Clinical trial footprint in BRICS: Improvements seen but needs further affirmative action

BRICS represents 42% of the global population and 25% of the world's gross product.[1] Their gross domestic product (GDP) growth has enabled BRICS countries to increase expenditures and investments in health, build infrastructure, and improve life expectancy.[2] The BRICS countries rarely present as a whole group in international statements and actions, and as a result, the BRICS countries are generally seen as five separate countries rather than an entity. BRICS countries are undergoing an unprecedented socioeconomic transformation and rapid urbanization.[3] The transformation has brought a shift in the spectrum of disease, from communicable diseases to noncommunicable diseases.[4] The mortality rate and disease burden of noncommunicable diseases in the BRICS countries have increased significantly in recent years,[5,6] while the threats of major communicable diseases and emerging infectious diseases are still significant challenges for the vulnerable populations, causing a double burden of diseases in BRICS countries.[7,8]

In this edition of PICR, Manoharan *et al.*[9] have collected data from the World Health Organization International Clinical Trials Registry Platform (WHO ICTRP) and the World Bank database for the total number of trials registered between a 5-year period from 2018 to 2023 in BRICS countries and G7 countries. The objective was to compare trends in clinical trial conduct between these two economic-political blocs. The study showed that 2,77,536 trials from the BRICS and G7 were registered in the WHO portal during the period and China and the US had the most trials among the BRICS and G7, respectively. Data also showed that between 2018 and 2022, the gap between the leading clinical trial countries in BRICS and G7 steadily reduced (mainly between China and the USA). The clinical trials sector remains dominated by North America and Europe, collectively accounting for over 80% of active commercial clinical trial sites. However, increasing need for globalization has led to clinical trials being conducted in a wider number of countries, in particular emerging regions.[10] The emerging regions of South America, the Middle East, and Asia (excluding Japan) currently account for just under 10% of all commercial clinical trial sites globally. Although they remain regions of interest due to large treatment-naïve patient pools (~30 million potential patients), faster recruitment rates, and lower costs, conducting trials in these markets is not without its challenges. Economic uncertainty, regulatory barriers, and clinical trial quality are key concerns for the conduct of trials in emerging markets.

The study also identified that the most common indication for clinical trials among the BRICS countries was cancer. India had 39,765 trials registered on the portal with COVID-19 studies (2056; 51%) followed by oncology (1936; 48%) and neurology (1602; 40%) being the top 3 disease areas. Clinical trials in oncology account for over 30% of trials currently running in Brazil, significantly more than any other indication. Clinical trials in cardiovascular indications are estimated to account for <10% of active clinical trials[11] even though, ischemic heart disease is the leading cause of death in Brazil.[12] Russia was ranked 10th globally based on the number of commercial clinical trial sites with just under 7000 in 2016.[10] Trial sites grew at a rapid phase from 2016 to 2022 in Russia as seen by trial density data in the study, with nearly 60% of clinical trials currently running in Russia being in Phase III. The number of trials has drastically come down with all multinational organizations either winding down studies or not placing any new studies in Russia, Ukraine, and Belarus due to the current geopolitical situation.

According to the World Bank, approximately 67% of the Indian population live in rural areas. Health-care provision in rural areas remains poor, and as a result, a high proportion of the population have to travel long distances to receive basic medical services and partake in clinical trials. Although health-care expenditure as a proportion of GDP has increased in India, it remains low compared to other countries and out-of-pocket payments are high in order to subsidize public health-care services. The Indian drug discovery and development and, as a corollary, the clinical trials conducted in the country have to cater to affordability and access, on the one hand, and diseases which are more prevalent such as malaria, dengue, and tuberculosis.[13] The number of active commercial clinical trial sites in India has decreased over the past 5 years, estimated at 1884 in 2016, and this is due to the regulatory streamlining that occurred between 2012 and 2015. India

currently has ~350 global clinical trials registered in India's public registry (Clinical Trials Registry – India CTRI) between 2020 and April 2024.[14]

The only country where the number of trials has increased is China. Robust annual GDP growth (6.9%)[15] in the past decade has resulted in strong investment in health care. The launch of the Major New Drug Innovation Program has seen a significant investment in drug development. Even so, there are challenges there that also stymie the drug development process. Nearly 50% of active commercial clinical trials in China are for oncology indications. India and China have achieved major strides in vaccine development, regulation, and production. The creation of the BRICS Vaccine Research and Development (R and D) Center will have a significant impact on vaccine cost and accessibility. This will also mean that a larger number of vaccine studies will occur in the near future in BRICS.

Regulatory approval delays present a significant challenge for conducting clinical trials in India, Brazil, and South Africa with study start-up times in the mid third to lower third in the ranking of countries.[16,17] China has a fairly competitive approval and start-up timeline that allows study enrollment to proceed at a fast pace allowing China to catch up with other countries which has a much more faster trial approval and start-up timelines. Long approval timelines for global clinical trial projects cost R and D pharmaceutical companies' valuable time and money. In approximately 80% of clinical trials, enrollment timelines are then not met or are delayed,[17] and for each day of trial delays (start-up and conduct), pharmaceutical R and D companies stand to lose from $600,000 to $8 million per day.[18]

Currently, most emerging countries including BRICS require additional investment to improve health-care facilities, training, and regulations to ensure that all aspects of the health-care infrastructure are able to support the complex practicalities of running a clinical trial. In China, there is a significant push by the government since the past decade to set up GCP directorates in the hospitals in order to facilitate both clinical trials sponsored by pharmaceutical R and D companies and academic clinical trials. India has moved to set up Phase I centers of excellence as of 2023, but there is no impetus for government institutions in India to be participating in clinical trials in spite of this becoming a standard recommendation of the Subject Expert Committees. Given the variety of challenges currently faced in emerging markets, sponsors may not be able to use a "one-size-fits-all" approach by running clinical trials in the same way as in developed G7 markets. Therefore, in the short term, many pharmaceutical companies may choose to take a cautious approach in placing global clinical trials at the same time investing in training and partnerships with hospitals and sites before committing fully to the conduct of trials.

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