Review Article

DOI: 10.7860/JCDR/2024/70716.19608

Bridging the Divide: Tackling Recruitment Challenges in Indian Clinical Trials: A Narrative Review

Ethics Section

SHAMBHAVI S GHOTANKAR[1], RAJENDRA DEVKAR[2], MADHURA DESHMUKH[3]

ABSTRACT

India's clinical trial landscape has witnessed rapid growth over the period, with the recent introduction of remote trial patient monitoring utilising technologies like Artificial Intelligence (AI). The vast and diverse population, combined with well-established medical infrastructure and skilled professionals, makes India an ideal location for conducting clinical research. Many international pharmaceutical companies have chosen to outsource their operations to India as well. However, despite India emerging as a significant hub for clinical trials, recruiting participants still presents unique challenges. This review aimed to shed light on the hurdles faced in recruiting participants in Indian clinical trials and explore potential solutions to bridge this gap. It has been highlighted that overcoming the challenges in recruiting participants in Indian clinical trials requires a multi-faceted approach involving various stakeholders. Along with the powerful steps taken by the government in reforming policies and regulatory norms, certain innovative and effective strategies need to be designed to streamline the processes of participant recruitment.

Keywords: Clinical research, Drug development process, Participants, Phase 1 to Phase IV, Randomised control trials

INTRODUCTION

Randomised Controlled Trials (RCTs), are generally acknowledged as the gold standard for assessing the efficacy and safety of medical interventions [1], and they play a vital role in advancing medical research and bringing new treatments to patients. The recent pandemic has increased the need for more clinical studies for medications and vaccines. The Coronavirus Disease-2019 (COVID-19) pandemic has significantly impacted various clinical research methods, including patient recruitment, obtaining informed consent, and implementing interventions, which were traditionally conducted in person by the research team. The pandemic disrupted these processes, leading to the development of alternative methods to keep clinical research going while keeping participants and researchers safe. As a result, remote trial patient monitoring has become a significant trend to continue ongoing studies and perform new ones during the lockdowns. Pharmaceutical and medical device businesses have developed these remote monitoring techniques by utilising technology like blockchain and Artificial Intelligence (AI) [2]. Technology-reliant clinical trials are a significant development that will benefit the field in the future [3].

However, the success of clinical trials relies heavily on recruiting a diverse and representative participant pool [4]. India, a country emerging as a significant hub for clinical trials, still faces unique challenges in recruiting participants. Poor recruitment is a major hindrance to the successful conduct of RCTs, and careful review of the causes of these obstacles and the development of reliable solutions to enhance enrollment are of key importance. Numerous global investigations about patient acquisition challenges have suggested tactics such as newsletters and patient reminders, educational and financial incentives for physicians, open-versus placebo-controlled trials, patient travel support, and professional networking. Additionally, they have tested recruitment procedures [5]. These tactics have been developed through extensive research on a population in the West with a distinct socio-cultural context; further research is necessary to see how applicable these tactics are to recruiting campaigns in emerging nations such as India [1].

One of the main bottlenecks in the drug development process (Phase II to Phase IV) has been identified as recruiting the intended sample size within the specified time limit in clinical studies. It takes up more time than any other clinical trial component, resulting in missed deadlines and increased expenses. Secondly, healthy volunteers are frequently of reproductive age; they must either take legal forms of birth control or, in certain situations, abstain from sexual activity during the whole study, which becomes quite difficult, particularly for the ladies [6]. Recruitment and retention of participants (for conduction and smooth implementation) are of key importance in clinical trials, particularly in India, which has the highest potential for delivering successful trials. Identification of the factors influencing the recruitment procedure and documenting appropriate measures to reduce these hurdles will help in planning robust clinical trials in the future. This review aimed to shed light on the hurdles faced in recruiting participants in Indian clinical trials and explore potential solutions to bridge this gap.

Background on Indian Clinical Trials and Current Scenario

India's clinical trial landscape has witnessed rapid growth in recent years, attracting pharmaceutical, biotech, and academic trials worldwide. The vast and diverse population, combined with well-established medical infrastructure and skilled professionals, makes India an ideal location for conducting clinical research [7]. India fully complied with Trade-Related Aspects of Intellectual Property Rights (TRIPS) in 2005 [8,9]. Since then, in an effort to promote clinical trials in India, the government has been striving to modify the laws and policy framework. Furthermore, there are other reasons (low operational costs, a large population with diverse ethnicity, high prevalence of acute and chronic diseases, well-equipped establishments, and research facilities, etc.,) why international pharmaceutical companies have chosen to outsource their operations to India [9-11].

Despite this, foreign companies are still facing several challenges such as language and cultural barriers, socio-economic factors, awareness, and willingness, along with the effects of genetic diversity on drug testing [12]. Furthermore, given the nation's ongoing boom in clinical trial activity, there is a good reason to be concerned about the dearth of personnel who have received the necessary International Council for Harmonisation of Technical Requirements of Pharmaceuticals for Human Use (ICH) Good Clinical Practice (GCP) training [13]. Clinical research outsourcing is also a result

of a lack of clinical investigators. Insufficient patient participation in research results in inadequate data collection to demonstrate the safety and effectiveness of an experimental product. To more precisely assess trial progress and addressable bottlenecks, divide the recruitment and enrollment periods, and track success for each.

Importance of Participant Recruitment

Recruiting participants is the basis of clinical trials. The fact that conducting trials is expensive is as innovative and shocking as stating that the sky is blue or that a lot of people like ice cream. Hard data, however, is difficult to come by, and estimates of the true cost might differ significantly based on the indication, the number of participants in the study, and other elements like whether or not the trial compares a novel medication to an already available one. The participation of individuals from diverse backgrounds ensures that research outcomes reflect the broader population. This inclusivity is crucial for valid and reliable results that can be generalised to different ethnicities, ages, genders, and socio-economic groups [14].

CHALLENGES IN RECRUITING PARTICIPANTS IN INDIAN CLINICAL TRIALS

Throughout the existence of clinical trials, many of the same challenges have presented themselves repeatedly. Now, however, things are different since sophisticated investigation and analysis have clarified the precise reasons behind this.

Limited awareness and understanding: One significant challenge revolves around the limited awareness and understanding of clinical trials among the Indian population. A study in Pune, India found that people know clinical trials are about medicine and progress but don't understand how they work. Even though they see the benefits, 80% are worried about side-effects and don't want to join. It shows the need of better education to help people make informed choices about participating in trials [15]. Many people perceive participation in clinical trials as risky or experimental [16]. A lot of healthy individuals frequently employ screening tests as a way to "get a free health check-up" or to get paid a little sum of money in exchange for their time and travel. When they receive the results of the screening test, these individuals frequently decide not to participate [17]. Most potential participants actually do not listen to or even understand the risks of participation in the trial.

They often fail to make a distinction between research and treatment, due to which they expect high payment for participation. The answer to this problem lies in shifting the focus of research to the patient, spending more time and resources on discussions with patients, family engagement, and general demystifying of the trial procedure and what it takes to be a participant. While opinions are gradually shifting toward this idea, individuals who have already made the shift are finding it simpler owing to technological advancements. Patient education has been presented and distributed more effectively because of digital health technology. Addressing this misconception through educational campaigns and utilising various media platforms can help create awareness and foster a positive perception of clinical trials [18].

Sociocultural factors: Sociocultural factors (cultural and regional diversity) significantly influence participant recruitment in Indian clinical trials. Stigma associated with clinical trials in certain communities can daunt potential participants. Furthermore, cultural beliefs in India might occasionally make it difficult for a doctor to fully disclose a patient's diagnosis and the dangers involved in taking part in scientific research. The importance of family in healthcare decision-making cannot be overstated, as family members are typically involved in informed consent discussions [7,15]. Overcoming this stigma requires targeted community engagement programs and fostering trust by involving local opinion leaders and influencers. Additionally, ensuring language proficiency, a culturally sensitive approach, and addressing the concerns of diverse communities are crucial to enhance recruitment efforts.

Additionally, India is among the world's most genetically diverse countries. Genetic diversity presents new difficulties for medication testing and development, even though it is thought to be a benefit in patient recruitment. Despite the fact that every region has its language or languages and culture, due to migration, there is a mixture of individuals from various groups throughout the nation [15].

Inadequate infrastructure and resources: The lack of adequate infrastructure and resources is a significant challenge in recruiting participants, particularly in remote areas of India. The scarcity of medical facilities and research centers can limit accessibility, discouraging potential participants from enrolling. To address this challenge, there is a need for increased investment in healthcare infrastructure and the establishment of research centers in underserved regions. Additionally, ensuring the availability of trained personnel, adequate funding, and technological resources will greatly facilitate participant recruitment [19].

Regulatory and ethical considerations: Stringent regulatory guidelines and ethical considerations are vital for ensuring participant safety and maintaining the integrity of clinical trials. However, navigating complex regulations and bureaucratic processes in India can pose challenges. Streamlining regulatory procedures, improving transparency, and providing clear guidance can facilitate smoother recruitment processes. Upholding high ethical standards and ensuring proper oversight throughout the entire trial process should remain a top priority [20].

Protocol related issues: The intricacy of a research protocol is positively correlated with the challenges encountered in patient recruitment. The majority of research techniques entail the use of placebos. It is more difficult to persuade patients and their families to take part in a study if one of the arms is a placebo. This is particularly true for studies involving critical intervention conditions, pain management, and psychiatric disorders, where the actual treatment is crucial to the patients' conditions. It is challenging to recruit treatment-naïve patients for an oncology trial if it is one of the inclusion criteria. It continues to become harder to convince patients and their families to agree to participate in the trial, even though the protocol offers rescue drugs and patients can opt out at any moment [21].

In order to perform multiple tests as part of certain study protocols, patients must stay in the hospital for extended periods of time. Some patients may find such a lengthy wait to be extremely demanding, which could limit their willingness to participate in and stay in a study. Requirements for a wash-out time and restrictions on concurrent drugs are two further factors that impact patient retention and restrict patient recruitment. Complicated research protocols and regular protocol visits put patients and their families under more stress. This becomes especially important in paediatric trials when parents and kids need to get used to strict study regimens and academic obligations [21].

EFFECTIVE STRATEGIES TO IMPROVE RECRUITMENT IN INDIAN CLINICAL TRIALS: A PERSONAL VIEWPOINT

Overcoming the challenges in recruiting participants for Indian clinical trials requires a multi-faceted approach involving various stakeholders. The Indian government has taken significant steps by implementing policies and regulatory reforms aimed at streamlining processes and improving participant recruitment [21,22].

In addition to these, some strategies that could be used at an individual level to improve recruitment in the trial may include:

Create a powerful recruitment team: For any clinical trial to be successful, a strong recruitment team is required. Individuals with experience in patient recruitment, as well as those with expertise in the medical condition or disease being examined, should form the team. Collaborative efforts between research organisations, government bodies, and NGOs can further enhance participant recruitment and address sociocultural barriers.

Use social media and online advertising: Patients can be recruited for clinical trials using online advertising and social media. Online advertising can assist in reaching a broad audience of potential volunteers by targeting specific demographics and using terms related to the illness being studied. Social media channels like Facebook and Twitter can also be used to inform people about clinical trials and encourage them to participate.

Use Electronic Health Records (EHR): Electronic Health Records (EHR) can be a useful tool for patient recruitment. Researchers can quickly find potential participants by scanning EHRs for patients who match the eligibility criteria for a clinical study. EHRs can also be utilised to track patient outcomes and the trial's progress. Lower drop-out rates are a direct outcome of recruiting appropriately matched participants, and greater recruitment expenses may arise from participant attrition, either as a replacement or as a means of making up for anticipated losses during the recruitment phase.

Establish trust and transparent communication: It is critical to establish trust with potential partners. Ensure transparency by explicitly communicating the aim, processes, risks, and benefits of the experiment. Maintain open channels of contact throughout the process and provide simple information resources. Encourage questions and swiftly resolve concerns to foster a sense of security and involvement.

Simplify the recruitment procedure: Simplify the enrollment procedure to lower hurdles for potential participants. Use electronic permission forms and user-friendly web platforms for registration. To enhance accessibility, reduce paperwork and simplify eligibility criteria. Consider offering remote or mobile enrollment alternatives to improve convenience.

A cross-sectional questionnaire-based study involving 121 respondents from four geographical locations in India reported that the majority (90%) had knowledge about CTs, whereas only 7% had confirmed signing consent forms. The total awareness-attitude score significantly varied across locations (27% for the southern zone, 53% for the central zone, and 52% for the western zone), and this was negatively associated with education [22].

CONCLUSION(S)

Recruiting participants in Indian clinical trials is faced with several challenges. This has been attributed to factors such as lack of awareness about clinical trials, cultural beliefs and superstitions, fear of side-effects, and concerns about exploitation and lack of trust in the healthcare system.

Negative publicity and past instances of unethical trials reported in the media have led to a widespread mistrust of clinical research among the Indian population. Additionally, the current regulatory challenges in India, such as the requirement for audio-visual recording of the consent process and restrictions on the number of trials per site, can also impede the recruitment process. Furthermore, the cost and logistical challenges associated with participating in clinical trials, such as travel expenses and time commitment, can deter potential participants from enrolling. Lastly, the complex study designs and restrictive inclusion/exclusion criteria, which are the core principles of clinical trials, can limit the pool of eligible participants and pose challenges to recruitment efforts and the conduction of outcome-based quality research.

To address these challenges, it is important to devise innovative and effective strategies for clinical trial recruitment in India. These strategies could include increasing public awareness and education about the importance and benefits of clinical trials, improving trust in the healthcare system through transparent and ethical practices, collaborating with community leaders and influencers to overcome cultural barriers and dispel myths, providing support for travel and logistical arrangements for participants, simplifying study designs and eligibility criteria to expand the pool of eligible participants, and streamlining the regulatory process to facilitate efficient recruitment.

REFERENCES

[1] Kadam RA, Borde SU, Madas SA, Salvi SS, Limaye SS. Challenges in recruitment and retention of clinical trial subjects. Perspect Clin Res [Internet]. 2016;7(3):137-43. Available from: https://dx.doi.org/10.4103/2229-3485.184820

[2] Tagde P, Tagde S, Bhattacharya T, Tagde P, Chopra H, Akter R, et al. Block chain and artificial intelligence technology in e-Health. Environ Sci Pollut Res Int. 2021;28(38):52810. Available from: https://dx.doi.org/10.1007/s11356-021-16223-0.

[3] Clinical Trials and Biomedical Research in India- Legal and Regulatory Framework [Internet]. Nishithdesai.com. 2023 [cited 2024 Jan 22]. Available from: https://www.nishithdesai.com/fileadmin/user_upload/pdfs/Research_Papers/Clinical-Trials-in-India.pdf.

[4] Howley MJ, Seth J, Sechopoulos S, Malamis P. Getting to clinical trial diversity [Internet]. Applied Clinical Trials. 2023 [cited 2024 Jan 22]. Available from: https://www.appliedclinicaltrialsonline.com/view/getting-to-clinical-trial-diversity.

[5] Oncology clinical trial market size, application analysis, regional outlook, 2020-2030 [Internet]. BioSpace. 2022 [cited 2024 Jan 22]. Available from: https://www.biospace.com/article/oncology-clinical-trial-market-size-application-analysis-regional-outlook-2020-2030/.

[6] Chaudhari N, Ravi R, Gogtay NJ, Thatte UM. Recruitment and retention of the participants in clinical trials: Challenges and solutions. Perspect Clin Res [Internet]. 2020;11(2):64-69. Available from: https://dx.doi.org/10.4103/picr.PICR_206_19.

[7] PTI. India emerging as favourable destination to conduct global clinical trials: Report [Internet]. Economic Times. 2023 [cited 2024 Jan 22]. Available from: https://economictimes.indiatimes.com/industry/healthcare/biotech/healthcare/india-emerging-as-favourable-destination-to-conduct-global-clinical-trials-report/articleshow/99951510.cms.

[8] New DKT. lift.ac.in. [cited 2024 Jan 22]. Available from: https://wtocentre.iift.ac.in/FAQ/english/TRIPS.pdf.

[9] Imran M, Najmi AK, Rashid MF, Tabrez S, Shah MA. Clinical research regulation in India-history, development, initiatives, challenges and controversies: Still long way to go. J Pharm Bioallied Sci [Internet]. 2013;5(1):02-09. Available from: https://dx.doi.org/10.4103/0975-7406.106553.

[10] Fogel DB. Factors associated with clinical trials that fail and opportunities for improving the likelihood of success: A review. Contemp Clin Trials Commun [Internet]. 2018;11:156-64. Available from: https://dx.doi.org/10.1016/j.conctc.2018.08.001.

[11] Delhi N, Mondal S, Abrol D. Institute for studies in industrial development [Internet]. Org.in. 2015 [cited 2024 Jan 22]. Available from: https://isid.org.in/wp-content/uploads/2022/09/WP179.pdf.

[12] Kumar G, Chaudhary P, Quinn A, Su D. Barriers for cancer clinical trial enrollment: A qualitative study of the perspectives of healthcare providers. Contemp Clin Trials Commun [Internet]. 2022;28(100939):100939. Available from: https://www.sciencedirect.com/science/article/pii/S2451865422000564.

[13] Language Connections. Clinical Trials in India: What are the Challenges [Internet]. Language Connections. 2015 [cited 2024 Jan 22]. Available from: https://www.languageconnections.com/clinical-trials-in-india-what-are-the-challenges/.

[14] National Academies of Sciences, Engineering, and Medicine; Policy and Global Affairs; Committee on Women, Bibbins-Domingo K, Helman A. Why diversere presentation in clinical research matters and the current state of representation within the clinical research ecosystem. Washington DC, DC: National Academies Press; 2022.

[15] Joshi V, Kulkarni AA. Public awareness of clinical trials: A qualitative pilot study in Pune. Perspectives in Clinical Research. 2012;3(4):125-32. Doi: 10.4103/2229-3485.103593.

[16] Mowlabaccus WB, Jodheea-Jutton A. Participant perception, still a major challenge to clinical research in developing countries- A mixed methods study. PLoS One [Internet]. 2020;15(7):e0236563. Available from: https://dx.doi.org/10.1371/journal.pone.0236563.

[17] Regulatory strategy for Medical Devices-FDA consulting Makrocare.com.[cited 2024 Apr 20]. Available from: https://www.makrocare.com/devices/regulatory/regulatory-strategy/.

[18] Kuwabara A, Su S, Krauss J. Utilizing digital health technologies for patient education in lifestyle medicine. Am J Lifestyle Med. 2020;14(2):137-42. Available from: https://dx.doi.org/10.1177/1559827619892547.

[19] Briel M, Elger BS, McLennan S, Schandelmaier S, vonElm E, Satalkar P. Exploring reasons for recruitment failure in clinical trials: A qualitative study with clinical trial stakeholders in Switzerland, Germany, and Canada. Trials. 2021;22(1):844. Available from: https://dx.doi.org/10.1186/s13063-021-05818-0.

[20] Thoma A, Farrokhyar F, McKnight L, Bhandari M. Practicaltips for surgical research: How to optimize patient recruitment. Can J Surg. 2010;53(3):205-10.
[21] India's regulatory reforms for clinical trials. EPS. Available from: https://www.epsi-global.com/locations/india/article01.html.
[22] Pillai GS, Sheeba CS, Barman M, Sen A, Sundaram N, Dickson M, et al. Knowledge and awareness of clinical trials among trial participants in India: A multicentric questionnaire-based cross-sectional study. Indian J Ophthalmol. 2024;72(2):275-80. Doi: 10.4103/IJO.IJO_3041_22.

PARTICULARS OF CONTRIBUTORS:
1. Researcher, Department of Central Research Facility, Dr. D. Y. Patil Medical College, Hospital and Research Centre, Dr. D. Y. Patil Vidyapeeth, Pune, Maharashtra, India.
2. Social Worker, Department of Central Research Facility, Dr. D. Y. Patil Medical College, Hospital and Research Centre, Dr. D. Y. Patil Vidyapeeth, Pune, Maharashtra, India.
3. Researcher, Department of Central Research Facility, Dr. D. Y. Patil Medical College, Hospital and Research Centre, Dr. D. Y. Patil Vidyapeeth, Pune, Maharashtra, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Madhura Deshmukh,
Researcher, Department of Central Research Facility, Dr. D. Y. Patil Medical College, Hospital and Research Centre, Dr. D. Y. Patil Vidyapeeth,
Pune-411018, Maharashtra, India.
E-mail: madhura.deshmukh@dpu.edu.in

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Mar 15, 2024
- Manual Googling: Apr 09, 2024
- iThenticate Software: May 13, 2024 (9%)

ETYMOLOGY: Author Origin

EMENDATIONS: 6

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was informed consent obtained from the subjects involved in the study? NA
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Mar 14, 2024**
Date of Peer Review: **Apr 04, 2024**
Date of Acceptance: **May 14, 2024**
Date of Publishing: **Jul 01, 2024**