

Clinical trial trends over the last 5 years among the BRICS (Brazil, Russia, India, China, and South Africa) nations

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Abstract

Purpose: Although the Americas and Europe have historically dominated the global research landscape, emerging economies – Brazil, Russia, India, China, and South Africa (BRICS) have significantly increased their contributions in recent years. This article studies clinical trial trends in the BRICS nations between 2018 and 2022 and compares it with trends in the G7 nations (comprising Canada, France, Germany, Italy, Japan, the UK, the USA, and the European Union). This will help stakeholders in planning drug development strategies.

Materials and Methods: Data were collected from the World Health Organization International Clinical Trials Registry Platform (WHO ICTRP) and the World Bank database. An electronic search was done for the total number of trials registered between January 1, 2018, and March 15, 2023. Information was analyzed based on the year of registration, therapeutic area, type of intervention, sponsorship, and type of special population. The trial density indices (TDIs) were calculated based on population (Xi) and gross domestic product (GDP) (Yi) using author-derived formulae.

Results: Altogether 2, 77, 536 trials from the BRICS and G7 were registered. China and the US had the most trials among the BRICS and G7, respectively. Between 2018 and 2022, the gap between the BRICS and G7 steadily reduced. The most common indication for clinical trials among the BRICS was cancer. Based on population, the TDI was the highest in China and the lowest in Russia. In proportion to the GDP, the TDI was maximum in Russia and minimum in India.

Conclusion: There is a remarkable reduction in the gap in clinical trial trends between the BRICS and G7 nations. Among the BRICS, India and China are at the forefront in drug development. There is scope for improvement in trial density based on India's population and GDP. Stakeholders are likely to utilize the strengths of the BRICS as an attractive destination for investment in this area.

Keywords: Brazil, Russia, India, China, and South Africa, clinical trials, developing nations, trends, trial density, World Health Organization International Clinical Trials Registry Platform

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INTRODUCTION

Brazil, Russia, India, China, and South Africa, collectively known as BRICS, are five emerging nations that are expected to occupy the top rungs of the economic ladder by the year 2050.^[1,2] This organization aims to improve cooperation and dialogue and to establish consensus with respect to matters such as trade, development, health, education, security, and finance among its members.^[3] The mutual benefits derived from this alliance have massively boosted their status in the global economy. Currently, the BRICS serves as a leading competitor to the advanced economies – G7 nations (comprising Canada, France, Germany, Italy, Japan, the UK, the USA, and the European Union). The contribution of the BRICS conglomerate to the global gross domestic product (GDP) based on the purchasing power parity is 31.5% overtaking that of the G7 by 0.8%.^[4]

This competition also spills over into the field of clinical research. A large unmet need for new drugs and molecules that can effectively treat and prevent diseases still exists globally. A steady rise in the GDP translates to higher investment in drug development, and a key player in this area is the pharmaceutical industry. Clinical trials of pharmaceutical products contribute significantly to the economic growth of a country by improving resources and infrastructure and increasing capital. In addition, a hike in the number of clinical trials enhances health-care outcomes and the overall quality of life of the population.^[5,6] Statistics from the World Health Organization (WHO) indicate that the Americas and Europe dominated the research landscape in terms of number of clinical trials registered annually. However, since 2016, there has been a paradigm shift in this hierarchy with the Western Pacific region occupying the top ranks. This change has been attributed to the increase in the number of trials registered in Japan and China.^[7] A similar uphill trend has also been reported in other emerging economies.^[8] Pharmaceutical companies are also showing increasing interest in establishing trial sites in developing nations due to their large and diverse population and high disease burden. However, this does not come without its challenges. Regulatory barriers, focus on local pharmaceutical companies, and natural as well as man-made calamities could be possible deterrents.

Our study aims to portray the changing clinical trial trends over the last 5 years (2018–2022) within the BRICS nations. It also outlines the difference in the trends between the BRICS and the G7 nations during the same time period. This will be of value to various stakeholders in planning strategies and implementing policies in drug development.

MATERIALS AND METHODS

Our study was performed using data from the WHO International Clinical Trials Registry Platform (WHO ICTRP) and the World Bank database. The Ethics Committee approval is not applicable for this study as all the data are available in the public domain. We performed an electronic search for the total number of clinical trials registered for 5 years from January 1, 2018, to March 15, 2023, among the BRICS and G7 nations [Figure 1]. All studies registered in the portal were included irrespective of the recruitment status. The data in each search page were manually cross-checked to omit data that were not relevant to the search terms used.

We identified the various therapeutic areas in which trials were registered. These included cancer, COVID-19, diabetes, hypertension, cardiology, respiratory medicine, infectious diseases, nephrology, neurology, and liver diseases. The studies were classified based on whether they involved drugs, vaccines, or others. Trials on vaccines were identified by applying filters, and drug trials were tallied separately by manual scrutiny. The remaining trials which were grouped under “others” comprised biologics, stem cells, blood and related products, biomarkers, devices, procedures, radiotherapy, nutraceuticals, natural remedies, dentistry, and dermal cosmetics. Next, the number of clinical trials performed in special populations (pediatric and geriatric) was identified. The distribution of sponsored and nonsponsored trials among the BRICS nations was also observed. The World Bank database^[9] was used to gather information regarding the GDP and total population of the respective countries in the BRICS bloc. The trial density indices (TDIs) for the study period were calculated based on population (X_i) and GDP (Y_i) using the following author-derived formulae:

BRICS: TDI based on population (expressed as X_i):

$$X_i = \frac{\text{Total number of trials}}{\text{Average population}}$$

BRICS: TDI based on GDP (expressed as Y_i):

$$Y_i = \frac{\text{Gross Domestic Product (in billion USD)}}{\text{Total number of trials}}$$

Finally, the data collected were entered into an Excel file and analyzed using bar graphs and pie charts.

RESULTS

The BRICS and G7 nations combined registered a total of 2, 77, 536 clinical trials between 2018 and 2022. Out of this, 1, 21, 046 (43.6%) were from the BRICS and 1, 56,

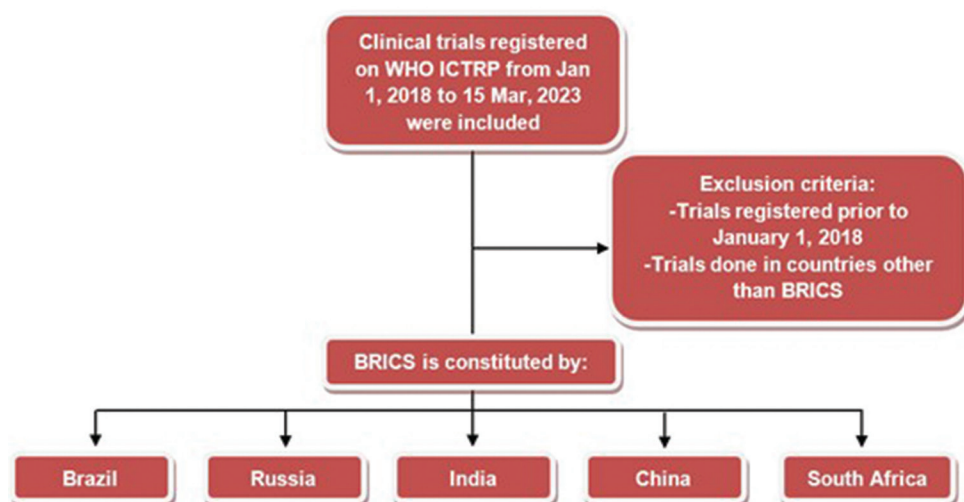


Figure 1: Schematic representation of the inclusion/exclusion criteria for the study. BRICS: Brazil, Russia, India, China, and South Africa, WHO ICTRP: World Health Organization International Clinical Trials Registry Platform

490 (56.4%) from the G7. Among the G7, the US (55,151) had the greatest number of trials, and among the BRICS, China outranked the other nations (67,081) [Table 1]. There was no significant change in the trial distribution during the study period among the G7 countries. However, the trend over the last 5 years clearly indicates a bridging of the gap between the BRICS and G7 blocs. The difference in the total number of trials between the two blocs dropped from 12,199 in 2018 to 3834 in 2022, i.e., by 68.6% [Figure 2]. The hike in the contribution from the BRICS is noteworthy – from 37.6% in 2018 to 42.4% in 2022. This can be attributed to an increase in the trials conducted mainly in India, followed by China. Canada (11,084) had the lowest number of trials among the G7, and South Africa (1,826) had the lowest number of trials among the BRICS.

When the data from 2018 and 2022 were compared, it was seen that the contribution from India increased from 33% to 40%, whereas that of China remained the same at 51%. Brazil showed a 4% decrease, Russia showed a 2% decrease, and South Africa showed a 1% decrease.

Overall, the most common indication for trials in the BRICS bloc was cancer (37%), and the least common indication was liver disease (1%). When the member countries were analyzed individually; cancer trials topped the list in Brazil (27.4%), Russia (41%), China (47.7%), and South Africa (20.5%). However, in India, the maximum number of trials was done in the field of COVID-19 (23.2%), and cancer came a close second (21.8%). Each country had the lowest number of trials in the area of liver disease (Brazil – 0.6%, Russia – 0.3%, India – 2.1%, China – 0.6%, and South Africa – 0%) [Table 2].

Table 1: Country-wise distribution of clinical trials registered in Brazil, Russia, India, China, and South Africa and G7 nations between 2018 and 2022

Rank	Country	Total number of trials (2018–2022)	Percentage
1	China	67,081	24
2	US	55,151	20
3	India	39,765	14
4	Japan	27,630	10
5	Germany	18,884	7
6	France	17,515	6
7	UK	14,842	5
8	Italy	11,384	4
9	Canada	11,084	4
10	Brazil	8354	3
11	Russia	4018	2
12	South Africa	1828	1

Table 2: Country-wise distribution of clinical trials registered in Brazil, Russia, India, China, and South Africa in various therapeutic areas between 2018 and 2022

Rank	Therapeutic area	Brazil	Russia	India	China	South Africa	Total
1	Oncology	738	653	1936	7489	150	10,966
2	Neurology	466	220	1602	2066	40	4394
3	COVID	625	180	2056	1355	105	4321
4	Respiratory medicine	204	175	789	1866	148	3182
5	Nephrology	149	54	591	691	42	1527
6	Cardiology	144	100	298	840	45	1427
7	Diabetes	77	32	718	491	53	1371
8	Infectious diseases	170	110	325	470	134	1209
9	Hypertension	102	60	361	331	16	870
10	Liver diseases	18	6	187	90	0	301

In terms of vaccine trials, China (53.5%), India (23.3%), and Brazil (10.3%) were at the forefront. A similar pattern was observed with respect to research on drugs (China – 50.9%, India – 25.5%, and Brazil – 10.9%). Brazil contributed to a whopping 65.6% of studies in the geriatric population, whereas the number in the other nations was dismally low. In the pediatric population, China had the maximum

number of trials (40.6%), followed by India (34.9%). China also had the highest number of sponsored trials (55.5%), and Brazil had the highest number of nonsponsored trials (22.7%).

Using the author-derived formulae for the TDI, it was found that China had the highest X_i (47.6), followed by Brazil (39.5). South Africa (30.7), India (28.8), and Russia (27.5) had relatively lower values. In terms of the TDI based on the GDP, Russia was the first (0.41), followed by China (0.23), South Africa (0.21), and Brazil (0.20), while India (0.07) had a disappointingly low Y_i [Figure 3].

DISCUSSION

Our study provides a glimpse of the clinical trial trends and patterns seen among the BRICS nations between 2018 and 2022. Our results indicate a noticeable change in the research landscape among the BRICS between 2018 and 2022. The narrowing of the wide chasm between the developed and developing worlds can be explained by a number of reasons. First, the BRICS nations have a combined population of 3.27 billion, which accounts for 40% of the world’s population.^[10] This number combined with diversity in terms of race and genotype as well as naivety of the patient pool provides an impetus for research. Second, these developing countries have a high disease burden, accounting for 40% of the global burden.^[11] As per the 2019 WHO Global Health Observatory data, ischemic heart disease remains one of the leading causes of disability-adjusted life years (DALYs) in Brazil, Russia, India, and China. In South Africa, the most common cause of DALYs is HIV/AIDS.^[12] The BRICS also bears 49% of the world’s burden of tuberculosis (TB), 40% of all TB-related mortality, and more than 60% of the multidrug-resistant TB burden.^[11] In addition, these nations are also playing a growing role in the R and D of neglected diseases, with a focus on the leading causes in

their own countries.^[13] Third, developing countries like the BRICS are becoming hotspots for trial initiation as global sponsors wish to utilize the cost-effectiveness of these nations. The low labor costs decrease the cost of clinical trials. The BRICS nations also fall within the purview of the “pharmerging” markets, where Big Pharma has observed its highest growth in sales revenue. As a result, they are inclined toward modifying their strategies to adapt to these pharmerging markets.^[14] Yet, another factor observed from our results is that China seems to be a major driver in narrowing the gap between the BRICS and G7. China currently occupies the first position in terms of number of registered clinical trials. In addition to its large population, disease burden, and cost-effectiveness, China’s economic growth rate and improved regulatory milieu have probably contributed to its overtaking the US, which has always been a dominant player in the field.^[15]

In terms of therapeutics, oncology had the highest number of trials in Brazil, Russia, China, and South Africa. The COVID-19 pandemic caused an enormous demand for drug and vaccine development, and the BRICS nations accounted for 30% of COVID-19 deaths worldwide.^[11] Considering the fact that China was the epicenter of the COVID-19 pandemic, one would expect that the maximum number of trials would have been conducted here. However, our results show that 47.6% of the registered COVID-19 trials were from India, whereas only 31.4% were from China. This can be explained by the fact that conducting clinical trials in response to a novel acute infectious disease is daunting. The high morbidity and mortality rates may have forced the health-care system to divert its resources away from clinical research.^[16] It is possible that there was a lack of inclination toward research in the early phases as the foremost priority was placed on control measures. After the suppression of the first wave of COVID-19, China implemented strict lockdown measures

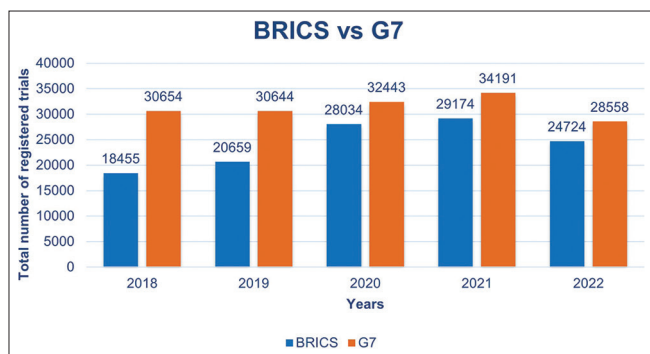


Figure 2: Clinical trial trends in Brazil, Russia, India, China, and South Africa and G7 nations between 2018 and 2022. BRICS: Brazil, Russia, India, China, and South Africa

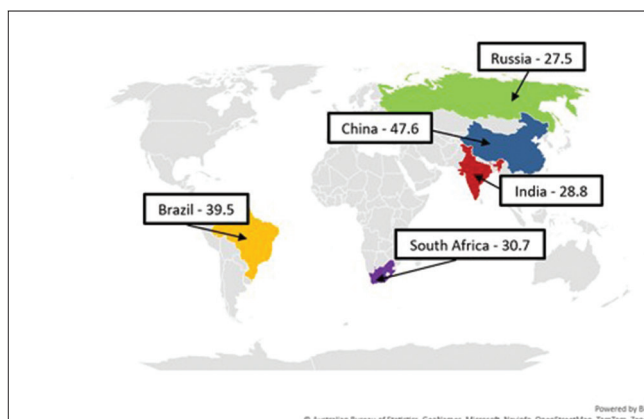


Figure 3: Global representation of the trial density index based on population (X_i) among Brazil, Russia, India, China, and South Africa

and several clinical trials never began, and several others were terminated prematurely as a result of the inability to perform on-site visits, quarantine requirements, and travel restrictions. There is also a likelihood of trials not being registered on portals during this crisis period.^[17]

Our results show that the density of trials in the BRICS nations is much lower than what would be expected when considering the magnitude of their areas and populations. Despite the fact that India is the only member state showing an increase in contribution to the total number of trials between 2018 and 2022, the TDI of India in proportion to its population as well as the GDP remains low. One of the key challenges faced by global sponsors for the conduct of clinical trials in emerging economies is the tedium of local guidelines or the lack of clarity thereof. The time for the overall approval may take around 10–14 months in Brazil and China, whereas the US completes it within 3–6 months.^[18] In South Africa, time to market can be as long as 4 years due to huge backlogs in the health department. Language serves as an impediment in Brazil, Russia, and China. The regulations in these countries are in their local languages, namely, Portuguese, Russian, and Chinese. In addition, documents for trial registration require translation serving as an additional administrative burden to sponsors.^[19] Efforts are being made to break down these linguistic barriers. The website of the Brazilian Regulatory Agency, Agencia Nacional de Vigilancia Sanitaria, currently has contents in English as well; however, these are limited when compared to the Portuguese version.^[20] India has an advantage here owing to the large number of health-care professionals proficient in English.^[21] The lag between the BRICS and G7 can also be due to an increased focus on local pharmaceuticals. For instance, new drugs produced by Russian enterprises are usually put only on their domestic markets. In an attempt to decrease dependence on imports, Russian regulations mandate collaboration between global pharmaceutical companies and local establishments to relocate their production facilities in-country.^[13,22,23] The percentage of Phase I trials in low- and middle-income countries is dismally low (6%) in comparison to the US and other high-income nations.^[24] The lack of adequate infrastructure and facilities are lacunae that need to be addressed in this regard. Economic crises, issues with quality control, corruption, and population vulnerability are other risks faced by Big Pharma.^[25]

There have been attempts to harmonize and formulate unified regulations for the BRICS nations. However, linguistic barriers, constantly changing regulatory requirements, and the need for local clinical trials are challenges faced by policymakers. Identification of

research gaps by mapping of clinical trial trends, as done in this study, will be of value to researchers, sponsors, and policymakers in planning and decision-making.

Limitations

The limitation of our study is that it only includes data from the WHO ICTRP portal. This may not represent the exact scenario of clinical trial trends as not every trial is registered in this portal. Data from national registries could not be included as a result of linguistic barriers. The European Union is a nonenumerated member of the G7. However, it was not included for the purpose of our study as it comprises 27 member states, including France, Germany, and Italy.

CONCLUSION

There is tremendous potential among emerging economies in the field of clinical trials. It is imperative that the significance of this contribution is recognized and encouraged. Currently, among the BRICS, India and China are at the forefront. However, there is considerable scope for improvement in the TDI based on India's population and the GDP. Stakeholders are likely to utilize the strengths of the BRICS as an attractive destination for investment in this area. Possibly, the BRICS could emerge as a world leader in drug discovery and development in the near future.

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Conflicts of interest

There are no conflicts of interest.

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