Global Burden of Cancer Inequality

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FROM THE EDITOR IN CHIEF
Motivating Health Equity
Audiey C. Kao, MD, PhD

It was one of the hottest and muggiest days of the summer, and I was lunching al fresco with friends at a neighborhood pub. As we ate, drank, and chatted, my gaze happened upon a person sitting on the sidewalk down the street. After parting ways, I went to pick up a prescription and realized this person was actually motionless, his head slumped on his chest. A sign was propped on his left side describing his life circumstance and asking for money. As I walked into the store, my mind was whirling: Was it heat stroke? Should I do something? Is he dead?! He’s fine. Where’s my wallet?

Waiting in the pharmacy line gave me a moment to ponder what to do next. I decided to check on this man and bring him something cold to drink. Hesitating briefly, I approached him, bent down, and jostled his right shoulder. This roused him and I introduced myself. He said, “I’m okay.” I gave him a couple of fruit smoothies. He shook my hand. I started home.

Those of us with means and standing can expect to live longer, fuller lives than ever before. Those of us with less or little struggle to simply get through a day. In the city where I live, a recent study found that 2 neighborhoods, one predominantly black and the other mainly white, had a life expectancy gap of 30 years.\(^1\) Inequity in health status of this magnitude is not accidental but a consequence of transgenerationally entrenched power structures that produce and reproduce inequity over time.\(^2\) This is a justice problem and cannot be fixed without tackling social, political, and economic root causes that advantage some of us and disadvantage some of us. With the reemergence of white nationalism and xenophobic bigotry, structural racism and its harms to individuals’ and communities’ health demand urgent attention, especially from those called upon to care for the sick and injured.\(^3\)

Physicians are expected to embody medicine’s ethical oaths and codes, to apply clinical knowledge and skills without prejudice. Yet evidence of racial and ethnic disparities in health care persistently reveals unequal treatment, even after accounting for differences in access to care and patient
preferences. This evidence cannot be ignored or rationalized away, and the US medical profession must not ignore or discount its role in this nation’s history of segregation and racism. The impact of this legacy—still evident in the number of underrepresented minority physicians and false beliefs about biological differences among racial groups—must be understood in terms of how our past has situated our present. We, as members of the medical profession, are obliged to confront this past. Only then can the medical profession aspire to make good on a commitment to mitigate, and to eliminate over time, inequities in health status and outcomes.

The *AMA Journal of Ethics* is committed to catalyzing greater appreciation for and understanding of health equity and to motivating “assurance of the conditions for optimal health for all people.” This editorial commitment is not a new one, as the journal has published a variety of content on health equity. That said, motivating health equity requires deep examination of critical issues that are particularly complex and potentially divisive. From a micro or individual perspective, how should personal accountability factor into health equity? How much should we expect individuals to take responsibility for their own health status? From a macro or policy perspective, how far are we willing to stray from what economists call Pareto efficiency? Should society accept resource allocation decisions that make some people better off while making some people somewhat worse off? The journal invites submissions examining these and other thought-provoking ethical questions.

Furthermore, each issue of the journal will explore some dimension of health equity, regardless of whether the theme is humor in health care (forthcoming in July 2020) or Native American health (forthcoming in October 2020). An entire theme issue dedicated to racial justice and health equity is slated for February 2021. Foci of particular interest include innovations in bias training, organizational responses to unequal treatment, policy solutions to root causes of health status disparities, legal approaches to historical injustices and trauma, and social activism of health care professionals.

As I crossed the intersection, a driver waiting for the light to turn green flashed me a “thumbs up.”Emoji acknowledgment aside, I thought of the man on the street corner, his vulnerability, his future, and how we can do more.

**References**

1. Schencker L. Chicago’s lifespan gap: Streeterville residents live to 90. Englewood residents die at 60. Study finds it’s the largest divide in the


Audley C. Kao, MD, PhD is the editor in chief of the AMA Journal of Ethics.
FROM THE EDITOR
Malignant Disparity and the Ethics of Global Cancer Prevention
Zachary Tabb, MD

In the 21st century, cancer is projected to be the single greatest killer in the world.° While nearly 10 million deaths due to cancer occurred globally in 2018, approximately 70% of those deaths occurred in low- and middle-income countries (LMICs), underscoring that cancer is a reflection of global inequality. Governments will not be able to treat their way out of cancer.° Up to half of cancers are preventable, but several issues challenge prioritizing prevention. Prevention often lacks the social visibility and market appeal of treatment and depends on sustainable behavior change. Moreover, prevention is held to a different standard than treatment; while treatment is assessed by whether it leads to a return equal to its cost, prevention is expected to produce a net positive return. Accordingly, prevention remains neglected.

This theme issue of the AMA Journal of Ethics is devoted to exploring ethical complexities of cancer prevention in LMICs. Evident disparities between cancer control programs in LMICs and in high-income countries illuminate practical challenges to reducing morbidity and mortality of individual patients and at the national level. In providing care to patients in low-resource settings, how should clinicians overcome barriers to access? Where screening services are limited, clinicians must decide whether and when a suboptimal approach is better than none.

Of risk factors for cancer, tobacco remains the leading contributor to cancer incidence worldwide.° Clinicians have an increasingly vital role in prioritizing smoking cessation in light of the rising use and market penetration of cigarettes in LMICs.° The role of global tobacco control regulation, such as the World Health Organization Framework Convention on Tobacco Control,° remains paramount in preventing youth from lighting their first cigarette (or e-cigarette), but its impact will depend on how it is implemented and enforced.

Cervical cancer in many LMICs is the leading cause of cancer death in women.° In these settings, human papillomavirus vaccination policy typically targets
girls alone, but a more equitable policy might be a gender-neutral one that includes vaccinating boys to prevent male-specific cancers while reducing spread of the virus. Given health care access disparities, emerging home-based, self-sampling, cervical screening initiatives could have greater impact on cancer rates than existing facility-based approaches. As oncology research and clinical trials continue, biobanks will play an increasingly important role in deepening our understanding of complex cancer pathophysiology by serving as long-term repositories of biological material for research. Ethical issues in biobanking emerge in practice, however, and researchers must navigate informed consent processes in LMICs. Finally, examining principles of international law, particularly regarding patent protections, holds promise for identifying and addressing barriers to accelerating new developments in cancer prevention technology. This issue of the *AMA Journal of Ethics* examines these timely, complex ethical issues.

References


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CASE AND COMMENTARY
How Should Vaccine Campaigns Balance Need for Clear Communication Against Need for Timely Administration of Large-Scale Programs?
Paul Ndebele, PhD and Sithembile Ruzario, MSc

Abstract
Limited understanding of public health disease prevention programs often leads to resistance, which ultimately results in low vaccine uptake. This article suggests how public health practitioners can improve public understanding of cervical cancer and HPV vaccination programs, which is key to improving health literacy, using culturally appropriate materials and approaches to boost public acceptance of vaccine programs.

Case
Dr M was trained in the United States but has returned to her native country to serve as the chief medical officer of a regional health district. This low-income country’s Ministry of Health has decided to fund human papillomavirus (HPV) vaccinations in Dr M’s district, given the recent increase of cervical cancer incidence. Understanding of HPV and cervical cancer is almost nonexistent in Dr M’s district, and she is extremely concerned about how to discuss risks and benefits of vaccination and obtain informed consent from parents of the 9- to 14-year-old girls. Dr M greets a girl’s mother, Ms A, at a district health center and begins to counsel Ms A about the HPV vaccine and cancer prevention. Ms A listens attentively and then asks in English, “Are you saying this cancer is an infection like HIV?” Dr M responds, “The cancer is caused by an infection, a virus. HIV is also a virus. But this vaccine protects you from HPV, not HIV.” Dr M attempts to clarify, but Ms A doesn’t appear convinced. “And this cancer, it grows in her belly, like a pregnancy? So, this vaccine will be like preventing pregnancy?” Dr M wonders which source of confusion to address first and then explains, “The vaccine will not affect whether she can have a family.” Ms A wonders, “If I say no to this vaccine, the cancer will grow, and she will not have children?” Dr M wonders how to respond.
Commentary
This case is a common one in low-income countries whose public health and health care delivery systems are dependent on foreign-trained practitioners. The challenges associated with the implementation of public health prevention programs in low-income countries go beyond patient-clinician communication. This commentary investigates how vaccine campaigns should balance ethical demands to clearly communicate risks and benefits with clinical and public health demands to efficiently administer large-scale programs. Using examples from some of our work conducted in an HIV prevention study setting in Malawi, we provide some suggestions for how clinicians and public health practitioners can improve public understanding of cancer prevention programs, with a focus on improving stakeholder engagement and health literacy.

Limited Understanding
Community members in low-income regions might have limited health literacy. Some might lack adequate vocabulary to describe either a specific disease or vaccines, and there can be confusion about disease causation.\(^1\),\(^2\) Nevertheless, lack of knowledge of a specific disease and of a vaccine for that disease should not be taken to imply that there are no cases of that disease in a region or that community members have no experiences with vaccination or other prevention strategies. Community members might simply view disease causation differently.\(^3\) For example, some might believe that a disease caused by a virus is instead caused by witchcraft.

Conversely, those implementing public health programs might lack knowledge of community members’ understanding of disease. Because they might not understand local traditions or appreciate their importance and impact, some public health professionals might fail to engage with community members in ways that facilitate local uptake of prevention programs or awareness of their importance. Lack of engagement might also be due to limited financial, personnel, or training resource investment in a public health intervention; a fundamental need for speedy public health intervention implementation;\(^4\) and to overemphasis on boosting numbers of patients vaccinated or insufficient respect for patients’ or parents’ rights to make decisions about whether to accept or reject an intervention for themselves or a child.\(^5\),\(^6\)

Communication Goals
In many low- and middle-income regions, limited understanding or lack of knowledge of cervical cancer and prevention can interfere with vaccination uptake.\(^7\) Refusal or hesitancy to vaccinate one’s child against measles in the United States is one example.\(^8\) If disease prevention programs do not
facilitate adequate explanation of an intervention’s benefits or overemphasize an intervention’s potential harms as a way to manage litigation risk, even patients or parents with high health literacy might refuse an intervention. Acceptance of any intervention depends on understanding not only risks and benefits but also the problem being addressed, why a proposed intervention is a useful solution, and the implications of the proposed intervention. Accordingly, acceptance of an HPV vaccine requires understanding cervical cancer and its associated risks, understanding the need for vaccination, understanding the risks and benefits of vaccination, and—more importantly—understanding the implications of present and future implications of vaccinating children before they’re sexually active. In the case, Dr M and fellow practitioners need to balance an ethical imperative to communicate clearly with community members about cervical cancer and the potential risks and benefits of vaccination with public health demand for efficient intervention. An efficiently implemented, administered, and executed vaccine campaign begins by promoting uptake in communities.

Engaging Community Members
Public health practitioners need to become familiar with how patients’ cultural and religious beliefs, for example, inform or obstruct their understanding of cervical cancer and HPV vaccines. In particular, clinicians and health educators from resource-rich regions should be aware of how their relative power and authority is perceived and experienced by those whom they seek to serve and should consider how to express respect for individuals’ self-determination in the context of community. It is particularly critical to express respect when discussing beliefs about disease causation that are “wrong” from an allopathic perspective, since a key to intervention uptake is making patients and community members allies in the overall public health effort. In the case, expressing respect for the region’s cultural and religious values would mean ensuring that women public health practitioners are the ones who interact with, and introduce the program to, local girls and their mothers.

Navigating Cultural Pluralism While Cultivating Common Need
One way to help ensure that community members start to feel the need for cervical cancer vaccination is to facilitate their understanding of cervical cancer’s regional severity and incidence. In the case, Dr M and fellow clinicians can focus on helping community members understand HPV vaccination as a way to preserve girls’ and women’s lives. Some might argue that it is only fair to extend vaccination to boys as well, since they are the ones who transmit the virus to girls during sexual intercourse. In some regional religious groups, sex is permitted only in marriage and some might fear that vaccinating
children constitutes an endorsement of premarital sex. But Dr M and colleagues can perhaps draw upon regional marital and family-oriented values to problematize health beliefs that are wrong from an allopathic standpoint and to motivate the public health interests of children today, who might be the adult regional family leaders of tomorrow.

**Disarming Misinformation, Improving Understanding**

Low levels of health literacy can exacerbate language barriers and frustrate communication about risks and benefits of an intervention. When critical information about an intervention is not well understood by those who bear the risk of receiving it, gaps in understanding can be filled by misinformation and spread as rumor. Public health practitioners’ awareness of and capacity to disarm rumored misinformation is critical to the success of public health interventions.5,12,13 Furthermore, some languages do not have English-equivalent words14 to accurately describe cervical cancer, symptoms, treatments, or vaccines from an allopathic perspective. In such cases, public health practitioners and clinicians can use visuals to clearly describe cervical cancer and stories from everyday life to explain vaccinology. In Malawi, for example, agricultural pictures are used to try to explain placebos, double blinds, and randomization15,16 and lay language is used to facilitate a prospective research subject’s consent to enroll in a trial.17,18

When explaining HPV vaccination, public health practitioners must clearly describe a vaccine’s prospective short-term and long-term reproductive health risks and benefits or, if a vaccine is experimental, its risks and possible benefits. Some individuals might be familiar with vaccinations for diseases such as measles and tetanus that have been administered in low-income regions of the world in recent decades. If so, clinicians can draw upon known examples to help community members understand how mortality from these diseases was reduced by vaccine programs and to suggest reasons to hope for mortality reductions of an HPV vaccine.

**References**


16. Ndebele P, Wassenaar D, Masiye F, Munalula-Nkandu E. Trial participants’ understanding of randomization, double-blinding, and placebo use in low literacy populations: findings from a study


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CASE AND COMMENTARY

How Should Physicians in Low- and Middle-Income Countries Regard Electronic Nicotine Delivery Systems to Facilitate Smoking Cessation?

Thomas E. Novotny, MD, MPH, DSc (Hon) and May C. I. van Schalkwyk, MBBS, MPH

Abstract

Electronic nicotine delivery systems (ENDS) have been widely referred to as “safer,” “healthier,” and more “effective” smoking cessation aids, but little evidence supports such claims. New concerns about pulmonary injuries associated with ENDS suggest reasons for concern about these products’ health risks and potential for nicotine addiction. Nevertheless, multinational tobacco companies heavily market ENDS to retain customers with nicotine addiction, and global progress against tobacco use might slow as a result. The tobacco industry has managed to divide the tobacco control community by offering hope of harm reduction without actual evidence of ENDS’ effectiveness or long-term safety. Low- and middle-income countries need this evidence to assess ENDS’ value in mitigating tobacco use.

Case

Dr L, a family medicine physician in a middle-income country, sees Mr G, a 47-year-old man with moderately controlled hypertension and hyperlipidemia. Mr G has a 50-pack-per-year smoking history and has tried, without success, to quit. Over the last 3 months, he has cut his smoking from 2 packs to 5 or 6 cigarettes per day. Mr G explains enthusiastically to Dr L that he’s finally been able to reduce his regular cigarette use by using electronic (e-)cigarettes, which, along with tobacco cigarettes, are heavily marketed in his neighborhood. “I’ve been told that e-cigarettes don’t contain the cancer-causing toxins in real cigarettes, so I feel better about smoking these instead, and I love the flavors.”
Dr L has worked with many patients who struggle with smoking cessation and with family members who struggle with the consequences of having a family member who smokes. While some recent research suggests that e-cigarettes offer a better means of smoking cessation than other methods, significant uncertainty remains about the effects of long-term e-cigarette use. “This is good progress. I know it’s hard because cigarettes are everywhere here,” said Dr L. Then, trying to clarify, he added, “Nicotine concentrations in e-cigarette oil blends can still be harmful, and there could be other carcinogens in these blends, so it’s important that you continue to try to wean yourself off the habit altogether.”

Mr G looked crestfallen, and Dr L considered how best to respond.

Commentary
The US Food and Drug Administration (FDA) defines electronic nicotine delivery systems (ENDS) as noncombustible tobacco products including “vapes, vaporizers, vape pens, hookah pens, electronic cigarettes (e-cigarettes or e-cigs), and e-pipes,” as well as devices with flavored nicotine-containing “pods” that attach to them. Use of these products has grown enormously since the 2003 invention of e-cigarettes by a Chinese pharmacist whose father died of lung cancer. Manufacturers marketed these products first in China and subsequently in the United States, notably without any regulatory oversight. The Family Smoking Prevention and Tobacco Control Act, which established FDA regulatory authority over tobacco products, was not signed into law until 2009. Some in the public health community welcomed ENDS as a potential harm-reduction approach to the continued global tobacco epidemic, reasoning that any reduction in cigarette use should outweigh any potential risks of ENDS.

In 2016, the FDA officially deemed that it had regulatory authority over the manufacture, import, packaging, labeling, advertising, promotion, sale, and distribution of ENDS. Of note is that the FDA has not approved ENDS for smoking cessation. A 2016 Cochrane review reported low-quality evidence supporting ENDS’ efficacy in aiding quitting. However, in 2018, Public Health England of the United Kingdom (UK) provided a summary of available evidence to support the clinical use of ENDS. Multinational tobacco companies and some experts have promoted these products with implied claims of their safety and cessation efficacy. In fact, recent findings suggest that US smokers use these products more than they do FDA-approved cessation aids (such as nicotine replacement, bupropion, and varenicline) to help them quit.
Despite the international marketing success of ENDS, consumers and clinicians should be cautious about these products’ use. Evidence suggests that ENDS pose risks for human cardiac events, pulmonary toxicity, and cancer. Recent studies have also shown increased exposure to toxic volatile organic compounds (carcinogens) among adolescent smokers and have found potentially toxic metals in e-liquids. Nicotine itself is a neurotoxin that poses a particular risk for the developing child and adolescent brain. ENDS use is now considered an epidemic among young persons in the United States. Therefore, clinicians should carefully evaluate the clinical utility and the risks of ENDS for those addicted to nicotine who use them long-term. Clinicians have a duty of care to be up-to-date on the literature on ENDS, including recent developments regarding safety and efficacy.

**Counseling Mr G**

Any practicing clinician who has advised a patient to quit smoking understands the extraordinary difficulty these patients face in overcoming nicotine addiction and other behavioral reinforcements that sustain tobacco use. Nonetheless, most experts agree that counseling and various approved cessation medications improve quitting success, especially when combined. Mr G, a heavy smoker, is at significant risk for serious illness (especially for the many cancers caused by smoking), and he presents an ethical challenge for his primary care physician. Mr G has accessed ENDS in an effort to reduce the harms of heavy smoking, and he has probably seen or heard advertising that reinforces his decision. Although there are approved medications and alternatives, these are likely to be more expensive than ENDS and are not always covered by health insurance. An ethical dilemma confronting Dr L is that ENDS are commercial products marketed by multinational tobacco companies as “healthier,” even though they have not yet been fully vetted for cessation treatment. Dr L’s dilemma is also emblematic of a wide gulf between different public health agencies’ and professionals’ positions on ENDS. The UK’s National Health Service, for example, suggested that the risk of harm from ENDS is worth ignoring as it is a safer alternative to smoking, while others believe that the risk of sustained nicotine addiction and unproven claims about ENDS should be more strongly considered in the clinical treatment of tobacco use.

How should Dr L proceed? Both the physician and the patient in this case correctly understand that ENDS might have less carcinogenic potential than combustible tobacco products. Dr L also correctly understands that the overall
risks for long-term ENDS use are still unclear. ENDS will certainly sustain Mr G’s nicotine addiction, which is dangerous for patients with cardiac risk factors such as hypertension and hyperlipidemia. Moreover, Mr G continues to use cigarettes, for which there is no safe threshold of consumption.

Dr L wisely reinforces Mr G’s progress in reducing his daily cigarette use, but, just as wisely, Dr L recognizes the need to assist Mr G in weaning himself completely from nicotine. In this case, there needs to be a mutually agreed-upon endpoint to Mr G’s ENDS use. Just as with nicotine replacement therapy, Dr L needs to work with Mr G to set a date by which he completely ceases using any tobacco product, including ENDS. Reinforcing Mr G’s intention to reduce his risk of tobacco-related disease will support his autonomy in this effort.

**Considerations for Dr L**

*Guidelines.* As part of efforts to end the tobacco epidemic, the World Health Organization (WHO) Framework Convention on Tobacco Control (FCTC)—the first international health treaty—provides guidance for cessation assistance at the national level. The FCTC recommends cessation supports and treatment of tobacco dependence as key components of a comprehensive, integrated tobacco control program. In particular, the FCTC guidelines call for development of national strategies for evidence-based clinical treatments that are free of conflicts of interest with “commercial and other vested interests of the tobacco industry.” Health professionals everywhere arguably have a duty to advocate for such evidence-based measures as part of quality-focused and equitable health care systems in their countries.

*Conflicts of interest.* Further muddying global perspectives on ENDS are efforts of a large multi-national tobacco company to promote the Foundation for a Smoke-Free World. Led by a former WHO deputy director, this Foundation has dedicated millions of dollars to ending smoking, which “means eliminating the use of cigarettes and other forms of combustible tobacco worldwide.” While continuing to vigorously market cigarettes throughout the world, the tobacco company now markets new heat-not-burn tobacco products in the United States in an attempt to keep its customers. These products also have not been evaluated for safety or cessation efficacy. The WHO correctly states that if the company “were truly committed to a smoke-free world, the company would support these [WHO FCTC] policies.” Instead, the company “engages in large scale lobbying and prolonged and expensive litigation against evidence-based tobacco control policies such as those found in the WHO FCTC.” The risk to public health
posed by this paradoxical effort cannot be underestimated. Spending millions of dollars on high-level lobbying annually\(^3^7\) and obfuscating new product risks are effective tools to sustain profitability. The newfound commitment to a smoke-free world is likely to be more of the same.

**Recommendations**

Clinicians such as Dr L need to rely on evidence-based information about ENDS and also to be aware of multinational tobacco industry initiatives to preserve their market share and sustain demand for potentially deadly tobacco products. ENDS might have many more health risks than originally identified and should have already been subject to careful scientific scrutiny. Dr L should support this patient’s commitment to reduce his tobacco use. He should recommend other proven cessation aids as alternatives to ENDS. Dr L can also meet with him more frequently and perhaps support his quit attempts with telephone contact and referrals to other cessation support services such as telephone quitlines.\(^3^8\)

Given the growing evidence of health risks of ENDS and the still-tenuous evidence that there are population benefits to using these largely unregulated products, there is no compelling ethical or clinical justification for clinicians to recommend vaping for smoking cessation. Clinicians should advise patients, as Dr L has, to eventually eliminate any form of nicotine delivery, regardless of their global locale. When deciding how to treat and advise Mr G, Dr L should be guided by fundamental ethical considerations of clinical care, as articulated by the WHO.

Most health practitioners want to do what is best for their patients. Non-maleficence (“first do no harm”), beneficence (doing good) and trust are fundamental ethical principles at the heart of clinical care. Health practitioners also seek to ensure that patients are given adequate information, are consenting to treatments and procedures voluntarily, and have the capacity to understand and appreciate the potential benefits and risks of the care they receive. Health practitioners seeking to provide the best possible care to their patients in the most ethical manner may find it difficult to balance the right to information with the need to avoid information overload.\(^3^9\)

Dr L should also incorporate procedural justice considerations by explaining how he made his recommendations and which values and evidence he used to inform these recommendations. In this way, he would ensure transparency of his decision making with his patient.

The advertising blitz and the subsequent rift over the utility of ENDS in a normally unified public health community will likely continue. ENDS use has
been firmly established in many high-income countries, even those with functional regulatory authorities.\textsuperscript{40} In low- and middle-income countries (LMICs), however, clinicians and consumers need more information and more alternatives to assist smoking cessation rather than just accepting ENDS as an unproven cessation tool. LMICs suffer from information asymmetries regarding ENDS, as these products established consumer markets before clinical guidelines or regulatory regimes for them were established.\textsuperscript{41}

New Problems for ENDs

In August 2019, reports of severe pulmonary injury associated with ENDS gave rise to more concerns about these products’ use among public health authorities.\textsuperscript{42} An epidemic of these injuries caused a variety of jurisdictions to temporarily ban the sale of ENDS and to issue warnings not to use products that have been altered with any additives, especially cannabinoids.\textsuperscript{43} Until more is known about the role of ENDS in these injuries, additional caution about recommending ENDS use should be exercised.\textsuperscript{44}

References


33. Tobacco Tactics. Foundation for a Smoke-Free World. 
34. Foundation for a Smoke-Free World. Request for proposal: advancing industry transformation—Smoke-Free Index. 


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The viewpoints expressed in this article are those of the author(s) and do not necessarily reflect the views and policies of the AMA.
CASE AND COMMENTARY

When Is a Suboptimal Approach to Cancer Screening Better Than None?

Ramy Sedhom, MD and Bishal Gyawali, MD, PhD

Abstract
Cancer care in low-resource regions is complex, as resources and infrastructure for cancer care and prevention are limited. Mortality rates for breast cancer in particular are higher in regions where treatments are unavailable, unaffordable, or cost ineffective. Clinical breast examination is a reasonable screening approach, although its effects on mortality have not yet been shown. This article recommends focusing on early detection of symptomatic disease (ie, downstaging) and treatment of early detected breast cancers with potentially curative strategies.

Case
Ms P, a 59-year-old woman who lives in a remote, low-income region, has worried about cancer ever since her mother died from metastatic breast cancer a year ago. As the family’s sole income earner, she would not be able to support her children if she developed a serious illness. When visiting Dr A for her child’s earache, she tells Dr A that she wishes she could get a mammogram so that any cancer could be detected and treated early.

There are only 2 clinics in the country where mammography is available, and Ms P has access to neither without making a long journey that she cannot afford. However, Dr A does have an ultrasound machine. Although ultrasound is generally not accepted as a way to screen for breast cancer, Dr A has experience using ultrasound in a variety of diagnostic and screening contexts, and perhaps using it would ease Ms P’s mind. Dr A wonders whether to offer to examine Ms P via ultrasound.

Commentary
The global burden of cancer—including breast cancer—is growing, with low-income countries (LICs) contributing to the majority of new breast cancer
cases and deaths. Indeed, LICs now contribute to roughly 53% of global breast cancer incidence. In addition, because the resources and infrastructure for cancer care and control are limited in LICs relative to high-income countries (HICs), the mortality rates for breast cancer are higher in LICs. In fact, breast cancer remains the number one cancer killer among women in LICs. Thus, the patient described in the vignette is appropriately concerned about her risk of breast cancer and her likely outcome, given that she resides in an LIC. However, whether screening is the appropriate solution remains a challenging question.

Screening for breast cancer in LICs presents a paradoxical dilemma. On the one hand, no screening would lead to increased odds of presentation at advanced-stage disease for which treatments are unavailable, unaffordable, and cost ineffective. On the other hand, LICs are not equipped to both implement a screening campaign effectively and deal with the downstream consequences of screening-detected lesions, most of which end up not being cancer. Debate persists even about whether mammography screening is appropriate in HICs. The United States Preventive Services Task Force (USPSTF) assigns a grade B recommendation for biennial mammogram screening for women aged 50 to 74 who are not at high risk. (The USPSTF recommendation grades range from A (highest) to D (lowest), where grade B implies recommended service based on high certainty of moderate benefit or moderate certainty of moderate to substantial benefit.) For the sake of discussion, let’s assume this recommendation applies to women in LICs. Since Ms P is in this age group, should mammography screening be recommended, despite not being locally available? And should ultrasound screening be offered instead because she can’t afford the journey for a mammogram? If neither is appropriate, what alternatives are there for Ms A’s care?

**Mammography in LICs**

For screening to be appropriate, it “must be acceptable, equitable, accessible, sustainable, and economically efficient for the target population.” The aim of a screening campaign for cancer thus could be different in low- and middle-income countries vs HICs. In resource-poor settings, focusing on mitigating symptomatic disease should be prioritized rather than, as in developed nations, focusing on cancer detection in asymptomatic women. For example, a cohort study from Uganda revealed that 77% of breast cancer patients at a national cancer hospital had advanced disease, defined as stage III or IV. Thus, LICs should focus more on reducing advanced-stage diagnoses by using campaigns to educate women and to encourage symptomatic women to
come forward for diagnostic evaluation. For Ms P, living in an LIC, tumor detection at the earliest stage should be the clinical and ethical priority.

An important aspect of the debate about cancer screening in LICs is the effect of screening on all-cause mortality vs cancer mortality. For example, although mammography reduces breast cancer-related deaths among women in Ms P’s age group, overall life expectancy for women in LICs is less than that of HICs. The upshot here is that, while it is important to address Ms P’s concerns, it is also important to consider that screening mammography has failed to improve all-cause mortality, even in HICs.

If we consider the costs, inconvenience, and inaccessibility of mammography in LICs, together with the infrastructure needed to implement it, there is arguably less justification to spend limited resources for this screen, given its limited evidence of effectiveness and potential for harm. In sum, the inconvenience of a mammogram could be justified for diagnostic purposes if Ms P has symptoms, but probably not for screening.

### Ultrasound in LICs

In general, as mentioned in the case, ultrasound is not recommended as a screening modality. Even when ultrasound is used as an adjunct to mammography, its effect on reducing breast-cancer mortality is uncertain, and screening with adjunct ultrasound actually increases false positives in women at high risk.

For Ms P, there is a small chance that ultrasound would be helpful and a risk of harm from a false positive.

However, in deciding whether to offer Ms P ultrasound, we need to consider not only the evidence but also the economic context. Screening is not a one-time detection intervention; for a screening program to function well and be clinically and ethically justifiable, resources must be sufficient to respond to the downstream follow-up required for patients in whom a lesion is detected, including referral, confirmation diagnostics, and treatment. If Ms P’s local center doesn’t have mammography, it probably doesn’t have sufficient resources for biopsy, surgery, radiation, and other procedures. Given the lack of follow-up capacity, the risk of harm from a false positive should be regarded as clinically and ethically prominent.

Previous cost-effectiveness studies suggest that treating stage I breast cancer is the best breast cancer control strategy for LICs. Ideally, all cases
of breast cancer would be discovered early and referred to a surgeon. However, many LICs lack surgery, pathology, and radiation facilities. Nearly 80% of patients in LICs require surgical oncologic care, but 75% will not have timely access. Other studies similarly show that women in LICs lack access to appropriate pathology and radiotherapy services. How, then, should we advocate and care for patients like Ms P?

The goal of screening is not just to detect but to treat detected disease. For Ms P, diagnosis and treatment will remain challenges, so is it ethically appropriate to pursue tumor detection if treatment is not available to her? A breast cancer diagnosis could cause distress, physical harm, and unknown downstream consequences. If appropriate clinical care for a detected lesion is unavailable, one could argue that it’s not ethically justifiable to screen without capacity to treat.

**Screening for Asymptomatic Disease vs Early Detection of Symptomatic Disease**

Diagnostic delay is an important cause of late-stage diagnosis for women in LICs. Previous studies have evaluated patient delays (lag from initial symptoms to presentation to a clinician) and clinician delays (lag from a patient’s first presentation to diagnosis or treatment). Patient delay can be due to a patient’s lack of awareness of breast cancer symptoms, severity of disease progression, lack of access to a qualified clinician, or lack of financial means to pay for treatment. Lack of breast cancer experience and knowledge among primary care clinicians and quality deficiencies in cancer care contribute to clinician delays in LICs, although this topic has been less extensively investigated. We recommend as a national screening strategy that LICs prioritize early detection among patients with symptomatic disease to help reduce the kinds of delays just described. Interventions to reduce delays in care would increase the number of patients with potentially curable breast cancer who seek care and reduce breast cancer mortality while minimizing expenditure of limited resources. To address the needs of women like Ms P and the population needs of LICs, clinical breast examination (CBE) could be a reasonable middle-ground approach.

Many women with breast cancer in LICs seek care when their cancers have progressed beyond curability. Treating advanced disease is less hopeful and more expensive and requires complex infrastructure and the availability of multiple subspecialties. By contrast, treating women whose breast cancers are detected early can be done with less costly surgery, radiotherapy, and limited-time adjuvant treatment. CBE has been proposed by the International
Agency for Research on Cancer as an alternative to mammography to detect breast cancers at an earlier stage.\textsuperscript{30} In Malaysia, for example, there was a 41.7\% reduction in the proportion of patients presenting with advanced-stage breast cancer within 5 years of introducing a cancer surveillance program that included CBE screening.\textsuperscript{29} In Indonesia, CBE was nearly as effective as mammography,\textsuperscript{31} and, in India, annual CBE was estimated to be as effective as mammography but only half the cost.\textsuperscript{32,33} Because detecting cancer at an early stage when treatment is more affordable is important for LICs, CBE can be an important tool of cancer control in LICs if implemented properly.

For Ms P, CBE would likely be more appropriate than mammography. Preliminary data from trials in low-income settings suggest that CBE screening can lead to downstaging of breast cancer, although its effect on mortality hasn’t been shown.\textsuperscript{34,35} Because a substantial proportion of women in LICs present with late-stage breast cancer,\textsuperscript{29,36} for women like Ms P and others in LICs, downstaging is critical.

**Recommendations**

The feasibility of CBE has been established in LICs.\textsuperscript{35,37} Our argument is not that CBE is a good screening tool but that it is a more pragmatic choice than mammography in LICs. For screening programs to be effective and affordable, high-quality treatment must be available. Accordingly, socioeconomic and other barriers to treatment should be addressed as part of cancer control policy in LICs. In addition, what needs to be available are good pathology, surgery and radiotherapy, supportive care services, surveillance and monitoring systems, and a cancer registry. Screening without good follow-up care across the cancer continuum makes little clinical or ethical sense, as one could argue that resources devoted to breast cancer screening would be better spent on public and professional education such as tobacco cessation, alcohol control, and healthy diet and lifestyle promotion. We propose that health services in low-resource regions test CBE in a small district and monitor the program’s feasibility, acceptability, effectiveness, and cost.

**References**


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*The people and events in this case are fictional. Resemblance to real events or to names of people, living or dead, is entirely coincidental. The viewpoints expressed in this article are those of the author(s) and do not necessarily reflect the views and policies of the AMA.*

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HEALTH LAW

Can International Patent Law Help Mitigate Cancer Inequity in LMICs?
Srividya Ragavan, SJD and Amaka Vanni, PhD

Abstract
Although low- and middle-income countries (LMICs) bear 75% of the cancer burden globally, their available resources to treat cancer constitute less than 5% of global health resources. This inequity makes it imperative to take appropriate measures to treat and prevent cancer in LMICs, which should include consideration of trade and patent policies. This article highlights some impediments to effective use of existing policies to promote access to treatment and prevention measures in LMICs and offers recommendations about next steps.

Introduction
Cancer incidence is rising globally, resulting in financial, physical, and emotional distress to families and burdening public health services. According to the World Health Organization (WHO), the global cancer burden was estimated to have risen from 14.1 million new cases in 2012 to 18.1 million new cases in 2018 and from 8.2 million deaths in 2012 to 9.6 million deaths in 2018.1 Low- and middle-income countries (LMICs) bear 75% of cancer deaths.2 Asia and Africa, for example, have a higher proportion of cancer deaths (7.3% and 57.3%, respectively) compared to their incidence (5.8% and 48.4%, respectively) than other countries due, in part, to enormous inequities in cancer treatment.3 Indeed, the available resources to treat cancer in LMICs compose less than 5% of the global share of resources for cancer control.4 Correspondingly, only 10% of children diagnosed with cancer in LMICs are cured compared with more than 80% of such children in high-income countries.4 A WHO finding that less than 30% of low-income countries report having treatment services available compared to more than 90% of high-income countries underscores the enormous inequities in cancer treatment and access to cancer medications.5 These disparities make it critical to focus cancer control efforts on LMICs.
In these countries, many new cancer medications are exorbitantly expensive relative to individual income. For example, one company’s egregious original price tag of Rs 280 428 per month (about $5000 at that time) for sorafenib tosylate, a drug for treating primary kidney cancer and advanced liver cancer, was nearly 5 times higher than the median annual income in India. Like this drug, many cancer drugs are unaffordable for large number of patients diagnosed with cancer in poorer nations.

Efforts to effectively improve access to medicines by reducing costs of cancer medications should look to international trade agreements and, particularly, TRIPS flexibilities for compulsory license (explained below), which can (and should) be used to address health burdens, such as the HIV/AIDS epidemic. Just as in the case of an epidemic, efforts to address cancer should be mindful of the labor and economic loss that ensue when productive individuals are lost to disease. In order to be involved effectively in such efforts, the medical community must appreciate how international trade and patent prescriptions interact with efforts to improve access to cancer medication, especially in LMICs where such access remains inadequate. The focus of this essay, therefore, is on how international patent law can help mitigate the cancer burden in LMICs.

**Global Trade Policies and Cancer**

The inclusion of intellectual property (hereafter, IP) within the global trade framework was a defining moment for global access to medication. In broad terms, IP rights are legal tools designed to result in public benefit by promoting private rights. Thus, IP rights recognize innovations by awarding monopoly rights to the creator as a means to incentivize creativity. In 1995, when the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS agreement), which forms a part of the larger World Trade Organization (WTO), became effective, it required all member states to provide a 20-year term of protection for all pharmaceutical innovations. The TRIPS agreement provided limited flexibilities for countries to weigh IP rights against public health and developmental needs. Specifically, Article 31 of the TRIPS agreement allows for compulsory license, a mechanism that permits a third party to produce a patented product or process without the consent of the patent owner. The patent owner still retains the right to the patent and receives royalties for the products made under the compulsory licence. However, this provision allows a sovereign government to authorize the licensing of a patent to produce a generic version of the drug, enabling greater access to it during a public health crisis.
Nevertheless, the inadequacies of the compulsory license during global public health crises—particularly the HIV/AIDS crisis—forced member states to adopt, in 2001, the Doha Declaration on the TRIPS Agreement and Public Health. The Doha Declaration affirms the right of member states to implement policies to enable access to medicines to address a national public health crisis.\(^\text{10}\) Thus, Article 31 of the TRIPS agreement in conjunction with the Doha Declaration reaffirms the rights of sovereign nations to “protect public health and enhance access to medicines.”\(^\text{11}\) Importantly, while the Doha Declaration reaffirmed member countries’ ability to compulsorily license a patent for the production of generic drugs to address a public health crisis, it underscored the existence of member countries that are unable to take advantage of the compulsory license because they lack the manufacturing capabilities to even produce generic medications. Hence, the WTO General Council, in 2005, adopted Article 31(bis),\(^\text{12}\) which allows for export of generic drugs from member countries that can produce licensed medication to member countries that lack manufacturing facilities but need the medication. Through this provision, the TRIPS agreement allows nations to act either individually or as a regional group in granting compulsory licenses to export pharmaceutical products to member countries with insufficient or no manufacturing capacities. However, the definition of what constitutes a national public health crisis has remained contentious.\(^\text{13}\)

To date, there has been limited use of compulsory licenses for cancer drugs. In fact, only 2 countries have issued compulsory licenses for cancer treatment to reduce the cost of medication. India’s first (and so far only) compulsory license was for sorafenib, a drug to treat kidney cancer,\(^\text{14}\) and Thailand granted compulsory licenses over 3 cancer medications: erlotinib (for small cell lung cancer), letrozole (for early breast cancer) and docetaxel (for breast cancer).\(^\text{15}\) Both countries cited the high cost of the patented drugs as the reason for issuing compulsory licenses to improve access to these medicines in their patient population.\(^\text{16}\)

Despite their limited use, compulsory licenses in these countries were hugely contentious.\(^\text{17}\) Specifically, both countries were unilaterally targeted by the United States through the Special 301 process, which identifies nations whose domestic IP laws and policies are perceived as creating market access barriers to US business interests. As a result, India and Thailand have featured in the Priority Watch Lists compiled annually by the Office of the US Trade Representative under Section 301 of the Trade Act of 1974 for having instituted legitimate health safeguards.\(^\text{18}\) Unilateral US actions have been on
shaky legal grounds because the trade regime only provides for multilateral dispute settlement. That the United States, as a rule, unilaterally forces trade concessions from countries using negotiated flexibilities to alleviate a public health crisis has resulted in interventions by the WHO and the United Nations in favor of countries that lack the same bargaining power as the United States. Nevertheless, US actions have made countries hesitant to use compulsory licenses to increase access by lowering the cost of cancer medications.

Notwithstanding the TRIPS agreement’s provision for compulsory licenses, other impediments from patent policies have stymied efforts to provide access to medication. Some examples of pharmaceutical patent-related impediments include evergreening and the cost and use of public funds to create private property. Additionally, barriers to competition from follow-on products during the postpatent period include provisions for data and market exclusivity for clinical trial data and provisions that act as a barrier to national interventions. The following section discusses 2 issues that most affect access to cancer medications: data and market exclusivity provisions that affect national interventions (eg, preventive measures).

**Patents and Cancer Prevention**

One of the important policy barriers to addressing cancer inequities concerns provisions for data exclusivity. Data exclusivity protects clinical trial data for a given period of time. Typically, the clinical trial data submitted by the innovator drug company is protected by separate data and market exclusivity periods that run parallel with the patent protection term. During the term when data exclusivity prevails, competing generic drug companies cannot rely on clinical trial data to get approval for follow-on products. Thus, the data cannot be submitted to gain approval for a generic drug from the US Food and Drug Administration (FDA). During the term of market exclusivity, the FDA accepts applications but does not grant market approval for a generic manufacturer’s drug, thus ensuring additional monopoly protections for the drug. Thus, data and market exclusivities work as an additional layer of protection over patents.

For manufacturers of innovator pharmaceuticals, protection of clinical trial data provides an additional economic opportunity in that it creates a new market for the clinical trial data. In the United States, a biologics drug that is important for treating cancer or autoimmune diseases, for example, can benefit from 20 years of patent protection and an additional 4 years of data exclusivity and 8 years of market exclusivity, resulting in a guarantee of a total
of 12 years of market exclusivity,\textsuperscript{25,26} and the FDA grants new chemical entities a total data exclusivity period of up to 5 years.\textsuperscript{27} The European Union currently allows 8 years of data exclusivity for the originator’s preclinical and clinical test data.\textsuperscript{28} Pharmaceutical companies have slowly increased the period of data exclusivity, however. In the United States, in addition to data and market exclusivity, there is paediatric exclusivity that runs for 6 months and an orphan drug exclusivity that runs for 7 years.\textsuperscript{29} In fact, the United States had sought to extend exclusivity for data in its bilateral and regional agreements. For example, the United States-Mexico-Canada Agreement, sought a 10-year data exclusivity for new biologics, which would have represented an increase in the term of exclusivity for Mexico and Canada,\textsuperscript{30} although the final text approved on December 13, 2019, does not include the 10-year exclusivity requirement.\textsuperscript{31}

Importantly, extended data exclusivity periods may effectively provide market exclusivity for compounds that fail patent scrutiny and thus help maintain high pharmaceutical prices because even when a patent is declared invalid, access to data is unavailable for generics. So, if Company A has a drug whose active ingredient is found unpatentable, the drug falls into the public domain and hence should be available to the generic drug manufacturer. Nevertheless, on account of data exclusivity laws, the generic drug company will be prevented from using the clinical trial data to have its drug approved. Indirectly, this restriction results in awarding Company A market exclusivity even though it does not have any innovation in the market. Thus, with expensive medications such as cancer drugs, data exclusivity delays the entry of generic drugs into the market until the data protection period is over, and it indirectly allows the innovator pharmaceutical company to monopolize the market for even off-patent materials.

**Conflict Between Global Trade and Cancer**

A recent dispute under the WTO’s dispute settlement process involving several nations highlights the intersection between patents and trademarks as well as the importance of domestic interventions to efficiently preserve public health. In the Australia plain packaging case,\textsuperscript{32} several countries disputed Australia’s plain packaging laws. The law required that tobacco products not use logos, brand name, imagery, or promotional text on their packaging. The objective was to standardize the appearance of the packets to reduce the appeal of tobacco products and thereby prevent health consequences from smoking. The law is part of Australia’s national comprehensive strategy to improve public health by reducing the use of, and exposure to, tobacco products. The complaining countries claimed that the
plain packaging requirements restricted trade and violated key aspects of the TRIPS agreement—particularly, the companies’ ability to protect and promote their trademarks. The complaint was that, in restricting the use of trademarks to preserve public health, Australia interfered with the IPs of the complainants. The WTO panel found that plain packaging requirements can and do make a meaningful contribution to Australia’s objective of curbing tobacco use and exposure in order to prevent cancer despite its violation of trademark rights. The panel reiterated the importance of taking preventive measures to protect humans and prevent public health risks, given the extensive evidence of smoking as a key contributor to lung cancer.

The Australian law provides a useful model for other countries interested in instituting such preventive measures. In fact, in 2016, the United Kingdom (UK) statutorily imposed plain packaging for tobacco products. The law came into force when the Supreme Court of the UK refused to consider an appeal by the tobacco industry against the law. This case sheds light on how LMICs could align domestic public health objectives with emerging multilateral public health policies in the area of cancer prevention as well as cancer treatment.

**Conclusion**
The past decade’s trade and patent policies have largely turned access to medication in LMICs into a luxury. Effective interventions for cancer treatment and prevention are thus needed in LMICs to reduce both human and financial costs of the cancer burden. Such interventions necessitate strategic policymaking and the inclusion of TRIPS flexibilities in proposed national legislation to enable the legislation’s passage and efficient implementation. Although the inclusion of flexibilities in the TRIPS agreement has led to increased access to cancer medications, data and market exclusivity continues to pose impediments to access. It is therefore imperative that policies to prevent and treat cancer employ many-pronged approaches, which should involve both the medical and the trade community. Importantly, the medical community’s interest in treating and preventing cancer should inform the global trade agenda. As interventions employed to tackle HIV/AIDS have shown, concerted and coordinated policy interventions can lead to desired results. The same should hold true for cancer. The bottom line is that the increased global incidence of cancer cries out for improved access to medications for cancer prevention and treatment.

**References**
1. World Health Organization. Latest global cancer data: cancer burden rises to 18.1 million new cases and 9.6 million cancer deaths in 2018


12. TRIPS Agreement—Article 31bis. 


21. Correa CM; South Centre. Pharmaceutical innovation, incremental patenting and compulsory licensing. 


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AMA CODE SAYS
AMA Policies and Code of Medical Ethics’ Opinions Related to Cancer Prevention in Low- and Middle-Income Countries
Andi Sirokman

Abstract
Cancer is the second leading cause of death globally. Death rates from cancer reflect global inequality; approximately 70% of deaths from cancers occur in low- and middle-income countries (LMICs). Due to high costs of cancer treatment and limited access to resources, these countries are unable to use treatment as a primary means for reducing cancer burden. Thus, redirecting focus from treatment to prevention in LMICs and considering prevention as a global public health imperative are critical. The AMA Code of Medical Ethics and policies can guide efforts to promote and support cancer prevention in LMICs.

Global Burden of Cancer Inequality
Cancer is the leading cause of death globally, accounting for about 1 in every 6 deaths.1 Deaths from cancer reflect global inequality, as approximately 70% of deaths from cancer occur in low- and middle-income countries (LMICs).1 Increasing and already-high costs of cancer treatment, combined with a lack of access to resources, contribute to the highly concentrated burden of this disease in LMICs. These and other factors make it impossible for LMICs to use treatment as the primary means of reducing the cancer burden. Thus, shifting the focus from treatment to prevention in LMICs is critical to furthering this goal. Between 30% and 50% of cancers are preventable, but prioritizing prevention in these countries presents its own set of unique challenges.¹ The American Medical Association (AMA) Code of Medical Ethics offers guidance on disease prevention and health promotion that is applicable to addressing cancer in LMICs.

Preventive Medicine
Preventive medicine aims to protect, promote, and maintain the health of individuals, communities, and populations by taking steps to avert, rather than respond to, disease or sickness. The AMA is clear in its support of
preventive medicine and of cancer prevention in particular. AMA Policy H-425.997, “Preventive Services,” states: “Our AMA encourages the development of policies and mechanisms to assure the continuity, coordination and continuous availability of patient care, including professional preventive care and early-detection screening services.”

Preventive medicine practice in LMICs presents unique challenges, however. AMA policies recommend that physicians and other health professionals become sufficiently familiarized with the country (or countries) in which the preventive services will be offered. AMA Policy H-425.984, “Clinical Preventive Services,” states: “Practicing physicians should become familiar with authoritative clinical preventive services guidelines and routinely implement them as appropriate to the age, gender, and individual risk/environmental factors applicable to the patients in the practice at every opportunity.” Similarly, AMA Policy H-425.986, “Challenges in Preventive Medicine,” states: “In concert with other groups, physicians should study local community needs, define appropriate public health objectives, and work toward achieving public health goals for the community.” Thus, in piloting programs to support cancer prevention in LMICs that are responsive to community needs, following Opinion 8.5, “Disparities in Health Care,” physicians should “cultivate effective communication and trust by seeking to better understand factors that can influence patients’ health care decisions, such as cultural traditions, health beliefs and health literacy, language or other barriers to communication and fears or misperceptions about the health care system.”

In addition, the AMA Code states that preventive services being considered should be supported by evidence of improved outcomes or quality of life and should be cost effective. Since studies do indeed show that services that help to prevent cancer improve both outcomes and quality of life, developing and implementing cancer prevention services in LMICs that are cost effective is crucial to reducing premature cancer mortality. To further these efforts, physicians should “support research that examines health care disparities, including research on unique health needs of all genders, ethnic groups, and disadvantaged populations, and on developing quality measures and resources to help reduce disparities.”

Health Promotion
Supporting cancer prevention efforts everywhere, and especially in LMICs, is a duty of everyone in health care. Opinion 8.11, “Health Promotion and Preventive Care,” emphasizes and expands on this idea by stating:
Medicine and public health share an ethical foundation stemming from the essential and direct role that health plays in human flourishing. While a physician’s role tends to focus on diagnosing and treating illness once it occurs, physicians also have a professional commitment to prevent disease and promote health and well-being for their patients and the community. Health promotion should be a collaborative, patient-centered process that promotes trust and recognizes patients’ self-directed roles and responsibilities in maintaining health.6

Opinion 8.11 offers more specific guidance for physicians. It asserts that individual physicians should:

(a) Keep current with preventive care guidelines that apply to their patients and ensure that the interventions they recommend are well supported by the best available evidence.
(b) Educate patients about relevant modifiable risk factors.
(c) Recommend and encourage patients to have appropriate vaccinations and screenings.
(d) Encourage an open dialogue regarding circumstances that may make it difficult to manage chronic conditions or maintain a healthy lifestyle, such as transportation, work and home environments, and social support systems.
(e) Collaborate with the patient to develop recommendations that are most likely to be effective.
(f) When appropriate, delegate health promotion activities to other professionals or other resources available in the community who can help counsel and educate patients.
(g) Consider the health of the community when treating their own patients and identify and notify public health authorities if and when they notice patterns in patient health that may indicate a health risk for others.
(h) Recognize that modeling health behaviors can help patients make changes in their own lives.6

Additionally, it states that, collectively, physicians should:

(i) Promote training in health promotion and disease prevention during medical school, residency and in continuing medical education.
(j) Advocate for healthier schools, workplaces and communities.
(k) Create or promote healthier work and training environments for physicians.
(l) Advocate for community resources designed to promote health and provide access to preventive services.
(m) Support research to improve the evidence for disease prevention and health promotion.6

The selections from the AMA Code featured here speak broadly to preventive medicine and health promotion and offer guidance on responding to ethical challenges associated specifically with cancer prevention in LMICs.

References

   https://www.who.int/news-room/fact-sheets/detail/cancer.


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STATE OF THE ART AND SCIENCE
Why Consider Self-Sampling for Cervical Cancer Screening in Low- and Middle-Income Countries?
Victoire Fokom Defo, MD and Joël Fokom Domgue, MD, MPH

Abstract
Molecular detection of high-risk human papillomavirus (HPV) in genital cells is being widely endorsed as a preferred tool for cervical cancer screening globally. In low- and middle-income countries (LMICs) where cervical cancer remains a leading killer, HPV testing is an appealing, accessible alternative to traditional cytology (ie, Pap smear) screening that enables women to self-collect specimens. This article examines self-sampling and its suitability as a strategy for cervical cancer prevention in LMICs that would promote equitable access to cervical cancer screening.

Introduction
Cervical cancer is preventable but remains one of the most commonly diagnosed cancers around the world. More than 85% of new cases occur in low- and middle-income countries (LMICs), which bear 90% of the burden of cervical cancer mortality, primarily due to low coverage rates for cervical cancer screening services. Since cervical cancer is preceded by infection with high-risk strains of the human papillomavirus (HPV), screening tests have been developed to detect the presence of these high-risk HPV types in cervical cells. HPV testing is more sensitive than the traditional cervical cancer screening modality, cytology (ie, Pap smear), which has been successfully used to reduce the burden of cervical cancer in high-income countries. Compared to cytology, HPV testing is less resource intensive and can be done using either a clinician-collected cervical swab or a specimen collected by the woman (self-sampling).

HPV self-sampling is an innovative technique for cervical cancer screening that empowers women by allowing them to collect their own specimen in private, at a time and place of their choosing and when and where they are comfortable. It has the potential to overcome many of the identified barriers
to accessing cytology in LMICs. Specifically, self-sampling removes the need for a pelvic exam, clinic setting, and a trained clinician. This strategy not only is acceptable to both women and clinicians but also is adapted to hard-to-reach and rural communities with limited transportation options and distant health facilities. As a result, it can potentially improve access to and uptake of screening, particularly among underscreened women and LMIC populations.

In view of the above, HPV self-sampling might reduce social inequalities in access to cervical screening services.

Nevertheless, HPV self-sampling in LMICs might be associated with a number of ethical challenges, including concerns about autonomy, opportunity costs, and limited health care resources. For implementation of HPV self-sampling screening programs in LMICs to be successful, it is imperative to understand and address the opportunities and challenges of self-sampling so as to realize its substantial benefit to women's health while limiting its potential harms.

**Specimen Collection and Results Disclosure**

In the context of cervical cancer screening, the procedure for self-sampling is simple and does not require specific training (see Figure 1). Briefly, the woman is given a kit containing the necessary tools for self-collection, including a swab (or brush), a tube, and an envelope or zipper storage bag. To perform self-sampling, she chooses a private place (at home or at work) where she feels comfortable, takes off her underwear, and puts one leg on a chair or bench. She then holds the free end of the swab's handle and gently pushes the other end to the top of the vagina. When the swab is inserted in her vagina, the woman turns the handle 2 or 3 turns, then removes the swab completely from her vagina, puts it into the tube, snaps the swab handle to break it, and caps the tube. Finally, she puts the tube into the envelope and seals it. The sealed envelope is either mailed to the laboratory or handed to a community health worker or health care practitioner who takes it to the lab. The procedure is easy and does not take more than 2 to 3 minutes. Generally, the laboratory is owned or equipped by the institution or entity that sponsors the cervical cancer screening program. In most Latin American and Asian countries, the implementation of HPV screening programs is mainly supported by governments, while in Africa, these programs are usually supported by nongovernmental organizations and research funds.
Figure 1. Procedure for Self-Collected Vaginal Sampling

Processing and disclosing the results takes several steps (see Figure 2). In the lab, the technician processes the specimen contained in the tube, then runs the HPV test using an automated machine that provides results after a couple of hours (for rapid HPV analyzers). When the analysis is complete, the lab technician reads the result (positive or negative), which is returned to the woman via mail or through the community health worker or her health care practitioner. In any case, the screening result is generally accompanied by an interpretation of the result with recommendations about next steps. In the context of primary screening, a negative HPV test result indicates that the woman is at very low risk of developing cervical cancer within the next decade. She is therefore advised to repeat the test after 5 to 10 years. A positive HPV test result indicates that the woman has acquired the virus responsible for cervical cancer and might require further evaluation in a health care facility. Depending on the resources available and the appearance of the cervix, she might benefit from immediate treatment (with ablation or excisional therapy) or undergo additional workup, ie, a triage test—visual inspection with acetic acid (VIA) or visual inspection with Lugol’s iodine (VILI), cytology, biomarkers like OncoE6, or HPV genotyping—which may be complemented by colposcopy and/or biopsy (if available) to determine if she has a cervical precancerous or cancerous lesion that requires immediate treatment.
Figure 2. Proposed Cervical Screening and Treatment Algorithm With Primary HPV Testing for LMICs

Potential benefits. Self-sampling for cervical cancer screening might offer many benefits to women in LMICs. By respecting women’s privacy, self-sampling might encourage screening participation in underscreened populations and in LMICs. Although cancer screening consultation is generally sensitive, self-sampling allows for screening without undergoing pelvic examination. It has been reported that lack of privacy for women is one of the important reasons behind forgoing screening in LMICs. Further perceived barriers to screening include fear and shame, especially when it would involve unnecessary exposure of private parts in the presence of male health care practitioners, which might negatively impact women’s self-confidence. Women also need to be assured that the privacy of their results is maintained. Interestingly, HPV testing (especially polymerase chain reaction-based assays) was found to be as accurate on self-collected specimens as on clinician-collected specimens, suggesting that women can effectively replace health care practitioners in collecting samples for HPV testing. Health care practitioners, after adequate training and supervision, can safely provide management and follow-up of HPV positive women in primary care settings.
Efforts to create awareness of women’s privacy rights should be directed at both women and clinicians. First, educational interventions aimed at raising women’s awareness of their duties and rights should be fostered in LMICS. Second, appropriate training of community health workers and health care practitioners would improve their understanding of patients’ rights to access and control information. Third, national or regional guidelines on cervical cancer prevention in LMICs should highlight policies that govern women’s privacy.

Other benefits of self-sampling for cervical cancer screening in LMICs include (1) superior clinical performance of HPV test compared to cytology or visual screening methods (VIA/VILI), allowing for the proper detection of cases of cervical cancer precursors; (2) potentially longer time interval between screening rounds (from 2 to 3 years with cytology or VIA/VILI to 5 years or more with HPV test), and (3) initiating screening at an older age (21 to 25 years with cytology or VIA/VILI vs 30 to 35 years with HPV testing), thereby reducing the number of screening rounds in a woman’s lifetime.19 Moreover, self-collected HPV testing has proven to be more cost effective than cytology in LMICs.20,21 Of note, in most limited-resource settings, women do not have health insurance, and health care expenditures are often paid out of pocket. For all these reasons, self-sampling is of value in LMICs, where unfamiliarity with the screening concept, lack of time, need for spousal permission, fear of financial burden, and fear of social marginalization are known obstacles to cervical cancer screening.7,22

Screening with HPV self-sampling is thus considered to be one of the most practical approaches for early detection of cervical cancer in LMICs, and it is the most effective in reducing the burden of disease at an affordable cost.19,20,21 Ethically, providing self-sampling as an alternative to other screening programs for prevention of cervical cancer in LMICs is a significant and reasonable act of beneficence.

Potential limitations. There are also potential limitations to adopting HPV self-sampling for cervical cancer screening in LMICs. Due to the high sensitivity of HPV testing, there is concern that it might lead to the overdetection of cervical dysplasia and thus unnecessary interventions (such as needless treatment, colposcopy, and/or biopsy) for both transient HPV infections and less serious cervical lesions that would have otherwise resolved on their own, subjecting those affected to unnecessary physical and mental burdens.23 This consideration is of utmost importance in LMICs, where there is a shortage of follow-up and treatment facilities as well as a lack of
trained clinicians who can adequately manage and support HPV positive women.\textsuperscript{24} Thus, educating patients and practitioners and to some extent reinforcing health care infrastructures are major components of implementing HPV self-sampling in LMICs.

In addition to the HPV test’s potential for false positive results, HPV self-sampling poses potential challenges to the workflow of clinicians and laboratory specialists.\textsuperscript{25} The introduction of self-sampling might change the makeup of the services and workforce required in already resource-constrained settings. Indeed, facilities equipped with HPV machines might require (1) lab technicians who are trained to run the test and report the results; (2) community health workers who have been trained to properly explain the self-sampling procedure, adequately transport the self-collected specimens to the laboratory, and appropriately interpret and disclose the HPV results to women in the community; and (3) skilled clinicians to manage and follow up with women who tested positive. Implementing these changes would require decision makers to discuss and choose to respect the rights of women in LMICs to equal and appropriate treatment.

The fact that HPV is mainly transmitted through sexual contact might also affect how women interpret the screening results in ways that cause harm. While a negative HPV result might be perceived as a sign of reproductive health, some women who receive a negative test result (especially those with multiple previous or concurrent sexual partners) might consider themselves as being less vulnerable to the virus, and this false belief could induce them to engage in more risky sexual behaviors. Conversely, women might fear that a positive HPV test would bring them shame, blame, and even abandonment by their husbands and families, so some might prefer not to know the test result because of their fear of a positive result.\textsuperscript{26,27} Furthermore, women in patriarchal societies might fear the stigma associated with a positive result; for example, they might worry about male partners suspecting them of having other sexual partners.

Developing culturally appropriate messages and educational materials aimed at mitigating women’s feelings of guilt when HPV positive or feelings of invincibility when HPV negative might encourage women to participate in cervical cancer screening and might decrease the stigma of treatment. Such health promotion messages through face-to-face education with pictures and diagrams and through local media need to be aimed at both women and men.
Conclusion
HPV self-sampling as a global strategy for cervical cancer prevention is more respectful of women’s privacy and more accepted and cost effective than cytology and visual screening, and it has the potential to reduce social inequalities in access to screening in LMICs. However, it is associated with a number of policy and ethical concerns, including issues related to privacy of information, disclosure and interpretation of results, and potential harms of screening. These considerations need to be accounted for to successfully introduce self-sampling for cervical cancer screening at the community level in LMICs.

References


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POLICY FORUM: PEER-REVIEWED ARTICLE
How Should Cervical Cancer Prevention Be Improved in LMICs?
Weyinshet Gossa, MD, MPH and Michael D. Fetters, MD, MPH, MA

Abstract
Cervical cancer has become rare in high-income countries but is a leading cause of mortality among women in low- and middle-income countries (LMICs). This inequity is due to economic, social, and cultural factors and should be seen as an epidemiological tragedy. This article examines ethical considerations that should compel policymakers and international donors to prioritize cervical cancer prevention in LMICs.

Introduction
In this article, we offer an ethical argument to support policies that prioritize cervical cancer prevention in low- and middle-income countries (LMICs). We first examine the inequity between high-income countries (HICs) and LMICs in the burden of cervical cancer and highlight cultural factors impeding effective cervical cancer prevention. We then consider how the ethical values of beneficence, nonmaleficence, social justice, and gender equity can be drawn upon to compel policymakers and international donors to prioritize cervical cancer prevention in LMICs. Finally, we review extant literature on cervical cancer prevention in LMICs.

Cervical Cancer Inequity
Inequity between HICs and LMICs in cervical cancer burden. Cervical cancer is among the top five most common cancers and a major cause of mortality among women in LMICs, more than 85% of the cervical cancer global disease burden occurs in LMICs. An estimated 569,847 new cases of cervical cancer and 311,365 cervical cancer-related deaths occurred globally in 2018,
with most occurring in LMICs.7 In particular, cervical cancer mortality is highest in Africa, Latin America and the Caribbean, and Asia.7 Age-standardized incidence and mortality rates (ASRs) were highest in Southern, Eastern, and Western Africa and Melanesia and lowest in Western Europe, North America, Australia and New Zealand, and Western Asia (see Figure).7 While cervical cancer ASRs are lower overall in HICs, there is international variation5 by race, ethnicity, and region. For example, in the United States, the highest cervical cancer incidence and mortality rates occur among black women and in the South.8 This variation is attributable primarily to socioeconomic status, although cultural factors are also influential.8 Within Europe, cervical cancer incidence is highest in Eastern Europe, largely due to the lack of uniformly implemented population-based screening and vaccination programs across the region.9,10

Figure. Age Standardized (World) Incidence Rates, Cervix Uteri, All Ages

Failure to prevent cervical cancer in LMICs. Cervical cancer rates are high in LMICs despite cervical cancer being preventable and prevention methods, such as human papillomavirus (HPV) vaccination and cervical cancer screening, being highly cost effective.11,12 In 2012, HPV vaccination would have cost $0.23 per capita in low-income countries and $0.40 per capita in upper-middle-income countries, and screening and treatment of precancerous lesions and early cervical cancer would have cost $0.26 per capita in low-income countries and $0.87 per capita in upper-middle income countries.13 GAVI, the Vaccine Alliance provides support for HPV vaccinations
in LMICs and has negotiated vaccine delivery pricing since 2013—lowering it from over $100 per dose to $4.50-4.60 per dose—although cost is still a barrier to implementing national HPV vaccination programs in LMICs.14

**Causes of Inequity**

Differences in incidence and mortality rates are due to economic, social, and cultural factors.

*Economic factors.* There is limited availability and implementation of effective prevention programs in LMICs.2,3,4,5 Many screening programs in LMICs are pilot programs. Only a few countries—most of them HICs—have scaled up to national programs with at least 70% coverage.15,16 HPV vaccination coverage is also low in LMICs, as only 14% of LMICs had national HPV vaccine programs in 2016 compared to 55% of HICs.14

More generally, there is limited funding for cervical cancer prevention in LMICs. In 2016, low-income countries accounted for 9.6% of the global population but only 0.4% of total global health spending, and lower-middle income countries accounted for 39.3% of the global population but only 3% of health spending.17 By contrast, HICs accounted for 16.6% of the global population and 81% of global health spending.17 Development assistance for health (DAH), while less than 1% of total global health spending, accounted for 25.4% of health spending in low-income countries in 2018.17 While reproductive, maternal, newborn, and child health received 32.1% of DAH, only 2% of DAH was allocated to noncommunicable diseases (NCDs), including cancers, which account for 62.1% of the global disease burden.17 Both maternal health and cervical cancer are women’s health issues, but cervical cancer receives less attention and financial support.

*Social and cultural factors.* Resource scarcity is the main reason for limited cervical cancer prevention capacity in LMICs, but social and cultural factors also influence utilization of available preventive services. In particular, utilization is undermined by lack of knowledge about cervical cancer and preventive services, limited accessibility, stigma associated with acquiring disease via sexually transmitted infection, and cultural and religious beliefs.18 Low HPV vaccine uptake in LMICs is in part due to concerns about the vaccine’s safety, effectiveness, and benefits. Attempts to use informed consent processes as opportunities to respond to these concerns have not eliminated some people’s suspicion that informed consent processes are ploys to absolve vaccine givers from responsibility for harm.19 Vaccine hesitancy, however, is not unique to LMICs and has become a global
phenomenon, probably best addressed by engaging and partnering with local community members.

Colonial legacy. Most low-income countries are located in Africa, where cervical cancer rates are the highest and health, economic, and social inequities persist. Colonialism led to economic degradation, sociopolitical instability, cultural shifts away from traditional practices, decreased social cohesion, and high disease burden. This historical context must be considered in the drive to resolve the ethical and policy issues impeding cervical cancer prevention.

Ethical Values

Beneficence and nonmaleficence. Kinsinger defines beneficence as “an act of charity, mercy, and kindness with a strong connotation of doing good to others including moral obligation.” Beneficence goes hand-in-hand with nonmaleficence (“do no harm”); these 2 principles require health care provision that produces more benefit than harm. In the context of cervical cancer, prevention is the morally right thing to do to avert unnecessary morbidity and mortality. The 1978 World Health Organization (WHO) Alma-Ata Declaration established that health is a “fundamental human right.” Women in LMICs have a right to health regardless of their locality, and the WHO’s goal for health care to ensure the well-being of all individuals must hold true for women in LMICs.

Social justice. Social justice applied to health typically involves fair distribution of resources, which requires population-based considerations of competing demands. Cervical cancer in LMICs usually presents at an advanced stage due to lack of prevention, and this, along with lack of adequate treatment, leads to higher costs and ultimately higher mortality. Treatment for cervical cancer requires trained health professionals to administer surgery, radiotherapy, and chemotherapy as well as infrastructure, equipment, diagnostic capability, and adequate medication supply. Costs of these resources make availability of treatment for cervical cancer in LMICs inadequate; hence, prevention is critical. A social justice perspective, then, suggests that international donors should adequately fund and prioritize prevention. Resource allocation for prevention has led to significant decrease in cervical cancer incidence in HICs, and similar outcomes can be achieved in LMICs.

Gender equity. Gender equity demands fair treatment of women and men based on their needs, preferences, and interests. Gender inequity is at the
core of global cervical cancer inequity. Worldwide, women experience inequity in education, employment opportunity, income, and political representation, and gender gaps in these areas are widest in developing nations. Gender equity has not been achieved even in HICs, such as the United States. However, women in LMICs have even less access to education and lower income than women in HICs and, as a result, have less opportunity to access preventive services. Lack of knowledge about cervical cancer and low socioeconomic status have been associated with lower rates of cervical cancer screening and HPV vaccination in LMICs. In addition, cervical cancer is stigmatized in LMICs due to its anatomic site, grim prognosis, and being caused by sexually transmitted infection (via socially condemned behavior).

Prevention
The WHO serves as a critical beacon for guiding cervical cancer prevention in LMICs, recommending HPV vaccination for girls ages 9 to 13 years and cervical cancer screening for women ages 30 to 49 years at least once using HPV testing, cytology, or visual inspection with acetic acid (VIA), depending on availability. While support from GAVI is allowing more LMICs to introduce national HPV vaccine programs, this support is expected to end in 2020. Lower vaccine prices, more international funding support, and expanded vaccine programs are needed to augment screening in LMICs.

Among screening methods used in LMICs, VIA and HPV testing are deemed more effective and less costly than cytology. However, that cytology is still regarded as the gold standard for cervical cancer screening in HICs suggests the importance of questioning the fairness of administering suboptimal screening to women in LMICs due to resource scarcity. We advocate using the most effective screening methods that are available, feasible, and culturally acceptable in LMICs. In particular, VIA and HPV testing are appropriate in the absence of other more effective screening methods. Over the long-term, however, we advocate for investment in and development of effective, less costly, and easy-to-use methods that are culturally acceptable. Commitment and political will are needed to expand prevention efforts from pilot and demonstration projects to national programs.

Conclusion
In summary, cervical cancer prevention in LMICs is due not just to resource scarcity but to pervasive inequity. Arguments based on beneficence, nonmaleficence, social justice, and gender equity all strongly support the imperative to improve the availability of and access to cervical cancer screening and HPV vaccination in LMICs. Although there are limits to how well
these Western values can be applied internationally, we suggest that they be used to illuminate ethically and clinically relevant features of historical legacies of colonialism and to remind stakeholders that solutions should not be imposed by the West. Rather, the West is obliged to collaborate with LMICs to prevent cervical cancer deaths. Resource allocation for cervical cancer prevention should be a policy priority for national and international leaders to promote gender and health equity in LMICs.

References

10. Altobelli E, Lattanzi A. Cervical carcinoma in the European Union: an update on disease burden, screening program state of activation, and


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POLICY FORUM
How Should Global Tobacco Control Efforts Be Prioritized to Protect Children in Resource-Poor Regions?
Stella Aguinaga Bialous, DrPH and Yvette van der Eijk, PhD

Abstract
The tobacco industry’s aggressive marketing of tobacco products and electronic (e-)cigarettes is well documented. Yet existing restrictions on tobacco and e-cigarette marketing are poorly implemented in most low- and middle-income countries. Ongoing challenges include weak implementation and enforcement of some aspects of the WHO Framework Convention on Tobacco Control and a lack of consensus among health professionals on how to address the tobacco industry’s health claims related to e-cigarettes and other novel tobacco products. We argue that, despite these challenges, countries must prioritize the implementation and enforcement of restrictions on tobacco and e-cigarette marketing as these products represent not only a serious public health threat but also a violation of children’s rights.

Need for Tobacco Regulation
The WHO (World Health Organization) Framework Convention on Tobacco Control (FCTC) entered into force in 2005 and, as of July 2019, it had 181 parties. The FCTC lays out a number of demand- and supply-side measures to reduce tobacco use, including restrictions on direct and indirect tobacco marketing. Parties to the FCTC acknowledge that tobacco marketing, which comes in many forms (advertising, events sponsorships, promotions, point of sale displays, attractive packaging, innovative product designs, social media advertising) serves to encourage youth tobacco use. Indeed, the greatest impediment to FCTC implementation has been the tobacco industry, as its political influence and strategies have served to block, delay, or weaken tobacco marketing restrictions, particularly in low- and middle-income countries (LMICs).
The FCTC has had significant success in promoting tobacco control globally and in reducing the prevalence of tobacco use in several countries.\textsuperscript{1,5,6,7} The 2019 \textit{WHO Report on the Global Tobacco Epidemic: Offer Help to Quit Tobacco Use} estimates that the global prevalence of tobacco use declined from 22.5\% in 2007 to 19.2\% in 2017, with middle-income countries experiencing a lower rate of decline than high- and low-income countries.\textsuperscript{1} Data from the 2019 report also indicate that tobacco use among youth remains high and that electronic (e-)cigarette use among youth has increased. The report estimates that 24 million 13- to 15-year-old children smoke and 13 million use smokeless tobacco products.\textsuperscript{1}

As discussed below, an ongoing challenge in curbing youth tobacco and e-cigarette use is the marketing of these products to young people. Comprehensive bans on tobacco and e-cigarette marketing are lacking but are essential to protecting young people from nicotine addiction and serious health problems in later life.\textsuperscript{1,8} We argue that tobacco and e-cigarette marketing is a violation of fundamental children’s rights and that, accordingly, LMICs should prioritize the implementation of comprehensive bans on tobacco and e-cigarette marketing.

\textbf{Circumventing Marketing Restrictions}

Although many LMICs have restricted tobacco advertising, others have yet to implement a comprehensive approach to tobacco marketing.\textsuperscript{1} Displays at the point of sale are still common, despite the abundance of evidence showing that point-of-sale tobacco displays serve as advertisements and encourage youth smoking.\textsuperscript{9,10,11} The tobacco industry continues to vigorously oppose proposed legislation that would ban such advertising, as observed recently in South Africa.\textsuperscript{12,13}

Social media and other internet sites are an increasingly popular tobacco marketing venue that has yet to be addressed by tobacco control policies.\textsuperscript{14,15} A recent study of teenage internet users in Java, Indonesia, found that 80\% were exposed to cigarette adverts on YouTube, 58\% on websites, and 57\% on social media platforms such as Instagram. Smoking prevalence of 10- to 18-year-olds in Indonesia has also increased from 7\% (in 2013) to 9\% (in 2018).\textsuperscript{16} Youth, who are more frequently exposed to online and social media advertising than older adults, are particularly vulnerable to this marketing strategy, which often presents no disclosures that social media posts—which portray smoking as a normal, glamorous social activity—are sponsored adverts.
At the eighth session of the Conference of the Parties to the WHO FCTC in October 2018, the parties decided to create a working group that would recommend measures that could be added to existing policies to support the implementation of marketing restrictions, specifically by addressing social media and other online channels.\(^8,17\) However, other obstacles to tobacco control remain.

The use of flavors and innovative design features, such as flavor capsules, are an ongoing challenge for tobacco control, although the parties to the FCTC continue to support regulation of novel tobacco and vaping products.\(^2,8\) Tobacco companies increasingly rely on the use of flavors and product design features for market appeal, as marketing mediums, such as mass media or product packaging, become less available to them.\(^18\) Research has consistently found that tobacco companies add flavors, particularly menthol, to cigarettes to make them more attractive and palatable to youth—and also more addictive.\(^19,20\) Capsule cigarettes, which contain a crushable flavor capsule in the cigarette filter, are a novelty that appeals primarily to youth.\(^21,22,23\) Since their global launch in 2007, capsule cigarettes have grown rapidly in popularity, especially in Latin American countries.\(^24\) Nonetheless, very few countries have banned tobacco additives and flavors\(^22\) or regulated product engineering to ensure that tobacco products are not designed to appeal to youth.

**Underregulation of Novel Tobacco Products**

There is a range of policies addressing new tobacco products such as e-cigarettes, including pod-based products and heated tobacco products. Existing regulatory policies range from a ban on sales (in 28 countries), to regulation of or a ban on marketing (in 67 countries), to minimum age of purchase policies (in 36 countries, where the minimum age ranges from 16 years in Belgium to 21 years in Honduras and Palau).\(^25\) Other countries have not implemented any regulations at all. In the United States, the unregulated entry of these products in the market led to a reversal of progress towards eliminating tobacco use among youth. In 2011, 15.8% of US high school students reported smoking cigarettes in the past 30 days; this proportion fell to 8.1% in 2018.\(^26,27\) However, the proportion of high schoolers using nicotine increased overall from 24.2% in 2011 to 27.1% in 2018, as the proportion using e-cigarettes increased from 1.5% to 20.8% during the same period.\(^26,27\)

The promotion of these novel products as a safer alternative to cigarettes has created a chasm in the public health community that has served the tobacco industry well. The Conference of the Parties to the WHO FCTC has
recommended a range of policy options, including a ban on such products.\textsuperscript{28} One unifying agreement is that these new products must, if allowed in the market, at minimum be regulated in a way that prevents their use by youth.

Although research shows that these products may cause significant harm,\textsuperscript{8,29} measures to restrict their being marketed to, and accessed by, youth, have been unsuccessful. For example, in the United States, sales of these products to minors is banned, but that has not been sufficient to deter their increasing use among adolescents.\textsuperscript{30} Similarly, Canada experienced an increase in vaping among youth from 8.4\% in 2017 to 14.6\% in 2018 after it allowed these products in the market, despite regulations banning sales to minors.\textsuperscript{31,32}

In a July 2019 statement, the CEO of one such company (JUUL, creator of a pod-based vaping product) stated that he was sorry that children were using JUUL, which controls over 70\% of the vaping market in the United States, and admitted that more research was needed to understand the health impacts of vaping.\textsuperscript{33,34} With the launch of JUUL in several other countries, including Indonesia, policy measures should be implemented urgently to regulate the marketing and sales of these novel tobacco products, especially to youth.

Tobacco and E-Cigarette Marketing and Children’s Rights
The FCTC is based on human rights principles, notably that all people, including children, have a right to the highest attainable standard of health.\textsuperscript{35} The role of tobacco control in realizing this right is increasingly recognized.\textsuperscript{35,36,37,38}

Children’s rights are articulated in the 1989 Convention on the Rights of the Child (CRC), which all countries (except the United States) have ratified.\textsuperscript{39} Several articles of the CRC should be called on to support enforcement of stricter tobacco control measures (see Table). According to Article 6 of the CRC, governments should ensure that children survive and develop healthily, and Article 24 states that children have a right to “the highest attainable standard of health.”\textsuperscript{39} Article 33 of the CRC states that children should be protected from the illegal use of harmful drugs.\textsuperscript{39}
Nicotine is a toxic and highly addictive drug, yet it is widely available and marketed to youth in contravention of the CRC. By allowing tobacco companies to market their products via point-of-sale displays, social media influencers, and flavors and other product novelties, governments are failing to protect children from illegally using and developing a lifelong addiction to a toxic product that, for many of them, will result in chronic diseases and premature death.

Article 36 of the CRC states that children should be protected from exploitative activities that harm their welfare, yet the tobacco industry’s marketing messages exploit children’s impressionability and desire to fit into the adult world by portraying smoking—and, more recently, vaping—as a normal, glamorous adult activity. Tobacco companies have acknowledged this intent in their own internal communications. In the words of a 1973 tobacco industry report: “The fragile, developing self-image of the young person needs all of the support and enhancement it can get ... this self-image enhancement effect has traditionally been a strong promotional theme for cigarette brands.”40 The tobacco industry’s marketing activities are a textbook example of child exploitation for a corporation’s financial gain, with devastating impacts on children’s health and overall welfare. Therefore, a state’s failure to adequately restrict tobacco marketing constitutes a failure to adequately protect fundamental children’s rights, particularly their right to health and their right to be protected from harmful drugs and exploitation.

Table. Articles of the Convention on the Rights of the Child Relevant to the Issue of Tobacco Marketing

<table>
<thead>
<tr>
<th>Reference</th>
<th>Relevant Text</th>
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<tbody>
<tr>
<td>Article 6</td>
<td>“States Parties shall ensure to the maximum extent possible the survival and development of the child”</td>
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<tr>
<td>Article 24</td>
<td>“States Parties recognize the right of the child to the enjoyment of the highest attainable standard of health.”</td>
</tr>
<tr>
<td>Article 33</td>
<td>“States Parties shall take all appropriate measures, including legislative, administrative, social and educational measures, to protect children from the illicit use of narcotic drugs and psychotropic substances.”</td>
</tr>
<tr>
<td>Article 36</td>
<td>“States Parties shall protect the child against all other forms of exploitation prejudicial to any aspects of the child’s welfare.”</td>
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*Quotations from Human Rights Office of the High Commissioner, United Nations.39*
Moving Forward

The 2019 *WHO Report on the Global Tobacco Epidemic* demonstrates that progress has been made in implementing the FCTC. However, significant gaps remain, particularly in protecting vulnerable youth from tobacco and e-cigarette marketing, including marketing of flavored products.

Several countries provide examples of a tobacco policy agenda that protects youth. Point-of-sale tobacco advertising is banned in several countries, and others—such as Iceland, Thailand, Belarus, the United Kingdom, and Australia—also ban the display of tobacco products at the point of sale. In these countries, the bans are estimated to have reduced overall adult daily smoking prevalence by 7%. Indonesia recently implemented a ban on online tobacco advertising, after finding that at least 141 platforms—including Facebook, YouTube, and Google—were showing cigarette adverts. Bans on tobacco flavors or on sales of products with flavors (including menthol) have been implemented in Canada and parts of the United States and will be implemented in Turkey and the European Union in 2020. Several countries, such as Brazil, Singapore, and Australia, have banned the sale and marketing of all e-cigarettes and heated tobacco products. Proper enforcement of such policy measures is pivotal for their success.

Additionally, countries should continue or enhance efforts to monitor and evaluate tobacco use among youth (following the example of more than 70 countries that already do so) as well as strengthen efforts to monitor tobacco industry strategies to circumvent regulations. For example, the current youth prevention programs promoted by the tobacco and vaping companies are as ineffective as previous tobacco industry-sponsored “youth smoking prevention” initiatives.

Conclusion

Countries without comprehensive tobacco regulation still have a window of opportunity to prevent their children from becoming victim to tobacco or e-cigarette use. Countries that have yet to ban tobacco displays and point-of-sales advertising, ban social media and other online tobacco marketing, ban all tobacco additives and flavors, and ban or strictly regulate access to e-cigarettes and heated tobacco products should do so. However, to achieve the goal of tobacco control, gaps in policy implementation will need to be addressed, and tobacco and e-cigarette marketing bans will need to be strictly enforced. Although these measures may appear restrictive, they are necessary not only to protect children’s health but also their fundamental
rights to health and to be protected from harmful drugs and exploitation. Countries are morally and legally obligated to fulfil these measures as parties to the FCTC as well as to the CRC.

References


41. Glantz SA, Gardiner P. Local movement to ban menthol tobacco products as a result of federal inaction. *JAMA Intern Med.* 2018;178(5):711-713.


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Dr Bialous has served as a consultant to the Secretariat of the WHO Framework Convention on Tobacco Control and has presented in a public hearing in Brazil on that country's regulation of electronic nicotine delivery devices. Dr van der Eijk had no conflicts of interest to disclose.

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How Should Low- and Middle-Income Countries Motivate Equity in Cancer Prevention and Control?

Justin M. List, MD, MAR, MSc and Jeremy M. O’Connor, MD, MHS

Abstract
Cancer continues to be a prominent cause of morbidity and mortality in low- and middle-income countries (LMICs). Many LMICs, however, lack adequate data to better understand and respond to trends in cancer incidence. This article highlights crucial roles that government and public-private coalitions can play in cancer surveillance in LMICs. In particular, local and global investment in LMICs can build essential structures for cancer prevention and early detection, including public health surveillance systems and cancer control coalitions. Using examples from LMICs that show the promises and pitfalls of these approaches, this article argues that comprehensive cancer control can motivate health equity.

Global Cancer Burden
Low- and middle-income countries (LMICs) bear a larger burden of cancer mortality than high-income countries (HICs), with as many as 70% of cancer deaths occurring in LMICs. Fewer resources to allocate to cancer, a rising rate of cancer incidence due to improvements in life expectancy from reduced infectious disease mortality, and exposure to other risk factors common in HICs, such as smoking tobacco, physical inactivity, and changes in dietary patterns, account for some of these trends and inequities.

Effective cancer prevention and control require multilevel policy interventions to reduce cancer inequities, defined as disparities in multiple measures of cancer control, including cancer screening, incidence, morbidity, mortality.
Using lessons from HICs and LMICs, we focus on 2 key levers in public health for improving cancer prevention and control and thereby reducing cancer inequities in LMICs: public health surveillance systems and cancer control coalitions.

**Public Health Surveillance for Inequity**

The World Health Organization (WHO) defines public health surveillance as “the continuous, systematic collection, analysis and interpretation of health-related data needed for the planning, implementation, and evaluation of public health practice.” Toward this end, 3 types of cancer registries provide different levels of cancer-related data: population-based cancer registries (PBCR), hospital-based cancer registries, and pathology-based cancer registries. A PBCR collects all reportable cancer occurrences from multiple sources in a defined area and is best suited to capture population-level disease burden and inform approaches for cancer control.

An effective cancer registry supports a core set of functions related to data: collection, dissemination, analysis, and application. In the United States, the Surveillance, Epidemiology, and End Results (SEER) Program serves as a robust and well-coordinated system of local and national cancer registries containing data on cancer screening, incidence, treatment, and outcomes. The SEER registry is an example of a registry that helps streamline the dissemination, analysis, and application of data by making data readily available to researchers, providing statistical software for data analysis, and publishing reports for the public in order to increase awareness and understanding of cancer surveillance.

Cancer registries at the local and regional levels can provide particularly useful information for tailoring prevention and awareness strategies when local trends differ from national and regional trends. For example, a recent study using data for New York City (NYC) found racial and ethnic differences between NYC and national trends in the incidence of early adult-onset colorectal cancer. In another example, regional data from an Egyptian PBCR suggested that breast cancer incidence was higher among urban-dwelling women than women in rural areas, even when controlling for known risk factors. Researchers and health officials are now considering environmental and other risk factors to understand these differences.

Although these examples at the local and national level illustrate the importance of accurate data collection as the foundation of effective public health surveillance, publicly available data suggest that current PBCRs cover
just 2% of Africa, 6% of Asia, and 8% of Central and South America.\textsuperscript{12,13} Lack of accurate population-level data and of systems to collect and organize it puts LMICs at a severe disadvantage when setting priorities for nascent cancer control initiatives.

What are the best ways for LMICs to build and run PBCRs? The International Agency for Research on Cancer (IARC) categorizes the core components necessary to build and run PBCRs into 2 domains: political/administrative and institutional/professional.\textsuperscript{7} The political/administrative domain includes local and national health department involvement and a cancer registry as part of a health information system for planning and managing services for cancer prevention and treatment. The institutional/professional domain includes key leaders needed to oversee a registry, cancer specialists, hospital directors within the geographic catchment area, and death registry departments.

Resource constraints cannot be overstated as a barrier to building PBCRs. For example, PBCRs incur not only fixed costs but also labor costs, as cancer registrars, who collect and process cancer data, play a crucial but often overlooked role in the organization and operation of cancer registries.\textsuperscript{8} In some LMICs, cancer is not defined as reportable per national legislation,\textsuperscript{14} making it even more difficult for stakeholders to make the case for government funding for registries. In contrast, all 50 US states now have programs that report incident cases of cancer to registries.\textsuperscript{9} The first study estimating resources used for total costs of cancer registries in select countries found that fixed and variable costs of maintaining registries were borne mostly by nongovernmental host institutions, such as local universities, and supported financially by multiple sectors.\textsuperscript{14} Governments can play a key role in encouraging development of registries through legislation, but it is often critical for governments in LMICs to develop partnerships with nongovernmental institutions to operate them.

A paucity of cost data for operating registries can limit how robustly stakeholders can support staff, labor, and technology resources. For the purposes of sustainability, LMICs and their global partners should estimate fixed and variable costs as early as possible, given the diversity of public-private partnerships (PPPs) for PBCRs found throughout LMICs. Although tools such as the IARC's Global Initiative for Cancer Registry Development support crucial capacity building across LMICs,\textsuperscript{13} LMICs need further investment from and coordination with other stakeholders to expand PBCRs as a tool for identifying cancer disparities.
Cancer Control Coalitions
In addition to cancer registries, cancer control coalitions offer a potentially wide-reaching opportunity for informing population-level cancer prevention activities, which include raising awareness about cancer, supporting PBCRs, and generating multisector approaches for outreach to populations. Cancer control coalitions often bring together individuals from health departments, academic institutions, community-based organizations, advocacy groups, and health care systems in order to set agendas for increasing awareness and for prevention, early detection, and access to care.

In the United States, Centers for Disease Control and Prevention (CDC) funding and strategic planning advanced the growth of these coalitions in the late 1990s through the development of cancer control programming.15 In San Francisco, a broad, community-based cancer coalition—San Francisco Cancer Coalition—was launched in 2016 to address 5 of the most common cancers according to PBCR data, and the coalition prides itself on raising awareness of the physical and social environments and other social determinants of health that impact cancer outcomes and health equity.16 Indeed, the emergence of coalitions has tracked with steady gains in cancer prevention and control. For example, the NYC Citywide Colorectal Cancer Control Coalition, convened by the NYC Department of Health and Mental Hygiene, set clear goals to increase screening colonoscopy rates and eliminate racial and ethnic screening disparities in the early 2000s.17 Engaging diverse partners in the coalition, it focused on public awareness and physician education, easing the referral process for colonoscopies, promoting colonoscopy quality, supporting patient navigation in screening, and promoting public health messaging in communities known to have low screening rates. By 2013, gaps reflecting racial and ethnic inequities had closed and the colonoscopy screening rate had risen from 42% to 69% in NYC.17

Although fewer in number compared with high-income countries, examples of coalition building exist in LMICs. In one case, better defined as a PPP, the Rwandan Ministry of Health worked closely with a pharmaceutical company, medical device company, the American Society of Clinical Pathology, and the CDC, among others, to devise a comprehensive plan for cervical cancer prevention, screening, and treatment.18 The plan included a national human papillomavirus (HPV) vaccination campaign, expanded cervical HPV infection screening and treatment, and pathology education.18 Often noted as an example of a highly successful PPP because of its population health results,19 this unique constellation of partners helped create roadmaps for PPPs in other LMIC settings.
Despite the potential for success that coalitions and PPPs hold, many challenges must be addressed throughout the lifespan of a coalition or PPP in order to achieve or sustain improvements. Partnership members’ funding and organizational priorities can change or even conflict with a coalition’s or PPP’s mission and framework. And power differentials among stakeholders in the coalition or PPP can stall progress on stated shared goals. In LMICs, in particular, one risk is that coalitions or PPPs will draw resources away from an already fragile health infrastructure—for example, by diverting local health worker labor from essential core health care functions to report writing for funders.\(^\text{19}\)

The participation of corporations and other private sector or nongovernmental organization members can present additional conflicts of interest within a coalition or PPP. Corporate participation can give companies unfair market advantages or negatively impact governmental and public health priorities, and, in some cases, products of a particular corporation (eg, tobacco and food industry corporate partners) can be at odds with or thwart public health goals.\(^\text{20}\) For example, one foundation’s holdings in a corporation presented potential conflicts of interest on multiple levels,\(^\text{19}\) at least in part because some products, such as soda, promote obesity,\(^\text{21}\) which is a risk factor for certain cancers.\(^\text{22}\)

Given this context, how might LMICs chart an ethical way forward? One way is for governments and public health agencies to follow a coalition governance framework that enforces evidence-based public health priority setting to keep policy design at arm’s length from private sector partners and evaluate effects on health and the health care system of potential partners’ products in order to mitigate risk and vet the appropriateness of potential partners.\(^\text{23}\) As a result of careful consideration, some potential partners might be excluded from coalitions and others might be given clearly defined participatory guardrails.

Successful cancer coalitions also foster accountability and shared decision making among coalition members, diversified funding, and flexible structure and prioritize evidence-based work plans.\(^\text{24,25}\) Engaging a convening entity, such as an academic institution or health department; revising goals based on emerging data; reviewing local assets and challenges; and periodically re-evaluating stakeholder representation can further strengthen coalitions.\(^\text{17}\) Effective communication, both within a coalition and between a coalition and its audiences, requires understanding the media landscape, crafting messages
that resonate with intended recipients, and purposeful coordination among 
coalition stakeholders and external partners. Lessons learned from places 
such as NYC, San Francisco, and Rwanda provide guideposts for HICs and 
LMICs trying to reduce cancer inequities.

Conclusion
Public health surveillance systems and cancer control coalitions are necessary 
but not sufficient for ending cancer inequities between HICs and LMICs, and, 
in the case of coalitions, how a coalition’s membership and governance are 
structured affect progress toward achieving equity in cancer prevention and 
control. Of course, ending cancer inequity requires more policy interventions 
than we have discussed, including those aimed at (1) collecting population-
based behavioral risk and environmental data and establishing cancer 
screening registries, (2) maintaining an adequate health care workforce, 
providing health education concerning prevention and early detection, (4) 
increasing access to preventive services, (5) controlling tobacco use, and (6) 
establishing programs to address the social determinants of health. In 
addition, advancing knowledge about and solutions to cancer inequity is a 
process that is most effective when it is bidirectional—that is, with relevant 
experiences in LMICs informing policies in HICs and vice versa. In the end, the 
degree to which we improve cancer outcomes in LMICs and eradicate global 
inequities in cancer control is dependent in part upon the degree to which 
people and societies make a commitment to focus on cancer surveillance in 
LMICs.

References
1. Torre LA, Siegel RL, Ward EM, Jemal A. Global cancer incidence and 
mortality rates and trends—an update. Cancer Epidemiol Biomarkers 
room/fact-sheets/detail/cancer. Published September 2018. 
Accessed May 19, 2019.
according to the Human Development Index (2008-2030): a 
17. Itzkowitz SH, Winawer SJ, Krauskopf M, et al. New York Citywide Colon Cancer Control Coalition: a public health effort to increase colon


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MEDICINE AND SOCIETY
How Should Biobanking Be Governed in Low-Resource Settings?
Aminu Yakubu, Nchangwi Syntia Munung, and Jantina De Vries, PhD

Abstract
Development of biobanks in Africa raises ethical questions related to particular features of African cancer research contexts, such as underresourced health care and research infrastructures and low-average research literacy. This article describes ethical challenges of informed consent, benefit sharing, and stigmatization and proposes navigating these challenges by developing a comprehensive governance framework to ensure African leadership in biobanking research programs in Africa.

Biobanking in African Research
Recent years have seen increased efforts to capture global genetic diversity in an attempt to ensure that the benefits of genomic innovation filter down to all people around the globe, including Africans. Efforts such as the Human Heredity and Health in Africa (H3Africa) Consortium and the Bridging Biobanking and Biomedical Research Across Europe and Africa (B3Africa) Consortium are aimed at achieving this diversity, increasingly through the inclusion of African researchers and populations in genomics studies. These initiatives either set up new biobanks or strengthen the capacity of already existing ones.

Biobanking—the practice of collecting, curating, and archiving biospecimens for research purposes—is one key tool that is available to scientists to accelerate genomic cancer research. A biobank stores large numbers of samples and associated data and makes these resources available for further research. To serve its purpose as a research resource, biobanks are expected to (1) have defined mechanisms for accessing biospecimens, (2) ensure that the use of biospecimens is in accordance with the informed consent of the participants who donated the samples, (3) have policies for biospecimens disposal, and (4) have a benefit sharing plan.
Several features of the African research context raise ethical challenges for biobanking. In most African countries, these include, for instance, limited resources available for research, health and research institutions that are understaffed or have underskilled workers, old or outdated infrastructure, and limited or no regulation of biobanking.\textsuperscript{6,7,8} Prevailing norms that govern research also raise ethical challenges for informed consent, given that the African context tends to prioritize values like communitarianism and reciprocity over respect for autonomy.\textsuperscript{9} While respect for autonomy is important, relations between people and considerations of community benefit are considered equally important. Taken together, these features raise a range of ethical challenges including not only consent for the storage and reuse of biospecimens, but also limited country regulations for the export of biospecimens, benefit sharing, and genetic discrimination and stigmatization.

**Challenges of Obtaining Informed Consent**

Although informed consent holds a special position in research, in biobanking research, consent is also required to store a specimen—sometimes for an indefinite period of time—as well to use specimens for unspecified future research. Yet consent forms are often specific to a particular study, for which biospecimens’ aims and uses are defined. This apparent clash between consent for a specific study and consent to future unknown uses of biospecimens has caused considerable debate in bioethics. Broad consent, which is consent for future research subject to a number of restrictions,\textsuperscript{10} has been proposed as an appropriate consent model for African genomics research and biobanking.\textsuperscript{11} It has also been recommended for secondary research on unidentified biospecimens in the revised Common Rule that guides research in the United States.\textsuperscript{12} While a growing body of evidence suggests that African research participants recognize broad consent as the “best compromise,”\textsuperscript{13,14,15} it has also been argued that broad consent increases the risk of exploitation of African research populations,\textsuperscript{16} which suggests that a decision to use broad consent is context dependent and that there might be particular instances when its use is inappropriate.

Broad consent has been proposed for African genomics research,\textsuperscript{17} but given the appeal of communal values in most African settings, it is important that broad consent be accompanied by governance mechanisms that incentivize biobanks to promote the interests of biospecimen providers\textsuperscript{11} as well as communities’ health and research needs. Toward this end, genomics research and biobanking initiatives are setting up data and biospecimen access committees (DBACs) to review secondary biospecimen use and consider risks posed to study communities. DBACs are critical not only in mitigating risks of
multiple uses of samples and data but also in building trust between researchers and study communities. Trust is particularly important because DBACS are expected to serve as custodians of samples and to provide some oversight of the use of samples and data with an aim of benefiting study communities.

Exporting and Regulating Samples
One motivation for establishing biobanks in African countries is that doing so will hopefully give those countries and the people whose samples are included in the biobank more control over uses of stored biospecimens. Regulation of biobanking in most African countries is limited, which makes oversight of biobanks challenging. Lack of national regulation enables some unethical practices to go unchecked. An example is specimen transfer without recourse to local country authorities or respect for persons from whom samples were collected, which occurred during the 2014–2016 Ebola virus disease (EVD) epidemic. Biospecimens from EVD patients were shipped out of Sierra Leone and Liberia to be stored in biobanks in other countries. People from whom specimens were collected were not informed that their samples would be taken out of their country of residence; nor were they informed that their samples would be used for health research. Biobanks in countries in which these samples were stored have expressed unwillingness to provide some form of oversight of the samples or access to the samples to researchers or government authorities from countries in which specimens were collected. This example shows that absence of national regulatory frameworks makes it difficult for governments to insist that samples be returned.

To eliminate these kinds of scenarios, which have been described as exploitative “parachute” research (a practice whereby scientists in high-income countries go to low-income countries to collect specimens and publish findings in prestigious journals without properly crediting collaborators in LMICs or returning benefit to study communities), it is important for African governments to develop national guidelines for biobanking. Moreover, given the trend toward multicountry African biobanking, harmonizing countries’ regulations might help facilitate health research across the continent.

Benefit Sharing
Research conducted using biobank resources benefits researchers from Western countries in tangible and intangible ways. When research is commercially driven (eg, pharmaceutical research), expectation of benefit is
more tangible than in knowledge-driven research, which mostly aims to build general scientific knowledge. Ethically, this is important because access to technology, literature, and other resources affords researchers’ institutions in high-income countries (HICs) opportunities to use biobank samples in more ways than their African counterparts.

One way to ensure that research is beneficial to all stakeholders is to engage various stakeholders (for example, study communities, policymakers, funders, African researchers, HICs collaborators, and research ethics committees) in discussions of what would constitute likely research benefits and how these could be actualized through biobanking. Two of the most direct ways in which biobanking can benefit Africa is by helping to build research capacity and by ensuring that young African students and scholars have opportunities to lead in ethical uses of samples for health research.

Risk of Genetic Discrimination

A recurring fear in population-level genomics research is that genetic information could be used to stigmatize or socially undermine certain groups, particularly those with stigmatized health conditions, such as podoconiosis, human African trypanosomiasis, epilepsy, and some psychiatric or mental health conditions. Historically, some interpretations of biological evidence have been ethically and scientifically troubling. One example of overinterpretation was the conclusion that South African San people’s lack of an allele associated with skin pigmentation and their ability to sense a bitter taste confer a survival advantage in the Kalahari desert; the latter “may reflect a need in hunter-gatherers to avoid toxic plants.” Problematic interpretations of evidence can also be used to support negative stereotypes, as was the case in a description of a Māori “warrior” gene as a “marker” for alcohol and tobacco use. What these examples suggest is that, at a minimum, researchers must consider the risk that their research and interpretations of results can be perceived by some as offensive, stigmatizing, or otherwise scientifically or ethically inappropriate.

Governance Framework

In a partial response to some of these challenges, a set of principles to ensure inclusion of African populations in biobanking research has been proposed by the Ethics and Regulatory Issues Working Group of the H3Africa Consortium. Recognized in this framework is the need for African researchers to lead in the conceptualization, planning, and implementation of research using stored biospecimens. This framework also recognizes the need for robust governance mechanisms that explicitly promote fairness in
research by ensuring that African populations and researchers are not exploited when participating in international biobanking programs. Such governance mechanisms must provide a role for local country governments to help make decisions about storage and use of specimens collected from their citizens. This role could be recognized through a designated government entity for research or through institutions where African investigators are based. Key to good governance is a mechanism for providing feedback to the ethics committees that approve uses of specimens that are collected from African people and stored in African biobanks. Equally important is promoting fairness in research by ensuring that decisions about access to biobank resources in African countries are made by representatives from African institutions, that African researchers are given preferential access to biobank resources, and that reuse of specimens is prioritized for research about conditions of importance to African communities by African researchers and co-investigators.

References


18. Freudenthal E. Ebola’s lost blood: row over samples flown out of Africa as “big pharma” set to cash in. *Telegraph.* February 6, 2019: https://www.telegraph.co.uk/global-health/science-and-


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ART OF MEDICINE
Risks, Benefits, and Conundrums of Cancer Screening
Nick Love, PhD

Abstract
This graphic narrative is a fictional case report illustrated using paint pens and histological micrographs collaged with Adobe Illustrator. The story of Mr P and his physician recapitulates an ethical dilemma presented by cancer screening: screening can save lives, but it also generates diagnostic morbidity and incurs costs.

Figure. Detail from Corpora Amylacea

(Click here to view entire the entire graphic narrative.)

Media
Oil and acrylic paint pencils on paper; micrographs of histologically stained tissue captured using SPOT software and collaged with Adobe Illustrator.

**Caption**
This graphic narrative is drawn from the artist’s experience working in a department of pathology. Drawing on the aesthetic beauty of histologically stained tissue, the graphic relates a story of uncertainty in medicine, represents risk of diagnostic morbidity, and visually considers psychological burdens of disease. The illustrations and micrograph collages aim to provoke a viewer’s consideration of risks, benefits, and costs of cancer screening and workup techniques while the precision of the digital images contrasts with the imprecision of analog histological staining techniques.

**Nick Love, PhD** is a pathology fellow and fourth-year medical student at Stanford University School of Medicine in Stanford, California. A biology undergraduate of the University of North Carolina at Chapel Hill, he also attended Cambridge University and the University of Manchester in the United Kingdom, the University of Bergen in Norway, and the RIKEN Center for Developmental Biology in Japan.

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**Editor’s Note**
This is the winning artwork of the 2019 John Conley Art of Medicine Contest.

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ART OF MEDICINE
Girl and Rooster
Ayotunde Ayobello, MD

Abstract
This colorful oil painting suggests how a fearless child can inspire compassion, particularly regarding our clinical, political, and ethical orientations to ongoing practices of separating children from parents at the US southern border.

Figure. Girl and Rooster
Media
Oil on canvas.

Caption
In this painting, a trip to the countryside takes an exciting turn when my 5-year-old daughter finds and picks up a rooster. The bird appears thoroughly displeased, but she basks in the moment, fearless. This painting seeks to represent a confluence of fearlessness, innocence, and compassion. This set of themes has potential to inspire people to end ongoing policies and practices of separating children from parents at the US southern border that are ethically problematic and clinically relevant.

Ayotunde Ayobello, MD is a third-year psychiatry resident at the Virginia Tech Carilion School of Medicine in Roanoke, Virginia. He is an avid oil painter with professional interests in child and adolescent psychiatry, ethics, and medical humanities.

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PERSONAL NARRATIVE

Six Tips for Giving Good Health Care to Anyone With a Cervix
Ryan K. Sallans, MA

Abstract
Cervical cancer is most frequently diagnosed in patients ages 35 to 44, but risk persists as individuals age. Among patients who are regularly screened via the Pap test, cancer is rare and death rates have dropped dramatically in the United States. Nevertheless, access to regular screening can be difficult for transgender men (individuals assigned female at birth but with a male gender identity) due to misinformation, discomfort scheduling appointments, fear of being mistreated or of refused services, lack of insurance, and clinicians’ lack of knowledge. This narrative explores 6 barriers to cervical cancer screening for transgender men and offers recommendations for eliminating cervical cancer inequality.

Need for Transgender Gynecological Care
Death rates from cervical cancer have dropped dramatically in the United States due to the effectiveness of the Pap test in detecting cervical cancer, which has allowed clinicians to treat abnormal and precancerous cells. Yet transgender men (individuals assigned female at birth but with a male gender identity) obtain cervical cancer screening less frequently and are less likely to be up-to-date on Pap tests than cisgender women (individuals assigned female at birth and with a female gender identity). According to the 2015 US Transgender Survey, although transgender men are vulnerable to chronic undetected human papillomavirus (HPV) infections, only 27% report having had a Pap smear in the past year compared to 43% of women in the general population. Barriers like the ones presented below may prevent transgender men from scheduling appointments and accessing life-saving screenings. First, however, I offer a personal perspective on the need for cancer screening.
Testosterone Therapy and Pelvic Pain

During the summer of 2006, I celebrated the completion of my first year on testosterone. Over the course of that year, I documented many physical changes as my body morphed from a female to male shape. I had undergone chest surgery (a bilateral mastectomy with nipple grafts), but I still had other body parts—uterus, ovaries, fallopian tubes, vagina, and cervix—that required screening typically marketed only to female patients. The last time I had had a pelvic exam and Pap test, I was 19 years old, and I was now turning 26. Although cervical cancer is most frequently diagnosed in patients ages 35 to 44, it was important to me to schedule another exam, not only to make sure that my tissues were healthy but also to address my ongoing extreme pelvic pain.

After initiating hormone therapy—in my case, testosterone—transgender male patients can experience cramping and pain that can last more than 6 months. My pelvic pain had been ongoing day and night for almost 4 weeks. At the time, I didn’t know that this was a common symptom of testosterone use, so I was concerned. Although motivations and reasons for seeking gynecological care vary, in my case, I had dysphoria about my reproductive organs; I was tired of dealing with pelvic pain; and I was concerned about uterine, cervical, and ovarian cancer. (Please note that there is currently no evidence that testosterone therapy increases risk for ovarian, uterine, or cervical cancers among transgender men.) Not having a desire to retain my uterus, I hoped my exam would render me eligible for a laparoscopic total hysterectomy and an oophorectomy. If so, I would be joined by a low percentage of transgender men who have had a hysterectomy. In a 2015 survey that included more than 8000 trans male respondents, 14% reported having had a hysterectomy and 57% reported wanting one someday.

Barriers

1: Gynecological care for men. Scheduling an appointment for gynecological care, including a Pap test and pelvic exam, and then following through with the appointment can be emotionally difficult for transgender men. I wanted to see a clinician about my concerns, but I was afraid to call and schedule an appointment because I didn’t know if anyone would take me as a patient. I’d had negative experiences with clinicians and staff in the past, so even if someone would see me, I was worried about how I’d be treated.

I gained courage by having a female friend call her obstetrician’s gynecology office and ask if anyone would see a trans man as a patient. The office responded, “We’ve never worked with a trans man before, but send him our
It was a relief to hear this kind of response in 2006, given the lack of clinical education and training in how to respond to transgender patients’ obstetrics and gynecological needs. This lack of training persists. A 2015 survey of obstetrics and gynecology clinicians found that 80% of respondents reported not having received training in transgender care during residency, but almost 89% reported that they would be willing to provide routine Pap tests for transgender men. In my case, knowing the clinic was open to me, even if its staff didn’t have experience, diminished my anxiety—a little.

2: Is the target population gender and gender identity inclusive? When I called the clinic to make an appointment, the receptionist sounded surprised to hear a man’s voice ask for a pelvic exam. And as I walked into the clinic, I had to ignore that women was the only word on the sign. The door closed behind me, and I kept my head down as I approached the front desk. I wasn’t sure how people would react to seeing a man in a waiting room full of women. I was relieved that the front desk staff greeted me with a smile and treated me like any other patient.

3: Gynecological clinical encounters with trans men. Transgender patients’ positive experiences in health care settings increase the likelihood of their remaining compliant with recommendations, including for screenings. If you’re a clinician or a staff member, the upshot here is that patients’ first encounters could be their last if they feel terrible about what happened to them there. So, the first time a trans man patient has a Pap test, it is important to talk with him about the procedure, including speculum use, swab insertion, and total time it typically takes to complete a physical examination. Approaching patients using a trauma-informed care model can help alleviate transgender men’s anxieties about having their body parts examined and their experience of dysphoria or discomfort.

Although I went to my appointment alone, I accompanied a transgender male friend to his and joined him in the exam room. While my friend was still fully clothed, the clinician reviewed his health history. She informed him that if he had discomfort with any of the language she used, he should let her know his preferred terms. Trans men might be uncomfortable with clinically accurate terminology associated with body parts, so when patients prefer different language, clinicians should mirror their language.

Testosterone causes atrophy and dryness of vaginal tissue; for trans men or cisgender women who do not engage in penetrative vaginal sex, a speculum can be especially uncomfortable. My friend was extremely anxious about
speculum insertion, due to never having had penetrative sex, so this particular clinician did well to assure him that she would use an appropriately sized speculum for his anatomy. Pediatric-sized speculums, however, are not always helpful, and over lubrication should be avoided. The clinician continued to communicate each step she would take and described what my friend might feel. She then asked him to disrobe from his waist down. Upon completing the exam, she left the room to allow him to put his clothes back on and later returned to answer his questions. This was a positive encounter for my friend and also for me as an observer. This clinician became a trusted caregiver in our community of trans men, and we all began supporting each other in making and attending appointments.

4: Gendering and body parts. Another barrier to care that transgender men tend to experience, if insured, is receiving notice of denial of claims coverage by an insurer. Clinicians can help prevent this occurrence with clear billing communication. After an appointment, for example, a clinician should note the patient’s gender in his health record and notify stakeholders that this might be different than what is on his insurance card. If gender markers, like pronouns or names, are mismatched for a gender-linked procedure, like a Pap test, or gender-linked body parts, like a cervix, it’s helpful to trans men patients when clinicians explain to the billing department the organ-specific services rendered. Taking these steps might decrease the number of insurance claims that a trans man patient is denied.

After my clinician determined that a hysterectomy would be the best treatment for my symptoms and concerns, I informed her that all of my documentation—including driver’s license, birth certificate, and insurance card—affirmed my identity as a man. She stated that she would note specific organs present in my health record and submit forms for precertification to my insurance company. Although my procedure was precertified, 4 months later a postpayment audit flagged the claim due to my being a man, prompting my insurer to request a refund. My clinician helped me appeal by writing a letter noting the medical necessity of the service she provided to me, and the appeal was eventually approved. In my case, the clinician advocating for me increased my trust and desire to return for future care.

5: Inadequate lab results. Inadequate tests or samples are more common among transgender male than cisgender female patients, requiring return office visits and repeat screening. Often, the lab notes list “inadequate sample,” “atrophy,” or “dysplasia” as a reason for abnormal or inconclusive results. Not wanting to undergo another exam, a trans man patient receiving
such results might not return to a clinic but might remain concerned about the results. In order to decrease the odds of an inadequate test, clinicians should inform the labs they use that a patient on testosterone (which causes thinning of vaginal tissue) had a cervical swab and also note whether the patient is amenorrheic. Taking these steps can decrease the chance of abnormal results, confusion, error, or sample disposal by the lab. For example, the tissue sample taken after my hysterectomy came back with a note about cervical dysplasia, but I didn’t find this alarming because my clinician explained that my long-term testosterone use caused cervical epithelial atrophy, which can mimic dysplasia.

6: Sex practice diversity and risk awareness. Both transgender men patients and clinicians can be misinformed about screening guidelines and risks. Some trans men lack not only understanding of risk factors for HPV but also general gynecological knowledge. Some clinicians might assume that trans men are less likely to be at risk for HPV because they might also assume that trans men don’t have penile/vaginal penetrative sex. This assumption is wrong. There are a wide range of sexual practices in which trans men might be interested, including penetrative vaginal, anal, or oral sex with partners who have penises that produce sperm. Minority stress due to gender-related discrimination and victimization has a negative impact on health; alcohol use, a history of psychosocial distress, and a history of sex with men only are risk factors for sexually transmitted infections in trans men.

Anyone With a Cervix
Transgender men need to see themselves reflected in data, research, and cervical cancer screening guidelines published in authoritative, reliable sources. When conducting research for this article, I noticed that many sources continued to use anatomical words and pronouns intended to apply narrowly to cisgender women only. It is important to include trans men in cervical cancer screening recommendation language, for example, by stating clearly that screening is for women, transgender men, or anyone with a cervix.

Patients who identify as trans men find it acceptable and preferable to test for HPV with self-collected vaginal swabs. Clinicians should offer and provide self-collection swabs as an option to trans men patients, along with education about risks and benefits of HPV vaccination. Clinicians should also offer other forms of screening, such as urine tests for sexually transmitted infections, to increase the likelihood that trans men patients follow screening guidelines while being spared the discomfort of a pelvic exam. The more
frequently trans men have positive experiences in gynecological health care settings when seeking routine screening, the more likely they will be to practice regular screening and illness prevention. While I no longer need pelvic exams, I still visit my clinician’s office for hormone therapy monitoring and other health care because I have established trust and had positive clinical encounters. Everyone deserves equality in enjoying this level of quality and trust in their health care.

References

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