The global burden of women's cancers: A grand challenge in global health

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Health, equity, and women's cancers 1

The global burden of women's cancers: a grand challenge in global health

Ophira Ginsburg, Freddie Bray, Michel P Coleman, Verna Vanderpuye, Alexandru Eniu, S Rani Kotha, Malabika Sarker, Tran Thanh Huong, Claudia Allemani, Allison Dvaladze, Julie Gralow, Karen Yeates, Carolyn Taylor, Nandini Oomman, Suneeta Krishnan, Richard Sullivan, Dominista Kombe, Magaly M Blas, Groesbeck Parham, Natasha Kassami, Lesong Conteh

Every year, more than 2 million women worldwide are diagnosed with breast or cervical cancer, yet where a woman lives, her socioeconomic status, and agency largely determines whether she will develop one of these cancers and will ultimately survive. In regions with scarce resources, fragile or fragmented health systems, cancer contributes to the cycle of poverty. Proven and cost-effective interventions are available for both these common cancers, yet for so many women access to these is beyond reach. These inequities highlight the urgent need in low-income and middle-income countries for sustainable investments in the entire continuum of cancer control, from prevention to palliative care, and in the development of high-quality population-based cancer registries. In this first paper of the Series on health, equity, and women's cancers, we describe the burden of breast and cervical cancer, with an emphasis on global and regional trends in incidence, mortality, and survival, and the consequences, especially in socioeconomically disadvantaged women in different settings.

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Introduction

Cancer is a leading cause of premature death and disability worldwide, especially in women.[1,2] It is a rapidly growing crisis in low-income and middle-income countries (LMICs), where the epidemiological transition continues to shift the burden of disease from mainly infectious causes to chronic, non-communicable diseases (NCDs).[3] Many countries, especially those with weak, under-resourced health systems, are struggling to cope with the rapid rise in NCDs while high maternal and child mortality rates, and high mortality rates from infectious diseases (including malaria, tuberculosis [TB], and HIV/AIDS) and malnutrition still persist.

Worldwide, more than 2 million women are diagnosed with breast or cervical cancer every year, but where a woman lives (ie, in which country, region, or setting in relation to the nearest health-care services) and how she lives (eg, poor or otherwise socially disenfranchised) largely determines whether or not she develops one of these cancers, how early she presents to health-care services, and her access to affordable, good-quality diagnostic and treatment services. This pattern is

Search strategy and selection criteria

Studies for the economics analysis were retrieved through systematic searches on the following medical and social sciences electronic databases: Embase, Global Health, MEDLINE (OVID), Scopus, Web of Science, and Econlit. We combined variations of search terms related to "breast cancer"; "cervical cancer"; "low income", "middle income", and "developing" countries; the individually named countries of relevance; "economic burden" and "economic consequence". We searched Google Scholar, scanned the reference lists of the studies retrieved, and hand searched the resources and publications of institutional websites. Searches were limited to studies published in English between January, 1990, and July, 2015, containing original quantitative estimates of economic impact. We identified 4228 studies, of which 30 full text articles were included in our review.

Key messages

- Worldwide, the majority of women who die from breast cancer and most who die from cervical cancer live in low-income and middle-income countries. This situation is a largely preventable tragedy for hundreds of thousands of women and their families every year.
- Most women who develop breast or cervical cancer in a high-income country will survive; the opposite is true for women in most low-income and many middle-income countries. Where a woman lives, and her socioeconomic, ethnocultural, or migration status, should no longer mean the difference between life and death from these common cancers, for which cost-effective, life-saving interventions exist.
- The incidence of breast cancer is expected to increase rapidly with human development. Although invasive cervical cancer should be predicted to fall in emerging economies, this is not yet the case in many countries where patterns of sexual behaviour are increasing the transmission of oncogenic human papillomavirus subtypes, and population-based organised human papillomavirus vaccination and cervical screening programmes are not yet widely implemented.
- To understand the social, economic, and financial consequences of breast and cervical cancers, which take a disproportionate toll on women in low-income and middle-income countries in their prime of life, is of crucial importance. The efficacy and cost-effectiveness of interventions for breast and cervical cancer control must be critically evaluated to help inform and prioritise evidence-based, resource-appropriate programmes and policy making.
- Global efforts, especially in recent years, have led to substantial improvements in maternal health outcomes. Similar efforts are urgently needed to address breast and cervical cancer, which take the lives of three times as many women each year than complications of pregnancy and childbirth (ie, maternal mortality).

This is the first in a **Series** of three papers about health, equity, and women's cancers

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especially striking for cervical cancer, since around 85% of women diagnosed and 87% of women who die from cervical cancer live in LMICs.[3] Proven approaches exist to reduce these gross inequities, yet most women have few opportunities to access these life-saving interventions. In many countries, and in many resource-poor regions within countries, implementation of human papillomavirus (HPV) vaccination is limited,[4] as is the availability of—and access to—early detection programmes, cancer surgery,[5] essential cancer medicines,[6] radiotherapy,[7] palliative care,[8] and support for those who survive cancer, sometimes referred to as survivorship care.

Disability and premature death from breast or cervical cancer is a preventable tragedy for hundreds of thousands of women and their families every year. In 2012, breast and cervical cancer were responsible for the deaths of 522 000 and 266 000 women worldwide respectively;[3] as such, around half a million more women died from these two cancers alone than from complications of pregnancy or childbirth (303 000 maternal deaths in 2015, according to the UN Population Fund).[9] A further 152 000 women died from ovarian cancer and 76 000 from endometrial cancer.[3] But where do women's cancers fit in the global health agenda? In high-income countries, there is notable advocacy, media attention, and funding for research and treatment of cancer, but in many resource-poor settings, breast, cervical, and other gynaecological cancers are effectively neglected diseases.[10] That these diseases cause substantial disability, premature death, disruption of family life, and loss to the national economy, thus exacerbating the cycle of poverty,[11] has largely been ignored by the global health and development community.

Only 5% of global spending on cancer is directed toward the majority of countries (ie, LMICs) where the highest burden exists.[12] Health inequities are differences in health "…that are unnecessary, avoidable, unfair and unjust".[13] Poor health within countries and inequities between countries represent an unequal distribution of power, income, goods, and services that result from "ineffective social policies, unfair economic arrangements, and bad politics".[14] Cancers that mainly affect women present particular challenges in terms of achieving health equity. Elevation of the status of women will be one of the key drivers in reducing disparities in cancer outcomes within and between countries.

The *Lancet* Series on health, equity, and women's cancers seeks to provide an advocacy and action framework for radically improving progress toward closing the global cancer divide[11] for women. The three papers in the Series will focus on the global burden of breast and cervical cancer, the untapped potential of proven and promising interventions, the challenges and opportunities to take these to scale while strengthening health systems, and the provision of recommendations for translating evidence to policy, to reduce inequities and improve cancer survival for women.

In this first paper of the Series, we describe the burden of breast and cervical cancer, with an emphasis on global and regional trends in incidence, mortality, and survival; the social and economic effects on women and their families; and the disparities in cancer survival in socioeconomically disadvantaged women. Endometrial, ovarian, and other gynaecological cancers are important contributors to cancer mortality, but this Series will focus mainly on breast and cervical cancer, since these are two of the greatest contributors to cancer mortality and morbidity in women worldwide. As highlighted in this paper, breast and cervical cancer will continue to pose particularly important challenges and create opportunities to strengthen health systems in the coming decades. Cervical cancer is largely preventable through public health interventions, such as HPV vaccination for girls aged 9–13 years, and screening with treatment of pre-cancerous lesions is among the few cancer-related so-called "best buys" or "very cost effective strategies" according to WHO's Global Action Plan for the Prevention and Control of Noncommunicable Diseases (2013–20).[15] Both HPV vaccination and screening and treatment of pre-cancerous cervical lesions are also included in the package of essential interventions for cancer control in LMICs, in the *Cancer Volume of the World Bank Group's Disease Control Priorities, Third Edition* (DCP3).[16] Although breast cancer screening continues to generate substantial debate regarding the magnitude of benefits and harms, opportune ages, screening intervals, cost-effectiveness, and relevance to resource-poor settings,[17] improving access to early diagnosis and treatment for breast cancer can be cost effective, and promotion of breast cancer early diagnosis and treatment is listed in the DCP3 essential package.[16] We therefore address only these two cancers in this Series, because they fall under the domains of public health and public policy most relevant to women's cancers.

Causes and risk factors of breast and cervical cancer

The major known risk factors for breast cancer include female sex, age, and family history, and reproductive factors, including early age at menarche, later menopause, nulliparity, and first childbirth after age 30 years, all of which are independent risk factors.[18] Breastfeeding is independently associated with a reduced risk, with longer duration associated with a greater reduction in risk of developing breast cancer.[19] Overweight and obesity are associated with an increased risk for post-menopausal breast cancer, whereas the effect of these factors on pre-menopausal breast cancer is less clear and remains an area of active study.[20]

The most important risk factor for invasive cervical cancer is HPV, of which there are several major

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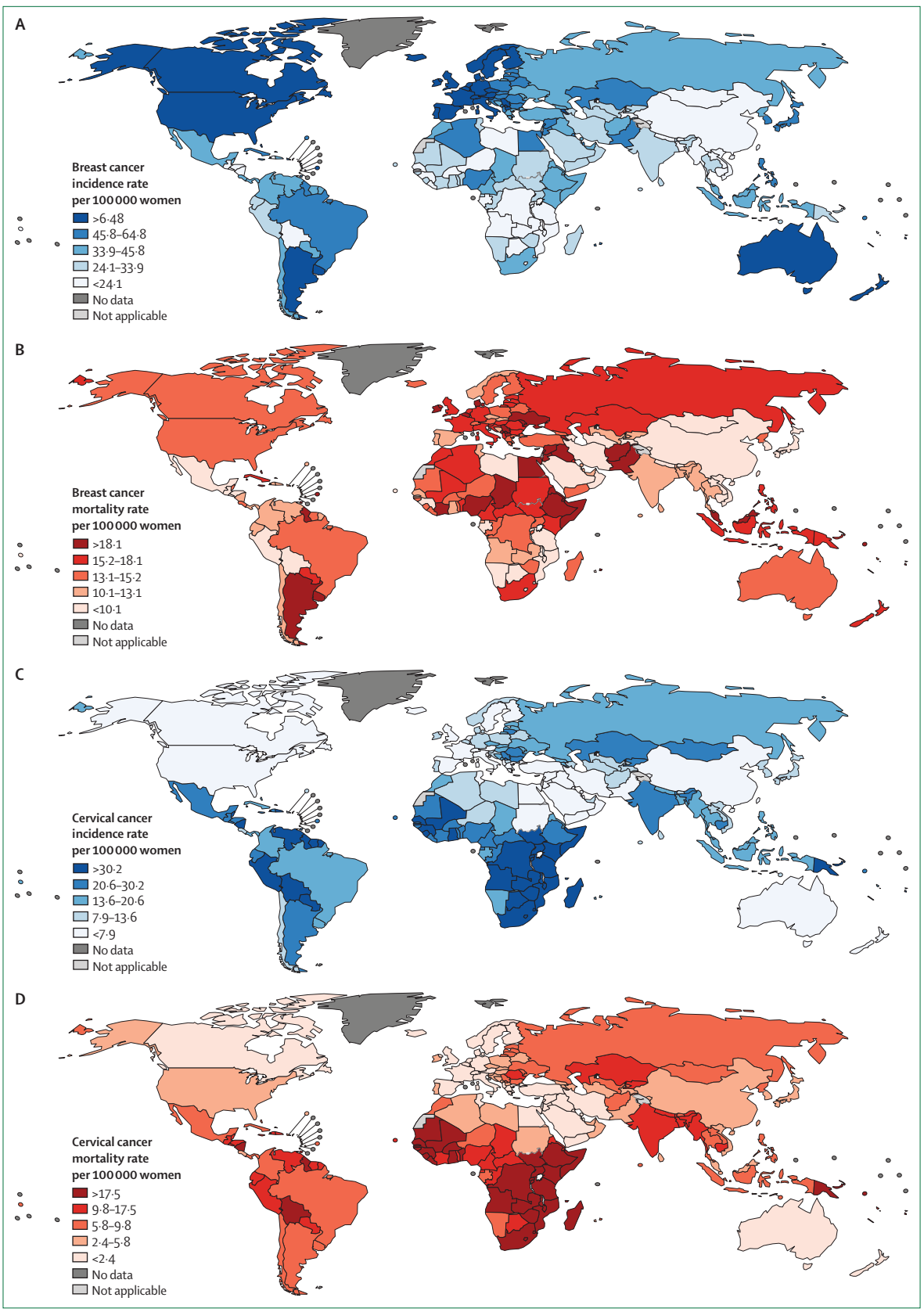

Figure 1: **Age-standardised global incidence and mortality rates of female breast and cervical cancer in 2012, with the range divided into quintiles**

(A) Breast cancer incidence rates. (B) Breast cancer mortality rates. (C) Cervical cancer incidence rates. (D) Cervical cancer mortality rates. The boundaries and names shown and the designations used on these maps do not imply the expression of any opinion whatsoever on the part of WHO concerning the legal status of any country, territory, city, or area, or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement. Data are from GLOBOCAN 2012. Maps produced by the International Agency for Research on Cancer.

For **data from GLOBOCAN 2012** see http://gco.iarc.fr/today/home

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oncogenic subtypes[21] (discussed further in Series paper 2).[17] Other independent risk factors include immunosuppression, especially through HIV infection,[22] and smoking.[23]

Breast and cervical cancer: incidence, mortality, and survival

Every year, 1·7 million women are diagnosed with breast cancer, making it the most common cancer in women

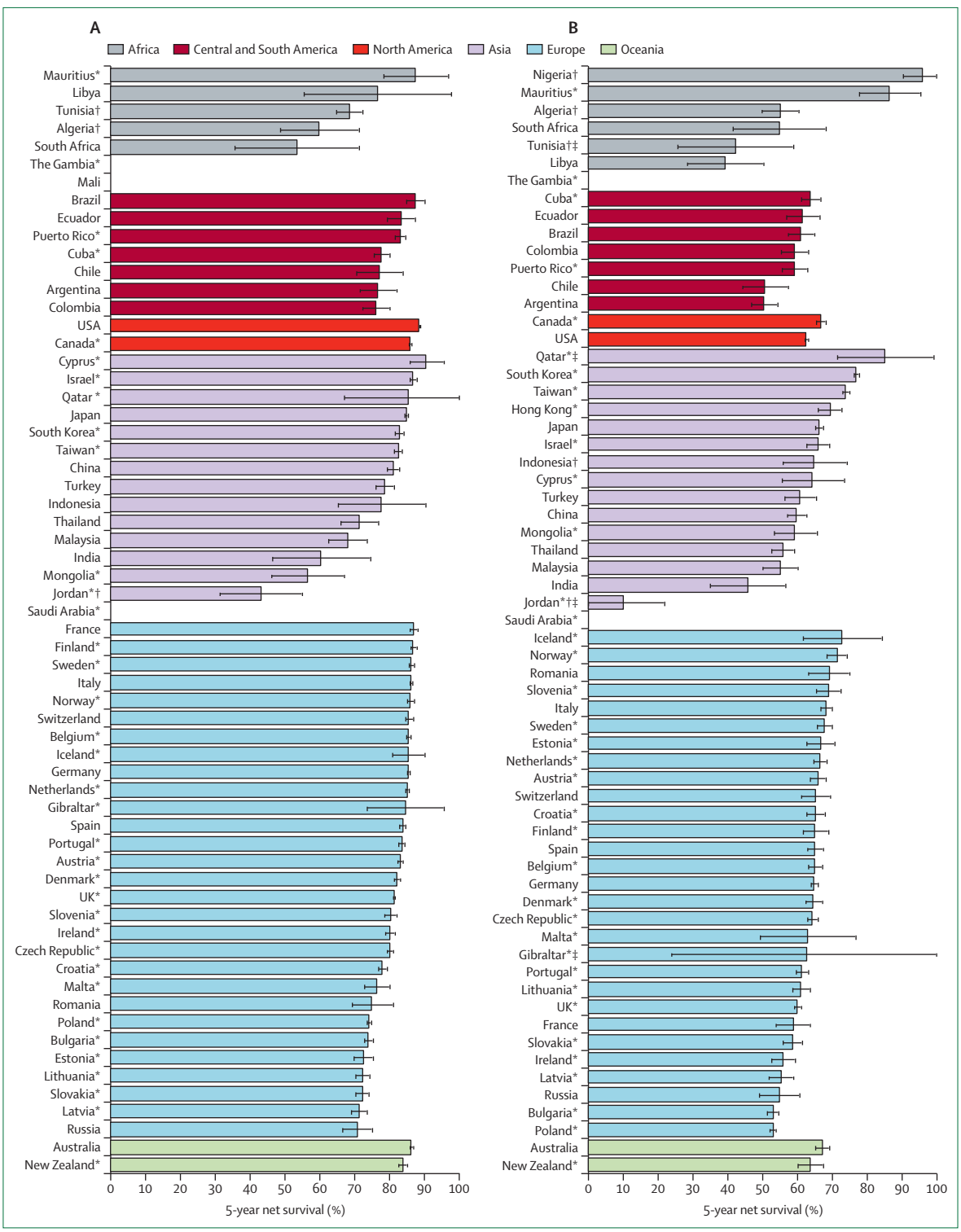
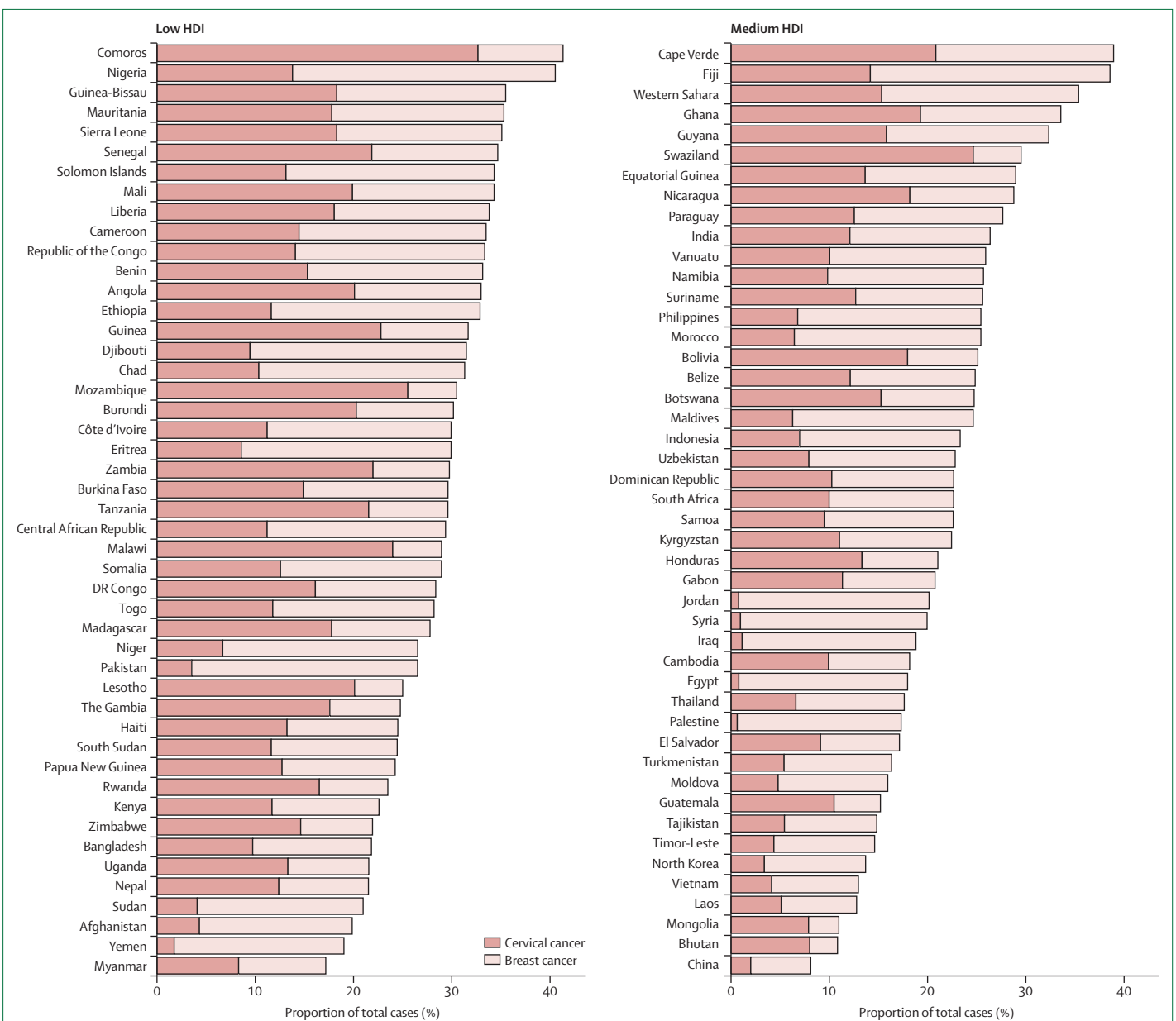


Figure 2: **Global distribution of age-standardised 5-year net survival (%) for women diagnosed aged 15–99 years with (A) breast cancer or (B) cervical cancer during 2005–09, by continent and country**

Survival estimates for each country are ranked from highest to lowest within each continent. Error bars represent 95% CIs. Survival estimates are flagged as follows: *100% coverage of national population. †Less reliable because the only estimate(s) available are from a registry or registries in this category. ‡Not age standardised.

worldwide.[3] Just over half of all cases (53%) occur in less developed regions.[3] The highest incidence rates are reported from countries in northern and western Europe (eg, Denmark, Belgium, and the UK), North America, Australia, and New Zealand (figure 1A), but breast cancer is not confined to high-income countries and is the most commonly diagnosed cancer in women in 140 countries. With an estimated 522 000 deaths in 2012, breast cancer is the leading cause of cancer death in women (accounting for 15% of all cancer deaths), ahead of lung cancer (491 000 deaths).[3] Breast cancer survival in most LMICs is lower than in high-income countries and mortality rates vary more widely than does incidence (figure 1B). For example, breast cancer mortality rates in the Pacific Islands (Fiji), the Caribbean (The Bahamas), sub-Saharan Africa (Nigeria), and southern Asia (Pakistan) are among the highest in the world.[3]

An estimated 530 000 women were diagnosed with cervical cancer in 2012.[3] It is the fourth most common cancer in women worldwide, but in 38 countries, including many in sub-Saharan Africa, it is the most common cancer affecting women. The highest incidence rates occur in this region (Malawi and Zimbabwe; figure 1C), although rates are also high in parts of



(Figure 3 continues on next page)

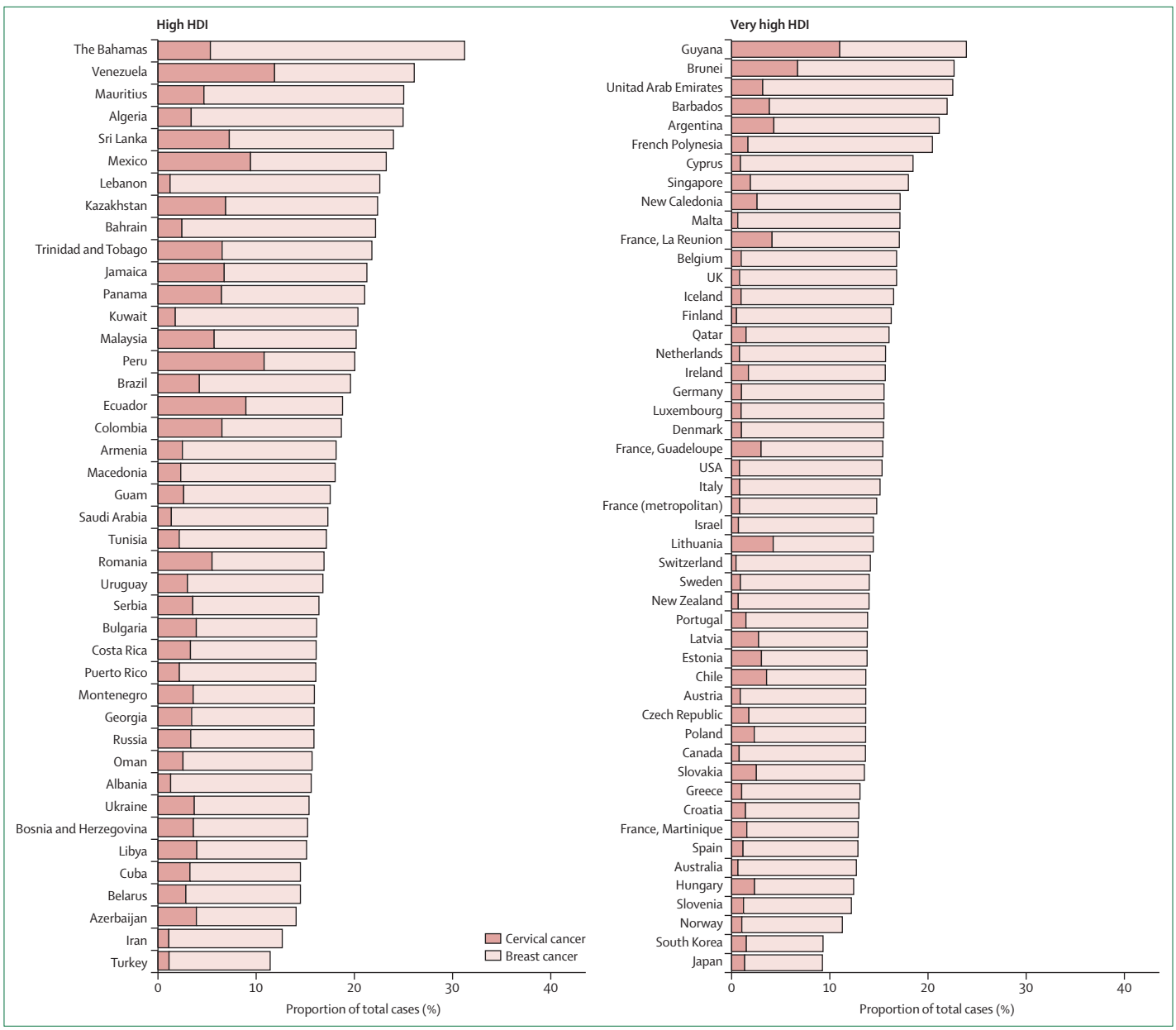


Figure 3: **The proportion of new cases of cervical and breast cancer in 2012 compared with the total cancer burden from all cancers combined in both sexes by country and HDI**
Proportions are sorted by HDI within these quartiles. HDI=Human Development Index. Data are from GLOBOCAN 2012.

Central and South America (eg, Guyana and Bolivia). Unlike breast cancer, the global map of cervical cancer mortality rates is more similar to that of incidence (figure 1D).

Global surveillance of cancer survival trends was recently initiated by the CONCORD-2 study,[24] which analysed individual data from 279 population-based registries in 67 countries for more than 25 million adults (aged 15–99 years) diagnosed with one of ten common cancers during the 15-year period 1995–2009. Net survival up to 5 years after diagnosis was estimated after correction for death from other causes. Data were available from 59 countries for almost 5·5 million women diagnosed with breast cancer. For women diagnosed during 2005–09, 5-year net survival was 80% or higher in 34 countries, but much lower in India (60%), Mongolia (57%), and South Africa (53%; figure 2). In the 10 years between 1995–99 and 2005–09, 5-year survival from breast cancer increased in Central and South America (eg, from 66% to 76% in Colombia). Data were available from 61 countries for 602 000 women diagnosed with cervical cancer.

Globally, the range of 5-year net survival varied greatly. For women diagnosed during 2005–09, 5-year net survival was 70% or higher in seven countries, in the range 60–69% in 34 countries, but below 60% in a further 20 countries.

A large international study followed up patients with cancer diagnosed in 1990–2001 in 12 countries undergoing major socioeconomic transition and noted similarly wide variations in cancer survival.[25] They describe 5-year survival for breast cancer by extent of disease: localised versus regional (indicating larger tumours or local spread to skin, chest wall, or regional lymph nodes), for countries with more developed or less developed health services. Information about the extent of disease was not available for the African countries in this study. Survival for women with localised disease was reported to be around 90% for countries with highly developed health services (Singapore and Turkey), compared with 76% in countries where they were less developed (Thailand, India, and Costa Rica), with a greater disparity for women with regional disease (75·4% for more developed health services *vs* 47·4% for less developed health services).[25]

Although each of these studies have limitations, they draw attention to the urgent need for major investments in population-based cancer registration, in vital statistics including cause of death, and in early detection programmes, health services infrastructure, and human resources.[24,25]

Women's cancers and human development

Breast and cervical cancer are indicative of the late phase of the epidemiological transition that characterises the rise of NCDs in general. Increasing life expectancy and declines in infection-related diseases (including cervical cancer) are offset by an upsurge in cancers more common in wealthier countries and associated with a so-called western lifestyle,[26,27] referred to as the cancer transition.[26] The Human Development Index (HDI) is a composite of three basic dimensions of human development:[28] a long and healthy life measured by life expectancy at birth; access to knowledge based on a combination of adult literacy rate and primary to tertiary education enrolment rates; and a decent standard of living, based on gross domestic product (GDP) per person adjusted for purchasing power parity (US$). HDI therefore places an emphasis on societal values and capabilities within a country and economic growth. In a comparison of the national incidence burden of the two diseases by level of HDI, the inequity is clear: cervical cancer comprises up to a third of all cancers diagnosed (in both sexes) in many low HDI settings, compared with less than 10% in most very high HDI countries (figure 3). In many low (and some medium) HDI countries, the combined burden of breast and cervical cancer represents a third of the total cancer burden in women; reductions in cervical cancer to rates recorded in very HDI countries would effectively reduce this proportion to 10–15%.

Breast cancer is the most common cancer in women in most countries, including many where cervical cancer is endemic. This fact suggests that breast cancer incidence is largely unrelated to national averages of the HDI. However, the relative magnitude and the extent to which breast cancer incidence is rising and cervical cancer incidence falling are markers of the extent of social and economic transition in a given country.[26] Changing reproductive patterns, including earlier age at menarche, later first childbirth, lower parity, and shorter duration of breastfeeding, are believed to be the major causes for the uniformly rising incidence of breast cancer in transitioning countries,[27] with overweight and obesity becoming increasingly important factors in post-menopausal breast cancer.[20] In some high-income countries, mammographic screening has generated transient rises and subsequent falls in breast cancer

Panel 1: Cancer survival disparities in North America and Europe

Disparities in breast and cervical cancer survival exist within and between high-income countries.[26,39–41] Age-adjusted 5-year survival from breast cancer varies by as much as 20% between EU countries, with lower survival recorded in eastern European countries than in the rest of the EU.[41] International differences in survival have been attributed to differences in stage at diagnosis, access to optimal treatment, and national levels of organisation and investment in health care. A European survey on the availability, reimbursement, and other barriers to access shows important disparities across Europe in access to cancer medicines.[42] Even within the EU, drug shortages limit access to older, inexpensive medicines that are essential for treatment (with either curative or palliative intent), such as tamoxifen for breast cancer, or cisplatin and 5-fluorouracil for cervical cancer. In view of their proven efficacy and low cost, these drugs, which are included in WHO's recently updated Essential Medicines List,[6] should be made universally available for all patients who need them.

To what extent differences in tumour biology versus social, economic, and other factors have a role in survival disparities within countries remains unclear. Several studies have reported a greater proportion of triple-negative breast cancers in African-American women,[43,44] a subtype associated with poor survival, than in white women. However, a recent population-based study in the USA[43] noted persistent differences in 7-year breast cancer-specific survival between African-American and white women, even for stage I disease. The difference in breast cancer-specific survival remained important even after triple-negative tumours were excluded. However, this study did not explore access and use of cancer services.

African-American women[43–51] and women from other ethnic minority populations in the USA,[43–47,50–52] the UK,[53] and Canada[54–56] tend to have lower participation in breast and cervical cancer screening programmes and, with some exceptions,[57] lower cancer survival than the corresponding national averages. Reasons for these disparities are poorly understood and include socioeconomic factors such as economic deprivation, geographical distance to cancer services, absence of health insurance, and other social and cultural factors that could affect health-care-seeking behaviour.[43–45,48,56]

In recognition of the magnitude and pervasiveness of these inequities, several regional, national, and international cancer organisations have established programmes and policies to reduce cancer disparities, not only for breast and cervical cancers but also for cancers more generally, in men, women, and children.

Panel 2: **Cancer incidence and survival in Indigenous women**

Indigenous people in many high-income countries have disproportionally worse health and lower life expectancy than their non-Indigenous counterparts. A study led by the International Agency for Research on Cancer comparing the scale and profile of cancer incidence in Indigenous and non-Indigenous populations in the USA, Canada, Australia, and New Zealand has shown high rates of cervical cancer in almost all jurisdictions, emphasising the need for targeted prevention strategies in these populations.[58]

Survival from breast and cervical cancer is lower in Indigenous women than the national averages in the USA, Canada, and Australia.[59–63] Vasilevska and colleagues[59] did a systematic review and meta-analysis of cervical cancer in Indigenous women in Australia, New Zealand, Canada, and the USA. Notably, they recorded no difference in the risk for cervical dysplasia or carcinoma in situ but they did report a raised risk of invasive cervical cancer (pooled relative risk 1·72) and cervical cancer mortality (pooled relative risk 3·45). As the Indigenous women had a higher risk of cervical cancer morbidity and mortality but no increased risk of early-stage disease, they suggest, "structural, social, or individual barriers to screening, rather than baseline risk factors, are influencing poor health outcomes".

However, little information remains about cancer incidence, survival, and the level of access to cancer services in Indigenous populations in low-income and middle-income countries. Recent global and regional reports reviewing cancer in Indigenous communities have highlighted the need for more attention to this issue.[58,64] Efforts to develop joint actions as a partnership between governments, health professionals, and the Indigenous communities will be crucial to reduce the elevated and avoidable burden of cancer in Indigenous populations worldwide.[58]

incidence, while decreases in the use of hormone replacement therapy (following publication of the Women's Health Initiative study in 2002[29]) was associated with a period of falling breast cancer incidence—a phenomenon that seems to have stabilised since 2007.[30] Meanwhile, survival has been improving and mortality has been decreasing in many high-income countries, due to a combination of more effective treatments,[24,31,32] earlier presentation, and improved access to care.[17]

Falling cervical cancer incidence and mortality rates in many countries in the past 30–40 years are associated with the implementation of effective population-based screening programmes in high-income countries or, in transitioning countries, a decreasing prevalence of factors associated with persistent infection with oncogenic subtypes of HPV.[33] However, some notable exceptions exist. For example, steady increases in cervical cancer incidence have been recorded in high-risk populations in Uganda[34] and Zimbabwe.[35] Increasing premature cervical cancer mortality is clearly evident from the cohort-specific mortality trends in some countries in eastern Europe and central Asia, including former republics of the Soviet Union.[36]

This so-called overlapping challenge whereby breast cancer incidence and mortality are increasing while the burden of cervical cancer is not yet declining is explored with an equity lens in a study from Mexico, using subnational time series data.[37] The report emphasises the need for integrated programmes that consider both prevention and treatment "underpinned by a life cycle approach to effectively respond to the burden of cancer faced by women globally".[37]

In 2012, Singh and colleagues[38] reported on global inequities in cervical cancer incidence and mortality as a function of variations in HDI, socioeconomic factors, health-care expenditures, and the Gender Inequality Index (GII) for 184 countries. GII is a composite score that includes reproductive health (maternal mortality ratio and adolescent birth rates), empowerment (proportion of women in parliament and those with secondary education), and economic status (labour force participation). Incidence and mortality were both correlated with human development and gender inequality. A 0·2 unit increase in GII was associated with a 24% increased risk of developing cervical cancer and a 42% increased risk of dying from the disease. Although GII as a composite measure has its limitations, this study suggests that not only poverty reduction but also increasing access to preventive health services and elevating the status of women are essential to reduce cervical cancer disparities.

Inequities in survival from breast and cervical cancer are not limited to the so-called global south, but also persist for women in North America and Europe (panel 1). Indigenous women, irrespective of country income level, face several barriers to cancer care, including prevention, early diagnosis, and effective treatments for these cancers (panel 2).

Prediction of the future burden

Figure 4 shows the predicted global burden of breast and cervical cancers in 2030. Data available from long-standing high-quality population-based cancer registries from medium, high, or very high HDI countries[65] suggest that if these average changes continue and were applicable to all countries of the world, the number of women diagnosed with breast cancer will increase to almost 3·2 million per year. Even if rates can be maintained at 2012 levels, a rise to 2·4 million new cases of breast cancer is predicted on the basis of demographic changes alone. For cervical cancer, even if the average decline were to occur in all countries worldwide, almost the same number of women will be diagnosed in 2030 as today—around 510 000 cases. However, if cervical cancer incidence rates were to remain unchanged, the number of women diagnosed annually is predicted to rise to more than 700 000 by 2030.

Wider effects on women, families, and society

Breast and cervical cancer are major contributors to the overall burden of disease in women worldwide. Breast cancer is the leading cause of life years spent with disability in 119 countries, whereas cervical cancer is the leading cause in 49 countries.[2] However, as a cause of

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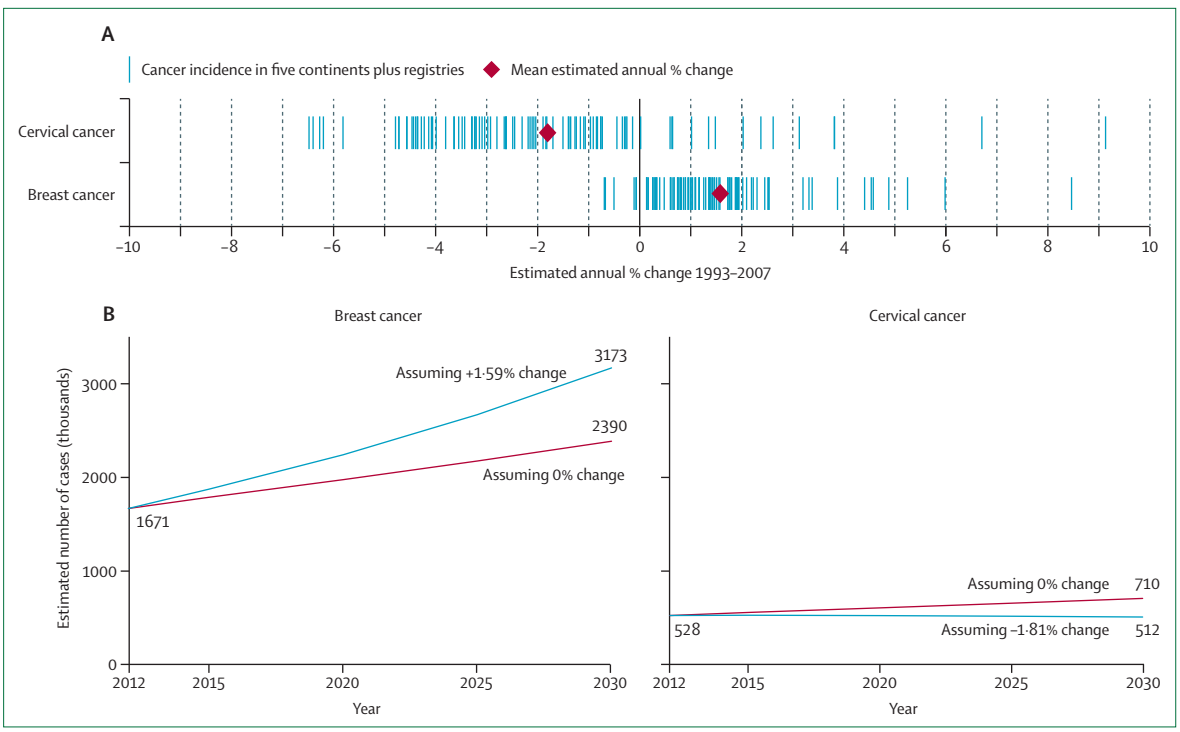

Figure 4: **Estimated and predicted incidence of breast and cervical cancer**
(A) Estimated annual percentage change 1993–2007 based on cancer incidence obtained from cancer registries included in several volumes of Cancer Incidence in Five Continents. (B) Predicted number of breast and cervical cases (thousands) in 2030 assuming average trends in the estimated annual percentage country are observed in every country up to 2030 seen in the incidence series, or assuming rates remain unchanged in every country from those estimated in GLOBOCAN in 2012.

For **Cancer Incidence in Five Continents** see http://Ci5.iarc.fr

For the **GLOBOCAN 2012 data** see http://gco.iarc.fr

premature death (as estimated through years of life lost), cervical cancer leads breast cancer in 23 countries, mainly in sub-Saharan Africa and parts of Central and South America. As figure 5 shows, the disability-adjusted life-years (a composite measure of years of life lost and life-years spent with disability) for cervical and breast cancer by four-level HDI are in opposing directions by HDI. The relative contribution of years of life lost and life years spent with disability to disability-adjusted life-years also differ substantially (figure 5). Breast cancer is a major contributor to the high overall cancer disability-adjusted life-years in very high HDI countries, with quite a large contribution of years of life spent with a disability. For cervical cancer, the overall magnitude of disability-adjusted life-years and the large years of life lost component in low HDI countries are striking.[2]

A comparative analysis of epidemiological data for breast cancer in the USA, Canada, India, China, Taiwan, Japan, South Korea, and Sweden[66] showed notable differences in the median age at diagnosis. The peak age at diagnosis was 40–50 years in Asian countries, and 60–70 years for western countries. Breast cancer has also been shown to occur earlier in life in African countries where such data have been reported, with a median age of approximately 45 years.[67–73] It remains unclear to what degree the earlier age at diagnosis is related to variations in the patterns of risk factors and breast cancer subtypes,

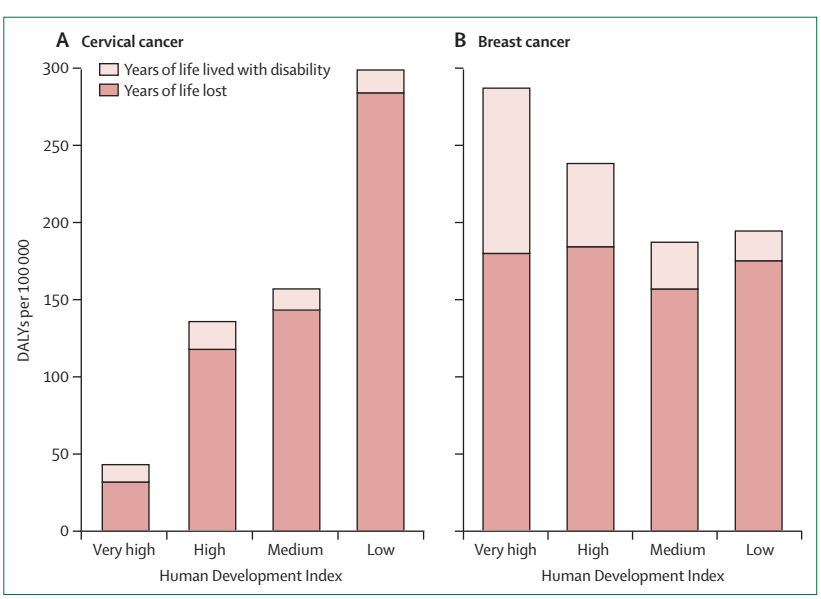

Figure 5: **Age-adjusted DALYs per 100 000 population for cervical and breast cancer in 2008 according to Human Development Index quartile**
(A) Cervical cancer. (B) Breast cancer. DALYs=disability-adjusted life-years. Data are from Soerjomataram and colleagues.[2]

or is rather merely a reflection of the differences in population structures between countries of low, middle, and high income (eg, the median age of women in The

Gambia is 20·5 years, compared with 41·6 years in the UK).[74]

The median age at diagnosis for invasive cervical cancer depends on the timing of exposure to oncogenic HPV subtypes, and on the latency between exposure, cervical dysplasia, and other factors that can affect the likelihood of progressing to invasive disease, as described in the multistage model of carcinogenesis.[75] Once exposed to an oncogenic HPV subtype, the risk of developing invasive cervical cancer is greatly affected by immune status, which in turn is related to age at exposure and general immunocompetence. Women who are HIV positive are at particular risk of progression to invasive cervical cancer,[22] especially in the absence of screening programmes.[76]

In high-resource countries, cervical cancer incidence rates increase until the age of 30–35 years, then remain stable throughout older ages,[3] most likely as a consequence of the delivery of effective screening programmes.[17] In the USA, the median age at diagnosis of invasive cervical cancer is 47–48 years,[77] compared with 55–59 years in India.[78] In one multicentre study in Limpopo, South Africa, the mean age at diagnosis was 41·3 years for HIV-positive women and 59·1 years for HIV-negative women.[79]

Clearly, breast and cervical cancer in low-resource settings disproportionately affect women in the prime of life, and, as such, have substantial economic and societal consequences. A mother's death has complex effects on the children and families she leaves behind. Women are central not only in direct caregiving for their own children, but more broadly in society, playing key roles in the socialisation, education, and health of children.[80,81] Women also make substantial—albeit under-recognised—contributions to the health-care labour force. Langer and colleagues[81] have described women's "crucial roles in the health care of families and communities [as] drivers of the wealth and health of nations". The *Lancet* Commission on Women and Health[81] in relation to policy for women's cancers is explored further in the third paper in this Series.[82]

Although a close link between maternal mortality and neonatal health has been established,[81,83,84] most studies have concentrated on the early weeks and months of a child's life, focusing on the direct effects of inadequate nutrition from breastfeeding. The impact of a mother's disability and untimely death on child survival and wellbeing at other key periods during the life course, including adolescence, is also important. Death from untreated and unpalliated cancer is slow, painful, and traumatic for patients and their families. To our knowledge, no published studies have specifically addressed the effects of a woman's death from cancer on her child's survival. In view of the rising mortality from women's cancers, and the young ages (ie, in the childbearing and child-rearing ages) at which so many women are affected, we suggest that the scope and scale of the consequences of women's cancers on the health and wellbeing of her children warrants further research.

Overwhelming evidence suggests that investment in women's health provides substantial economic returns.[81,85–88] Since the economic cost of cancer is estimated to be up to 4% of global GDP,[89] addressing the global burden of women's cancers should be regarded as a sound investment by governments.[11,90,91] The investment case is compelling given the major effect of these cancers on premature death and disability, with long-lasting social, financial, and economic consequences for the affected women, their immediate families, and their wider communities.

Beyond evaluating the cost-effectiveness of interventions for breast and cervical cancer control, more research is needed on the macroeconomic consequences of women's cancers. Of the 1676 255 studies on breast and cervical cancer examined by this Series, only 3% included an economics component. Furthermore, only one in ten of these were from a low-income or middle-income setting. Most of the economics studies identified were based in high-income countries and concerned cost-effectiveness assessments of interventions, often under trial conditions. Very few studies about the economic effects of advocacy or survivorship programmes were identified. If we focus on studies exploring the wider economic consequences of the two cancers, the cervical cancer studies are quite evenly spread across all World Bank income country classifications. However, no studies about the wider economic effects of breast cancer from low-income countries were identified.

Cancer affects the national economy and society at large through increased health expenditure, labour and productivity losses, and reduced investment in human and physical capital formation. At the microeconomic level, cancer has profound effects on women, their families, individual firms, and governments.[92,93] Importantly, much of the work done by women is not associated with monetary transactions and is therefore unlikely to be reflected in conventional macroeconomic indicators.[81] Any calculations aiming to assess the economic burden associated with breast and cervical cancer should therefore capture non-income-generating work, such as gathering water and firewood, preparing food, tending to livestock, and caring for children.

If we go beyond the individual effects on women and include their families, the likelihood of catastrophic expenditures is shockingly high in low-resource settings.[94,95] Not infrequently, families faced with enormous direct and indirect costs associated with cancer and its treatment are forced to sell assets and accrue debts.[96–99] This already dire scenario is often exacerbated by employment-related complications such as decreased productivity, job loss, dismissal, and reduction of work-related benefits.[100] A 2015 report of 9513 adults with cancer from eight countries in southeast

Asia[95] found that 1 year after diagnosis, 29% of adults had died, 48% experienced financial catastrophe, and just 23% were alive with no financial catastrophe. Low income was an independent predictor for financial catastrophe, as was education and stage at diagnosis.

A cross-sectional study undertaken between 2002–04 in Argentina,[101] which was a middle-income country at the time, reported a substantial socioeconomic impact on women with cervical cancer, with negative consequences on radiotherapy treatment compliance, despite the fact that 96% of patients reported their radiotherapy was free of charge, paid for either by social security, the hospital, or another agency. Study participants reported work interruption (28%), a reduction in hours worked (45%), loss of household income (39%) with nearly one in five families reporting a loss of 50% or more, a reduction in the daily amount of food consumed (37%), delays in paying for essential services such as electricity or telephone (43%), and the sale of property or use of savings (38%).

To understand the social, economic, and financial consequences of breast and cervical cancer on the health system is essential.[100–104] How the health system is structured and financed[16,105] dictates many of the socioeconomic determinants and inequities of access to health services. Additionally, the efficacy and cost-effectiveness of interventions for breast and cervical cancer control must be critically evaluated to help inform and prioritise evidence-based, resource-appropriate programmes and policies. An understanding of the political economy in which decisions on resource allocation are made, both nationally and internationally, is essential if we are to address the true consequences of breast and cervical cancer.[106,107] These policy implications are examined in greater depth in paper 3 of this Series.[82]

Conclusions

Huge global inequities exist in cancer survival for women. In low-resource settings, breast and cervical cancer disproportionately affect women in the prime of life, resulting in substantial economic and societal effects. A woman's country, region of residence, income level, socioeconomic status, ethnocultural status, or migration status should no longer affect the likelihood of dying from these common cancers.

Several global initiatives are broadening their approach to women's health along the life course, which could provide opportunities to address women's cancers.[108,109] The Global Strategy for Women's, Children's and Adolescents' Health (2016–2030) aims to accelerate efforts to end preventable maternal, newborn, child, and adolescent deaths by 2030. At the 2016 World Economic Forum, the new Every Woman Every Child high-level advisory group was announced to move the new strategy forward, and to ensure that "every women, child, and adolescent not only survives, but thrives".[110] Women's cancers have already received some high-level attention. On World Cancer Day, 2016, UN Secretary General Ban Ki-Moon released a statement that addressed the global inequities in women's cancers, and called for action to eliminate cervical cancer as a public health concern.[111]

International efforts have recently led to major improvements in maternal health outcomes: a similar global drive is urgently needed to reduce the effects of breast and cervical cancer, which currently take the lives of around 800 000 women every year. Cancer control for women could be introduced through the new Sustainable Development Goals. These topics are explored further in the second and third papers in this Series.[17,82]

Contributors

All authors were responsible for key messages and final draft. OG led the Series.

Declaration of interests

We declare no competing interests.

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