

# Breast and Cervical Cancer Screening: Investing in Health Care Systems

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**F**or decades, programs to address women's health in resource-limited settings have focused primarily on strategies to prevent deaths related to pregnancy and childbirth. Maternal mortality remains a devastating example of inequities in health outcomes worldwide – for example, a woman in a low and middle income country is still 65 times more likely to die of a pregnancy-related condition than a woman in a nation with greater resources.<sup>1</sup> Despite this persistent inequality, however, maternal mortality in low and middle income countries has actually declined 45% in the past 2 decades. Furthermore, as the global population ages and acquires more risk factors for non-communicable diseases such as diabetes, hypertension and cancer, it has become urgently clear that chronic diseases are a significant and growing issue impacting the reproductive and non-reproductive health of women,<sup>2</sup> especially poor women. Global health experts have thus started to outline a broader women's health agenda that recognizes the growing burden of non-communicable diseases along with key issues in reproductive health. This more expansive vision would address women's health throughout the life cycle—before, during and beyond the reproductive years.<sup>3,4</sup>

As breast and cervical cancers are the most common cancers among women worldwide, these diseases occupy a central place in the new global women's health agenda.<sup>5</sup> Rates of breast and cervical cancer are rising in low and middle income countries,<sup>6</sup> with about 450,000 new cervical cancer cases and 883,000 new breast cancer cases in less developed countries annually.<sup>7</sup> A woman with breast or cervical cancer in a low and middle

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income country is about twice as likely to die from her cancer than a woman diagnosed with these cancers in a high-income country,<sup>8</sup> and among adult women, the number of deaths from breast and cervical cancers in these countries now exceeds maternal deaths. Disparities in case fatality rates in low and middle income countries and high-income countries are due in part to limited access to effective and affordable diagnostic and treatment modalities, including pathology services, oncologic surgery, chemotherapy, and radiotherapy; but it are also due to higher rates of diagnoses in low and middle income countries made at a late stage of disease.<sup>9,10</sup> In the United States, through widespread awareness, screening, and access to care, 5% of women diagnosed with breast cancer present with incurable Stage IV disease,<sup>11</sup> whereas 25% of women diagnosed with breast cancer in Uganda present with Stage IV disease.<sup>12</sup>

In high-income countries, screening for cervical cancer has led to dramatic declines in the incidence of invasive cervical cancer,<sup>13</sup> while mammography screening for breast cancer, along with advances in treatment, has led to decreased breast cancer-related mortality.<sup>14, 15</sup> As awareness grows of the burden of breast and cervical cancer in low and middle income countries, screening and early detection are major areas of focus. We will discuss what is known about breast and cervical cancer screening and early detection strategies in low and middle income countries, and the limitations of current approaches. We will argue that with far-sighted investment and leadership, breast and cervical cancer screening programs could help realize the vision of a “life cycle” approach to women’s health.

The rationales for breast and cervical cancer screening or early detection are clear, though they are slightly different for each cancer. In order to build understanding of the policy and health system implications of screening programs, we will briefly describe some of the screening strategies employed for each type of cancer. Regular screening for cervical cancer can actually prevent the development of invasive cancer, since it ideally allows the detection and removal of precancerous lesions before they develop further. In the United States, for example, cervical cancer rates have dropped 75% since screening with Pap smears became widespread, whereas 85% of new cervical cancer cases now occur in low and middle income countries, where screening coverage is very low.<sup>16</sup> Cervical cancer screening techniques include cytology (through the Pap smear), visual inspection with acetic acid, and testing for human papillomavirus, which can be used to identify women at highest risk for cervical cancer. While there is no consensus on the optimal cervical cancer screening strategy for low and middle income countries, visual inspection with acetic acid is an inexpensive and straightforward technique that has been advocated for use in low and middle income countries including by the World Health Organization. In visual inspection with acetic acid, vinegar is applied to the cervix; if small areas of the cervix become white, suggesting a possible

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precancerous lesion, these areas can be frozen off immediately with gas such as carbon dioxide (cryotherapy). All of the existing screening strategies, however, require trained health providers operating within functional health care systems with the ability to refer patients to a higher level of care for more advanced diagnosis and treatment, and to track those in need of further monitoring.<sup>17</sup> Of note, primary prevention of cervical cancer through human papillomavirus vaccination has been widely (though inconsistently) adopted in high-income countries,<sup>18</sup> and will also have a dramatic impact on cervical cancer incidence in places where vaccination is available. Efforts to increase vaccines' availability in low and middle income countries are essential.<sup>19,20</sup>

In the case of breast cancer, the goal of screening or early detection is generally to detect cancer that may already be invasive, but at an earlier stage, when it is much easier to treat. Compared with cervical cancer, far less is known about optimal technologies for breast cancer early detection or screening in low and middle income countries. By definition, breast cancer screening entails the identification of asymptomatic lesions. The only screening strategy proven to reduce breast cancer mortality based on studies in high-income countries uses mammography, which can detect non-palpable tumors. Population-based mammography screening is not yet feasible for most low-income countries because of the expense and technical expertise required. However, in contexts where up to one-quarter of women may present with late-stage disease, initial strategies to identify women with palpable masses through clinical breast exam alone may have substantial benefit. Ongoing research in countries such as India and Sudan suggests that screening of entire communities with clinical breast exam by trained workers can bring women in with earlier stage disease.<sup>21,22</sup> There are not yet data to suggest that screening with clinical breast exams can reduce breast cancer mortality.

In contrast to screening of asymptomatic women, early detection efforts promote the diagnosis of symptomatic cancer at an earlier stage, through facilitating earlier presentation and expedited evaluation of women who have identified breast masses themselves. Many late-stage presentations in low and middle income countries result from initial delays in seeking medical care by women who already have breast symptoms, and subsequent system- or provider-level delays in obtaining a diagnosis and initiating treatment. These delays appear to result from low levels of community awareness, stigma and fatalism around cancer (especially breast cancer), limited primary care infrastructure, lack of health provider knowledge and skills, and availability of diagnostic and treatment capacity.<sup>23</sup> This provides opportunities for multiple levels of interventions beyond increasing capacity and infrastructure, though few studies have documented the impact of such interventions. In Malaysia, for example, a program to increase provider skills and public awareness was associated with a 50% reduction in late-stage presentations 4 years later.<sup>24</sup>

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There is great interest in implementing breast and cervical cancer screening programs in low and middle income countries among donors, non-governmental organizations, and governments. Even with proven techniques for screening for cervical cancer in low and middle income countries, however, the human and technical resources and infrastructure for effective and ethical implementation (as well as evaluation) are often lacking. One key principle is that cancer diagnostic and treatment services, as well as palliative care, must be available for patients who are identified as having possible invasive cancer during a screening or early detection campaign. Many women who have an abnormality on breast exam, as well as women with more extensive cervical lesions or suspected invasive cervical cancer, require immediate linkage to a clear referral pathway and robust diagnostic services including biopsies. Facilities must be able to ensure adequate follow-up and treatment of abnormal findings, including obtaining rapid high quality pathological interpretations of biopsy samples that are both accessible and affordable for the general population, including the rural poor. Evidence-based effective treatment must be available, accessible, and affordable for all women diagnosed with treatable breast or cervical cancer, and palliative care must be available for those who cannot be cured. It is also important to note that the establishment of cancer care facilities in itself can lead to earlier detection of cancer through increased public awareness of the availability of treatment. For example, at a large public hospital in Soweto, South Africa, from 2006 to 2012, the percentage of tumors diagnosed at stage III or IV declined from 66% to 46% after the establishment of a breast clinic as well as community campaigns.<sup>25</sup>

A second and equally important principle is that both breast and cervical cancer screening programs must emerge in concert with investment in systems for primary care. Without appropriate infrastructure for patient follow-up, screening programs can fail. This was seen in a group of demonstration cervical cancer screening projects led by the World Health Organization in Africa. In these settings, 40% of patients with visual inspection with acetic acid-positive lesions eligible for cryotherapy did not receive treatment – the majority of these were lost-to-follow-up. Depending on the screening technique employed, efficient and effective screening entails ensuring an adequate supply of trained outpatient clinicians located in community-based settings with water and electricity, training in and dissemination of clear and tested implementation protocols, the ability to identify and recruit the appropriate target population (for example, women aged 35-45 for cervical cancer screening, with an earlier start for HIV positive women), identification of patients who have already been screened, maintenance of equipment and consumable supplies, close tracking of patients with abnormal results to ensure proper treatment and referral, identification of patients who are lost to follow-up, and ideally resources such as patient navigation and transportation funds to facilitate receipt of needed treatment. Many women who have initial abnormalities

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on screening need longer-term follow up and repeat testing at the primary care level – for example, a woman who is human papillomavirus positive but visual inspection with acetic acid negative, or a woman with a mild breast abnormality who does not need immediate referral for a biopsy but does need a repeat clinical exam.

There is substantial opportunity for governments and international partners (whether academic institutions, donors, or non-governmental organizations) to invest in functional, far-sighted breast and cervical cancer screening programs. Much remains to be known about effective screening strategies in low and middle income countries, particularly for breast cancer, and research and evaluation must be key components of all screening or early detection programs. Small-scale campaigns can be of value if they are coupled with implementation research to guide broader scale-up and if they include efforts to strengthen referral systems as well as the primary care systems within which screening occurs. International support for training of local providers must be accompanied by detailed plans and funding for ongoing follow-up, including fostering development of local master clinicians who can lead future trainings. If screening and early detection are regarded as components of a larger health care system to address the burden of chronic diseases, investment in screening programs can catalyze the development of care delivery models. This would include development of documentation systems that can be a platform for other preventive or treatment services, especially for older patients who have had a less well-defined place in traditionally prioritized services such as prenatal care, family planning, and pediatric care. As it historically has done in the United States, cancer screening can be a means of bringing patients into health facilities, and provide important opportunities to screen women for other diseases, including hypertension and diabetes.

As the burden of non-communicable diseases including cancer continues to rise in low and middle income countries, building health systems equipped to care for chronic diseases is vitally important. This includes taking a deliberate and specific approach to women's health that encompasses non-reproductive and reproductive concerns while recognizing the critical roles of women's biology and the social force of gender on health. Screening for breast and cervical cancers can lead to reductions in incidence and mortality of two major causes of death among women, and can address the profound inequities seen in the incidence and mortality from these two cancers. However, screening strategies must occur in concert with both immediate and long-term investment in all levels of the health care system, including support for cancer diagnosis and treatment and for primary care. In such a context, screening can serve as an important opportunity to engage older women in health care, a platform for other preventive and treatment services, and a catalyst for a "life cycle" approach to women's health. As low and middle income countries grapple with adopting effective, acceptable and feasible strategies for

early detection of breast and other cancers, consideration of this broader approach will be imperative to these efforts' sustainability and success.

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