Cancer Groundshot: Building a Robust Cancer Control Platform in Addition To Launching the Cancer Moonshot

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Overview

Cancer Groundshot is a philosophy that calls for prioritization of strategies in global cancer control. The underlying principle of Cancer Groundshot is that one must ensure access to interventions that are already proven to work before focusing on the development of new interventions. In this article, we discuss the philosophy of Cancer Groundshot as it pertains to priorities in cancer care and research in low- and middle-income countries and the utility of technology in addressing global cancer disparities; we also address disparities seen in high-income countries. The oncology community needs to realign our priorities and focus on improving access to high-value cancer control strategies, rather than allocating resources primarily to the development of technologies that provide only marginal gains at a high cost. There are several low-hanging fruit actions that will improve access to quality cancer care in low- and middle-income countries and in high-income countries. Worldwide, cancer morbidity and mortality can be averted by implementing highly effective, low-cost interventions that are already known to work, rather than investing in the development of resource-intensive interventions to which most patients will not have access (i.e., we can use Cancer Groundshot to first save more lives before we focus on the moonshots).

Cancer remains the leading cause of mortality and morbidity in the world, with 19.3 million new diagnoses and 10.1 million deaths in 2020.[1–4] These numbers are accelerating every year; it is estimated that there will be 28.4 million new cancer diagnoses by 2040[1] (Fig. 1), with the biggest increase in incidence occurring in low- and middle-income countries (LMICs). However, high-income countries (HICs) will continue to host the highest proportion of patients with cancer worldwide[1]; cancer is already a leading cause of death in HICs.[1–5] A Global Cancer Observatory (GLOBOCAN) 2020 report estimated that nearly one-half of all new cases and 58.3% of cancer deaths for that year occurred in Asia, where 59.5% of the global population resides.[1,3,5] By contrast, Europe accounted for 22.8% of the total cancer cases and 19.6% of cancer deaths, while representing only 9.7% of the global population.[6] Of note, Asia (58.3%) and Africa (7.2%) have higher fatality rates than new-cancer incidence rates (49.3% and 5.7%, respectively).[3] In this article, we discuss the philosophy of Cancer Groundshot as it pertains to priorities in cancer care and research in LMICs and the utility of technology in addressing global cancer disparities; we also address disparities seen in HICs.

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CANCER GROUNDSHOT

Cancer Groundshot is a philosophy that calls for prioritizing strategies in global cancer control.[7] The underlying principle of Cancer Groundshot is that it is important to ensure access to interventions that are already proven to work before focusing on the development of new interventions. Indeed, as will be discussed below, most cancer deaths occur because patients lack access to proven diagnosis and treatment strategies, not because they lack access to the newest technologies or drugs.

GLOBAL DISPARITIES IN ACCESS TO CANCER CARE

There are major disparities in cancer care delivery and access among countries, and these directly impact cancer outcomes. Despite the low incidence of certain types of cancer in LMICs, mortality remains similar to or higher than that seen in HICs. The reasons for these disparities are multifactorial and stem from imbalances in resource distribution and in environmental exposures between HICs and LMICs. These imbalances create barriers to access for primary prevention, timely screening, diagnosis, and treatment, and they contribute to the poor health infrastructure in LMICs, differences in the distribution of cancer types, and differences in overall life expectancy.[1,3–5,8]

In 2020, 2.3 million new breast cancers were diagnosed worldwide,[1] with countries in Sub-Saharan Africa experiencing the most rapid increase in breast

PRACTICAL APPLICATIONS

- Cancer Groundshot is a philosophy that calls for prioritizing strategies in cancer control.
- It is important to ensure equitable access to proven interventions before focusing on new ones.
- Technology has the potential to address some inequities but should be rigorously evaluated before being deployed.
- Disparities exist not only between high-income countries and low-and middle-income countries, but also within high-income countries.
- The philosophy of Cancer Groundshot can be applied to addressing disparities both within high-income countries and between high-income and low- and middle-income countries.

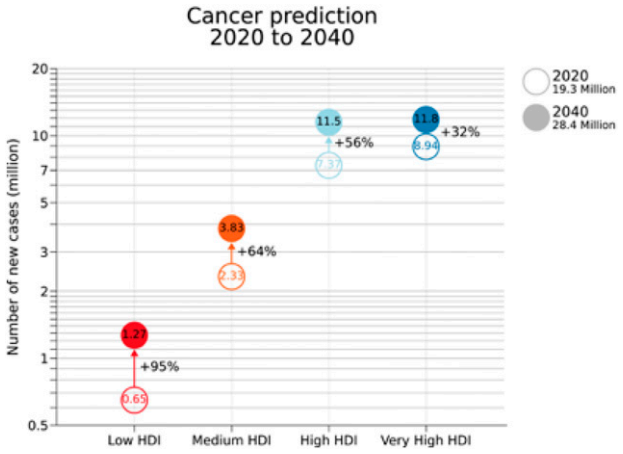

FIGURE 1. Projected Number of New Cases for All Cancers in Both Sexes in 2040, According to the Four-Tier Human Development Index
Source: Global Cancer Observatory (GLOBOCAN), 2020 (Available at https://gco.iarc.fr/tomorrow/en/dataviz/bubbles?mode=population).

cancer mortality.[9] Across 17 Sub-Saharan African countries, 77% of all diagnoses were stage III/IV.[9,10] A study conducted in five Sub-Saharan countries estimated that 28% to 37% of breast-cancer deaths in these countries could have been prevented with improved access to early diagnosis and treatment.[9]

Access to basic affordable cancer care is a challenge for LMICs[11]; this directly impacts cancer outcomes.[12] For instance, cervical cancer—the only cancer type that can be targeted for elimination with currently available prevention and treatment strategies—is still a common cause of cancer mortality in LMICs.[13] Therefore, access to proven diagnosis and treatment strategies should be prioritized, especially in LMICs where these strategies can have the greatest impact in reducing cancer morbidity and mortality.[7] This prioritization concept is the backbone of the Cancer Groundshot philosophy.[7] In fact, countries like Australia and New Zealand have targeted cervical cancer for elimination over the next decade in response to the World Health Organization (WHO) initiative to eliminate cervical cancer by 2035.[14] In recent years, there have been advances in the treatment of advanced cervical cancer, including the use of drugs such as pembrolizumab[15] and bevacizumab[16] that prolong median survival by a few months. However, Cancer Groundshot argues that LMICs with a heavy burden of cervical cancer and limited health care resources should not prioritize access to these drugs to treat a small number of patients with advanced cervical cancer; rather, the focus should be on prevention, screening, early detection, and early treatment campaigns that will help decrease the burden of advanced cervical cancer and the percentage of patients needing access to these modern, costly drugs.[17,18] Although the development of these modern drugs is consistent with Cancer Moonshot aspirations—and is indeed important for individual patients—prioritizing the elimination of cervical cancer represents the Cancer Groundshot philosophy.

Because of imbalances in global resource distribution, LMICs face several challenges to quality cancer care; however, access to new therapeutic inventions is not as important as it may initially seem for reducing the global burden of cancer. Less than 25% of the global population has access to basic curative services (e.g., cancer surgery or radiation therapy),[19–21] basic diagnostic facilities (e.g., pathology services or diagnostic imaging), or quality palliative care– and psychosocial services.[22,23] One study reported that there is an average of one pathologist for every 2.3 million people in most of Africa.[23] A Lancet commission found that nearly 90% of patients in LMICs do not have access to safe and timely surgery and radiotherapy.[19] By 2030, 45 million patients will require cancer surgery each year, yet less than 25% will be able to receive timely, safe, and affordable surgery.[11,19] Another report showed that more than 90% of patients in low-income countries do not have access to radiation therapy.[22–29] Additionally, WHO estimates that nearly 78% of patients who need palliative-care services each year live in low-income countries, but only 14% receive these services.[30,31] This reflects the omission of palliative care from the national health policies of many countries, the lack of trained staff, and inadequate access to affordable pain medications that are on the WHO Model List of Essential Medicines.[31,32] According to the Lancet commission, 99% of people in low-income countries do not have

access to basic, inexpensive, essential, and effective pain medications, despite the large global availability of these agents.[32] For example, an estimated 298.5 metric tons of morphine-equivalent opioids were distributed worldwide each year between 2010 and 2013, but only 0.1 metric ton went to low-income countries.[33,34]

Because of a global imbalance in training and professional opportunities, as well as income- and quality-of-life potential, LMICs face not only a shortage of services and resources, but also a shortage of cancer physicians and other workers needed to tackle the growing number of patients with cancer.[35,36] In LMICs, oncologists work for longer hours, taking care of a larger number of patients at a given time, with fewer resources and less job satisfaction.[36] It is estimated that by 2040, the world will need an additional 100,000 oncologists, most of whom will be needed in LMICs.[37]

Allocating resources toward strengthening the medical infrastructure, supply chain, and professional opportunities will lead to improved access to services that focus on cancer prevention, treatment, and survivorship; this focus has a greater potential to improve cancer morbidity and mortality than does spending resources on advances in treatment. Indeed, LMICs should not make the same mistake as HICs: focusing cancer control strategies on technological advances in expensive treatments that provide limited improvements in survival for a small number of patients, while a large proportion of the population still lacks access to basic cancer control services.[24]

RISING COST OF CANCER DRUGS

The rising cost of cancer treatment is a growing challenge for any nation's health care system and economy. New cancer drugs routinely cost upwards of $10,000 USD per month per patient.[38] This is higher than the monthly income of the average household in many countries, including HICs.[38–40] Although the absolute drug prices are lower in LMICs, when per capita gross domestic product is taken into account, cancer drugs are far less affordable in LMICs[38,39] (Fig. 2).

There is also growing concern that the incremental cost of cancer drugs does not provide incremental clinical benefit, thereby decreasing their treatment value.[41] Using the value frameworks proposed by ASCO, and the Magnitude of Clinical Benefit Scale (MCBS) proposed by the European Society of Medical Oncology, researchers have shown large discrepancies in the monthly prices and clinical-benefit scores of cancer drugs.[38–43] In fact, there is an inverse relationship betweenthe price of cancer drugs and the magnitude of clinical benefit, with the lowest benefit seen for drugs with the highest cost.[43] Thus, all countries should prioritize high-value drugs.[24,44]

The WHO Model List of Essential Medicines for cancer drugs provides a framework to help countries around the world prioritize important cancer therapeutics.[45] This list primarily contains classic chemotherapy agents that were approved decades ago and are available as generics (e.g., taxanes, platinums). More recently, the Model List added EGFR inhibitors for patients with lung cancer and immunotherapy for patients with melanoma. A survey of oncologists in 82 countries revealed that the drugs on the Model List of Essential Medicines are considered high-priority agents by clinicians working on the ground, especially in LMICs.[45] However, even these older generic chemotherapy agents can be unaffordable and lead to severe financial toxicity for patients.

"Financial toxicity" has been defined as the detrimental effect of excess financial strain, caused by the diagnosis of cancer, on the well-being of patients, their families, and society.[46] Studies have shown severe financial toxicity in LMICs, even with older generic cancer drugs used with curative intent. These drugs are frequently available only at full cost in LMICs, and they represent an out-of-pocket expense for the patient. For example, more than 75% of patients with acute leukemia in Nepal have to sell their property to afford treatment.[47] Financial toxicity is also increasingly recognized as an important outcome in individuals diagnosed with cancer in HICs, where health-insurance eligibility, coverage of cancer therapies, and out-of-pocket costs vary considerably between and within countries.[48]

LACK OF ACCESS TO NEW CANCER DRUGS IN LMICs

Lack of access to cancer drugs is usually a function of availability and affordability. We have discussed the affordability issue with cancer drugs, especially in LMICs. However, because of imbalances in the global distribution of resources, several cancer drugs are not available at all in LMICs. For example, one study showed that drugs like erlotinib, oxaliplatin, and gemcitabine (all generic agents on the WHO Model List of Essential Medicines) were available in only 10%, 36%, and 34%, respectively, of the 135 countries studied.[49] The causes for this lack of availability are multifactorial. A survey conducted by the European Society for Medical Oncology highlighted the following as the major barriers to access in LMICs: no reliable supplier, no commercial motive, manufacturing problems, budget capitation, and parallel export.[50]

Encouraging LMIC participation in clinical trials is often proposed as a way to provide access to new cancer medicines. This option should be considered in light of several caveats.

CAN CLINICAL TRIALS BE THE ANSWER?

A study of published Cochrane reviews revealed that, of the randomized clinical trials included in the Cochrane

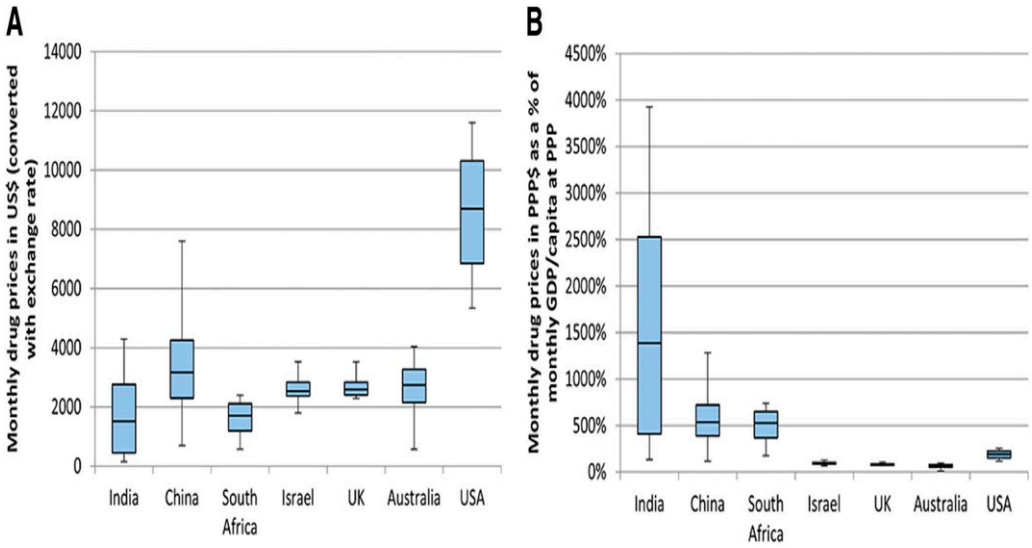

FIGURE 2. Cost and Affordability of Eight Patented Cancer Drugs in Seven Countries

(A) Prices were converted from local currency to USD (exchange rate, January 1, 2016) and expressed as box and whisker plots. (B) Monthly prices at purchasing power parity (PPP) were divided by the country's monthly gross domestic product (GDP) per capita.
Reprinted from Goldstein et al.[39]

guidelines for noncommunicable diseases, 90% (and more than 80% of participants) were from HICs[51] (Fig. 3). There is a considerable evidence gap for health-related publications between HICs and LMICs, which restricts the pool of knowledge and the perspectives on scientific activities that could improve cancer outcomes globally.[52] For example, although LMICs bear the largest burden of patients with cervical and breast cancer, most clinical

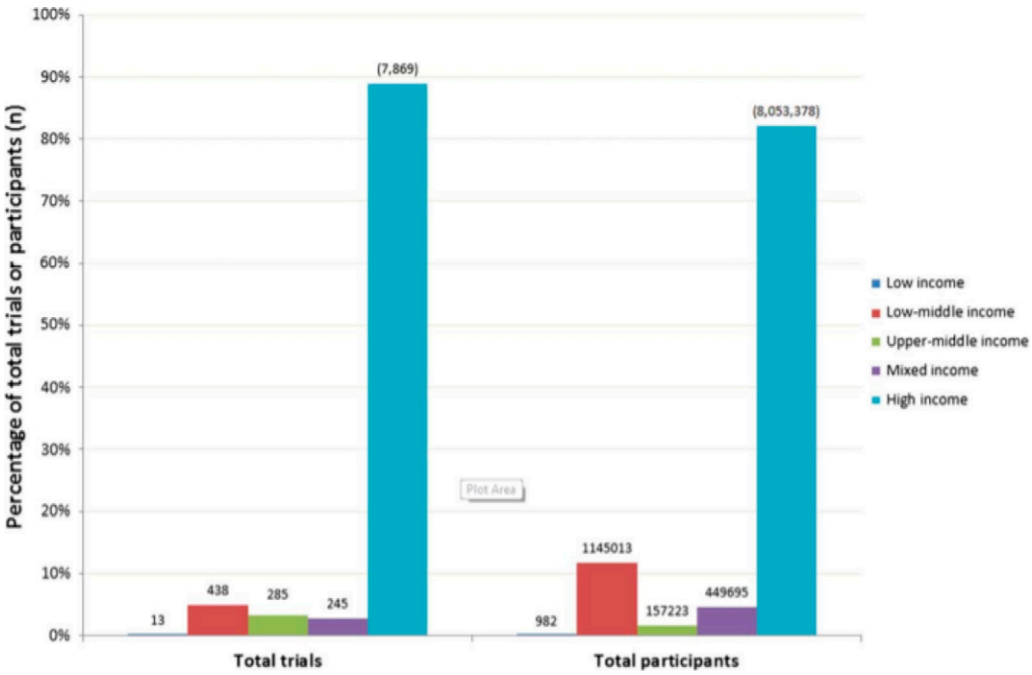

FIGURE 3. Number of Clinical Trials and Trial Participants Based on Gross National Income: 626 Cochrane Reviews of Noncommunicable Disease Studies

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trials for these cancers are conducted in HICs.[53,54] Therefore, it is imperative that LMICs participate in more research opportunities, including clinical trials.[55] Here, the philosophy of Cancer Groundshot again becomes relevant. When clinical trials are conducted in LMICs, researchers should prioritize pragmatic interventions that are relevant to, applicable to, and feasible for the patient population and local settings, rather than trials of new cancer drugs that will remain inaccessible or unaffordable locally.[56]

Although some argue that trials of new cancer drugs improve access for individual patients in LMICs, such trials cause net harm for scientific and ethical reasons, as discussed elsewhere.[57] Several randomized clinical trials use inferior control arms that would not be considered acceptable in HICs, but researchers conduct such trials in LMICs to get their "me-too" product approved in HICs,[57] a practice dubbed “research parasitism.”[58] Indeed, LMICs that participated in pivotal trials leading to U.S. Food and Drug Administration (FDA) approval of several such drugs still lack access to these agents many years later.[54] In one study, only 7% of countries that hosted trials for cancer drugs, directly leading to FDA approval, had market access to these drugs within 1 year of approval. Where applicable, drug approvals came more swiftly in HICs. Market access to medicines was lowest in Africa, followed by the Middle East.[54]

In contrast with clinical trials that test expensive systemic cancer therapies, studies of surgical interventions, repurposable drugs, frugal innovation techniques,[59] and cheaper strategies—including therapy de-escalation—can identify simple and cost-effective solutions to cancer care challenges in LMICs and HICs. These several areas of common interest for collaboration and mutual benefit were highlighted elsewhere (Fig. 4).[56]

We should also be cognizant that imbalances in the distribution of global resources create several barriers to conducting clinical trials in LMICs.[56,57,60] A lack of funding for clinical research is a common obstacle, with the majority of funding for clinical trials coming from Western countries or pharmaceutical companies.[61] However, several funding and collaboration opportunities have arisen in recent years, supported by organizations from HICs. These opportunities answer questions relevant to the local setting in LMICs.[62] Using the example of COVID-19, one would prioritize RECOVERY-type trials and dexamethasone-type interventions[63] (inexpensive, easy, worldwide access, substantial gains) over remdesivir-type interventions (costly, inaccessible, marginal gains).[64]

Barriers to access and lack of representation in cancer-drug clinical trials are not limited to LMICs. Although the number of cancer clinical trials and cancer drugs approved by the FDA has increased in the past two decades,[65] a lack of participant diversity remains a concern in HICs.[61,66] In a study of clinical trials that led to FDA approval of cancer drugs, female and Black patients were underrepresented compared with the general population (36% vs. 49.6%; $p < .001$ and 2.1% vs. 9.8%; $p < .001$, respectively).[61] Similarly, in the United States, the incidence of prostate cancer is nearly 70% higher in Black men and mortality rates are more than double those seen in the White population.[67] Yet Black participants made up less than 10% of the study population in two recent practice-changing clinical trials of darolutamide and apalutamide for patients with prostate cancer.[68]

CANCER TREATMENT IN AFRICA AND USE OF TECHNOLOGY

In this section, we use the example of Africa to discuss whether technology can be used to address cancer disparities in LMICs. In 2018, a World Health Assembly resolution called for a global strategy on digital health to support the drive toward universal health coverage in different countries.[69] And in 2019, WHO released its first guidelines that included strategies to help strengthen health systems.[70] As countries strive toward value-based care and universal health coverage, a critical look at the role of technology in health systems—includingmHealthis needed to reflect on care provision. In several LMICs, patients pay out-of-pocket for cancer screening, diagnosis, and treatment (including surgical, systemic, and radiotherapy services) , with chemotherapeutic agents costing three or four times more in Sub-Saharan Africa than in other equivalent LMICs.[71]

Patients in Sub-Saharan Africa engage with an average of three or four health care providers before receiving their cancer diagnosis[72]; among other issues,missing reagents, a lack of equipment, and stockouts may cause further delay in diagnosis and accessing therapy. It is within this scenario that one should interrogate the role of technology and whether it can be used to bridge the existing gaps in systems.

REALISTIC SOLUTIONS OR MISGUIDED PRIORITIES?

The use of mobile technologies is increasing, with the greatest expansion seen in low- and middle-income countries.[73,74] This has resulted in many countries having a phone penetration rate of more than 90%, which is greater than access to other forms of infrastructure (e.g., running water, electricity).[75,76] Data from the International Telecommunication Union show that, as of 2021, approximately 4.9 billion people (63% of the world’s population) are using the internet. This represents a 17% increase from 2019, with an additional 782 million people joining during the pandemic period. Internet penetration increased by more than 20%, and mobile subscriptions rose to a record 110 per 100 inhabitants, driven largely by increases in LMICs.[74]

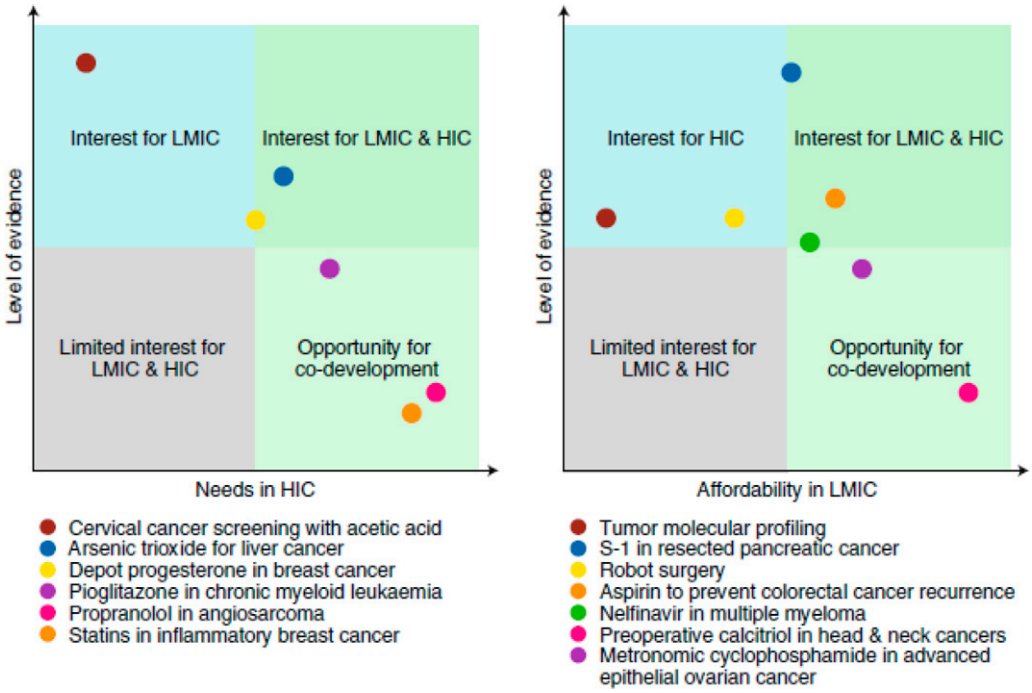

FIGURE 4. Opportunities for Collaboration Between High-Income Countries and Low- and Middle-Income Countries in Cancer Care.
Reprinted from Gyawali et al, with permission from the publisher.[56]
Abbreviations: HIC, high-income countries; LMIC, low- to middle-income countries.

How does this translate to clinical utility? A systematic review of seven mHealth projects in LMICs suggested a potential benefit for both clinical outcomes and adherence to treatment, as well as an improvement in health communication between patients and health workers, with use of the technology.[77] Another systematic review of the use of mHealth in Africa revealed that, of 44 projects conducted in 2006 and 2013, 19 were pilot studies and 11 were randomized controlled trials; these were primarily focused on patient follow-up and adherence to treatment protocols (8 studies); staff evaluation, monitoring and guideline compliance (2 studies); and data collection/transfer and reporting (1 study). Although these trials may provide a measure of the potential utility of mHealth in LMICs, they are limited by small samples and unknown scalability.

mHealth approaches may serve different functions in different health systems. In LMICs, mHealth has been used for health messaging, patient follow-up, childhood immunization, and clinic reminders,[78] but the majority of studies evaluating the usefulness of mHealth for liaising with clinicians regarding supportive cancer care have been conducted in HICs.[79] The use of mHealth approaches has demonstrated benefits for enhancing guideline adherence, preventing stockouts (e.g., monitoring central drug stores through mobile applications), and facilitating patient-reported outcomes around certain interventions or long-term programs.[79,80] mHealth initiatives have also been used to provide staff support, including drug reference– and clinical decision-making resources, for workers in remote areas. For instance, a pilot project in Botswana showed that it was possible to link specialists with health care workers to improve diagnostic accuracy and patient care.[81] This project has been replicated in many academic, training, and clinical centers in Africa; through the use of mobile applications (e.g., WhatsApp, Listserv), health workers in different specialties are able to connect and better coordinate patient care.

Pandemic-Induced Changes

With the unprecedented health care challenges of the COVID-19 pandemic, there has been growing acceptance of mHealth models; this includes expansion of mHealth roles in global oncology settings, especially in LMICs. The shift toward mHealth during the pandemic has helped to improve equitable access to learning resources, professional interactions, and knowledge-sharing through virtual platforms, such as Project ECHO and webinars run by the African Organisation for Research & Training in Cancer.[82] There has also been an increase in the number of virtual tumor boards and virtual patient-support group activities during the pandemic. In several LMICs, consultations and telemedicine visits occurred over smartphone-based platforms such as WhatsApp, Viber, or Zoom.[83] In addition, patient navigation is now leveraging technology to enhance follow-up and treatment adherence for many patients.

Artificial Intelligence and the Promise of Big Data

The role of technology is now expanding to machine learning, and several artificial intelligence (AI) applications are under way to determine the utility of this tool in health systems. A 2020 report of the Broadband Commission for Sustainable Development acknowledges that LMICs stand to gain the greatest benefit from AI, but they also potentially incur the most harm.[84] This warning is based on the idea that technologies should be developed to supplement systems rather than to replace them. Trials of imaging and pathology show the potential of leveraging machine- and deep learning to reduce imaging specialists' workflow,[85] which might be especially beneficial in resource-constrained environments.

However, AI is not the solution to the global imbalances in resources creating the scarcity of physicians and specialists and the poor diagnostic and treatment infrastructure in LMICs. For example, although Watson for Oncology tested their clinical decision–support AI tool in an LMIC setting after "training" it in the United States,[86] its use did not lead to better access to guideline-concordant treatment in LMICs because of differences in therapy availability and treatment-approach aggressiveness based on subpopulation characteristics (patient comorbidity burden, medical infrastructure, and safety-net resources). Because the majority of AI-based health applications are trained using data readily available from HIC populations, the proposed solutions might be biased or discriminatory when implemented in different contexts, such as in an LMIC health system. Although several areas for potential expansion have been proposed—including AI-enabled population health, preclinical research and clinical trials, clinical care pathways, patient-facing solutions, and optimized health operations that could help cover the continuum of care, from prevention through survivorship—AI's utility must first be proven in trials that are relevant to global and local health care needs. Implementation of common-sense, proven interventions should take priority over AI trials, especially in LMICs.[87]

Role of mHealth in Clinical Trials

Although mHealth is in use in several low-income countries for various clinical applications, there are few reports on its role in clinical trials. The use of this digital technology has met with several challenges. Respondents to a recent survey conducted by KNect365 shared their concerns about the use of mHealth in clinical trials.[88] These included issues around data security and privacy, technical operability, acceptability, usability, and internet connections, among others; these issues are also reflective of how mHealth could perform in health systems.

Data security and privacy Individuals' personal identifiable information and protected health information needs to be collected and stored privately, with measures in place for protection. Access to the internet, servers, and data-management tools can be difficult in LMICs, increasing vulnerability to cyberthreats. Some proposals to counter this include establishing frameworks for good data governance that will ensure protection of vulnerable populations, particularly those in LMICs. These may involve development of "ethical oversight and informed consent processes," strengthened data protection through the regulation of access controls, enhanced sustainability of ethical data use, and development and enactment of legislation relevant to data protection.[89]

System integration Many people in LMICs have phones that are only enabled for calls and texts, meaning that these phones may not be suitable for use in clinical trials or in more complex situations. Most mHealth-based health care projects are offered as mobile applications for smartphones. Smartphone-based research studies can pose an ethical dilemma: the cost of the phone itself and variable internet connectivity may worsen disparities between patients in high- versus low-income areas. Furthermore, mHealth applications are frequently unable to integrate with existing data health systems or electronic health records.

Internet connectivity Many mHealth applications require access to high-speed wireless internet connections. Secure, reliable, high-speed connections are needed for data entry, transmission, and access. Therefore, disparities in internet availability pose additional challenges for fulfilling mHealth's potential to improve equitable access to cancer care.

Usability Most mHealth applications are developed in English, which can create barriers in usability and lead to marginalization of nonnative English-speaking populations; this also poses problems related to informed consent. Additionally, mHealth literacy requirements ignore postcolonial challenges faced by most LMICs, including the restoration of indigenous language and knowledge while trying to comply with international education objectives in languages that were introduced by colonizers. Therefore, language and literacy biases in mHealth applications pose additional barriers for implementation in LMICs.

Scalability To date, many mHealth strategies have failed to demonstrate scalability of their approaches. Most of their data are from pilot studies; few of these have shown large clinical benefits.

Keys to Successful mHealth Use

Attempts have been made to define what constitutes a "successful" mHealth project in Africa. Aranda-Jan et al crystallized these down to four fundamental principles:

good tool design , stakeholder engagement, availability of technology and resources to support the initiative, and integration of digital health initiatives into the health care systems.[76]

Project design Good design involves a consideration for the context in which one is applying the tool—its accessibility, acceptability, and usability—and the needs of the intended patient population. mHealth tools must also be compatible with the sociocultural characteristics of the population in which they will be used. For instance, the use of a single phone per household or the controlling of the phone by the head-of-household could hamper the utility of mHealth tools in some settings. It is crucial to develop applications in languages relevant to the target population to improve the accessibility and relevance of these technologies.

Engagement of stakeholders Development of mHealth technologies should involve all potential stakeholders at the concept stage, to ensure that the unique needs, sociocultural characteristics, and existing expertise of the target population are considered and incorporated into the technology; this will enhance successful execution of mHealth projects.

Availability of technology and support To ensure the longevity and sustainability of mHealth technology, systems must be established to regularly support and upgrade the existing technology. Including the components for capacity-building into mHealth, and considering the resources available to maintain and support these technologies, can only serve to enhance and retain successful programs.

Integration into existing health systems Many governments and health care systems already have a digital strategy in place. Getting appropriate buy-in from the partners and designing tools that integrate with and complement existing digital resources ensures the relevance of the project and its potential for sustainability.

OVERSIGHT AND GOVERNANCE

WHO has helped to develop resources (e.g., handbooks) for the scaling up of digital health initiatives. These resources include the mHealth Assessment and Planning for Scale (MAPS) Toolkit[90] and the handbook for monitoring and evaluating digital health interventions.[91] More recently, WHO has tried to define key domains for providing guidance on the successful global integration of AI into health systems.[92] One meaningful development is WHO's attempt to homogenize the reporting of mHealth projects through the mHealth evidence reporting and assessment (mERA) checklist, developed by their mHealth Technical Evidence and Review Group. This checklist provides 16 items to be reported for all mHealth evidence points to assess the feasibility, usability, and sustainability of different interventions and technologies.[93] These steps will ensure that data collected across specialties and interventions are more uniform, reproducible across populations, and generalizable. This checklist could potentially help provide a framework for mHealth interventions in cancer care in different resource settings.

CAVEAT EMPTOR AND THE ROLE OF ONCOLOGISTS

It is important to consider the quality of care that these technologies provide. Quality measures look at the safety of care provided while weighing other considerations, such as the appropriateness of an intervention, its efficacy, its equitable distribution, its sustainability, and, ultimately, patient satisfaction. Cancer care is complex, multidisciplinary, and requires integration of different facets of the health care system to ensure access to services throughout the cancer care continuum. Considering the cost-effectiveness of different strategies and how they contribute to value-based care helps oncologists make decisions based on prioritized intervention strategies.

With LMICs representing the new hub for the development of "proof-of-concept" interventions, there has been a rush to embrace new technologies without adequately exploring their safety and efficacy. For instance, Sub-Saharan Africa is experiencing an increase in thermographic applications for breast cancer screening without real measures to adequately assess the utility of these applications. Because of the lack of regulatory measures, these applications are now being pitched to populations and policy makers as acceptable, cost-effective strategies to replace mammographic screening. Although these innovations are encouraging, one cannot bypass the crucial steps of reviewing the best evidence for efficacy and safety and providing appropriate regulation. There is a need for robust advocacy by the oncology community to develop trials and research studies to answer these key questions before technologies are implemented in LMICs.

As the number of smartphone applications and mHealth initiatives continues to expand, it is important to evaluate the added value and cost-effectiveness of these tools. Usability can no longer serve as an acceptable outcome; we must reflect on any new technology's ability to integrate with and support existing systems. Enhancing legislation that ensures the safety and efficacy of new technologies, and that strengthens security, privacy practices, and resources for electronic health records, is also crucial. In addition, a method is needed to standardize, increase awareness, and share knowledge acquired during the development and implementation of the already available mHealth options, to improve accessibility,

enhance uptake of these applications, and avoid unnecessary duplication of efforts.

The use of digital health maps coordinated by WHO, where individuals can list their mHealth initiatives alongside the use of the newly launched WHO guidelines and the mHealth evidence reporting and assessment (mERAS) checklist, are initial steps in this process. The oncology research community must collaborate and rethink the power and resource imbalances that are currently hampering the development and implementation of innovative designs of systems intervention; the community must also explore ways to incorporate mHealth and digital technology safely and equitably around the globe.

BOTTOM LINE ON TECHNOLOGY

Despite its "moonshot" appeal and potential for expansion, it is important to recognize that technology may contribute to deepening disparities. Of the 2.9 billion people worldwide who lack access to the internet, 96% live in low- and middle-income countries.[74] Technology is also not a panacea for drug development and allocation of health resources; the emphasis should be on strengthening equitable access to quality care worldwide. Introducing new technologies in LMICs should not precede evaluating how these strategies support the ultimate objective of equitable access to cancer care in a cost-effective manner.

GLOBAL ONCOLOGY IN THE HIGH-INCOME COUNTRY'S OWN BACKYARD

There are also many opportunities to reduce cancer morbidity and mortality through improving access to highly effective, low-cost cancer control interventions in HICs. In this section, we provide examples of low-cost interventions that are underused in the United States.

The United States leads the world in the speed of adopting innovative and expensive new therapies, and health care spending is nearly twice as high in the United States as in other HICs.[94] However, the United States has ranked consistently worse on key measures of health than other countries that spend far less.[94] Furthermore, health outcomes in the United States vary substantially by geographic area of residence,[95] socioeconomic status,[96] and race and ethnicity.[97] Disparities between the most advantaged and least advantaged populations in the United States are among the greatest in the world.[98] For example, the 2018 state-specific, age-adjusted cancer mortality per 100,000 population ranged from 120.8 in Utah to 181.8 in Kentucky (Fig. 5). Cancer mortality in Mississippi, West Virginia, Kentucky, and Oklahoma is of similar magnitude to, or exceeds, some of the highest cancer mortality rates in the world.[99] These disparities highlight the need to address barriers to access for existing highly effective—but underused—cancer control interventions that can modify potentially avoidable causes of morbidity and mortality.

The human cost of these cancer disparities is high. Approximately 610,000 people in the United States died from cancer in 2018,[101] and it has been estimated that at least one-quarter of those deaths could have been prevented with access to existing highly effective cancer prevention, screening, and treatment.[102] Cigarette smoking accounted for nearly 29% of cancer deaths and approximately 19% of new cancer diagnoses in 2018.[102] Smoking cessation at any time, including during cancer treatment, improves survival[103,104]; reducing the prevalence of cigarette smoking and exposure to secondhand smoke has been highlighted for decades as a public health priority that will reduce morbidity and mortality.[105] Yet as of 2018, approximately 20% of adults reported current

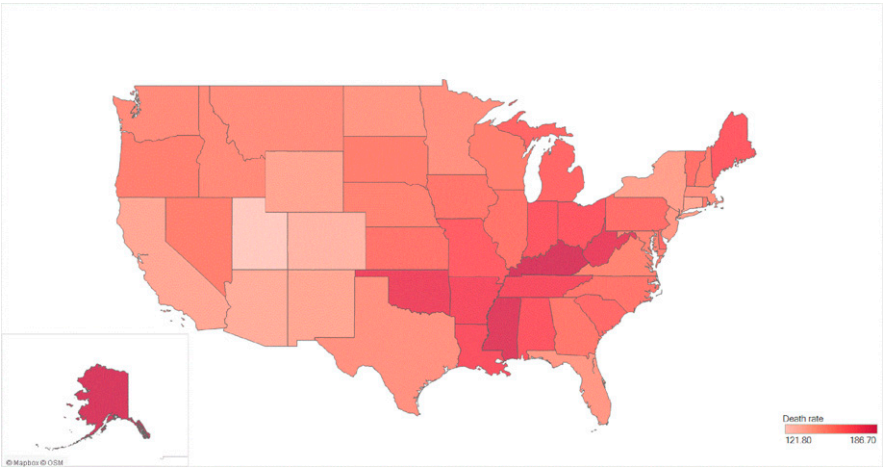

FIGURE 5. Age-Adjusted Cancer Mortality Rates in Male Patients: United States, 2020, by Congressional District.
Figure created using data from Islam et al.[99]

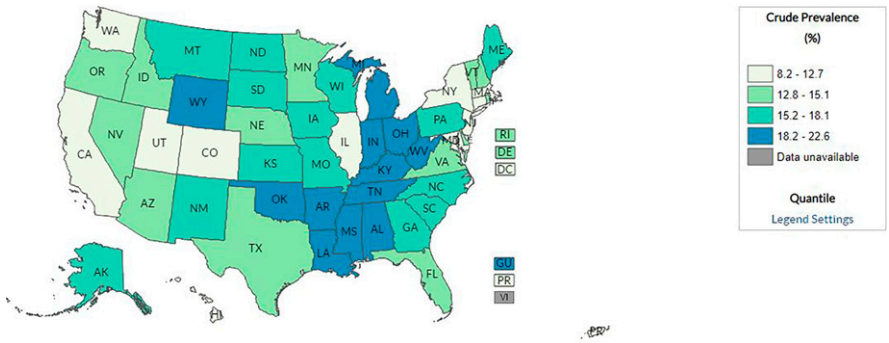

FIGURE 6. Prevalence of Current Smoking in U.S. Adults, 2020[100]

smoking, with substantial variation by state (Fig. 6), socioeconomic status, and health-insurance coverage.[106] Federal, state, and local policies are at the forefront of tobacco-control efforts. At the federal level, the United States lags behind other countries in implementing tobacco advertising bans, providing access to appropriate cessation treatment, adopting health warning labels, and implementing comprehensive smoke-free legislation.[107] Public smoking restrictions and increased cigarette excise taxes at the state level have been shown to reduce smoking prevalence,[108] and smoking-attributable cancer mortality is higher in states with weaker tobacco control policies and programs.[109] Effective and cost-effective smoking prevention and cessation strategies are available, yet underused, in the United States. Behavioral and pharmacologic interventions are successful and cost-effective for smoking cessation, yet less than 40% of current smokers report receiving counseling or medication for this purpose.[106] In 2014, the U.S. Surgeon General's report recommended increasing the average retail price of cigarettes to at least $10 per pack.[105] However, as of 2022, prices remain well below that amount in many states[110]; these states have the highest rates of cancer deaths associated with cigarette smoking[109] including, but not limited to, lung, oral cavity, pharynx, esophagus, and stomach cancers.[111] Furthermore, many individuals in these states die each year from noncancer smoking-related causes, including respiratory and vascular health conditions.[104,105]

Prevention and early detection of cervical cancer is another example of highly effective, low-cost care that is underused in the United States. More than 90% of cervical cancers are caused by infection with carcinogenic types of HPV.[113] Vaccines for HPV, which can prevent cervical and other cancers, were introduced in 2006 in the United States, yet uptake has been slow. As of 2020, less than 60% of the eligible population was up-to-date with HPV vaccination,[114] with substantially lower rates of vaccination seen in people without health insurance.[106] In addition to vaccination, cervical cancer can be prevented through Papanicolaou (Pap) testing, an inexpensive procedure that was introduced in the United States in the 1940s. Pap testing can detect preinvasive disease that, when treated in a timely manner, can prevent cervical cancer from developing. It can also detect invasive cervical cancer at an early stage, when treatment is more effective. More recently, primary HPV DNA testing (with or without Pap cotesting) was introduced; consensus guidelines have recommended routine cervical cancer screening for decades, to facilitate prevention and early detection,[115,116] with some variations in the recommended frequencies and ages of initiation and cessation. However, not all eligible women receive cervical cancer screening.[106] As a result, nearly 14,000 women are diagnosed with cervical cancer each year in the United States, with geographic variation in incidence (Fig. 7).[112] Of the more than 4,000 women who die from cervical cancer each year,[111] many have never been vaccinated or screened. Furthermore, many more individuals are diagnosed with, and die from, other preventable HPV-related cancers every year.

An important distinction between the United States and other HICs (and many middle-income countries) is the lack of universally available health-insurance coverage. In 2020, nearly 28.0 million people in the United States did not have health insurance at any point during the year.[117] Decades of research have demonstrated that health-insurance coverage is one of the strongest predictors of access to care and better health outcomes[118]; lack of health insurance plays a central role in disparities in cancer care and outcomes, and it underlies much of the large variation in cancer incidence, survival, and mortality by state,[119] socioeconomic status, and race and ethnicity.[120] The highest cancer mortality rates have been—and continue to be—in socioeconomically disadvantaged and uninsured populations,[121] with some evidence for widening disparities.[121]

Health-insurance coverage also protects individuals from experiencing financial hardship related to medical expenses, including difficulty paying medical bills, high out-of-pocket cost burden, distress about their financial situation, and delaying or forgoing recommended care.[122] Lack of health-insurance coverage and the associated deferral of care because of cost (including highly effective,

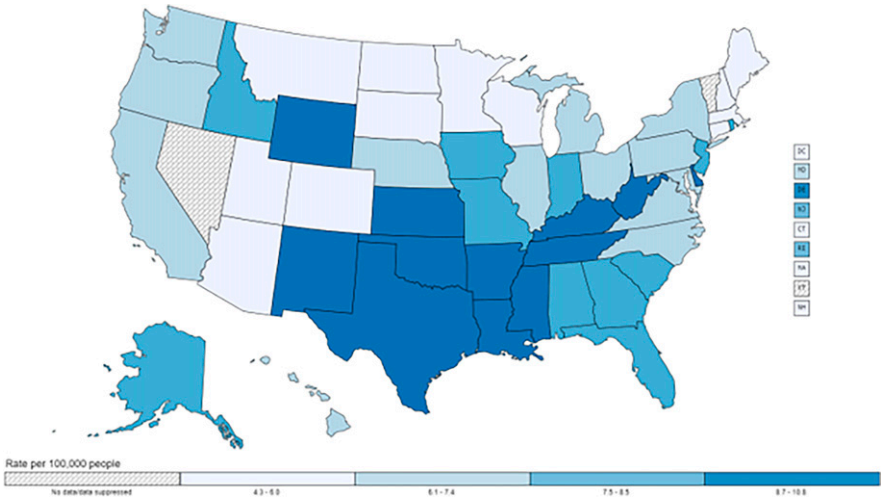

FIGURE 7. Incidence of Cervical Cancer in the United States, 2014 to 2018[112]

low-cost cancer prevention– and early detection interventions) contributes to the worse rates—and the subsequent human and economic costs—of preventable morbidity and mortality in the U.S. population compared with other developed countries (that spend far less on health care). Additionally, individuals diagnosed with cancer who are uninsured are less likely to receive timely and guideline-concordant cancer treatment and survivorship care, and they have worse survival.[123] For some cancers, patients without health insurance who are diagnosed with stage I disease have worse short- and long-term survival than do similar patients with private insurance who are diagnosed with stage II disease.[124,125]

Based in part on the large body of evidence related to the role of health-insurance coverage in improving access to care and health outcomes, the Patient Protection and Affordable Care Act was signed into law in 2010. This act included coverage of smoking-cessation treatment, cervical cancer screening, and other evidence-based, affordable prevention- and early-detection interventions, without cost-sharing, for individuals with private insurance or Medicare. However, coverage of smoking-cessation treatment for Medicaid enrollees, in whom the prevalence of current smoking is twice as high as in privately insured individuals, is state governed. The Patient Protection and Affordable Care Act also included multiple provisions related to expanding health-insurance coverage,[126] including expansion of the state Medicaid program income-eligibility threshold to 138% of the federal poverty line for all adults, with or without children, with incentives for states to provide this expansion. As of January 2022, 38 states and the District of Columbia adopted Medicaid expansion under the Patient Protection and Affordable Care Act; the other 12 states did not.[127] Medicaid expansion is associated with greater insurance coverage and access to care, higher rates of cancer screening, earlier stages of disease at diagnosis, improved survival, and lower mortality.[126,128–130] Additionally, states that expanded their Medicaid eligibility under the Patient Protection and Affordable Care Act saw declining disparities in access to care by income- or poverty status, race and ethnicity, and rural vs. urban residence; in contrast, there was little change in disparities in nonexpansion states.[131,132] As of 2020, the prevalence of uninsured adults was highest in nonexpansion states (Fig. 8), which also have higher cancer mortality, prevalence of cigarette smoking, and cervical cancer incidence. Furthermore, Medicaid expansion is associated with other economic benefits for states that choose to provide health-insurance coverage for low-income residents. Disparities in access to care between Medicaid expansion– and nonexpansion states are expected to widen; residents of expansion states are experiencing better access to care across the cancer control continuum, as well as better outcomesincluding improved survival—than those living in states that declined to expand Medicaid eligibility for their residents.

These examples of underused evidenced-based strategies to reduce avoidable cancer morbidity and mortality in the United States underscore the importance of improving equitable access to existing low-resource, highly effective care in HICs.

CONCLUSION

There is an important need for the oncology community to realign our priorities and focus on improving access to high-value cancer control strategies, rather than prioritizing the development of technologies that provide only marginal gains at a high cost. There are several easy ways to improve access to quality cancer care in both LMICs and HICs. Worldwide cancer morbidity and mortality can be reduced by implementing highly effective, low-cost interventions that

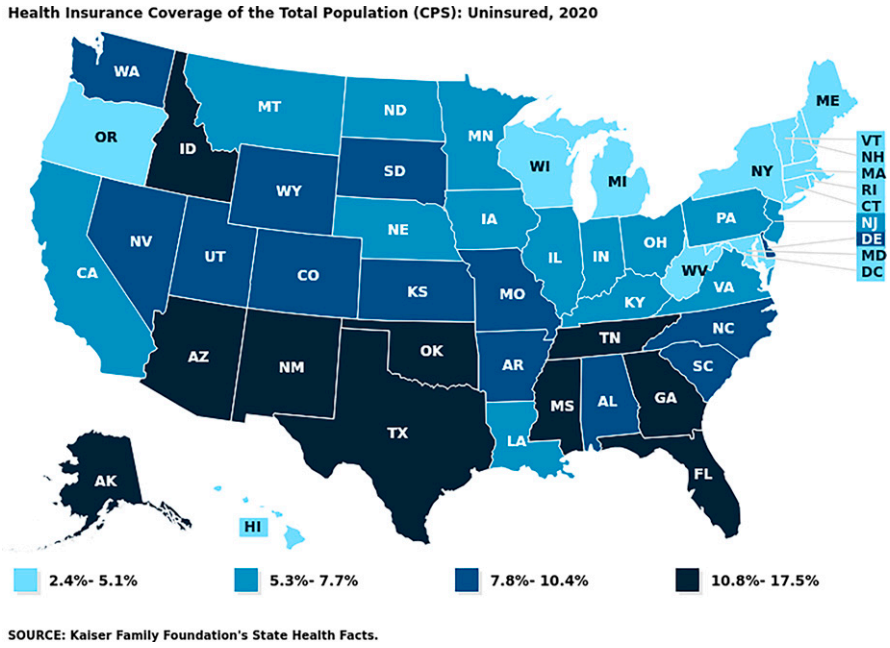

FIGURE 8. Percentage of Adults Age 18 to 64 Without Health-Insurance Coverage by U.S. State in 2020.
Data from https://www.kff.org/state-category/health-coverage-uninsured/.

are proven to work, rather than investing in the discovery of resource-intensive interventions to which most patients will not have access. We should focus onCancer Groundshot, to save more lives before we focus on the moonshots.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST AND DATA AVAILABILITY STATEMENT

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