; **341**: c3620.
- 30 Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D. Global cancer statistics. *CA Cancer J Clin* 2011; **61**: 69–90.
- 31 Progress in implementing measles mortality reduction strategies: India, 2010–2011. *MMWR Morb Mortal Wkly Rep*; **60**: 1315–19.
- 32 NCRP. Consolidated report of population based cancer registries, 2001–2004. Bangalore: National Cancer Registry Program, 2006.
- 33 Statistics Division, Ministry of Health and Family Welfare, Government of India. Rural health statistics in India, 2012. April 30, 2013. <http://nrhm.gov.in/images/pdf/publication/RHS-2012.pdf> (accessed Nov 20, 2013).
- 34 Sankaranarayanan R, Black RJ, Swaminathan R, Parkin DM. An overview of cancer survival in developing countries. *IARC Sci Publ* 1998; **145**: 135–73.
- 35 Reddy KS, Patel V, Jha P, Paul VK, Kumar AKS, Dandona L, for The Lancet India Group for Universal Healthcare. Towards achievement of universal health care in India by 2020: a call to action. *Lancet* 2011; **377**: 760–68.
- 36 Balarajan Y, Selvaraj S, Subramanian SV. Health care and equity in India. *Lancet* 2011; **377**: 505–15.
- 37 HLEG. High level expert group report on universal health coverage for India. New Delhi: Planning Commission of India, 2011.
- 38 Dikshit R, Gupta PC, Ramasundarahettige C, et al, for the Million Death Study Collaborators. Cancer mortality in India: a nationally representative survey. *Lancet* 2012; **379**: 1807–16.
- 39 Nair KS, Raj S, Tiwari VK, Piang LK. Cost of treatment for cancer: experiences of patients in public hospitals in India. *Asian Pac J Cancer Prev* 2013; **14**: 5049–54.
- 40 Mahal A, Karan A, Fan VY, Engelgau M. The economic burden of cancers on Indian households. *PLoS One* 2013; **8**: e71853.
- 41 Sengupta A, Joseph RK, Modi S, Syam N. Economic constraints to access to essential medicines in India. New Delhi: Centre for Technology and Development, Society for Economic and Social Studies, 2008.
- 42 Yamabhai I, Mohara A, Tantivess S, Chaisiri K, Teerawattananon Y. Government use licenses in Thailand: an assessment of the health and economic impacts. *Global Health* 2011; **7**: 28.
- 43 Anothaisintawe T, Teerawattananon Y, Tanthai N. Cost-utility of screening breast cancer with mammography once in a life time in Thai women. Bangkok: Health Intervention and Technology Assessment Program, 2013.
- 44 Almeida Ribeiro A, Sampaio MC, Barradas R. Condições de Saúde da população brasileira. In: Giovanella L, Escorel S, de Vasconcelos Costa Lobato L, de Carvalho Noronha J, de Carvalho AI, eds. Política e Sistemas de Saúde no Brasil. Rio de Janeiro: Fiocruz and Cebes, 2012: 143–81.
- 45 Moreno-Serra R, Smith PC. Does progress towards universal health coverage improve population health? *Lancet* 2012; **380**: 917–23.
- 46 Gadelha CAG, Maldonado J, Vargas M, Barbosa PR, Costa LS. A dinâmica do Sistema Produtivo da Saúde: inovação e complexo econômico-industrial. Rio de Janeiro: Fiocruz, 2012.
- 47 WHO. WHO model lists of essential medicines. October, 2013. <http://www.who.int/medicines/publications/essentialmedicines/en/> (accessed Nov 26, 2013).
- 48 Center for Global Development. Priority-setting in health: building institutions for smarter public spending. June 11, 2012. http://international.cgdev.org/sites/default/files/1426240_file_priority_setting_global_health_FINAL_0.pdf (accessed Jan 7, 2014).
- 49 WHO. Essential medicines selection: trastuzumab (addition)—adults. April 12, 2013. http://www.who.int/selection_medicines/committees/expert/19/applications/trastuzumab/en/ (accessed Nov 20, 2013).

- 50 Marquez P, Farrington JL. The challenge of non-communicable diseases and road traffic injuries in sub-Saharan Africa: an overview. Washington DC: World Bank, 2013.
- 51 Parkin DM, Sitas F, Chirenje M, Stein L, Abratt R, Wabinga H. Part I: cancer in Indigenous Africans—burden, distribution, and trends. *Lancet Oncol* 2008; 9: 683–92.
- 52 World Bank. World development report 2012: gender equality and development. Washington DC: The World Bank, 2011.
- 53 IARC. Cervical cancer incidence and mortality worldwide in 2008: summary. <http://globocan.iarc.fr/factsheets/cancers/cervix.asp> (accessed Nov 20, 2013).
- 54 Southern Africa Litigation Centre. Tackling cervical cancer: improving access to cervical cancer services for women in southern Africa. Nov 13, 2012. <http://www.southernafricalitigationcentre.org/1/wp-content/uploads/2012/11/CERVICAL-CANCER-Report1.pdf> (accessed Nov 20, 2013).
- 55 Ramogola-Masire D, de Klerk R, Monare B, Ratshaa B, Friedman HM, Zetola NM. Cervical cancer prevention in HIV-infected women using the “see and treat” approach in Botswana. *J Acquir Immune Defic Syndr* 2012; 59: 308–13.
- 56 GAVI Alliance. Human papillomavirus vaccine support. Oct 16, 2013. <http://www.gavi.org/support/nvs/human-papillomavirus-vaccine-support> (accessed Nov 20, 2013).
- 57 Glassman A. Separating the good from the bad on HPV. Dec 7, 2011. <http://international.cgdev.org/blog/separating-good-bad-hpv> (accessed Nov 20, 2013).
- 58 Strong L, Wali A, Sondorp E. Health policy in Afghanistan: two years of rapid change—a review of the process from 2001 to 2003, 2005. <http://crises.lshtm.ac.uk/files/2008/10/Health-Policy-in-Afghanistan-two-years-of-rapid-change.pdf> (accessed Nov 20, 2013).
- 59 US Government Accountability Office. Afghanistan reconstruction: despite some progress, deteriorating security and other obstacles continue to threaten achievement of US goals. July 28, 2005. <http://www.gao.gov/assets/250/247264.pdf> (accessed Nov 20, 2013).
- 60 Islamic Republic of Afghanistan, Ministry of Public Health. A basic package of health services for Afghanistan, 2005/1384. Nov 15, 2005. <http://moph.gov.af/Content/Media/Documents/BPHS-2005-FINAL29122010162945969.pdf> (accessed Nov 20, 2013).
- 61 Ministry of Public Health, Islamic Republic of Afghanistan. MoPH joins the family of NICE (National Institute for Health and Clinical Excellence), UK. May 19, 2013. <http://moph.gov.af/en/news/20391> (accessed Nov 20, 2013).
- 62 Engelgau MM, El-Saharty S, Kudesia P, Rajan V, Rosenhouse S, Okamoto K. Capitalizing on the demographic transition: tackling non communicable diseases in south Asia. Washington DC: World Bank, 2011.
- 63 Republic of Botswana. National health policy: towards a healthier Botswana. August, 2011. <http://www.bistand.iogt.se/Global/NHP> Nov 2011 Parliament.pdf (accessed Nov 21, 2013).
- 64 de Martel C, Ferlay J, Franceschi S, et al. Global burden of cancers attributable to infections in 2008: a review and synthetic analysis. *Lancet Oncol* 2012; 13: 607–15.
- 65 Peto R, Darby S, Deo H, Silcocks P, Whitley E, Doll R. Smoking, smoking cessation, and lung cancer in the UK since 1950: combination of national statistics with two case-control studies. *BMJ* 2000; 321: 323–29.
- 66 Ahmad Kiadaliri A, Jarl J, Gavrilidis G, Gerdtam UG. Alcohol drinking cessation and the risk of laryngeal and pharyngeal cancers: a systematic review and meta-analysis. *PLoS One* 2013; 8: e58158.
- 67 McTiernan A, Porter P, Potter JD. Breast cancer prevention in countries with diverse resources. *Cancer* 2008; 113 (suppl): 2325–30.
- 68 Mitra I, Mishra GA, Singh S, et al. A cluster randomized, controlled trial of breast and cervix cancer screening in Mumbai, India: methodology and interim results after three rounds of screening. *Int J Cancer* 2010; 126: 976–84.
- 69 Sankaranarayanan R, Nene BM, Shastri SS, et al. HPV screening for cervical cancer in rural India. *N Engl J Med* 2009; 360: 1385–94.
- 70 Sankaranarayanan R, Ramadas K, Thomas G, et al, for the Trivandrum Oral Cancer Screening Study Group. Effect of screening on oral cancer mortality in Kerala, India: a cluster-randomised controlled trial. *Lancet* 2005; 365: 1927–33.
- 71 Santesso N, Schünemann H, Blumenthal P, et al, for the World Health Organization Steering Committee for the Recommendations on the Use of Cryotherapy for Cervical Cancer Prevention. World Health Organization guidelines: use of cryotherapy for cervical intraepithelial neoplasia. *Int J Gynaecol Obstet* 2012; 118: 97–102.
- 72 André N, Banavali S, Snihur Y, Pasquier E. Has the time come for metronomics in low-income and middle-income countries? *Lancet Oncol* 2013; 14: e239–48.
- 73 Putthasri W, Tangcharoensathien V, Mugem S, Jindawatana W. Geographical distribution and utilization of mammography in Thailand. In: Regional Health Forum, vol 8, no 1. New Delhi: World Health Organization, Regional Office for South-East Asia, 2004: 84–91.
- 74 Anothaisintawee T, Teerawattananon Y, Wiratkapun C, et al. Developing and validating breast cancer risk prediction model in Thai women. Bangkok: Mahidol University, 2013.
- 75 American Cancer Society. Cancer facts and figures 2007. 2007. <http://www.cancer.org/research/cancerfactsstatistics/cancerfactsfigures2007/index> (accessed Nov 21, 2013).
- 76 Bakitas M, Lyons KD, Hegel MT, et al. Effects of a palliative care intervention on clinical outcomes in patients with advanced cancer: the Project ENABLE II randomized controlled trial. *JAMA* 2009; 302: 741–49.
- 77 Gorokhovich L, Chalkidou K, Shankar R. Improving access to innovative medicines in emerging markets: evidence and diplomacy as alternatives to the unsustainable status quo. *J Health Diplomacy* 2013; published online Aug 20. <http://www.ghd-net.org/abstracts/volume-1/8> (accessed Nov 21, 2013).
- 78 UK Government. UK and India to work together on evidence-informed healthcare policy and practice. June 14, 2013. <https://www.gov.uk/government/world-location-news/uk-and-india-to-work-together-on-evidence-informed-healthcare-policy-and-practice> (accessed Jan 8, 2014).
- 79 National Institute for Health and Care Excellence. NICE signs memorandum of understanding with the China National Health Development Research Center. Sept 28, 2010. <http://www.nice.org.uk/aboutnice/niceinternational/NICEInternationalChinaMoU.jsp> (accessed Jan 8, 2014).
- 80 St Jude Children’s Research Hospital. About international outreach. <http://www.stjude.org/stjude/v/index.jsp?vgnextoid=2f166f9523e70110VgnVCM1000001e0215acRCD&vgnextchannel=e41e6fa0a9118010VgnVCM1000000e2015acRCD> (accessed Jan 8, 2014).
- 81 All-Party Parliamentary Group on Global Health. Improving health at home and abroad: how overseas volunteering from the NHS benefits the UK and the world. 2013. <http://www.rcpsych.ac.uk/pdf/Improving%20Health%20at%20Home%20and%20Abroad%20-%20Final%20Report.pdf> (accessed Nov 21, 2013).
- 82 Oxman AD, Lavis JN, Lewin S, Fretheim A. SUPPORT Tools for evidence-informed health Policymaking (STP) 1: what is evidence-informed policymaking? *Health Res Policy Syst* 2009; 7 (suppl 1): S1.
- 83 Chalkidou K, Levine R, Dillon A. Helping poorer countries make locally informed health decisions. *BMJ* 2010; 341: c3651.
- 84 Rockefeller Foundation, Save the Children, UNICEF, World Health Organization. Universal health coverage: a commitment to close the gap. September, 2013. http://www.savethechildren.org.uk/sites/default/files/images/Universal_health_coverage.pdf (accessed Nov 21, 2013).
- 85 Johansson KA, Jerene D, Norheim OF. National HIV treatment guidelines in Tanzania and Ethiopia: are they legitimate rationing tools? *J Med Ethics* 2008; 34: 478–83.
- 86 Marquez PV, Farrington JL. No more disease silos for sub-Saharan Africa. *BMJ* 2012; 345: e5812.