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## Cancer Prevention in Low-Resource Countries: An Overview of the Opportunity

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### Abstract

Rising trends in the incidence of cancer in low- and middle-income countries (LMICs) add to the existing challenges with communicable and noncommunicable diseases. While breast and colorectal cancer incidence rates are increasing in LMICs, the incidence of cervical cancer shows a mixed trend, with rising incidence rates in China and sub-Saharan Africa and declining trends in the Indian subcontinent and South America. The increasing frequencies of unhealthy lifestyles, notably less physical activity, obesity, tobacco use, and alcohol consumption are causing a threat to health care in LMICs. Also, poorly developed health systems tend to have inadequate resources to implement early detection and adequate basic treatment. Inequalities in social determinants of health, lack of awareness of cancer and preventive care, lack of efficient referral pathways and patient navigation, and nonexistent or inadequate health care funding can lead to advanced disease presentation at diagnosis. This article provides an overview of opportunities to address cancer control in LMICs, with a focus on tobacco control, vaccination for cervical cancer, novel tools to assist with early detection, and screening for breast and other cancers.

### INTRODUCTION

Recent reports on the global burden of cancer estimate 18.1 million new cases and 9.6 million cancer deaths worldwide in 2018 (Fig. 1).<sup>1</sup> As the burden of communicable disease and cardiovascular disease continues, the incidence of cancer is on the rise in LMICs.<sup>2</sup> Regardless of the geographic area, social determinants of health (SDH) seem to play a crucial role in cancer control and its outcomes across the globe.<sup>3</sup> Even in higher-income nations, factors related to SDHs play a vital role in obtaining cancer screening, including sociodemographic factors, health literacy, cultural influences, lack of beliefs in preventive

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health, socioeconomic status, and lack of access to health care.<sup>4</sup> Also, patients' attitudes, beliefs (including fear of cancer), and an inadequate number of facilities equipped with cancer screening tools all prevent timely screening.<sup>5</sup> Unfortunately, limited allocation of resources to health care and a lack of implementation of government policies ultimately affect prevention and the disease burden. Although the incidence of cancer is increasing in LMICs, the cost of cancer is limiting its affordability.<sup>6</sup> Therefore, a focus on cancer prevention, early detection, and use of novel and cost-effective methods of screening are invaluable in lowering cancer incidence and the related financial burden on a country's economy. Herein, we describe the global burden of cancers related to tobacco use and other common cancers of the cervix, breast, and gastrointestinal tract, with an emphasis on potential opportunities for cancer prevention in LMICs.

## ADDRESSING THE BARRIERS TO SCREENING FOR THE MOST COMMON CANCERS

### Tobacco Use in LMICs

Tobacco use continues to be the largest preventable risk factor for the main noncommunicable diseases, including cancer.<sup>7,8</sup> Cigarette smoking increases the risk of at least 12 cancers, including acute myeloid leukemia and cancers of the bladder, colon and rectum, esophagus, kidney, larynx, liver, lung, oral cavity and pharynx, pancreas, stomach, and uterine cervix.<sup>7-9</sup> More than 24% of all cancer deaths globally are attributable to tobacco use.<sup>7,9</sup> Currently, more than 1 billion people in the world use tobacco products, and if nothing is done to help them quit and to prevent young people from starting, more than half of these people will succumb to premature deaths from tobacco-related diseases. In 2019 alone, the estimated death toll from tobacco-related disease was more than 8 million.<sup>8</sup> The economic burden is also staggering, approximately \$2 trillion (in 2016 purchasing power parity) from both higher health care costs and lost productivity.<sup>10</sup> Moreover, the burden is increasing in LMICs, where the majority of tobacco users now live.

However, there is encouraging news for public health: Tobacco control has a well-developed package of evidence-based interventions that are proven to work. These interventions are enshrined internationally in the Framework Convention on Tobacco Control (FCTC), the world's first public health treaty under the auspices of the World Health Organization (WHO).<sup>11</sup> Coming into force in 2005, the treaty now has 181 parties, and it undergirds the global approach to tobacco control. In most LMICs, the main provisions of the FCTC are barely implemented, which leaves plenty of room for improvement.

The most effective provision is the increase in excise taxes on tobacco products. The mechanism is simple: When governments raise taxes, companies raise prices to maintain profits, and higher prices lead to lower consumption. Typically, a 10% increase in tobacco prices leads to a 4% to 8% decrease in consumption.<sup>12</sup> This decreased consumption comes in large part from young people not initiating tobacco use. In fact, tax research unequivocally demonstrates two important dynamics: Young people and those in lower socioeconomic groups are more affected by changes in prices. Thus, lower-income people typically reap a disproportionate amount of the reward from these policies.

The other major benefit of tobacco excise tax increases is the increased revenue for government. Because tobacco products are typically inelastic (the decline in consumption is less than the increase in price), governments typically get the double benefit of higher revenue and reduced consumption. Nearly three dozen countries report investing these new tobacco tax revenues in health care, including two, Algeria and Mauritania, using the resources to address cancer specifically.<sup>11</sup>

A second effective provision is graphic warning labels on tobacco packaging. Research consistently shows that educating users, particularly young people, through packaging promotes quitting and reduces initiation.<sup>13</sup> It is inexpensive because governments place the financial burden on the tobacco companies while retaining full control over the messages and images on the package. In recent years, many countries have moved a step further to plain, standardized packaging of tobacco products, which removes all colors and logos. Because these characteristics have been proven to appeal especially to children and youth, their removal is having demonstrable positive public health effects.<sup>14</sup>

A third proven intervention is the banning of tobacco industry marketing.<sup>15</sup> It is well documented that one key part of the tobacco industry's success in attracting and maintaining customers is their relentless marketing. Removing their ability to communicate to the public undermines their efforts to find new customers and maintain existing ones. The challenge is that the industry finds many creative ways to communicate. For example, much tobacco marketing is done now through point-of-sale displays. Another major strategy is price discounting. Governments must be vigilant in addressing the tobacco industry's marketing innovations.

A fourth provision is smoke-free laws that prohibit smoking in public and workplaces. Exposure to second-hand smoke causes substantial morbidity and mortality annually, including an estimated 1.2 million deaths.<sup>8</sup> Approximately one-third of females and one-fifth of males are exposed to second-hand smoke. Smoke-free laws not only protect nonsmokers, especially children, but they de-normalize smoking, and it is well established that smokers are more likely to quit and youth are less likely to start when smoking is rarely observed in public.<sup>16</sup>

An important fifth intervention is the use of mass media campaigns to inform the public. Whereas incorporating learning about the dangers of tobacco use in school curricula is important and useful, targeted mass media campaigns are proving to be a better investment value. Young people are particularly responsive to social media sources, from which they typically get most of their information.<sup>17</sup>

### **Consumption of Smokeless Tobacco**

Although smoking remains the most common and deadly form of tobacco use, smokeless tobacco use is a major cancer risk factor for a number of cancers, most notably those of the head and neck.<sup>18</sup> Globally, more than 350 million people use a wide variety of smokeless tobacco products.<sup>19</sup> Though most smokeless users live in South and Southeast Asia (> 80%), the prevalence of smokeless tobacco use is above 10% in nearly 30 countries around the globe, and use is particularly concentrated in lower socioeconomic groups and increasingly

among youth.<sup>20</sup> Recent research suggests that the accessibility and affordability of these products is exacerbating this growing public health challenge. Most troubling is the lack of policy progress to tackle it, wherein interventions such as taxation and youth access lag behind other tobacco control efforts.<sup>21</sup>

There are three main barriers to successful tobacco control. First, the tobacco industry spends billions of dollars to market its deadly products. The messages of “cool” and “youthful” are ubiquitous and require perseverance by tobacco control proponents to counter. At the same time, the tobacco industry actively lobbies policy makers against public health provisions and even aggressively litigates regulations and policies that seek to reduce consumption. Last, weak governance, particularly in many LMICs, continues to be a major obstacle. Too often, governments are slow to react or do not make any effort to protect citizens from the obvious dangers posed by tobacco use. The FCTC has strong provisions in its Article 5.3 that help governments to insulate themselves from the pressure and influence of the tobacco industry, most notably by actively keeping the industry away from policy making.<sup>22</sup>

### **Cervical Cancer Prevention and Control**

Cervical cancer is an important public health problem among middle-aged women in LMICs, where screening programs do not exist or are ineffective, and a high risk of HIV infection exists. It is well established that persistent infection with one of the 13 high-risk types of HPV may lead to the development of high-grade cervical precancerous lesions such as cervical intraepithelial neoplasia grade 3 (CIN 3) and grade 2 (CIN 2) or adenocarcinoma in situ, which if left undetected or untreated may lead to the development of invasive cervical cancer.<sup>23</sup> Among the high-risk types, HPV 16 and HPV 18 cause 70% to 75% of cervical cancers and 50% to 60% of cervical precancerous lesions.<sup>24,25</sup> This knowledge has led to the development of two major approaches to cervical cancer prevention: HPV vaccination to prevent HPV infection and testing for high-risk HPV to facilitate the detection of cervical cancer precursor lesions.

There is conclusive evidence that cervical precancerous lesions can be prevented by HPV vaccination, and cervical cancer can be prevented with early detection and treatment of precancerous lesions. Given the effective and affordable interventions for preventing cervical cancer, and the fact that implementation of both prevention and early detection can lead to avoidance of cervical cancer, WHO has called on member states to commit and implement a global initiative to scale up preventive, screening, and treatment interventions to eliminate cervical cancer as a public health problem in the 21st century.<sup>26</sup>

**Global burden of cervical cancer**—The estimated age-standardized incidence rate of cervical cancer globally is about 13.1 per 100,000 women (range, 2 to 75 per 100,000 women), based on cancer data from 185 countries.<sup>27</sup> There were approximately 570,000 new cases of cervical cancer and 311,000 cervical cancer deaths in 2018.<sup>27</sup> Cervical cancer was the fourth most common cancer in women, ranking after breast cancer (2.1 million cases), colorectal cancer (0.8 million), and lung cancer (0.7 million). It was the leading cause of cancer-related death in women in eastern, western, middle, and southern Africa. The highest

incidence was reported from Eswatini (former Swaziland), with approximately 6.5% of women developing cervical cancer before age 75. More than one-third of the global burden of cervical cancer was contributed by China (106,000 cases; 48,000 deaths) and India (97,000 cases; 60,000 deaths). Globally, the average age at diagnosis of cervical cancer was age 53, ranging from age 44 (Vanuatu) to age 68 (Singapore). Cervical cancer ranked among the top three cancers affecting women younger than age 45 in 146 (79%) of 185 countries assessed.

Certain countries in West Asia and Maghreb with low incidence of cervical cancer (fewer than 5 in 100,000) have a low frequency of sexually transmitted infections and low prevalence of HPV infection, probably because of socioeconomic factors that reduce risky sexual behaviors.<sup>28</sup> A recent report hypothesized that overtransmission of a protective genetic variant, TP53 codon 72 proline allele, may also be responsible for the low risk in the West Asian population.<sup>29</sup> On the other hand, the high incidence of cervical cancer in sub-Saharan Africa, Latin America, and South Asia seems to be caused by increased background risk attributable to high rates of HPV persistence and HIV transmission.<sup>28,30</sup> Because the burden of cervical cancer in sub-Saharan Africa is substantial and is increasing, there is a great need for improved prevention to reduce morbidity and mortality from this disease.<sup>31</sup>

Information on cancer trends over time enables dynamic planning for changing patterns of cancer at the national level. In Asia, a disturbing pattern is the increasing trend in cervical cancer incidence rates and the narrowing urban-rural differences in incidence after several years of falling rates in China<sup>32,33</sup> and in sub-Saharan Africa.<sup>34,35</sup> The annual percentage increase in age-standardized incidence rates is about 9.2% in China.<sup>33</sup> In a pooled analysis of several prevalence studies, the overall prevalence of high-risk HPV infection was reported to range from 15% to 20% in China.<sup>36,37</sup> On the other hand, cervical cancer incidence rates have been declining with a concomitant increase in breast cancer, particularly in urban populations in India, possibly because of socioeconomic development, reduced parity, and increasing age at marriage.<sup>38</sup>

**Cervical cancer in immunocompromised women**—Precancerous cervical lesions and cervical cancer are more aggressive and progressive in immunocompromised patients. Given the high prevalence of precancerous cervical lesions among HIV-positive women, prevention measures are extremely important in HIV-positive women.<sup>39</sup>

Currently bivalent (targeting HPV 16 and 18), quadrivalent (targeting HPV6, 11, 16, and 18), and nonavalent (targeting HPV 6, 11, 16, 18, 31, 33, 45, 52, and 58) prophylactic vaccines effective in HPV-naive patients have been licensed in many countries, and new HPV vaccines are undergoing evaluation in India and China. The Indian vaccine is expected to be licensed in 2021. The WHO recommends that HPV vaccination be included in national immunization programs as part of a comprehensive strategy to prevent cervical cancer. It recommends two doses 6 or 12 months apart for 9- to 14-year-old girls and three doses over a 6-month period for those aged 15 and older and for immunocompromised patients irrespective of age.<sup>40</sup> There is recent evidence that even a single dose of HPV vaccine might protect against cervical neoplasia.<sup>41</sup> HPV vaccination has been followed by sustained protection against CIN2 or CIN3 and adenocarcinoma in situ associated with HPV 16/18

infection in young women who were not initially infected with high-risk HPV or HPV 16/18, and the occurrence of severe adverse events or adverse pregnancy outcomes was not significantly higher in recipients of HPV vaccines.<sup>32</sup>

Primary prevention of cervical cancer through HPV vaccination is a cost-effective preventive measure. HPV vaccination is being implemented in a number of sub-Saharan African countries with high vaccine coverage, improved community sensitization, and strong commitment from national governments (e.g., Rwanda, Botswana, Zambia), despite various challenges.<sup>42</sup> HPV vaccination has been associated with negative media coverage and negative advocacy in a number of countries.<sup>43,44</sup> Denmark provides an excellent example of how a country grappled with negative media coverage of HPV vaccination and the steady impact of action by national authorities.<sup>43,44</sup> These important national experiences provide valuable leads for successful vaccination implementation for countries beginning to plan for vaccine introduction.

**Screening for cervical cancer**—Cervical cancer can be prevented by screening for cervical precancerous lesions and treating them by screening with cytology or visual inspection with 3% to 5% acetic acid (VIA) or HPV testing. Cytology screening traditionally has been the cornerstone of cervical screening in high-income countries, where it has been followed by substantial decline in incidence and mortality.

The difficulty in implementing cytology or HPV screening in LMICs has led to the implementation of VIA screening and treatment of VIA-positive women with cryotherapy or thermal ablation.<sup>5</sup> The real-time result of screening with VIA allows a single-visit approach combining screening and treatment, thereby maximizing compliance to treatment. Given the feasibility of introducing VIA screening in public health services, several sub-Saharan African countries have implemented it. However, a major challenge with VIA screening has been the difficulties in quality assurance and in maintaining a consistent screening performance in the long run.

The fact that HPV testing is more sensitive, accurate, and reproducible in detecting high-grade lesions and more effective in preventing future invasive cancers than screening with liquid-based or conventional cytology, particularly in the post-HPV vaccination scenario, has led to increasing implementation of HPV screening in national programs.<sup>45</sup> Recent European guidelines strongly recommend primary HPV testing over cytology screening. The possibility of doing HPV testing by using self-collected cervical cell specimens facilitates reaching women who otherwise would not participate in screening. The high negative predictive value and the possibility of longer screening intervals for HPV-negative women are other advantages of HPV screening. It has been shown that even a single round of VIA or HPV screening has been followed by significant reduction in cervical cancer mortality in low-income countries.<sup>46,47</sup>

**Elimination of cervical cancer**—The goal set by WHO to reduce the incidence rate of cervical cancer to less than 4 in 100,000 women globally by vaccinating 90% of girls by age 15, screening 70% of women aged 35 to 45, and treating at least 90% of precancerous lesions detected by screening requires substantial investment by national governments. A

judicious combination of HPV vaccination, screening and diagnosis, and effective treatment of early invasive cancer and political commitment and allocation of adequate resources are critical for elimination in LMICs.

**Global Burden of Breast Cancer**—Breast cancer continues to be the most common cancer in women both in developed and developing countries. According to the GLOBOCAN 2018 estimates, WHO reports 626,679 women lost their lives to breast cancer in 2018.<sup>48</sup> Although the incidence of breast cancer is higher in high-income countries, with 74.4 per 100,000 in Western Europe, compared with 34.4 per 100,000 in Asia, the overall incidence is increasing in developing countries.<sup>49</sup> In 2018, among the 2.1 million cases of female breast cancers diagnosed worldwide, approximately 911,000 cases (rate of 34 per 100,000) were reported from Asia. Correspondingly, the overall outcomes of breast cancer vary with survival rates of 80% or more in North America, compared with 40% or less in low-income countries, demanding continued efforts across the continuum of cancer care in LMICs.<sup>49</sup>

**Epidemiology, prevention, and early detection of breast cancer**—The rising incidence of breast cancer among the younger women in LMICs is concerning. Whereas the median age of breast cancer for women in developed countries is 63, it is more common among younger women between age 45 and 50 and in India, Mexico, and Arab countries.<sup>50</sup> Given that the majority of LMICs have no screening guidelines in place, high-risk screening and chemoprevention options seem unfeasible. In this context, other preventive and cost-effective measures are optimal: mass cancer awareness and education camps, community health workers and navigator-based care delivery models, clinical breast examination (CBE), mobile technology, novel screening methods, addressing other risk factors such as obesity, and lifestyle modifications.<sup>51–53</sup> Although breast cancer prevention trials incorporating high-risk surveillance with imaging and risk reduction strategies with prophylactic mastectomy have shown success in *BRCA* gene mutation carriers, the uptake of these services is not cost-effective in LMICs.<sup>54–56</sup>

Despite the lack of collective agreement on the benefits of CBE, it continues to be an important tool and a standard of practice along with screening mammography.<sup>57,58</sup> Although the success of screening mammography with a 19% reduction in mortality for women age 40 to 70 appears promising, overdiagnosis continues to be a challenge.<sup>59</sup> Mammography is a potential option for screening, but the majority of LMICs lack screening guidelines and equipped facilities for cancer screening. Eventually, many patients succumb to advanced stages of disease at diagnosis and high mortality rates. Also, incomplete treatments and poor adherence continue to add to the burden at a societal level. To explore the use of triennial CBE in reducing the rate of advanced breast cancer and mortality, Sankaranarayanan et al<sup>53</sup> conducted a cluster randomized clinical trial in Trivandrum, India. In this trial, 115,652 women age 30 to 69 in 275 clusters were randomly assigned to receive CBE or no screening. CBE was performed by trained community health workers, who functioned as liaisons between the healthy women and physicians. This study demonstrated higher numbers of early-stage breast cancers in the CBE group compared with the control group (18.8 and 8.1 per 100,000 women, respectively).<sup>53</sup>

**Mobile mammography: a potential tool to improve access and screening in LMICs**—Previous studies reported mobile mammographic units as valuable screening tools in improving access for those with transportation barriers.<sup>51,60–68</sup> However, the utility of and adherence to screening mammography on fixed versus mobile units depended on sociodemographic factors and women’s perceived risk of breast cancer.<sup>61,64</sup> Whereas the users of fixed mammography units were noted to be from stable socioeconomic backgrounds, tended to be insured, and were adherent to screening,<sup>60,61,64</sup> mobile units’ users tended to be from underserved communities with transient lifestyles and living situations and were less adherent.<sup>65</sup> Vang et al<sup>67,68</sup> reported critical gaps and the challenges of the mobile units, such as the quality, incomplete imaging, higher recalls, limited use of newer technology (e.g., film-screen, full-field digital, tomosynthesis), and the lack of diagnostic imaging. Despite the expanding use of mobile mammographic units in several parts of the world, such as sub-Saharan Africa,<sup>62</sup> the association with sociodemographic factors and the recall rates continue to raise challenges for screening adherence.<sup>66</sup> Rodríguez-Cuevas et al<sup>66</sup> conducted a mobile mammography program in Mexico in 2005 and 2006 for women older than age 40. Among the 96,828 women submitted to mammography, only 1% of mammograms in the Breast Imaging Reporting and Data System were 0, 4, or 5. Among women with abnormal mammograms, 27.7% had breast cancer (ductal carcinoma in situ, 2.1%; stage I, 29.4%; stage II, 42.2%), and older age (age 50 and older) was found to be the only risk factor for having an abnormal mammogram. In LMICs with existing infrastructure, multidisciplinary evaluation of mobile mammographic units as a potential cost-effective opportunity will serve as a new avenue for screening.

### Head and Neck Cancers

Head and neck cancers (including cancers of the lip and oral cavity, larynx, oropharynx, hypopharynx, sinuses, and salivary glands) contribute 4.9% and 4.7%, respectively, to the global cancer incidence and mortality.<sup>69</sup> An estimated 76% of head and neck cancer cases and 84% of head and neck cancer deaths occur in LMICs,<sup>69</sup> and high rates of tobacco consumption, including smokeless tobacco, are a crucial concern for increasing rates of these cancers.<sup>70</sup> Although head and neck cancers are largely preventable, substantial morbidity, mortality, and financial burden could be avoided by early detection.<sup>71–73</sup> Head and neck cancers impose catastrophic economic burden on families of patients in LMICs.<sup>74</sup> One study of the economic effects of head and neck cancers in South Asia estimated that US \$16.9 billion was lost on account of these cancers every year in the region.<sup>75</sup> Another study conducted by Patterson et al reported an anticipated global cumulative loss of US\$535 billion during the years 2018 to 2030 due to head and neck cancers.<sup>76</sup> Surgery remains the treatment of choice for these cancers in LMICs since chemotherapy is very expensive and radiation facilities are limited.<sup>77,78</sup> Even surgical care is fairly limited and usually not specialized to handle head and neck cancers.<sup>79</sup>

### Liver Cancer

LMICs together contributed 83% of the global annual incidence of liver cancers and 82% of the global annual mortality from liver cancers in 2018, with China contributing more than 50% of these.<sup>80</sup> Poor survival rates make liver cancer the seventh most common cause of



cancer mortality worldwide (after lung, breast, prostate, colon, non-melanoma skin cancers, and stomach cancers).

Chronic infection with hepatitis B and hepatitis C viruses, alcohol, tobacco, aflatoxins, diabetes, and obesity are all associated with the disease. Cirrhosis is usually a precursor to liver cancer.<sup>81–83</sup> Hepatitis B vaccination, universal safety precautions for preventing transmission of blood-borne infections, blood product safety, supply of sterile needles and syringes to injectable drug users, and safe sex practices have been shown to reduce the transmission of hepatitis B and C.<sup>84,85</sup> Observational studies claim that coffee, statins, metformin, and aspirin have a protective effect against liver cancer.<sup>86–89</sup> Coffee even finds a mention in the 2018 clinical practice guidelines of the European Association for the Study of the Liver.<sup>90</sup> Several LMICs have incorporated hepatitis B vaccines into their national infant immunization programs, and some of these countries have reported declining rates of liver cancer.<sup>91</sup> Sonography is the standard surveillance test recommended by the American Association for the Study of Liver Diseases, the European Association for the Study of the Liver, and the Asia Pacific Association for the Study of the Liver.<sup>91–93</sup> Serum alpha-fetoprotein is sometimes used as an adjunct to sonography.<sup>94</sup>

### **Esophagus, Stomach, and Colorectal Cancers**

LMICs contributed 75% of the global annual incidence and mortality from esophageal, stomach, and colorectal cancers combined in 2018.<sup>80</sup> Contrast radiography and upper endoscopy have been used for screening stomach cancers. Observational studies suggest that the screening has contributed to early detection and mortality reduction, but there are no data from large randomized trials.<sup>95–103</sup> The value of screening asymptomatic people for gastric cancer is controversial even in areas with a high incidence of gastric cancer.<sup>104</sup> There are only limited data suggesting that such an approach may decrease the incidence of gastric cancer in high-incidence areas.<sup>105–108</sup> Therefore, routine radiographic, endoscopic, and *Helicobacter pylori* screenings of asymptomatic healthy people are not recommended.

Tobacco, alcohol, malnutrition, and HPV are identified as risk factors for squamous cell carcinoma of the esophagus.<sup>109</sup> Long standing gastroesophageal reflux disease, with Barrett esophagus as a usual precursor, is associated with increased risk of esophageal adenocarcinoma.<sup>110–112</sup> Benefits of screening for Barrett esophagus have been debated, without a firm consensus. The logistics of implementing such a screening strategy and the subsequent management of patients diagnosed with Barrett esophagus present enormous challenges in LMICs. Overall, the support for radiographic and endoscopic esophageal screening has been modest.<sup>113</sup>

Fecal occult blood test (FOBT) screening for colorectal cancers have shown mortality reduction.<sup>114</sup> Sigmoidoscopy, colonoscopy, and double-contrast barium enema are used to triage FOBT screening positives. Thailand implemented a successful pilot project demonstrating the feasibility of conducting an organized FOBT colorectal cancer screening program in LMICs, setting an example for other LMICs.<sup>115</sup>

## DISCUSSION

The incidence and mortality of cancer are increasing in LMICs; however, more than 70% of the commonly occurring cancers in LMICs have evidence-based prevention, screening, and early detection interventions. LMICs should therefore invest in low-cost cancer awareness, prevention, screening, and early detection programs that are locally feasible. Large investments in human resources would be needed for such programs.

Effective tobacco control measures should top the health agenda in LMICs. Several LMICs already have WHO FCTC-based legislation in place, and they should ensure tougher enforcement.<sup>116,117</sup> Smokeless tobacco use, which is very common in South Asia, is under-researched, and investments should be made in developing evidence-based interventions for smokeless tobacco control. Although increasing taxes and pack warnings<sup>118</sup> on tobacco products are effective evidence-based strategies, additional challenges exist because the majority of tobacco products sold in LMICs are nonpackaged (e.g., single cigarettes) and hence escape regulatory controls. Banning tobacco advertising and marketing (including surrogate advertising and marketing), enacting and enforcing tough smoke-free laws, and promoting effective mass media and social media campaigns targeting teenagers and youth would yield optimal returns on investments.

As studies of single-dose HPV vaccination continue to accumulate data,<sup>41,119–121</sup> two-dose nonavalent HPV vaccination as the standard of care (at least 6 months apart and before the 15th birthday) for girls (and boys if economically feasible) should be next on the list of LMIC health priorities.<sup>122</sup> Along with HPV vaccination, population-based cervical screening with VIA/HPV testing at 5-year intervals between the ages of 30 and 65 (two or three lifetime screens)<sup>123,124</sup> would help LMICs meet the WHO goal of global cervical cancer elimination. Despite the Global Alliance for Vaccines and Immunization subsidies of HPV vaccine, LMICs are still slow in the rollout of HPV vaccines, because of the costs and logistics associated with HPV vaccine delivery. International health agencies must work together to make HPV vaccination affordable in LMICs.

Because the age cohorts for breast cancer in women are much younger in LMICs, mammography as a population-based screening tool is likely to result in more harm than benefit. Based on the current evidence, breast self-examination, CBE, and sonography also cannot be recommended for population-based breast cancer screening in LMICs.<sup>125</sup> Breast cancer control programs in LMICs should therefore be currently limited to awareness programs with increased facilities to diagnose and treat symptomatic referrals.

Screening and early detection of liver cancer continue to be challenging in LMICs. Although liver sonography has been used with some success in Asian countries, it is not feasible in African countries. Therefore, all LMICs should adopt a universal hepatitis B vaccination policy for infants. Additionally, blood safety, universal safety precautions, and safe sex practices should be promoted, given the additional health benefits. Esophagus, stomach, and colorectal cancers are also increasing in LMICs, but these could be attributed to a combination of variables including, diet, physical activity, increasing lifespan, and improved diagnosis of the disease and disease registration processes. Radiographic and endoscopic

screening for these cancers, recommended in some high-income countries, is not feasible in LMICs because of inadequate numbers of service providers and necessary infrastructure. Therefore, focusing on tobacco and alcohol control, and FOBT screening where feasible, might be the best strategies for LMICs.

## CONCLUSION

Cancer incidence in LMICs is on the rise, requiring resources and implementation of cost-effective prevention measures. In addition, the increasing prevalence of obesity and lack of physical activity among people living in urban areas in LMICs will eventually result in sharp increases in noncommunicable diseases, including cancers. Investing in programs to aggressively address this problem is necessary now to prevent this future catastrophe.

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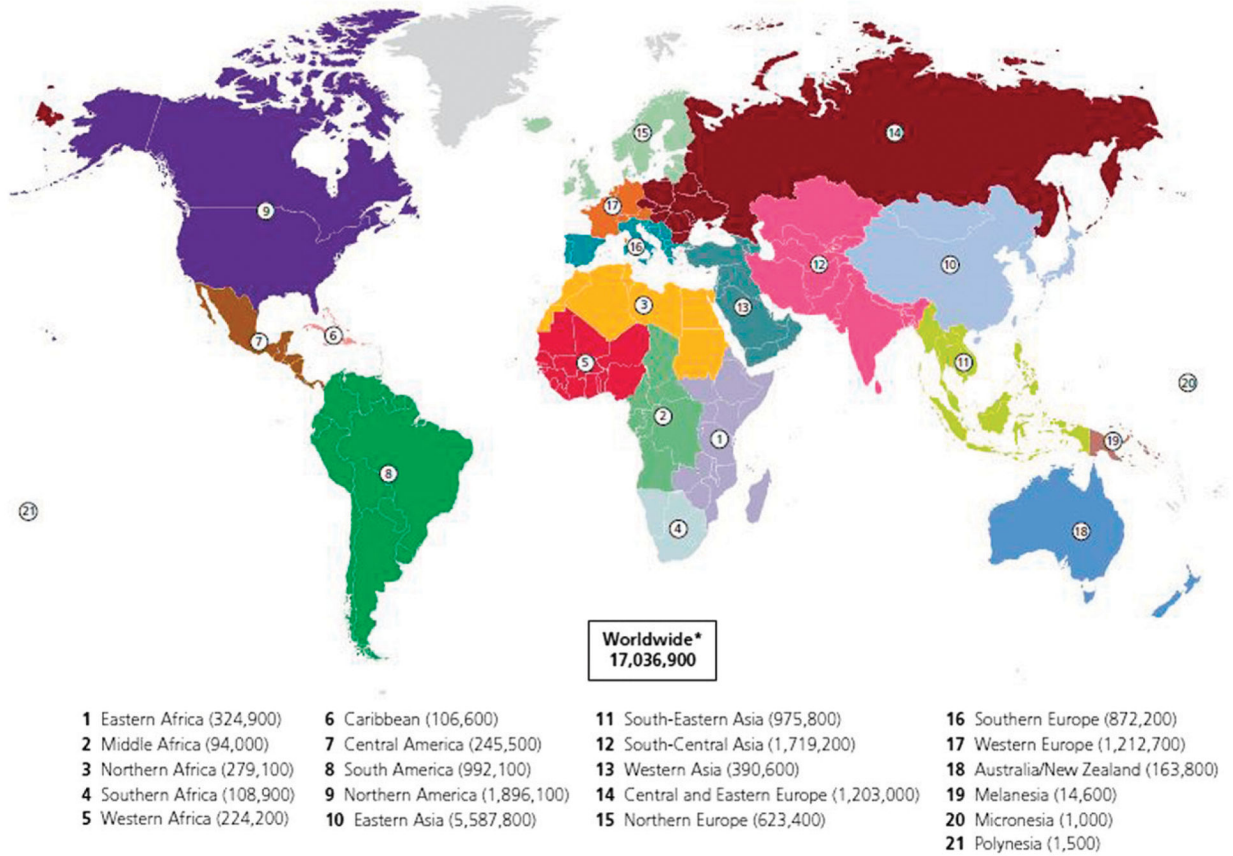


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### PRACTICAL APPLICATIONS

- Cancer incidence in LMICs is rapidly increasing, demanding the dedication of more resources and the implementation of cost-effective prevention measures.
- Cancer awareness and education through community health workers and navigators can improve cancer prevention, screening, and early detection in low-resource settings.
- Government support for comprehensive tobacco control programs—including higher taxes, graphic warnings, marketing bans, and accessible and free tobacco cessation programs—will reduce multiple tobacco-related cancers.
- Prophylactic HPV vaccines have a significant impact in reducing the risk of cervical cancer if deployed successfully to young girls (ages 9 to 14).
- Novel screening methods such as mobile mammographic units, detection of immunochemical fecal occult blood, and Papanicolaou test will assist in early detection of breast, colorectal, and cervical cancers, respectively.

Estimated Number of New Cancer Cases by World Area, 2018\*



\*Region estimates do not sum to the worldwide estimate due to calculation method.  
 Source: GLOBOCAN 2018.

**FIGURE 1.**  
 Estimated Number of New Cancer Cases by World Area, 2018