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IMPROVING REPRODUCTIVE HEALTH

Meeting the emerging challenge of breast and cervical cancer in low- and middle-income countries

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ABSTRACT

Cancer, particularly when it affects women and reproductive health, epitomizes the complexities and inequities of the epidemiological challenge faced by low- and middle-income countries. Women in resource-poor settings face a double cancer burden: the backlog of preventable cancer, and the emerging challenge of cancers that cannot be prevented but whose impact could be dramatically reduced through early detection and treatment. Disparities in cancer incidence, mortality, and other health and non-health outcomes are exacerbated by gender inequity and compounded by discrimination and stigma. The combination of these barriers implies a multiplicative challenge for women who face cancer, particularly when the disease is associated with reproduction. The horizons of maternal and reproductive health should extend to include the life cycle of healthy changes and illness that are embodied in longer life for women. Numerous opportunities exist to strengthen health systems through sexual and reproductive and women and health platforms and better meet the challenge of cancer.

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1. Introduction

Low- and middle-income countries (LMICs) face a double health burden of increasingly prevalent chronic and noncommunicable disease coupled with an overlapping backlog of disease and illness associated with poverty, preventable infections, and reproductive health problems. This has been referred to as a protracted and polarized epidemiological transition in which diseases that were once considered only of the poor now cease to be the only diseases of the poor [1]. Cancer, particularly the malignancies that most affect women, encompasses a group of diseases that epitomize the complexities and inequities of this epidemiological challenge faced by LMICs [2].

The “double burden” of cervical and breast cancer faced by women in less developed countries is emblematic of the cancer transition [2]. Cervical cancer is declining in incidence in most high-income countries, yet it is far from controlled in LMICs. At the same time, breast cancer though historically less common, is increasing in incidence. Thus, women in resource-poor settings face a cancer

burden that includes the backlog of preventable cancer and the emerging challenge of all other cancers that cannot be prevented with existing scientific knowledge. This emerging challenge is most clearly shown for breast cancer—a noncommunicable disease for which primary prevention is very difficult and there is no known vaccine.

Furthermore, a cancer divide exists that is especially evident for women and is exacerbated by gender discrimination [2]. The cancer divide refers to the disparities in incidence, mortality, and other health and non-health outcomes that are directly related to inequities in access and differences in underlying socioeconomic, environmental, and health conditions. As a result, preventable risk, disease, and suffering from cancer-related ill health and death are increasingly concentrated among poor and marginalized populations.

For LMIC health systems to respond effectively to these compounded challenges, a broader vision is required that goes beyond the false dichotomy of communicable versus noncommunicable disease and breaks down the barriers that have been created [3]. The transition in cancers of women clearly demonstrates the need and the potential to adopt this more holistic view and organize health systems to respond to the needs of people rather than around specific diseases. The horizons of maternal and reproductive health should extend to include the life cycle of healthy changes and illness that are embodied in successfully having women live longer.

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This paper describes the transition in women's cancers and reviews the cancer divide as it relates to the health of women. The conclusions highlight some of the opportunities for strengthening global and national programs, particularly in the context of the agenda that has been put forward by the 2011 United Nations high-level meeting on the prevention and control of noncommunicable diseases. Data are taken primarily from GLOBOCAN 2008 [4], and complemented by recent estimates published by the Institute for Health Metrics and Evaluation [5].

2. The women's cancer transition

A comparison of breast and cervical cancer trends in LMICs highlights the complexities of the cancer transition for women. In all parts of the world other than the poorest countries of Sub-Saharan Africa and South East Asia, breast cancer kills more women than cervical cancer [6].

At the same time, cervical cancer incidence and death are increasingly concentrated among the poor. The disease, despite the options for early detection and treatment in precancerous stages that were developed decades ago, still kills approximately 200 000 women each year, of whom almost 25% are younger than 50 years [5].

Indeed, the burden of these two cancers, both associated with reproduction in women, now exceeds that of many other priorities for women's health in LMICs. This is largely due to the success of efforts in public health focused on women. As a result of declines in maternal mortality, overall more adult women die of breast and cervical cancer each year than of deaths in childbirth. Considering the subgroup of women of reproductive age (15–49 years) in LMICs, and if current trends continue, the ratio of maternal deaths to breast and cervical cancer deaths will be almost 1:1 by 2025 [5].

Cervical cancer is increasingly a disease of poor countries. In 1980, LMICs accounted for approximately 80% of both incident cases and of deaths, and by 2010, the figures had increased to almost 90%. In LMICs between 1980 and 2010, incidence increased by 24% and death by 19%. In comparison, there was an impressive decline in high-income countries of approximately 30% in both incidence and mortality [5].

The contrast with breast cancer makes the transition more evident. In the case of breast cancer, both incidence and mortality are increasing throughout the world, but especially in LMICs. In LMICs between 1980 and 2010, breast cancer incidence increased by 60% and mortality by 53%, compared with 47% and 20% in high-income countries. Thus, the proportion of deaths from breast cancer that occur in LMICs increased from 49% to 63%. As of 2010, deaths from breast cancer in LMICs surpass deaths from cervical cancer by about 50% (approximately 88 000 deaths). In contrast, in 1980 there were approximately 142 000 cervical cancer deaths compared with 122 000 breast cancer deaths. The gap between the burden of breast and cervical cancer is closing, even in the poorest countries, as breast cancer incidence and deaths are increasing at a faster rate [2,5].

Time series of mortality for Mexico and Costa Rica also demonstrate the cancer transition for women. In Costa Rica, the transition is well underway and breast cancer mortality has exceeded cervical cancer mortality since at least the mid-1990s (the years for which data are available) and the difference is now approximately 14 versus 5 per 100 000 women. In the case of Mexico, cervical cancer mortality peaked at close to 16 per 100 000 women in the late 1980s and then steadily declined to a rate of less than 8 in 2008. Breast cancer mortality rose steadily reaching over 9 per 100 000 by 1995 and has remained relatively stable since [6]. Similar trends have been documented for high-income countries (Denmark, Japan, Singapore) and emerging economies (India, China) [7].

Data from within Mexico also demonstrate the transition. In wealthier states, breast cancer mortality surpassed cervical cancer mortality since the mid-1980s. In the poorer states, cervical cancer still exceeds breast cancer but the gap is narrowing rapidly, primarily because of impressive declines in cervical cancer mortality [2].

Breast cancer, often mistakenly thought to be a disease of older as well as wealthy women, is increasingly affecting reproductive-age populations in LMICs [8]. Although demographic transition explains a part (the populations of LMICs are younger), it seems unlikely to be the only factor behind these major differences in the age distribution of onset of the disease. Twice as many breast cancer cases of women aged 15–49 years have been reported in low-resource compared with high-resource regions [5].

Based on age-adjusted data, 66% of breast cancer cases in low-income, 62% in lower middle-income, and 44% in upper middle-income, compared with 33% in high-income countries, are diagnosed before age 54. Late diagnosis and lack of access to treatment combined with younger age at diagnosis explain the large differentials in age at death: 54% of deaths in low-income countries are before age 54, compared with 20% in high-income countries (Fig. 1) [9].

The differences in age at diagnosis are even more striking when late stage of diagnosis is taken into account. Although data are scarce, several LMICs report 60%–70% of cases detected in advanced stages of the disease [10] when cure is much less likely even with access to appropriate, high-quality treatment [11]. Late detection is indeed one of the major challenges to developing an effective response to breast cancer in LMICs.

3. The cancer divide for women

Women face specific and particularly difficult challenges that exacerbate their risks of dying and suffering from cancer. These risks

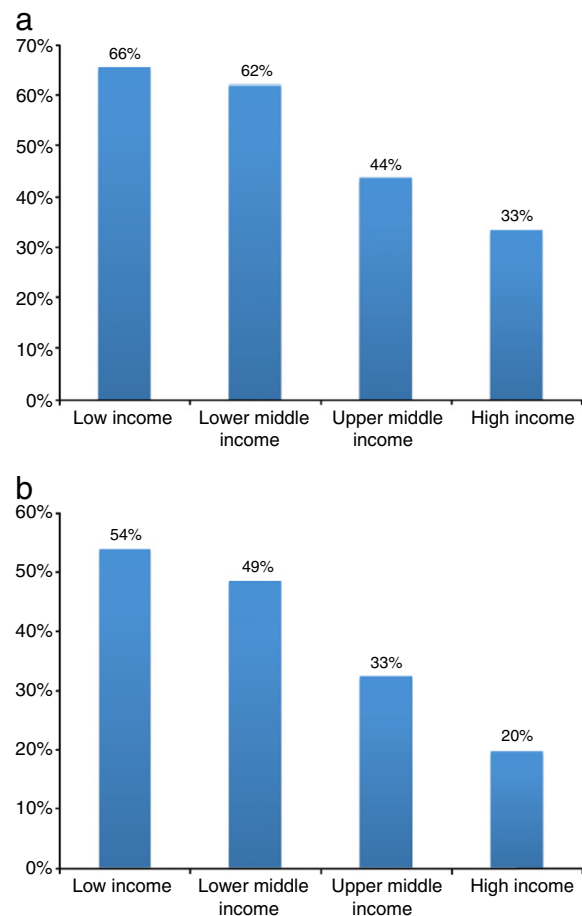


Fig. 1. Age of breast cancer (a) diagnosis and (b) mortality. Percentage younger than 54 years by country income level. Source: GLOBOCAN 2008 [4] and World Bank World Development Indicators 2010 [8].

are in fact associated with all cancers and many other diseases regarding the extent that women face additional barriers to accessing health care.

Chronic illness places severe economic pressures on families and repeat health incidents generate financial catastrophe and impoverishment. The risks of falling into poverty or being excluded from education may be especially severe for women. Female-headed households are at high risk of catastrophic health expenditures as they often rely on a single source of income. Women, and especially young women, are also the most likely source of care-giving in a family struck by a disease like cancer.

Women diagnosed with cancer face multiplicative barriers, especially for cancers associated with reproductive health. Any cancer diagnosis often leads to discrimination and stigma, especially in LMICs [12]. For women this is compounded by discrimination associated with gender, which often expresses itself in issues associated with reproduction [2]. The removal of a breast or loss of reproductive potential can make a woman unmarriageable or lead to abandonment. Thus, the cancer divide—the disparities in outcomes between rich and poor—is associated with and exacerbated by the barriers faced by women in accessing knowledge, as well as prevention, treatment, and palliation.

Social exclusion and cancer often go hand-in-hand and in particular for cancers associated with reproduction. Illness compounds exclusion, especially for diseases like cancer where treatment makes the disease impossible to hide and requires physical mutilation, such as with breast cancer. In LMICs protective legislation tends to be weaker, and ignorance about the etiology, prevention, and treatment of cancer more widespread. In this context, cancer patients and their family members face discrimination. Women, who already suffer discrimination both inside and outside the home, face yet another layer of obstacles.

The difference in the probability of surviving a treatable disease such as cervical or breast cancer is closely related to differences in access to high-quality services for prevention, early detection, and treatment. The ratio of mortality to incidence for breast cancer is twice as high as in high-income countries [13]. The vast majority of deaths—in the case of breast cancer between two-thirds and three-quarters—are considered avoidable with better access to knowledge and health services. Furthermore, the proportion of deaths that can be avoided is significantly higher in low-income compared with higher-income countries [2]. The polarization of the breast cancer burden implies that it will increasingly be poor women who die of the disease despite the possibility of improved outcomes through early detection and treatment. This is already true for cervical cancer given that the vast majority of deaths—most of them preventable even before the development of a vaccine—occur in LMICs.

One of the most pernicious aspects of the cancer divide is lack of access to pain and palliation. An almost 580-fold difference exists in opioid consumption per death from HIV or cancer in pain between the 20% poorest countries of the world and the 20% richest countries of the world. There are also huge variations in access even within regions and countries with similar levels of income that can be reduced by strengthening health systems and regulatory frameworks [2]. Little is known about gender differentials in access to pain, although it is reasonable to suspect that these exist, particularly if women face social exclusion associated with reproductive cancers. Thus, additional research on this issue is required. This could help guide the development of specific and targeted policies.

4. Strategies for action

There is substantial scope for action to close the divide between rich and poor for both breast and cervical cancer in LMICs even where the most advanced early detection and treatment options are not in place. Indeed, in the USA, significant improvements in breast cancer survival were achieved prior to the introduction and availability of mammography [10].

The implementation of effective screening programs for cervical cancer in LMICs has and will continue to substantially reduce morbidity and mortality in the short and medium term. Furthermore, the deployment of the vaccine against HPV could eventually prevent the majority of future cervical cancer cases [14]. The reductions of the price of the vaccine in 2011, particularly for the Pan American Health Organization (PAHO) Revolving Fund and for GAVI-eligible countries, is an important step forward [2].

The lack of public education and awareness in LMICs has been recognized as a significant barrier to better breast cancer outcomes [15,16]. Recognition of the problem among policy makers, the press, and even the public health community is also low [17]. In many low-resource countries, misconceptions about breast cancer discourage many women from seeking treatment [18]. Breast health outcomes cannot improve unless women and the healthcare decision makers in their community understand the benefits of early detection and are willing to support timely diagnosis and treatment.

Innovative strategies to reduce breast cancer morbidity and mortality are necessary and must focus on applying a diagonal approach to health systems strengthening efforts—addressing disease-specific priorities while improving health systems objectives [19–21]. In most LMICs, and unlike in the case of cervical cancer, breast cancer has yet to be incorporated into the broader women and health or antipoverty and health agendas. Breast cancer has not been incorporated into primary, maternal, or sexual and reproductive health platforms because it is assumed to be a disease of older women. This has led to important missed opportunities to reach women with messages and interventions for early detection and around the potential of treatment to cure disease [15].

Specific actions can include training community health workers to identify risk factors, such as family history, and conducting clinical breast exams alongside family planning, prenatal care, and safe motherhood activities. In addition, there are important examples of certain aspects of treatment being conducted at the primary and secondary levels of care, even without an on-site oncologist, through the use of telemedicine and other communications technology. This requires careful case and care management from a tertiary center and training of local staff and especially nurses. Yet, preliminary results suggest that some care can be shifted and even enhanced [2].

On the treatment side, financing has often been seen as an insurmountable obstacle, particularly in the case of breast cancer. However, several countries are responding to this challenge by developing and implementing large-scale programs of financial protection to women at all income levels. One of the most complete programs is Mexico's Seguro Popular Catastrophic Insurance Fund. Examples have also been documented in several other Latin American countries including Colombia, Peru, and the Dominican Republic, and existing evidence suggests that countries in other regions are beginning to develop similar programs. Many important lessons can be gleaned from these programs and help other LMICs to put programs in place. For example, existing efforts demonstrate that coverage of treatment must be accompanied by investing in early detection and primary prevention [2].

Placing cancers of women, particularly breast cancer, on national health agendas requires leadership and stewardship. Civil society led by women—patients and others—has been a strong motivating factor in high-income countries and the same can be true in LMICs [22]. The strength of the voice of women with breast cancer can and should be harnessed, not only to promote an agenda around breast cancer, but more generally for the health of women.

National agenda setting must take a broad outlook [23]. These efforts can be further strengthened by incorporating and encompassing broader goals of overall human development and economic growth, as well as across cross-cutting issues such as climate change and gender equity.

Building a strong evidence base, including cancer registries, but also evaluation and implementation research will be essential to developing and maintaining successful policies and programs. The Breast Health Global Initiative (BHGI) has developed novel and useful guidelines that can enable government and other leaders to help establish priorities that are linked to the level and availability of resources [24].

Almost two decades ago, Nobel Laureate Amartya Sen wrote about the concept of “missing women” to describe women’s disadvantages in overall mortality [25]. Sen noted that the deficit of women or unequal ratio of women to men in many parts of the world largely resulted from gender inequity in access to medical and social advancements. Poor women fare worse in many health outcomes compared with their male counterparts within the same context, but also with women in higher economic strata. Women, and especially those who live in poverty, face multiple layers of disadvantage in the opportunity to survive.

Cancer constitutes a critical and increasingly important example of the disparities faced by women in LMICs. Numerous opportunities exist to strengthen health systems through sexual and reproductive and women and health platforms. Harnessing these opportunities will help to close some of the most gaping facets of the cancer divide.

Conflict of interest

Felicia Knaul is founding president of a not-for-profit foundation, “Tómatelo a pecho,” dedicated to promoting awareness of breast cancer. She lives with breast cancer. Harvard Global Equity Initiative, directed by Felicia Knaul, has or is negotiating financial support for conference and dissemination of research from Johnson & Johnson, Celgene, Endo, and AstraZeneca. The Mexican Health Foundation receives support in the form of donations from numerous pharmaceutical and other private sector corporations based in Mexico and for research led by Felicia Knaul from Sanofi-Aventis, GlaxoSmithKline, Roche, and Chinoin. Julie Gralow receives research funding from Amgen, Novartis, Genentech, and Roche. The other authors have no conflicts of interest to declare. Financial support in relation to this article was provided to the Harvard Global Equity Initiative by Susan G. Komen for the Cure (Grant#: SG11-0311-01-E).

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