







Global Equity in Clinical Trials: An ASCO Policy Statement

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ABSTRACT

ASCO is a global professional society representing more than 50,000 physicians, other health care professionals, and advocates in over 100 countries specializing in cancer treatment, diagnosis, prevention, and advocacy. ASCO strives, through research, education, and promotion of the highest quality of patient care, to create a world where cancer is prevented or cured, and every survivor is healthy. In this pursuit, health equity remains the guiding institutional principle that applies to all its activities across the cancer care continuum. This ASCO policy statement emphasizes the urgent need for global equity in clinical trials, aiming to enhance access and representation in cancer research as it not only improves cancer outcomes but also upholds principles of fairness and justice in health care.

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INTRODUCTION AND BACKGROUND

Despite significant advancements in cancer treatments, profound disparities in outcomes persist, particularly among vulnerable populations.^{1,2} Low- and middle-income countries (LMICs) bear a disproportionate lack of clinical trial representation despite a higher burden of cancer-related deaths compared with high-income countries (HICs). Clinical trial design in LMICs frequently does not match global disease burdens nor meet the needs of the country or region of study. In a review of over 12,000 clinical trials, researchers found that almost 90% of trials and 82% of participants were from HICs.³ According to a recent systematic review, all 694 phase III randomized clinical trials (RCTs) evaluating anticancer therapies published from 2014 to 2017 found that trials are conducted predominantly in HICs (92%), are more likely to be industry-funded than LMICs (73%), and prioritize cancers that do not match the global burden of disease.⁴ Several other studies point to the misalignment of funding compared with the global burden of cancer and publication bias against research led by LMICs.²⁻⁶ In one analysis of global cancer research funding from 2016 to 2020, investment in LMICs amounted to 0.5% of total global funding.⁷ The uneven distribution of clinical trials in LMICs can be attributed to limited funding opportunities, a lack of research infrastructure, workforce shortages, and complex regulatory environments.⁸⁻¹¹

Inadequate clinical trial representation limits our ability to understand the nuances of cancer care in different populations, which in turn hinders progress toward personalized medicine and optimal treatment strategies. It also may limit our ability to understand and address the impact of social determinants of health on cancer outcomes. Lack of diversity in clinical trial results exacerbates longstanding inequities in

clinical care.¹² Research predominantly conducted in HICs fails to account for the diverse genetic and environmental factors that influence cancer incidence, disease outcomes, and treatment response. Stakeholder policies on global equity vary, reflecting the complex nature of the problem. Although some organizations prioritize improving access and representation in clinical trials, others focus on maintaining research capacities in HICs. Striking a balance between global equity and the maintenance of scientific rigor is crucial to achieve meaningful progress in cancer research.

The benefit to changing perspectives, improving global equity, and increasing global access to clinical trials is evident from past successes, such as the response to the HIV/AIDS epidemic. The international community rallied to increase resources, funding, and research collaborations, resulting in remarkable advancements. Applying similar principles and resource allocation to cancer research could transform the landscape of clinical trials and, in turn, enhance cancer care delivery and improve outcomes and access globally.

ASCO and other organizations have advocated for diversifying clinical trials and improving the representation of racial and ethnic minorities. In 2021, ASCO released an Equity, Diversity, and Inclusion (EDI) Action Plan, which includes aims to create an environment where clinical trials will more accurately represent patients with cancer globally, respective of social determinants of health, race/ethnicity, age, sexual orientation, gender identity, and geographic location.¹³ ASCO and the Association of Community Cancer Centers have collaborated on initiatives and issued a research statement on improving EDI in cancer clinical trials.^{14,15} ASCO also has issued a separate policy statement affirming its commitment toward achieving health equity in the United

States.¹⁶ In addition, ASCO's foundation, Conquer Cancer, has provided over \$182+ million US dollars (USD) in research funding through 8,700 grants and awards in 88 countries, with a strong focus on funding programs aimed at EDI.^{17,18} Additionally, EveryGrant is administered in collaboration with Conquer Cancer to help organizations develop and deliver grant programs to cancer researchers.¹⁹ These efforts are motivated by ASCO's organizational vision of a world where cancer is prevented or cured, and every survivor is healthy.

Ensuring equity in clinical trials conducted in LMICs is critical to overcoming global health challenges. Addressing these challenges can benefit LMICs but they also can have a positive impact on the broader global community. Because the cancer burden in LMICs encompasses more than 100 countries that include different patterns and characteristics of cancer, collecting comprehensive and diverse demographic data from multinational trials would greatly benefit our understanding of cancer biology and provide a better picture of the true global cancer burden. These efforts also have the potential to expedite medical innovation and create more safe and effective therapies that cater to diverse populations, including those within HICs.

It is estimated that the global economic cost of cancers from 2020 to 2050 will be \$25.2 trillion USD.¹⁵ Today, LMICs bear the highest mortality rate.²⁰ A global effort to address the disproportionate human cost of cancer in LMICs would greatly benefit the world economy and has the potential to inform policy decisions within HICs. By addressing these challenges, LMICs have the potential to contribute significantly to global oncology research and provide valuable insights into diverse patient populations.

Addressing these challenges requires collaborative efforts among all stakeholders, including patients and their caregivers, researchers, research institutions, regulatory authorities, patient advocacy groups, pharmaceutical companies, and other clinical trial sponsors. Strategies such as streamlining regulatory processes, improving infrastructure and research capabilities, fostering long-term partnerships between contract research organizations and research centers, and increasing patient and health care provider awareness about clinical trials can help overcome barriers that now prevent greater patient enrollment in cancer clinical trials.

There is a growing focus on global collaboration in clinical research.¹² Efforts are underway to conduct multinational oncology trials, enable secure data sharing for cancer genomics research, advance precision oncology, improve clinical trials for rare cancers, enhance coordination of cancer research, and support for pooling expertise and resources, to name a few (Table 1). Although these are encouraging, their consensus around how to close gaps in global cancer research has been elusive and there is a need for more concerted global efforts by stakeholders if we are to achieve progress in treatment and in health equity.²⁰

In summary, this policy statement emphasizes the urgent need for global equity in clinical trials (Table 2). By recognizing the burden of cancer in LMICs, acknowledging disparities among populations, addressing clinical barriers, and promoting humanitarian aims, we can drive meaningful change in cancer research. Diversifying trial representation, increasing access to resources, and strengthening research capacity on a global scale will promote greater understanding of cancer biology, enhance the validity of research findings, and facilitate more rapid completion of important clinical studies, while also promoting the principles of fairness and justice in health care, improved cancer outcomes, and ensuring that progress in cancer care benefits all individuals affected by the disease.³⁷

GOVERNMENT AND REGULATORY BARRIERS

Complex regulatory requirements have resulted in a decline in RCTs compounded by the general lack of funding outside of industry support.³⁸ Regulatory policies designed by government agencies to streamline processes and avoid exploitation are often needlessly complex, dismissive, and costly, and include tedious approval processes.^{9,39} Registration and approval of new and innovative drugs used in clinical trials in LMICs is fraught with several hurdles and often require multiple, duplicative ethical approvals at exorbitant costs to research teams and burdensome, poorly structured ethical review processes by untrained staff, resulting in failed projects.^{40,41} Global supply chain management of clinical supplies is disrupted by administrative requirements, including country-specific import and export licensing and other regulatory requirements, which in turn cause start-up delays.⁴²

The relatively small health budgets in most LMICs strains capacity and commitment to research funding. Low prioritization of clinical trials is manifest in the lack of policies to promote clinical research, oversight of enrollment procedures, incentives for excellence in research output, and suboptimal investment in academic health institutions.^{43,44} Researchers from LMICs face poor representation in global health forums that engage policymakers and research institutions to demonstrate the impact of local research on patient outcomes, health systems improvement, and economic growth.⁴⁵ In addition to financial constraints, LMICs often deal with investigators who have rigid regulatory policies that are challenging for local counterparts and may even be culturally insensitive (eg, the requirement for a standard arm in clinical trial design not covered by public health insurance). There often is not a framework for adapting research design that can accommodate local context and recommendations.⁴⁶

An analysis completed by Schipper⁴⁷ for the European Parliament of trials conducted by commercial sponsors for European Union marketing authorization found that trials conducted in LMICs are more vulnerable to unethical and unregulated clinical trial design, lack of compliance with

TABLE 1. Sample List of Global Collaborative Efforts

Organization	Description	Purpose
AC ³ T ²¹	AC ³ T is a public-private partnership fostering and implementing cancer clinical trials led by investigators in Africa	AC ³ T aims to build oncology clinical trial capacity in African countries while improving patient outcomes. AC ³ T brings together stakeholders that include government and nongovernmental organizations, leading oncologists, and multinational pharmaceutical companies to create coherence and leverage capabilities and initiatives to empower African clinicians and primary investigators to strengthen clinical trial capacity in Africa while improving patient outcomes
AORTIC ²²	AORTIC is an Africa-based nongovernmental organization that is dedicated to cancer control and palliation in Africa	AORTIC emphasizes the development of National Cancer Control Programs. AORTIC maintains and supports ongoing regional and country cancer training programs in palliative care and develops resources that support cancer care. They also cultivate partnerships with global cancer organizations, the media, and technology providers, and leverage AORTIC membership expertise and regional professional organizations, policymakers, the private sector, health care workers, community groups, and noncommunicable disease alliances while prioritizing synergy of efforts
ATLAS ^{32,33}	A collaboration between academia and industry accruing the largest global database of rare cancers driving genomic and other studies	High on the ATLAS agenda is drug development and other early-stage trials, collaborative research and regulatory practices to enhance innovative drug access, and genomic studies in Asia through the establishment of a pan-Asian cancer research group to increase cancer clinical trials. The ATLAS projects will further enhance stakeholder engagement through a multiplication of efforts in the region Through collaborative efforts, Asia has accrued the largest global database of rare cancers driving genomic and other studies through the MASTER KEY project. The Asia Cancer Clinical Trial Network, also known as the ATLAS Project, focuses on drug development and other early-stage trials, collaborative research, regulatory practices to enhance innovative drug access, and genomic studies through the establishment of a pan-Asian cancer research group to increase cancer clinical trials. The MASTER KEY and the ATLAS projects will further enhance stakeholder engagement through a multiplication of efforts in the region
CLICAP ^{34,35}	Consortium that works to improve lung cancer research in Latin America	CLICAP strives toward improving lung cancer research in Latin America. Composed of more than 75 lung cancer researchers from most Latin American countries, the consortium performs cutting-edge research to address regional needs in various disciplines and has produced many journal articles as well as a series of training courses for continuing medical education in the field of thoracic oncology
GA4GH ²³	International community dedicated to advancing human health through genomic data	GA4GH builds technical standards and policy frameworks and tools that expand responsible, voluntary, and secure use of genomic and other related health data
GOCCHI ²⁴	Cooperative oncology research group that promotes collaboration between Chilean cancer centers	GOCCHI's objectives are to plan, promote, and develop oncologic research in Chile while rigorously following the currently accepted scientific methodology; increase the level of work in the oncologic specialty in the country; promote and optimize relationships between private and public cancer care and research centers and between these and the Ministry of Health and universities; and prepare and present reports, studies, and research related to matters related to oncology
GAICO ²⁵	A cooperative group of specialists dedicated to oncology and developing and designing clinical trials in Argentina	GAICO has its own or contracted structure that allows it to manage research from the design and writing of research protocols and informed consent models, management of regulatory start-up efficiently and quickly, ethics committee and regulatory health authority reviews, training and coaching of the research teams of the participating sites, including researcher meetings, quality control monitoring and external quality assurance unit, data management, analysis of data, and final report. All of this is carried out under a system of SOPs that guarantees standardization of tasks and predictability
GECOPERU ²⁶	A cooperative group founded in 2005 in Peru that works to develop cancer research in the fields of basic sciences, epidemiology, translational research, and clinical trials	GECOPERU is a collaborative group focusing on the development of clinical trials, and epidemiologic and basic sciences research in cancer. It has developed an international network that has allowed members to participate in a significant number of clinical trials
H3Africa initiative ²⁷	Partnership between NIH, the African Society of Human Genetics, and the Wellcome Trust through the AESA	Organized to enable African researchers to carry out large-scale studies on African populations, H3Africa will make use of state-of-the-art genomic technologies, in combination with clinical and environmental analyses, with the aim of understanding the interaction of genes and the environment in health and disease. As part of this, H3Africa will create new research capabilities in Africa by enhancing infrastructure and supporting pan-African collaborations, as well as collaborations with researchers in the United States and Europe when appropriate
IMMONC ²⁸	A nonprofit foundation aimed at developing cancer research in Armenia and increase access to clinical trials for patients in the region	IMMONC has focused on launching several investigator-initiated studies to drive positive change in this area. These included clinical trials of investigational immunotherapy agents, observational registry studies for rare tumors, and trials of supportive therapy drugs The establishment of IMMONC in Armenia has led to a steady increase in the number of registered clinical studies. IMMONC collaborates with leading oncologists, researchers, and pharmaceutical companies in developed countries and ensures the sustainability of current efforts in Armenia through investing in capacity-building initiatives, providing continuous training and professional development opportunities for oncology professionals doing clinical research in Armenia

(continued on following page)

TABLE 1. Sample List of Global Collaborative Efforts (continued)

Organization	Description	Purpose
IARC ²⁹	Specialized cancer agency of the WHO	The objective of IARC is to promote international collaboration in cancer research. The Agency is interdisciplinary, bringing together skills in epidemiology, laboratory sciences, and biostatistics to identify the causes of cancer so that preventive measures may be adopted, and the burden of disease and associated suffering reduced. A significant feature of the Agency is its expertise in coordinating research across countries and organizations; its independent role as an international organization facilitates this activity. IARC has a particular interest in conducting research in low- and middle-income countries through partnerships and collaborations with researchers in these regions
ICH ³⁰	Network of regulatory authorities and pharmaceutical industry to discuss scientific and technical aspects of pharmaceuticals and develop ICH guidelines	ICH's mission is to achieve greater harmonization worldwide to ensure that safe, effective and high-quality medicines are developed, registered, and maintained in the most resource-efficient manner while meeting high standards
LACOG ³¹	A collaborative network of oncology researchers and institutions across the region that aims to promote and conduct high-quality clinical trials	Expansion of access to innovative treatments and improved patient outcomes by successfully conducting multinational trials in various cancer types, providing valuable data on treatment efficacy and safety, and allowed patients to access novel therapies
The SWOG Latin America Initiative ³⁶	Initiative developed by the SWOG Cancer Research Network whose mission is to significantly improve lives through cancer clinical trials and translational research	The SWOG Latin America Initiative works to foster research collaboration in South and Central America and develop research projects of high interest to both Latin American researchers and patient populations in Latin America, particularly projects that are also relevant to Latinos/Latinas in the United States

Abbreviations: AC³T, African Consortium for Cancer Clinical Trials; AESA, Alliance for Accelerating Science in Africa; AORTIC, African Organisation for Research and Training in Cancer; ATLAS, The Asian Clinical Trials Network for Cancers; CLICAP, The Latin American Consortium for the Investigation of Lung Cancer; GA4GH, Global Alliance for Genomics and Health; GAICO, Grupo Argentino de Investigación Clínica en Oncología; GECOPERU, Grupo de Estudios Clínicos Oncológicos Peruano; GOCCHI, Grupo Oncológico Cooperativo Chileno de Investigación; H3Africa, Human Heredity and Health in Africa; IARC, International Agency for Research on Cancer; ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use; IMMONC, Immune Oncology Research Institute; LACOG, Latin American Cooperative Oncology Group; NIH, National Institutes of Health; SOP, standard operating procedures.

international ethical standards, and lack of oversight for patient safety and rights. These gaps can compromise both quality and translational impact of research, create mistrust, and discourage future collaboration. It can also lead to missed opportunities to grow local skill sets, invest in infrastructure, and, most importantly, to nurture homegrown and cost-effective interventions. In many ways, failure to adapt clinical trial design to local culture and conditions is a violation of good clinical practice.

Addressing the challenges noted here requires a systems approach. Globally accredited universal frameworks should be developed to govern international clinical research design and operations, including participant rights, registration and approval of new drugs, funding mechanisms, and clinical trial reporting.¹⁴ One such effort is the WHO's International Clinical Trials Registry Platform, which was developed to ensure the accessibility of a single point of access on all clinical trials conducted globally.⁴⁸ Similar efforts will improve research transparency and have the potential improve both the validity and value of global cancer research in LMICs.⁴⁹

Recommendations to streamline clinical trials—especially in LMICs—are similar to those often suggested in the United States, including elimination of cumbersome paper trails, greater use of information technology, centralizing and strengthening ethical review, upholding autonomy of local institutions (including legal rights of study populations and

control and maintenance of biorepositories), and streamlining import/export requirements within global supply chain management. All LMICs should have an independent, government-backed clinical research institution to support, promote, and oversee public and private institutions and to ensure the quality of clinical trials in their country. Local partners should have the opportunity to contribute equally from inception to study completion, including provision of some financial support to maintain autonomy and reduce bias in outcomes reporting.^{50,51}

PATIENT-RELATED BARRIERS

Patient-related barriers noted in conducting clinical trials in LMICs are similar to vulnerabilities reported in underrepresented minorities within the United States and other HICs.¹² Themes such as distrust of the health care system, injustice, historical mishaps of the research industry, lower health literacy level, lack of understanding about clinical trial procedures and benefits, safety concerns, and fear of placebo are common in these patients. Many eligible patients are simply never asked to participate.^{52–56}

Although there are common global challenges to trial participation, barriers can also vary by country, community, and ethnicity. Failure to consider these differences in trial design and enrollment can widen clinical trial disparities. Many clinical trials do not ensure equity in various demographic

TABLE 2. ASCO Recommendations to Achieve Global Equity in Clinical Trials

ASCO Recommendations to Achieve Global Equity in Clinical Trials
Recommendations for government agencies
Leverage best practices from across the world to create efficient and effective regulatory frameworks, including review of trial conduct from sponsors
Incentivize further development and growth of global research collaborations and networks through mutually beneficial, multisector, long-term partnerships, and consortia
Enact policies that promote quality, good clinical practice skills, trial design, and registration of clinical trials that include country selection, data management, and reporting
Strengthen national and regional research infrastructure through independent, government-backed clinical research institutions to support, promote, and oversee public and private institutions and to ensure quality of clinical trials
Develop biorepositories that ensure high-quality biospecimens that meet the needs of researchers
Enhance and centralize ethical capacities in which every country or region, irrespective of economic development level, has research ethics committees to protect the dignity, integrity, and safety of its citizens who participate in research
Streamline regulations by improving import and export requirements within global supply chain management
Recommendations for funders and health care institutions
Invest, support, and reward local researchers through protected time for research, reduced clinical obligations, and recognition through equitable opportunities for contributions in academic publications, grant funding, international conference participations, and promotions
Facilitate local partnership contribution that is equitable, including provision of financial support to maintain autonomy and reduce bias in outcomes reporting
Support the use of information technology, including the development of distance learning and other resources with certified regional centers of excellence serving as training hubs
Develop interprofessional training in patient-oriented translational cancer research
Include and integrate local investigators as equal partners in research in a way that is clinically and culturally appropriate while upholding the autonomy of local researchers and their local institutions
Provide mentorship programs that engage stakeholders and assess feasibility and readiness of local investigators and research sites
Support local investigators through a well-trained research team in a manner that is context-specific and relevant to the clinical trial
Recommendations to trial sponsors and health care stakeholders
Invest and expand funding for clinical research infrastructure and research capacity strengthening
Promote and expand patient education and awareness efforts on clinical trial participation by including patient advocates, key opinion leaders in the community, religious leaders, and family units to obtain buy-in for clinical trial participants
Ensure the highest ethical review standards that provide study populations with autonomy in determining if a clinical trial is in their best interest and education regarding their legal rights in a culturally competent manner to ensure true informed consent
Provide patients with an equal right and priority to obtaining post-trial access to new therapies at a reasonable cost to the patient and local health system
Enact policies that require internationally recognized bioethics training to protect vulnerable populations

groups, including the elderly, adolescents and young adults, and sexual and gender minorities.^{57,58} In particular, the impact of new and innovative cancer drugs in the elderly should be an important area of study, elucidating the interplay between age-related biologic changes, multiple comorbidities, functionality, and pharmacodynamics to inform safe clinical practice. In view of such gaps in the United States, the US Food and Drug Administration issued guidance to encourage recruitment of the elderly (particularly those older than 75 years) in cancer clinical trials.⁵⁹ ASCO has separately issued a statement on improving the evidence base for treating older patients with cancer.⁶⁰

There is an urgent need for patient education and awareness about clinical trials and, in some areas, involving family units and communities can have a major influence on patients' willingness to enroll in clinical trials. Informed consent forms need culturally appropriate language to ensure that true informed consent is obtained and that patients and their families have a basic understanding of the clinical trial they are invited to participate in. Additionally, there should be

meaningful patient and public involvement as well as community engagement between researchers and stakeholders such as patient advocates, community and patient organizations, key opinion leaders in the community, religious leaders, and family units to obtain true engagement for clinical trial participation by patients. Meaningful participation requires involvement of patient and community representatives from the start of the process, including in trial design, execution, and results dissemination. This bidirectional approach will assist researchers in better understanding the patient population, help design trials that are acceptable to the target population, and ultimately will improve recruitment, enrollment, and retention. It can also lead to trial results that are disseminated—and meaningful—to the population of interest.^{61,62}

Other barriers that are unique to patients with cancer in LMICs or low-resource settings are the ethical concerns of financial coercion or undue inducement. In 2018, ASCO released a policy statement addressing financial barriers to patient participation in clinical trials in the United States.⁶³

Although the statement was specific to the US context, the same principles are applicable: provided that patient costs are reimbursed accurately, such payments do not exert undue influence as they do not result in a net benefit to research participants.⁶⁴ We suggest that this can also be addressed by offering equal access to reimbursement of reasonable costs in the screening and participation process, collecting true informed consent, and ensuring the autonomy of patients to reject clinical trials.

Patient retention on studies in some countries might be low because of fragmentation of the underlying care delivery system and logistical barriers such as excessive and long clinic visits or lack of transportation. Financial toxicity also plays a factor as patients in LMICs may bear the full cost of all treatment and nonmedical expenses and thus may stop their trial participation because of financial constraints. Patient retention can be improved with patient navigators engaging in the writing of realistic clinical trial protocols that fit the lifestyle of an average patient, the use of telemedicine, and home health workers.

Finally, the need for post-trial access to medication continues to be an ethical problem; regions and countries where studies are conducted should provide patients who have participated in clinical trials equal right and access. Likewise, those patients should be prioritized in getting access to these new therapies at a reasonable cost to the national health system.

PROVIDER-RELATED BARRIERS

There is a paucity of trained investigators and research staff, expertise, and motivation for the conduct of research in LMICs. The health care system is already strained because of a higher patient physician ratio leading to competing clinical demands and physician burnout, even without consideration for research activities. Furthermore, most local health systems do not invest in, support, or reward research productivity, thereby making it almost impossible for local investigators to thrive compared with investigators in HICs who benefit from study findings in tangible ways such as publications, grant funding, and promotions.

Shortages of health professionals also limit the ability of the health care system to conduct clinical trials. In addition to the limitation of the number of available providers and other clinical trial professionals, there is a significant training gap in research and ability to conduct clinical trials locally. There is an urgent need to develop interprofessional training in cancer clinical trials and patient-oriented translational cancer research. In addition to continuous training of local investigators, there should be integration of local investigators with investigators from HICs as partners in research with equitable opportunities for contribution in academic proceeds such as publications and participation in international conferences. Despite the incentives to conduct clinical trials globally, most clinical

trials with sites opened in other parts of the world still have key investigators originating mostly from HICs. There is a need for local investigator-led trials that are both clinically and culturally relevant, leveraging local expertise to facilitate trial implementation.

To address these provider-related barriers, local investigators should receive dedicated support from their institutions, including protected time for research, reduced clinical obligation, recognition for their contribution in globalized clinical trials, and capacity building to improve the health care system. Likewise, local LMIC investigators should be supported through a well-trained research team to balance the tasks associated with conducting clinical trials.⁶⁵ Dedicated capacity development in which capacity outcomes are as equally valued as research outputs is important to develop a sustainable health research system in LMICs.^{8,66}

International organizations may consider creating programs aimed at training and certification of cancer centers in LMICs and creating a comprehensive database of certified investigational sites along with detailed information on their recruitment capabilities. One example of these programs is the US National Cancer Institute's (NCI) Center for Global Health (CGH), which leads and coordinates research programs that include research training in LMICs to strengthen their capacity to conduct global research and add to the diversity of the cancer research workforce.⁶⁷ Likewise, NCI's Cancer Centers Program recognizes and designates US cancer centers that meet rigorous standards for transdisciplinary, state-of-the-art research that include global oncology research projects.⁶⁸ Leveraging these collaborative efforts, NCI's CGH conducts a periodic survey to assess global oncology activities to identify opportunities for cancer research and control collaboration.⁶⁹

INDUSTRY BARRIERS

From the industry point of view, conducting clinical trials in LMICs could facilitate increases in the number of clinical trials overall. However, concerns about site and health system constraints can discourage industry support. This includes poor quality of informed consent, inadequate scientific and ethical review processes, burdensome regulatory processes for new drugs and clinical trials, inadequate protection of the patients' rights, and lack of insurance for trial-related injury.¹⁴ Early-stage drug development trials (phase 0 and I) in LMICs are expected to bridge gaps in drug access, reduce cost of research, and improve subject recruitment. However, there is a paucity of trials seemingly because of labored, rigorous processes and mistrust of intentions. These limitations undermine credibility of clinical trials conducted in such environments and the subsequent support by the oncology community and regulatory bodies in HICs. Lapses in clinical trial design and operations, including failure to protect human subjects' rights and safety, have led to regulatory transformations and stringent guidelines in countries where these incidents occurred.^{70,71} Enhancing

good clinical practice is vital to clinical trial introduction in any new environment.⁷²⁻⁷⁴

Clinical research centers in LMICs often face unique challenges when it comes to patient enrollment in cancer clinical trials.⁸ Limited availability of time frames for patient recruitment and enrollment, lack of accredited facilities, shortage of trained human resources, a need for well-kept records, and absence of motivation for the conduct of research pose significant barriers. A lack of long-term investment in building sustainable research capabilities and capacity hinders the potential for greater participation in clinical trials and the generation of high-quality data. Because of these constraints, clinical research centers in LMICs may encounter difficulties in reaching and engaging eligible patients, which include language and cultural barriers, conducting comprehensive screening processes, overcoming logistical barriers, and implementation issues that can impede the efficient enrollment of participants.⁷⁵

Overcoming these challenges requires investment by the government or sponsors. The burden of funding is further complicated by the ethical necessity to provide a plan for long-term implementation of those expensive interventions and medications once proven effective in clinical trials.⁵⁶ Investing in building capacity and sustainability of access is necessary not only to a high-quality trial, but also to a successful outcome for patients once the trial is over. Both elements would positively affect overall survival of patients enrolled in clinical trials in LMICs after the trial.⁷⁶ Attention to building capacity and sustainability is both a responsibility and burden that could potentially hinder industry involvement in clinical trials.

In conclusion, to address global disparities in the clinical trial landscape, mutually beneficial, multisector, long-term

partnerships and consortia must collaborate to develop and enforce regulatory frameworks. Consortia must include all involved stakeholders including pharmaceutical sponsors, academic institutions, patient advocates, drug regulatory bodies, policymakers, communities, and research teams, among others. Policies that require clinical trial registration, good clinical practice skills by investigators, and internationally recognized bioethics training to protect vulnerable populations must be enacted to improve health outcomes. Clinical trial design, evaluation, and ethics training can be achieved through distance learning and other resources with certified regional centers of excellence serving as training hubs. Mentorship programs engaging stakeholders can leverage expertise to assess—and guide improvement in—the readiness of local clinical trialists and research sites. Potential trial sponsors should engage with local research collaborators to assess the feasibility of the collaboration, including registration, ethics regulations, and potential barriers to access for new innovations. Special attention should be given to protecting rights of patients in early-phase trials, using structured mentorship programs and transparent deliberation among stakeholders. Finally, recognizing the infrastructure necessary to conduct trials may not exist in LMICs, trials must be conducted in a way that is context-specific and relevant to the resources of LMICs involved.

This is a call to action. Progress toward better treatment and improved quality of life for all patients with cancer depends on global collaboration. Without full representation in clinical research by patients and clinicians in diverse communities, progress will be slowed—and the burden of cancer will continue to fall disproportionately on those least able to overcome it. By strengthening health system capacity and enhancing support for global research collaborations, especially in LMICs, we can narrow the gaps in equity, access, and outcomes.

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