ASIA SOCIETY POLICY INSTITUTE

CURE4CANCER

Advancing Global Health Equity:

Enhancing Clinical Trials Access and Cooperation to Save Millions of Lives from Cancer

REPORT >>

ADVANCING GLOBAL HEALTH EQUITY:

ENHANCING CLINICAL TRIALS ACCESS AND COOPERATION TO SAVE MILLIONS OF LIVES FROM CANCER

A REPORT FROM THE ASIA SOCIETY POLICY INSTITUTE AND CURE4CANCER

With a problem-solving mandate, the Asia Society Policy Institute tackles major policy challenges now confronting the Asia-Pacific in security and diplomacy; Trade, Investment, and Innovation; Climate and Energy; and Society, Technology, and Public Health. The Asia Society Policy Institute is a think- and do-tank designed to bring forth policy ideas that incorporate the best thinking from top experts in Asia and to work with policymakers to integrate these ideas and put them into practice.

Cure4Cancer (C4C) is an international movement that brings together patients, clinicians, scientists, policymakers, regulators, industry leaders, philanthropists, the media, and other closely related stakeholders in the global fight against cancer. The international movement is sustained through multi-stakeholder collaboration and cross-pollination among its global partners; thus, it cannot be limited to any single institution or country. Our mission is to accelerate the development of cancer cures and prevention through increased public awareness, cooperation, and regulatory harmonization on patient-centric international clinical trials.

Through research, analysis, and engagement, Cure4Cancer and its partners seek to accelerate the eradication of cancer as a major cause of death in a lifetime. The Asia Society Policy Institute serves as the movement's policy research and operational arm. For more information and a list of our partners and supporters, visit https://cure4cancerglobal.org/about-us/.

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PREFACE

Cancer is a leading cause of death worldwide, accounting for approximately 10 million deaths every year. Many cancer deaths are preventable if the disease is detected early and treated effectively. Clinical trials represent the critical step in translating scientific discoveries into lifesaving treatments and are widely regarded as the best treatment to improve the care of patients with cancer. However, access to clinical trials is limited to fewer than 5% of patients globally, with significant disparities among diverse communities. Consequently, the path for oncology research and development (R&D) is long and arduous and can take up to 10–15 years from laboratory discovery to regulatory approval for market access. Global regulatory harmonization of clinical trials and approvals of cancer therapies and prevention could reduce global cancer-related deaths by an estimated 10% to 20%, or 1 to 2 million lives per year. Yet, policy and regulatory processes for global clinical trials collaboration lag far behind the pace of scientific innovation, and the equity gap in access to clinical trials and precision oncology continues to widen.

A multiregional, multi-stakeholder approach is needed to break down barriers and accelerate the development and access to lifesaving treatments globally. To do this effectively, clinical trials should be adapted to become more patient-centric and expanded on a global scale, governments and regulatory bodies must work toward regulatory harmonization, and institutions must collaborate on international cancer research.

If this model is executed effectively, benefits could include but are not limited to the following:

- Advancing global public health equity;
- Reducing costs for industry, governments, and eventually all patients;
- Strengthening international collaboration on scientific research;
- Accelerating translation of scientific breakthroughs into treatments and prevention and, therefore, clinical breakthroughs;
- Saving millions of lives, bringing peace and reducing suffering for millions of families, and humanity as a whole.

This report explores the regulatory landscape and pathways for enhancing international cooperation in the fight against cancer, specifically discussing the potential for China to join the U.S. Food and Drug Administration's (FDA) initiative Project Orbis. This is the first Cure4Cancer report of a series that will study global health equity in other countries and regions including Australia and New Zealand, Southeast Asia, South Asia, the Middle East, Africa, and Latin America – as no country or region is spared the burden of cancer.

This first report will provide readers with a background on international cancer trials and show how the first case study on China, the country with the greatest cancer burden and highest number of cancer deaths, may help advance global health equity and accelerate the "cure for cancer" through regulatory harmonization initiatives such as Project Orbis. In the future, the Task Force will expand the case study to other countries and regions, showing more cases and different models of practice for enhanced international cooperation and policy harmonization.

CONTENTS

Today, people are living longer lives from successful cancer treatments that are the results of past clinical trials…. It is essential to have a wide range of people from different communities participate in clinical trials to reduce biases, promote social justice and health equity, and produce more innovative science.[1]

— National Institutes of Health

1. INTRODUCTION

As a leading cause of death, cancer accounts for approximately 10 million deaths globally each year.[2] Many of these 10 million lives lost to cancer could be saved through enhanced international cooperation. Global regulatory harmonization for clinical trials and cancer therapy approvals could reduce global cancer-related deaths by an estimated 10% to 20%, or 1 to 2 million lives per year, according to a study by the Bloomberg New Economy International Cancer Coalition.[3] However, studies have shown that the current patient participation in oncology clinical trials is fewer than 5% globally with significant disparities among communities, even though more than 70% of the same patients are either inclined or very willing to participate in such trials.[4]

FIGURE 1: LIVES LOST TO CANCER VS. TO WARS

Sources: Our World in Data, Martin School, University of Oxford. https://ourworldindata.org/counting-conflict-deaths. National Cancer for Biotechnology Information, National Institute of Health. https://pubmed.ncbi.nlm.nih.gov/33538338/#:~:text=Worldwide%2C%20an%20estimated%2019.3%20million,skin%20cancer)%20occurred%20in%202020.

The global community has been exploring ways to advance international public health equity in the fight against cancer. However, policy innovation and regulatory harmonization for international clinical trial collaboration are still lagging far behind the pace of scientific innovation partly due to bureaucratic hurdles, stakeholder silos, and cultural and geopolitical differences. Establishing more pragmatic policy frameworks that include multiple stakeholders is essential to overcome these challenges and promote international clinical trial collaboration.

This first Cure4Cancer report of a policy series underscores the potential impact of international regulatory harmonization, with a case study of China joining Project Orbis. Such cooperative initiatives could greatly streamline international regulatory processes and bolster global health equity by expanding access to clinical trials and precision oncology worldwide.

Beyond this specific case, the report presents alternative strategies, cases, and methods to foster robust and inclusive international cooperation in the fight against cancer – the common enemy of humanity.

2. BACKGROUND

2.1 GLOBAL HEALTH EQUITY

Health equity is defined as the absence of avoidable differences based on sex, gender identity, race, ethnicity, disability, sexual orientation, or other factors that affect access to care and health outcomes.[5] Achieving global health equity requires the identification and elimination of factors that create inequities in health outcomes in living conditions; education; socioeconomic status; geography; access to quality, culturally competent, and affordable health care; and so on. Monitoring and analyzing health inequities with data disaggregated by age, sex, race and ethnicity, education, income, disability, geography, and other factors and addressing gaps created by biases in data collection and analysis are critical to achieve this purpose. Equity, gender, rights-based assessment, and participatory approaches and tools should be used to systematically collect, analyze, and use evidence to design interventions for improved equity and ongoing monitoring of health inequities.

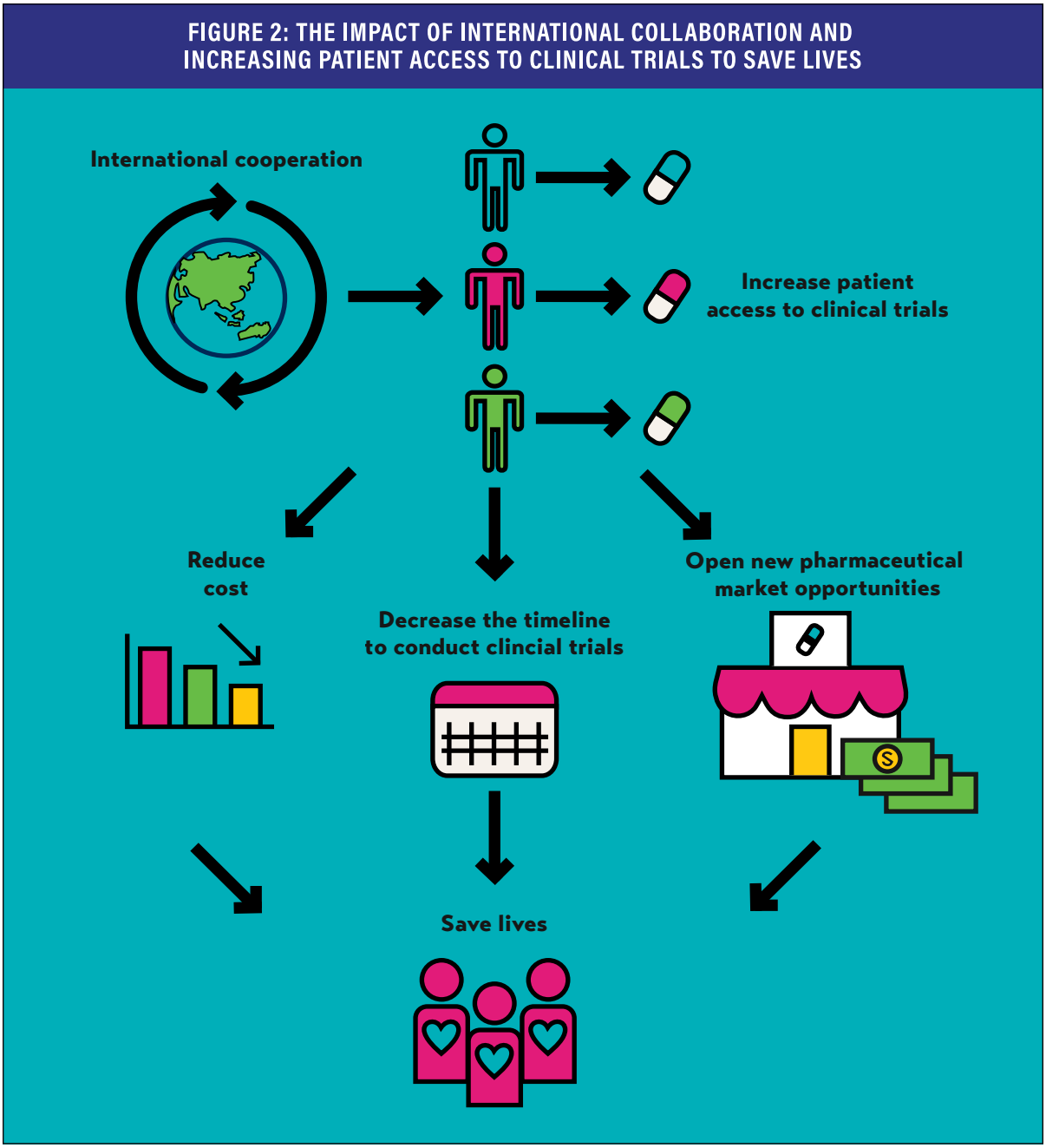
The significance of equity in oncology R&D cannot be overstated. Before the Covid-19 pandemic, an estimated $50 billion was spent annually on oncology R&D by the biopharmaceutical industry; the cost of clinical trials, which often last many years, is exorbitant, amounting to tens or hundreds of millions of dollars for each trial. Today, oncology R&D is estimated to cost the industry $80 billion per year according to the recent analysis.[6] As the cost of R&D continues to rise exponentially and other factors such as the Inflation Reduction Act may negatively impact industry profit margins, there is a growing recognition that the status quo is unsustainable. Advancing global health equity, therefore, is not only a prerequisite for the sustainable development of global public health but also a strategic business decision. Developing international clinical trials could prove essential for advancing global public health equity. International clinical trials stand to increase patient access in global communities, diversify participants, accelerate R&D timelines, reduce cost, and increase the worldwide impact of scientific results.[7] [8]

While the absolute number of completed clinical trials documenting how many patients have benefited from the trial is increasing, the inequity in the distribution of participation opportunities for patients is evident when considering geography, gender, race, ethnicity, income, education, language(s) spoken, and the economic development of the country in which the patients are located. To solve this problem, increasing the percentage of patients from diverse backgrounds who have access to clinical trials from the current fewer than 5% through international collaboration, could accelerate accrual and shorten the drug approval timeline from the traditional 10–15 years to a 2–3 year process.[9] This would save millions of patients waiting for treatments, lower the costs associated with clinical trials, open new

markets and revenue streams for pharmaceutical companies: these have the potential to contribute significantly to global health equity.

However, serious barriers to achieving this goal still need to be overcome. For example, among the 18,094,716 cases of cancer diagnosed in 2020 globally, China accounted for 24% of new diagnoses, as well as 32% of the nearly 10 million cancer deaths.[10] However, China, a country with the world's largest cancer burden, has not been sufficiently included or integrated into the international R&D and regulatory approval framework in terms of relevant data and cases over time. This also epitomizes the situation of many low- and middle-income countries with large cancer patient populations lacking

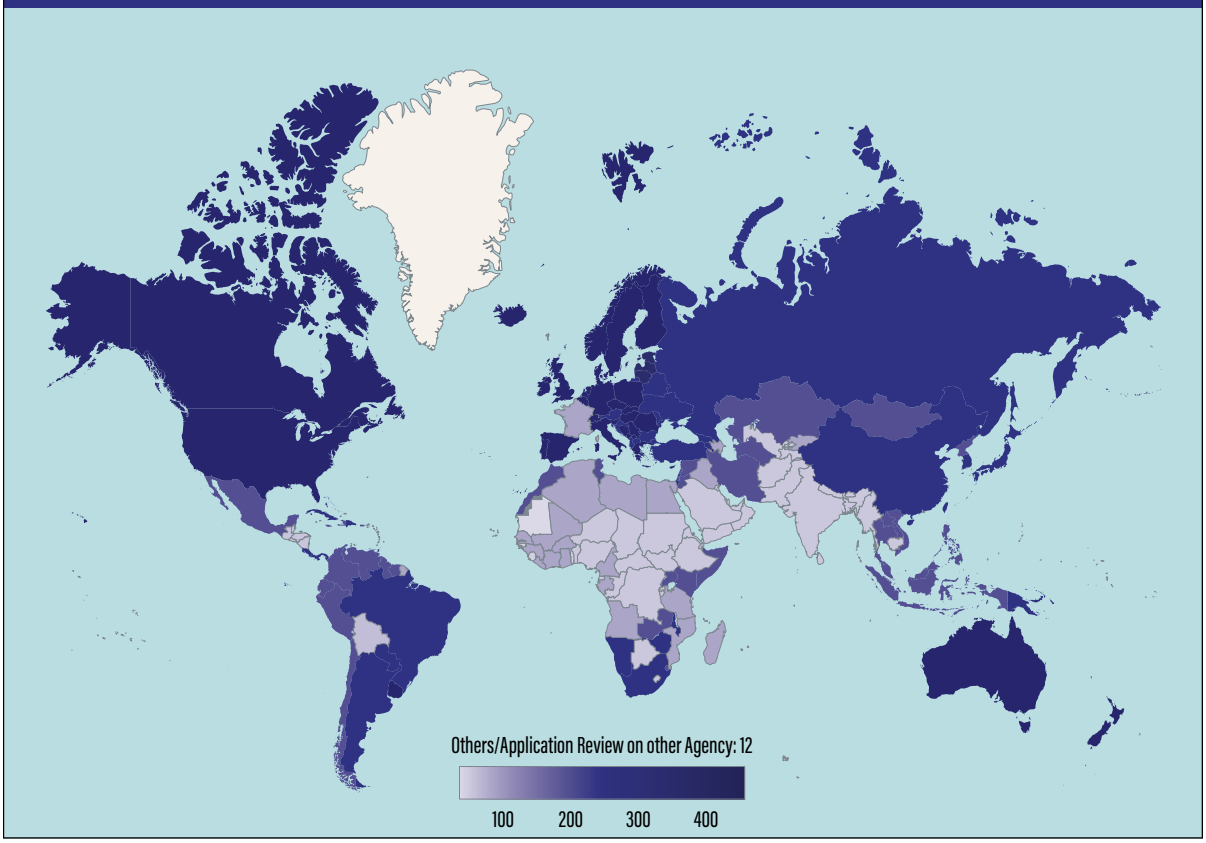
FIGURE 2: THE IMPACT OF INTERNATIONAL COLLABORATION AND INCREASING PATIENT ACCESS TO CLINICAL TRIALS TO SAVE LIVES



Source: https://www.nimhd.nih.gov/resources/understanding-health-disparities/diversity-and-inclusion-in-clinical-trials.html.

representation in the international regulatory landscape. As the global cancer burden is expected to continue to rise, the importance of equity in oncology R&D is gaining increasing recognition in both industry and academia. To integrate equity more deeply into oncology R&D, therefore, is not only a moral imperative but also a sound policy and business strategy that can lead to significant advances in cancer care.

FIGURE 3: ESTIMATED AGE-STANDARDIZED CANCER INCIDENCE RATES (WORLD) 2020



Source: World Health Organization GLOBOCAN 2020.

2.2 CLINICAL TRIALS AND THE FIGHT AGAINST CANCER

As the critical step of translating scientific discovery into lifesaving treatments and prevention, clinical trials are the key to making progress against cancer.[11] Clinical trials are research studies to test and evaluate how innovative cancer drugs, vaccines, and technologies perform for patients.[12] Continued human progress in cancer treatments and prevention is deeply reliant on access to clinical trials. By testing innovative therapies, these clinical trials have the potential to both save the lives of trial participants and expedite regulatory approvals of new cancer treatments that can help millions more patients battle the disease.

The clinical trial development process is constantly changing; for example, the technology for matching clinical trial patients to interventions based on AI algorithms is evolving. Regulatory agencies such as the U.S. FDA and the European Medicines Agency (EMA) have created novel and accelerated regulatory pathways to increase the flexibility of clinical trials design and execution. Remote monitoring and

clinical trial participation technology have the potential to decentralize the distribution of clinical trial patients away from major academic centers. Many factors, including the growing cancer drug pipeline and associated investments, as well as evolving patient identification, enrollment, treatment, and monitoring are demonstrating and driving the enormous potential of the clinical trial field.[6]

In sharp contrast to the breakthroughs and innovations in clinical trial development, there is also growing attention to the barriers that impede the advancement of cancer treatments research and development. Among these barriers, first and foremost is the lack of patient access to clinical trials.

The main barrier to finding lifesaving new cancer treatments or preventions is the time it takes to conduct clinical trials. Many factors contribute to this problem, but inadequate international regulatory coordination and cooperation is one of the more prominent ones: bureaucratic red tape, gaps in regulatory systems, less standardized institutional review boards with delays in clinical trial activation, and a lack of policy coordination between government regulatory agencies in different countries substantially limit clinical trial progress by resulting in delays in regulatory review and approvals, the cancellation of international cooperative regulatory projects, and grants and funding expirations while waiting for regulatory approvals. These consequences further lead to the observed stark disparity in clinical trial distribution. Such disparities exist between high-income countries (HICs) and low- and middle-income countries (LMICs) and between groups of patients from different socioeconomic levels or from rural/urban areas within a country, thereby compromising public health equity.

Better international standardization of clinical trials and their approvals can shorten the time needed to roll out a new cancer treatment from the traditional 10–15 year process to a 2–3 year timeline, accelerating biological discovery and having a positive impact on future funding and investments in more clinical trials. It can also lead to more affordable cancer treatments for more patients globally, more international academic collaboration and research output, and reduced R&D costs for all stakeholders. Conversely, if we continue with the current status quo of fewer than 5% clinical trial access with an expensive and lengthy R&D timeline, it is safe to say that the Cure4Cancer or the eradication of cancer as a major cause of death will not be achieved.

3. REGULATORY FRAMEWORKS SUPPORTING GLOBAL COOPERATION AGAINST CANCER: CANCER MOONSHOT WITH A CASE STUDY ON PROJECT ORBIS AND CHINA

Despite these challenges, regulators around the world have been working hard to promote better international clinical trials collaboration. Cancer Moonshot and Project Orbis are key examples.

Cancer Moonshot, launched in 2016 and reignited in 2022, is a signature project of U.S. President Joe Biden that is led by the White House, in collaboration with the National Cancer Institute of the National Institutes of Health (NIH) and other federal agencies. The White House Cancer Moonshot aims to “end cancer as we know it,” specifically reducing the cancer death rate in the United States by

at least half by 2047. Cancer Moonshot currently supports more than 70 programs and more than 250 research projects housed at the NIH.

As a core component of Cancer Moonshot, the FDA Oncology Center of Excellence (OCE) has already made progress toward this goal with the 2019 launch of Project Orbis, an initiative to set up an international regulatory infrastructure for simultaneous submission, review, regulatory action, and approvals of clinically significant new cancer treatments in multiple countries, instead of separate sequential applications in each country, thus avoiding duplicity and shortening the time needed for patients to access innovative cancer medicines. Current Project Orbis Partners (POPs) include the regulatory health authorities of Canada, Australia, Switzerland, Singapore, Brazil, the UK, and Israel.

Such initiatives promoting collaboration among international regulators allow cancer patients to receive earlier access to products in other countries despite significant delays in regulatory submissions. Pivotal clinical trials in oncology are commonly conducted internationally, and these global trials are increasingly important for investigating the safety and efficacy of cancer drugs for approvals.[13] Since its inception, Project Orbis has led to the multinational approval of 75 oncology drugs for patients across the world.[14] Major oncology disease categories were represented in the Orbis submissions, including solid tumor and hematologic malignancy indications.[15]

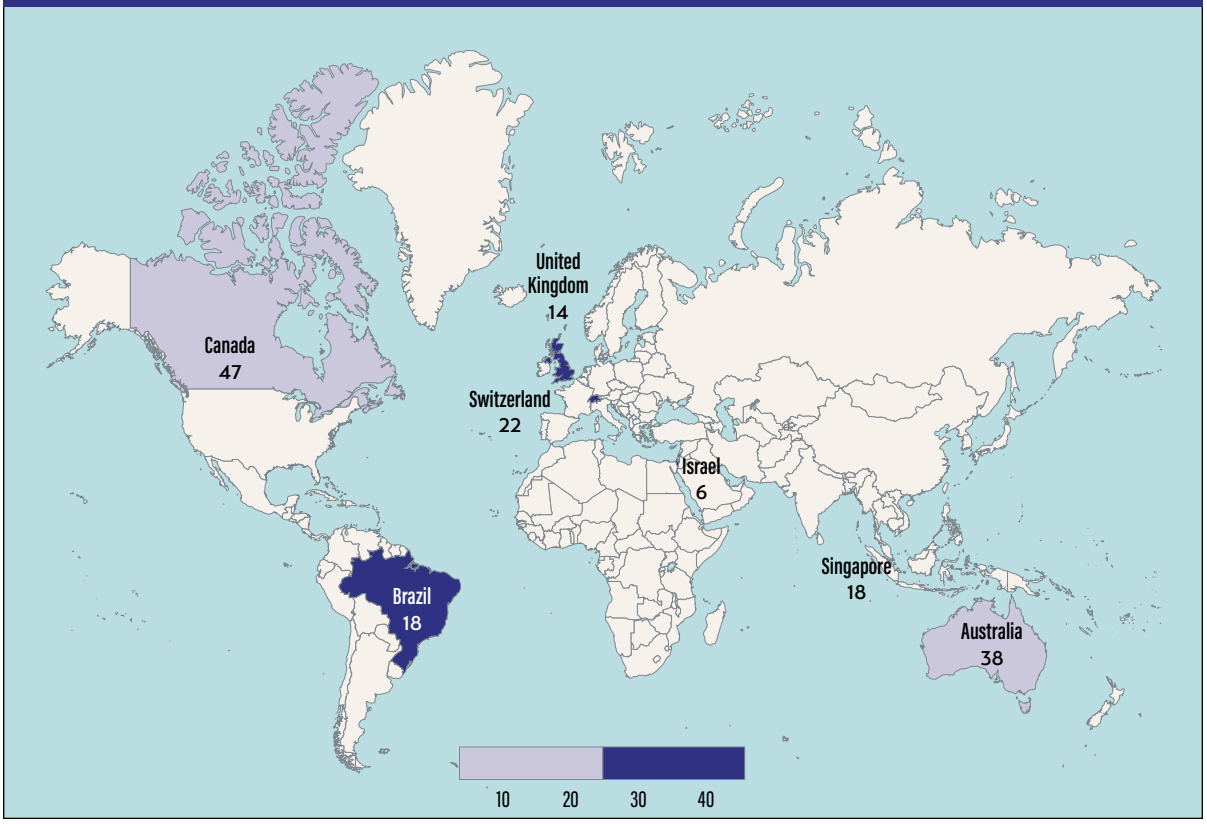
Still, these initiatives have much room for expansion in promoting international clinical trial collaboration and its diversity. Take Project Orbis as an example. The effectiveness of the project needs to be further developed from several aspects, including the limitation of the number of member countries and the limitation of the amount of corresponding data. Its current member countries account for only 21.64% of new cancer cases worldwide in 2020 – hardly representative of the vast

FIGURE 4 NEW CANCER CASES OF CURRENT PROJECT ORBIS PARTNERS AND AS A PERCENTAGE OF CANCER INCIDENCE WORLDWIDE IN 2020

COUNTRY/GLOBAL	CANCER CASES 2020, BOTH SEXES, ALL AGES
Global	18,094,716
Canada	274,364
Australia	200,021
Switzerland	60,483
Singapore	23,632
Brazil	592,212
UK	457,960
Israel	28,704
The United States	2,281,658
Percentage: PoP Countries / Global	21.64%

Source: World Cancer Research Fund International. https://www.wcrf.org/cancer-trends/global-cancer-data-by-country/

FIGURE 5: NUMBER OF APPROVALS IN PARTNERING COUNTRIES UNDER PROJECT ORBIS (2019-2023)



Source: U.S. FDA. https://www.fda.gov/about-fda/oncology-center-excellence/project-orbis.

global cancer population, leaving shortcomings in the timeliness, diversity, and equity of the programs it supports for approval.

Cancer experts and regulatory agency leaders from the United States and China have been discussing a potential agreement to collaborate in the fight against cancer through regulatory harmonization in multiregional clinical trials and the possibility of China joining Project Orbis. So far, China, with the world's highest cancer patient population and potentially the most impactful partner in this effort, remains absent from the initiative.

A feasible yet critical step in participating in the multilateral framework of Project Orbis for collaboration with member countries is to reach a policy agreement with the project initiator. A limited confidentiality agreement (LCA) between the United States and China could serve as a milestone to allow China's involvement in Project Orbis, hence joining the regulatory review with the FDA, enhancing international cancer collaboration on multiregional clinical trials, and facilitating the construction of the international regulatory system for global health. China's full membership in Project Orbis would require an agreement with each of the eight existing member countries, but the LCA between the United States and China would be the initial key step.

Progress toward the signing of an LCA has already been made behind the scenes over the past five years: regulators from both the United States and China held several rounds of dialogue and meetings on the

issue, and both sides recommitted to this goal at the fifth MSK-CTONG Annual Symposium held in December 2022. The United States and China share a common international regulatory background and have a history of cooperation: both are members of the International Council for Harmonisation (ICH) and have adopted international standards per ICH guidance documents, and each country has issued several guidance documents to further clarify respective regulatory requirements; thus, the bilateral review process would build on existing regulatory requirements and drive greater harmonization in regulatory decision-making.

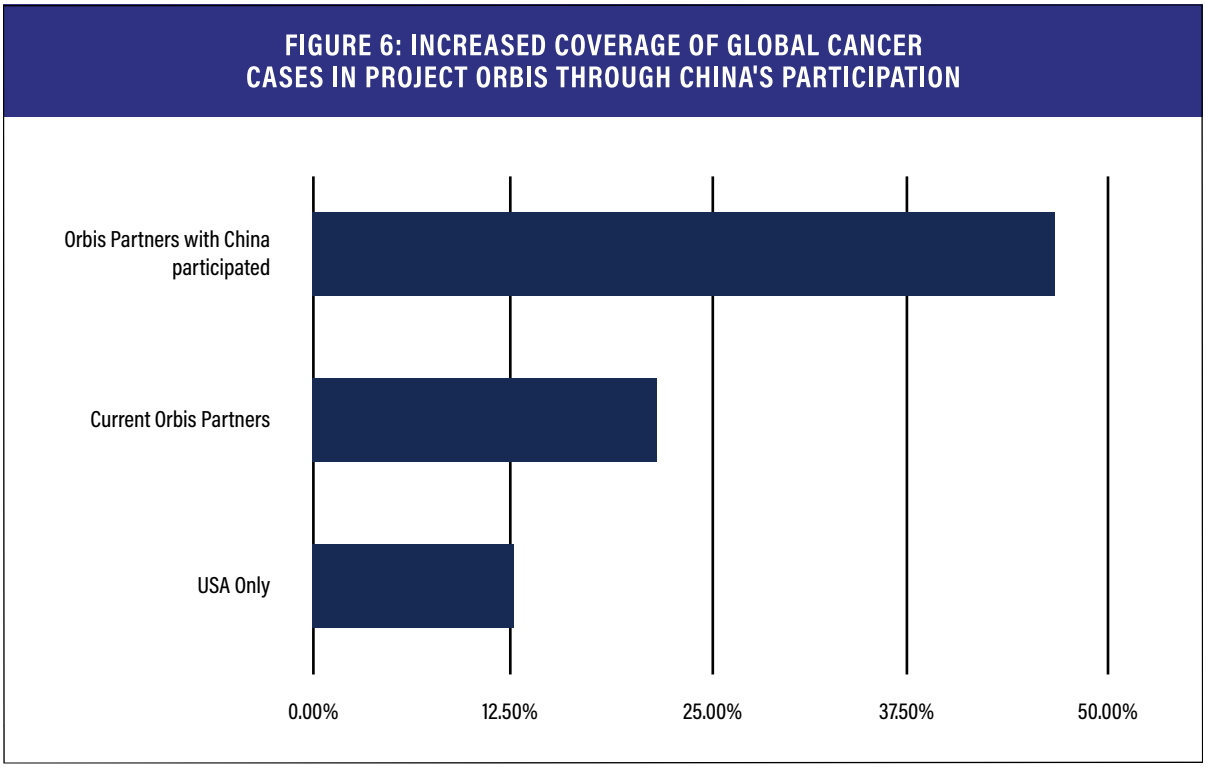
China's participation in clinical trials would yield manifold benefits for promoting public health equity, but it also faces obstacles and challenges.

3.1 BENEFITS

Population and data: With 1.4 billion people, China has the world's largest cancer patient population with unrivaled ability to accrue to clinical trials to accelerate the cure for cancer. The quantity of data in China available to researchers globally is simply unavailable anywhere else. The data in Table 2 shows that if China were to join Project Orbis, the number of new cancer cases in 2020 represented by the POPs would rise from 21.64% to 46.88%. Accounting for nearly 40% of the global annual cancer deaths, the prospect of the United States and China working together with other countries to fight the common enemy of humanity offers significant opportunity for success.

Standard setting: With the patient population and size of the China market, the global community is better served by including China's regulatory agencies, cancer researchers, doctors, and industry

FIGURE 6: INCREASED COVERAGE OF GLOBAL CANCER CASES IN PROJECT ORBIS THROUGH CHINA'S PARTICIPATION



Sources: U.S. FDA. https://www.fda.gov/about-fda/oncology-center-excellence/project-orbis. World Cancer Research Fund International. https://www.wcrf.org/cancer-trends/global-cancer-data-by-country/

leaders in the international standard-setting regulatory process. Simultaneous regulatory reviews allow global cancer breakthroughs to enter the China market earlier and impact more lives. The coordinated approval framework and the common application platform enable consistent requirements for approvability and interpretation of the regulatory requirements, which make clinical trials easier and faster to design and implement. Chinese cancer breakthroughs through multiregional clinical trials could also greatly benefit patients in all POP countries.

Urgency: China is the world's No. 1 cancer hotspot, with more than 4.8 million new cancer cases and 3.2 million deaths annually. The United States follows as No.2 in cancer burden, with about 1.9 million cases and more than 600,000 deaths annually. This makes the people of the two countries the largest number of cancer patients and natural collaborators as epicenters for cancer research and clinical trials, as well as humanitarian need, to fight against cancer, their common enemy. Leveraging China's extensive population of cancer patients, its involvement is poised to facilitate an uptick in clinical trials and to elevate the quality and diversity of global clinical trials. Such collaboration at the policy harmonization level to accelerate regulatory approvals addresses the urgency of the public health problem, and this is what millions of patients are now eagerly awaiting.

Reducing costs for all: The bilateral review process has the potential to eliminate or reduce delays in regulatory approval of innovative drugs in either market, thereby enabling patients in both countries to gain earlier access to therapies with reduced time costs and less costly expenses. One of the core measurable benefits of Project Orbis is a minimization in the lag times between FDA approval and approval in POPs. For example, in the first year of Project Orbis (June 2019 to June 2020), the median time gap between FDA and Orbis submission dates was 0.6 months with a range of –0.8 to 9.0 months. This demonstrates that the delay in marketing application submission and approval in Orbis countries can significantly be reduced, with several applications achieving parity or near-parity with FDA timelines. The reduction in time lag translates into faster access to approved medicines among participating countries, which is good for cancer patients, society more broadly, and innovator companies alike.

More data and lower regulatory hurdles translate directly into faster clinical trials and could lower costs for R&D. This has the potential to significantly improve the affordability of approved treatments for U.S. and global cancer patients and insurers, hence saving more lives.

Impact on the industry: The more diverse infrastructure of approval frameworks and the faster approval timelines among participating countries, if achieved by China's involvement in Project Orbis, can significantly improve the "return on" and the impact of clinical trials, which indicates substantial investment opportunities across the industry.

Reciprocity: This proposed agreement represents comprehensive reciprocity between the two sides, with any approvals in the U.S. market solely at the discretion of the U.S. FDA. On standards, this bilateral agreement will be built in accordance with those existing regulatory requirements set by the FDA and China's National Medical Products Administration (NMPA) and does not dilute any of the existing requirements. The FDA has specific requirements for data quality and applicability through multiregional clinical trials, and these standards will be upheld and strengthened through Project Orbis, applying to all its members. Shorter approval timelines will benefit patients in both China

and the United States, not to mention the rest of the world. And since the majority of the U.S. and international biopharmaceutical companies operate in both the United States and China, reducing the lag time for drug approvals in China and facilitating faster entry into the China market would benefit all such companies. This could also promote more communications with Chinese academic centers and establish more connections with clinical trial networks in China.

Global multilateral leadership and innovation: China's participation would provide a very strong incentive for other countries to join Project Orbis, further advancing the harmonization of international regulations, speeding up clinical trials, and saving more lives. This has the potential to firmly demonstrate U.S. global leadership and the ability to serve concrete global public goods. China has the same incentive. The United States and other countries can also benefit from Chinese innovation through co-development with China. In the coming years, China is poised to deliver many more innovative compounds that R&D and industry stakeholders could learn from. These results traveling more smoothly to more countries will be of great benefit to industry, academia, and patients in the United States, POP countries, and the rest of the globe.

Stabilize U.S.-China relationship and promote world peace: Genuine U.S.-China cooperation has the potential to help stabilize the U.S.-China bilateral relationship. However, opportunities for such cooperation are rare today. Cooperation on cancer trials through Project Orbis could be an exception. Both countries have a strong national interest in reducing cancer's death toll (through President Biden's White House Cancer Moonshot and the Healthy China 2030 initiative), as well as demonstrating global leadership, while the humanitarian nature of the effort may raise the issue above the domestic political turmoil that limits cooperation on other issues to achieve tangible achievements and further contribute to world peace.

3.2 OBSTACLES, SKEPTICISM, AND RESPONSES

Biosecurity and human genetics: Biosecurity is currently an especially salient concern for U.S. citizens and others around the world, particularly regarding China. However, the nature of Project Orbis is inherently secure: its objective is merely to share clinical trial data (not biological material) across national borders. Notably, clinical trials represent the critical step of translating scientific discovery into saving lives, and international trials have been conducted for decades, but without formal regulatory review coordination between the United States and China. Data sharing on cancer genetics is selective and annotated and has been routinely done in a secure, anonymous fashion for two decades (e.g., The Cancer Genome Atlas is publicly available). Clinical trial data sharing of cancer genetics is highly restricted with full protection of patient privacy.

Such data does not have national security implications. Existing regulations on human genetics provide expedited pathways for secure data sharing on cancer genetics so that international clinical trials and breakthroughs are not impeded.

Intellectual property protections: For some, China's potential involvement may raise concerns over intellectual property (IP) protections and the potential for this involvement to harm American and multinational companies. However, this is not relevant with Project Orbis.

First, IP protection is strengthened by the highly regulated and transparent process of international clinical trials. Second, clinical trials are intended to transfer existing scientific breakthroughs, for which the IP is already public knowledge (patented and published), into medical treatments that can then be made commercially available. Biopharmaceutical industry leaders are likely to welcome – and indeed have already expressed keen interest in – such an opportunity.

Biopharmaceutical companies normally need to submit their clinical trial data to individual countries' regulatory agencies separately for review and approval. Through international regulatory collaboration, they can choose to submit separately to each country or to FDA's Project Orbis for simultaneous regulatory review by multiple partnering countries to avoid duplication, reduce cost, and shorten the timeline to approvals.

Data quality and manipulation: There are also concerns about the quality and accuracy of data from China. However, international collaboration allows multiregional clinical trial sites to be subjected to regular and spontaneous FDA inspections and audits to ensure data quality. Empirically, international collaboration on regulatory infrastructure has been shown to strengthen data quality and prevent fraudulent data manipulation. In addition, the quality of the data can also be guaranteed due to the long-standing presence of third-party data monitoring of clinical trials.

Furthermore, data submitted should be consistent with ICH guidance and applicable to the patient population in the United States and China, given that both are members of ICH. China's regulatory reforms and ICH membership have led to its contributions to numerous pivotal international clinical trials in collaboration with the United States, collaborations that have resulted in FDA approvals of lifesaving treatments used by patients worldwide today. Project Orbis further strengthens the U.S.-led international regulatory infrastructure through enhanced types of cooperation with countries such as China.

LCA and process slowdown: Some concerns may arise over whether this LCA is unbalanced and will allow Chinese drugs to enter the U.S. market at a lower price and with lower requirements, to the detriment of U.S. patients and companies. In fact, pricing and reimbursement decisions will need to be made as a separate step following regulatory approval and are an important step that directly impacts patient access. On whether it will affect pricing in the industry, the bilateral confidentiality agreement is intended to enable greater information exchange and collaboration on regulatory decision-making. It is not linked to the pricing and reimbursement policies/processes in each country; pricing policies are determined by each government based on a number of factors that are not within the scope of the proposed bilateral agreement. Furthermore, price policy changes can happen, and are happening, in each country independent of policies around regulatory approval.

Regarding speed of approval, the U.S. FDA has issued its own decisions on drug approvals under Project Orbis ahead of other partner countries, so this joint review would not slow down the approval process in the United States or negatively impact U.S. patients. On the contrary, China's possible participation in the multilateral project would reduce lag time in drug availability for all patients. That said, to achieve reciprocity within the agreement, China needs to support multinational audits in this area and initiate capacity-building programs and relevant policy upgrades that will bring it closer to being on par with the United States on efficiency. The long-standing quarterly technical dialogue between the FDA OCE

and China's NMPA will serve to advance this goal. Besides, there are now different interpretations of ICH recommendations in terms of requirements for longer-term toxicology studies to be completed before and initiated in parallel with pivotal clinical trials that are slowing down the initiation of some Phase 3 cancer clinical trials in China. Differences in requirements for the chemical manufacturing and control sections of clinical trial applications and new molecular entity approvals are other areas where harmonization of requirements would enable simultaneous approvals across countries.

Strategic competition and geopolitics: The United States and China are engaged in wide-ranging global strategic competition. Concerns may be raised that any cooperation on biotechnology issues could advantage China in this competition. However, Project Orbis is an exceptional case. It is a global initiative led by the United States, both practically and symbolically. Most importantly, cancer is a common enemy of humanity, affecting millions of Americans annually – the American public will inherently understand that winning the battle against cancer would represent a collective victory by and for humanity the world over. This achievement will only further enhance the U.S. global leadership standing.

4. BROADEN THE SCOPE: MORE COOPERATION APPROACHES AND CASES

China joining Project Orbis is not the only significant case. When international clinical trial collaboration has been promoted to advance the international cancer cause, there are also more potential POPs, more ways to increase the diversity of member countries in the current policy frameworks, and more regulatory agencies with the potential for more policy innovation. In fact, there are many ways for different stakeholders to advance the shared goal of improving health equity in global oncology and saving the lives of more cancer patients through greater international collaboration, whether it is improving the international operational framework of clinical trials for pharmaceutical companies or increasing international participation in clinical trials at research institutions.

4.1 MORE POLICY HARMONIZATION INITIATIVES: PROJECT PRAGMATICA AS AN EXAMPLE

In 2022, The FDA OCE launched Project Pragmatica in partnership with the National Cancer Institute to simplify clinical trials and accelerate cancer treatment approvals.[16] Focusing on optimizing the design phase of clinical trials, this initiative aims to preserve trial randomization – while simplifying the overall trial process. By streamlining certain trials for drugs with known safety profiles, this project can help answer questions on overall survival more rapidly with a pragmatic trial that preserves randomization.

Compared to Project Orbis, which allows applicants to receive immediate, simultaneous reviews of their applications at the end of clinical trials, Project Pragmatica aims to make a long-term impact through the clinical trial conception and design phase. It does not require confidentiality agreements

with other country partners, making cross-border cooperation easier to achieve than is the case with Project Orbis. The OCE leader has already expressed the intention to welcome other countries including China to participate in Project Pragmatica. Thus, it could serve as a practical alternative for China (and other countries) to discuss the possibility of cooperation with the United States, starting with Project Pragmatica, prior to or parallel to discussions on joining Project Orbis. It is also worth discussing whether China could establish a similar "Pragmatica mechanism" to that in the United States. Cooperation would be greatly facilitated if both parties established similar mechanisms that do not require confidentiality agreements.

4.2 MORE POTENTIAL ORBIS/PRAGMATICA PARTNERS: INDONESIA AS AN EXAMPLE

In addition to China, Project Orbis and other international cooperation frameworks could consider more potential partner countries. Countries with a large change in cancer burden status or with new government policies to fight cancer are worthy of attention and further studies. For instance, in the Asia-Pacific region, Indonesia, a middle-income country with the largest population of Southeast Asia (270 million), is experiencing an increasing cancer burden. The latest data from GLOBOCAN for 2020 indicated a rise in new cancer cases to 141.1 per 100,000 in the population, with cancer deaths at 85.1 deaths per 100,000 population.[17] Both its cancer population and its geographic location in Asia would allow Indonesia to further broaden the sample size and diversity of the study population if it were to join Project Orbis.

In recent years, Indonesia has prioritized the strengthening and modernization of its health systems through the establishment and implementation of comprehensive cancer service guidelines. The government developed a National Cancer Control Plan containing 13 strategic goals that include increasing the quantity of standardized health service facilities and trained human resources, as well as the quality of healthcare delivery, patient safety, and technology and resources across the provision of cancer care. This effort was followed by the enactment of the population-based cancer registry in 14 provinces, with coverage for 14% of the whole population, which enables the generation of national cancer incidence data. Since 2018, the Indonesian government has committed to stepping up efforts to comprehensively increase access to cancer control, ranging from prevention, early detection and screening, diagnosis and therapy, surveillance, and research to palliative care and support and rehabilitation. These efforts have laid a foundation for further international cooperation opportunities.[18] The Indonesian government also stated that sustainable collaboration and coordination of all relevant stakeholders are imperative to achieve the cancer control goals.[19]

China's involvement in Project Orbis, if achieved, would set an example for many other countries in the world, including Indonesia. It could work as a potential starting-point for greater international collaboration, in a movement toward more diversity in trials and regulatory harmonization encompassing the United States, the Asia-Pacific, Africa, Latin America and the rest of the world.

4.3 MORE FEASIBLE APPROACHES

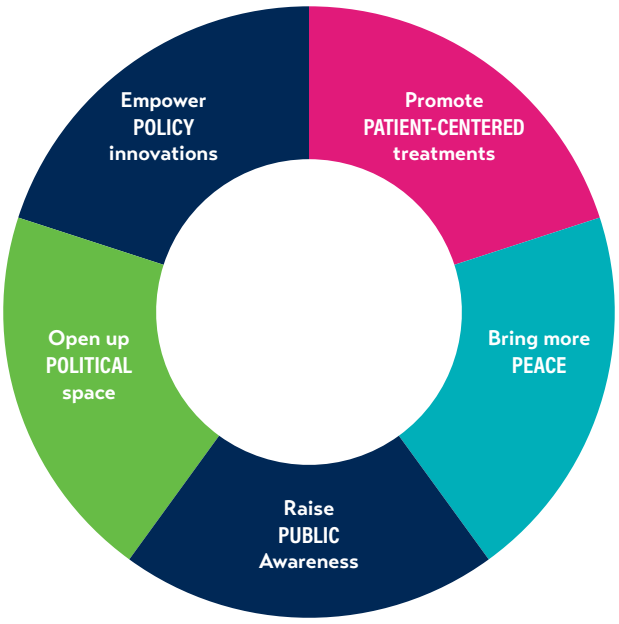
In addition to the direct call to increase the number of innovative policy mechanisms for international cooperation on cancer and expand the range of member countries, a number of approaches would be feasible in the short term, all requiring multi-stakeholders' cooperation.

Improving patient identification and enrollment: Ensuring effective and comprehensive patient-centric care requires a paradigm shift in how patients are identified and enrolled for treatments. Feasible approaches include (1) Technology Integration: utilizing technology tools, such as the development of an interactive international database, to help cancer patients input and update their details from diagnosis through treatment; (2) Hub-and-Spoke Model: adopting this network model whereby academic cancer centers serve as hubs, connecting distributed clinical research sites in diverse communities through spokes and ensuring broader access to trials regardless of patients' geographical locations; and (3) Prioritizing the principle of "bringing the trial to the patient" fostering and maintaining trusted clinician-patient relationships, thereby enhancing patient participation in trials.[4]

Promoting remote and hybrid treatment models: The future of patient-centric cancer care lies in optimizing remote and hybrid treatment models. Feasible approaches include (1) Telemedicine Adoption: integrating telemedicine technology comprehensively into clinical trials, including facets such as remote consent, toxicity monitoring, follow-ups, and direct medicine shipments to patients' residences; (2) Localized Treatment Access: engaging local physician practices, pharmacies, and even patient homes in clinical trials, facilitating accessible treatments and ensuring continuous care; (3) Prioritizing the need for diverse patient enrollment, ensuring representation from racial and ethnic minorities, older adults, and those from varied geographical and socioeconomic backgrounds.[2]

Enhancing public awareness: International stakeholders can jointly advocate for increased public awareness of clinical trials through collaboration, involving all stakeholders and patient advocacy groups. The global community, once sufficiently informed, could support worldwide campaigns such as Cure4Cancer by the Asia Society in partnership with Bloomberg New Economy to promote more dynamic policy innovations to advance the broader agenda of international clinical trial collaboration to achieve enhanced global health equity.

FIGURE 7: THE "5P"APPROACH: A COMPREHENSIVE STRATEGY OVERVIEW



Source: Cure4Cancer. https://cure4cancerglobal.org/.

5. CONCLUSION

Access to clinical trials is a key factor in translating scientific discoveries into breakthrough treatments for millions of cancer patients. Improving access to clinical trials could significantly accelerate drug approval timelines, saving the lives of millions of patients, reducing costs, and improving market access, and advancing global health equity. Greater global regulatory harmonization is critical to achieving the goal of promoting international clinical trials by overcoming numerous barriers.

Our case study of China's potential participation in regulatory harmonization initiatives such as Project Orbis shows how China's involvement in the existing international policy framework could benefit the global fight against cancer from multiple perspectives: bringing more data and population for oncology R&D, improving the establishment of global standards, reducing cost, increasing visibility, strengthening global multilateral leadership, stabilizing international relations, and finally advancing global health equity. Enhanced regulatory harmonization initiatives such as Project Orbis could achieve all these benefits and impacts by expanding global access to precision oncology through accelerated approval timelines in multiple countries.

Beyond this case, more methods and strategies exist to expand and refine these initiatives with the collaboration of all involved stakeholders and across multiple countries to further strengthen international clinical trials access and cooperation. In doing so, it is possible to revolutionize cancer care, improve global health equity, and save millions of lives while accelerating advances in scientific research, industry innovation, and global peace in the fight against cancer – our common enemy – for the betterment of all humanity.

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