Trials

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Understanding participation of persons with disabilities in clinical trial research in India—a retrospective analysis of inclusive language of protocols

Karikalan Nagarajan[1,2], Malaisamy Muniyandi[2,3*], Aswin Vickirananth Jeyachithra[4], Shelshia Muniappan[4], Nickson Rajamani[4], Pearl Maria Dsouza[5], Yasaswany Santhoshkumar[1], Ananda Kumar Balasubramanian[6], Bhaskara Chary Kothoju[3], Priscilla Rebecca[1] and Angayarkanni Balasubrammnaiyan[7]

Abstract

Background and objectives The under-representation of vulnerable groups in clinical trials, including persons with disabilities, could affect the applicability of trial findings to real-world public health interventions. We undertook this study to assess the extent to which persons with disabilities are excluded due to non-inclusionary language use in protocols from clinical trial research in India.

Methods We conducted a retrospective mixed-methods analysis of fully published clinical trial protocols relevant to India (January 2017 to December 2024), sourced from national and international databases. Inclusion and exclusion criteria were analyzed with a focus on seven disability domains as defined by the Rights of Persons with Disabilities (RPWD) Act: locomotor disabilities, blood disorders, neurological disabilities, speech and language-related disabilities, hearing and vision-related disabilities, intellectual disabilities, and others. We executed a structured five-step coding process to assess patterns of disability-based exclusion in clinical trial protocols, determining whether exclusions were based on specific diagnoses or broad descriptions and whether justifications or supportive mechanisms were provided. To contextualize the findings, additional information regarding the trial phase, study location, and disease focus was extracted. An inductive analysis explored the language and rationale being employed for disability-related exclusions.

Results Of the 11,975 records screened, 271 clinical trial protocols met the inclusion criteria. Among these, 117 (43.2%) protocols reported 126 instances of disability-related exclusionary language in the eligibility criteria. Exclusionary language pertaining to neurological disabilities accounted for the majority of exclusions (69.8%), followed by speech and language impairments (16.6%), blood disorders (9.5%), locomotor disabilities (3.1%), and hearing and vision-related disabilities (1%). Only 11.9% of these exclusions were explicitly justified based on diagnostic criteria, whereas 17.4% lacked any stated justification for disability-based exclusions. Exclusionary languages were notably higher in phase 3 trials (49.2%) and in international or multicentric trials (54.7%) compared to trials conducted in India (44.4%). Additionally, 5.9% of protocols specified a requirement for enhanced cognitive ability for informed consent, yet none included provisions for supportive decision-making mechanisms.

*Correspondence:
Malaisamy Muniyandi
muniyandi.m@icmr.gov.in
Full list of author information is available at the end of the article

Interpretation and conclusions Over one-third of clinical trial protocols had ambiguous eligibility criteria and exclusionary language which may potentially exclude persons with disabilities. This highlights the need for promoting the use of supportive, transparent, and non-exclusionary trial protocol language.

Keywords Persons with disabilities, Clinical trials, RPWD Act, Investigator discretion, Inclusivity, Ethics

Introduction

Clinical trials are widely regarded as the gold standard for evaluating the safety, efficacy, and effectiveness of drugs, vaccines, and other medical products and interventions. They serve as the cornerstone of evidence-based public health research, systems, and policies. Globally, the conduct of clinical trials has gained importance for its emphasis on scientific rigor, quality assurance, and regulatory compliance [1]. Trial guidelines and standards are continually evolving, developing, and being adapted to ensure high research quality. Alongside scientific advancement, there is a growing emphasis on ensuring that trials are designed and conducted in an equitable, inclusive, and accessible manner. Clinical trial protocols are expected to be designed to represent all population without exclusion due to selection bias and equally non-exclusionary language in determining eligibility. Considering their crucial role in improving population health, access to clinical trials must be distributed fairly, particularly for the vulnerable and marginalized groups [2, 3].

Under-representation and over-representation of certain population groups can influence the clinical trial outcomes and limit the applicability of findings to real-world public health interventions. While equity and inclusiveness in clinical research are increasingly addressed from the perspectives of gender, nationality, ethnicity, and socio-economic diversity, the inclusion of persons with disabilities remains notably underexplored. Studies from developed countries suggest that persons with disabilities are disproportionately excluded from clinical research. For instance, reviews of interventional clinical trials focused on the ten leading causes of global disability-adjusted life-years (DALYs) between 2010 and 2020 found that 35% of these trials explicitly excluded persons with disabilities [4].

India bears one of the highest burdens of persons with disabilities globally. Of the estimated one billion persons with disabilities worldwide, approximately 80% reside in developing countries, including India. According to census and survey data, the prevalence of disability in India is 2%, amounting to 26.8 million individuals. Considering the significant prevalence of disability and its obligations under the United Nations Convention on the Rights of Persons with Disabilities (UNCRPD), India enacted The Rights of Persons with Disabilities Act, 2016 (RPWD Act) which is framed around the social model of disability. This law formally recognized a wide range of disabilities and mandates equal opportunities for persons with disabilities across all spheres of life [5].

India continues to be a dynamic and rapidly growing hub for global clinical research. Its large, ethnically diverse population, coupled with a high burden of communicable and non-communicable diseases and a robust health research ecosystem, such as infrastructure, positions the country as a crucial site for global clinical trials [6]. In India, clinical trials are regulated through comprehensive guidelines and ethical frameworks. The Indian ethical guidelines for biomedical research have explicitly emphasized the right of vulnerable populations, especially persons with disabilities, to be included in health research and thereby benefit from its outcomes [7]. With reference to the social model of disability and the need to ensure inclusivity, we undertook this study to assess the status of potential exclusion of persons with disabilities in clinical trial research by analyzing the language of eligibility criteria in clinical trial protocols relevant to India.

Methodology

Study design

We conducted a retrospective mixed-methods analysis of fully published clinical trial protocols from studies relevant to India, spanning the period from January 2017 to December 2024. We considered protocols which are registered and fully available in trial registries and are protocols which are peer reviewed and published in high-index journals separately or as supplementary files. This timeframe was selected to align with the enactment of India's RPWD Act in December 2016, which marked a significant policy shift to promote the inclusion of persons with disabilities. The search encompassed protocols across a broad range of health domains, including communicable diseases, non-communicable diseases, rare diseases, and mental health conditions, without restricting any disease category, age, sex, or other demographic characteristics of trial participants. Multicentric trials that included India as one of the participating sites were also included. The study adhered to the PRISMA checklist.

Data sources and search strategy

We performed advanced searches across multiple databases, including ClinicalTrials.gov and the Clinical Trials Registry of India (CTRI) [8, 9], to retrieve fully available

published protocols. Using advanced search filters in ClinicalTrials.gov, we extracted published trial protocols that listed India as a study site within the specified study period. The search strategy incorporated criteria such as study location, study status, age, gender, and availability of publicly accessible study documents.

We used the CTRI website and PubMed to look for protocols registered under the Clinical Trials Registry of India. Through the CTRI website, we looked for clinical trial protocols registered between 01/01/2017 and 31/12/2024. Simultaneously, we also retrieved full-text clinical trial publications with CTRI registration numbers using PubMed's advanced search filters. In order to get protocol details, we also cross-checked the CTRI database using registration numbers.

Additionally, we thoroughly searched databases of biomedical journals with impact factors above 10 and indexed in Web of Science ($n = 176$). We also searched for journals (with any impact factor) known to publish trial protocols separately. As mandated by publication standards, we anticipated that studies published in these high-impact journals would include full protocols as annexes. Further screening of study protocols was done on the basis of how well-defined the inclusion and exclusion criteria were. All trial protocols, regardless of the trial phase, were included (Supplementary file).

Analytical perspective

The study aims to assess the inclusionary language of clinical trial protocols, with a focus on persons with disabilities. We considered the inclusion criteria defined in the protocols as the primary focus of our research analysis, because the external validity of clinical trial data relies on the study population's broad inclusivity across diverse variables such as disability.

Analytical framework

The inclusion and exclusion criteria of the protocols were thoroughly read, re-read, and reviewed by the study team for disability-related inclusions and exclusions. Seven disabilities were considered, which were categorized based on the types of disabilities specified in the RPWD Act. The disability domains were locomotor disabilities (including muscular dystrophy), blood disorders (thalassemia, hemophilia, and sickle cell disease), neurological disabilities (multiple sclerosis, chronic neurological conditions, Parkinson's disease, mental illness, and cerebral palsy), speech and language disability, hearing and vision-related disabilities (low vision, blindness, and hearing impairment, including deaf and hard of hearing), intellectual disabilities (including autism spectrum disorder), and other disability types (leprosy-cured persons, dwarfism, specific learning disabilities, and acid attack victims). The disability domains were categorized after consultations with experts involved in disability welfare and trained health experts, qualified social researchers, and a psychologist.

Three authors were involved in coding disability-related texts and phrases found in the protocols. An Excel data sheet and codebook were developed to systematically synthesize and categorize the disability-related domains in the protocols, using a predefined framework [10] (Fig. 1).

Coding process

A five-step process was used to assess patterns of disability-based exclusion in clinical trials.

i. The exclusion of persons with disabilities from the protocol was coded as "Yes" or "No." We read and re-read the texts specific to the inclusion and exclusion criteria, assessing them for terms or phrases related to different types of disability. If the protocol's research area of inquiry (disease or health condition) and the disability condition mentioned in the exclusion criteria overlapped, we coded it as "No" (for example, a study on the treatment of bleeding episodes in previously treated hemophilia that excluded current hemophilia patients, a study on participants with ataxia-telangiectasia that excluded hemoglobin C disease, sickle cell anemia, or thalassemia). However, if the health condition under study was not related to the excluded disability, we considered it as "diagnostically non-related exclusion" and coded it as "Yes."
ii. We examined whether the exclusion based on disability was attributable to a specific diagnosis or a generic description of disability conditions. Diagnostic criteria were used to determine whether exclusions were aimed at an entire disability category (e.g., "people with psychiatric illness") or a specific diagnosis (e.g., "schizophrenia"). This helped us understand whether exclusions were based on broad functional impairments or specific diagnostic conditions.
iii. We also evaluated whether any justification or reason was provided for disability-based exclusions. Regardless of the amount of justification offered for at least one disability domain, it was coded as "Yes"; if not, it was marked as "No."
iv. We examined the protocols for any mention of supportive mechanisms provided to enable persons with disabilities to participate in the study.
v. We extracted protocol-related information, such as the trial's phase, study location, and the disease or health condition focus.

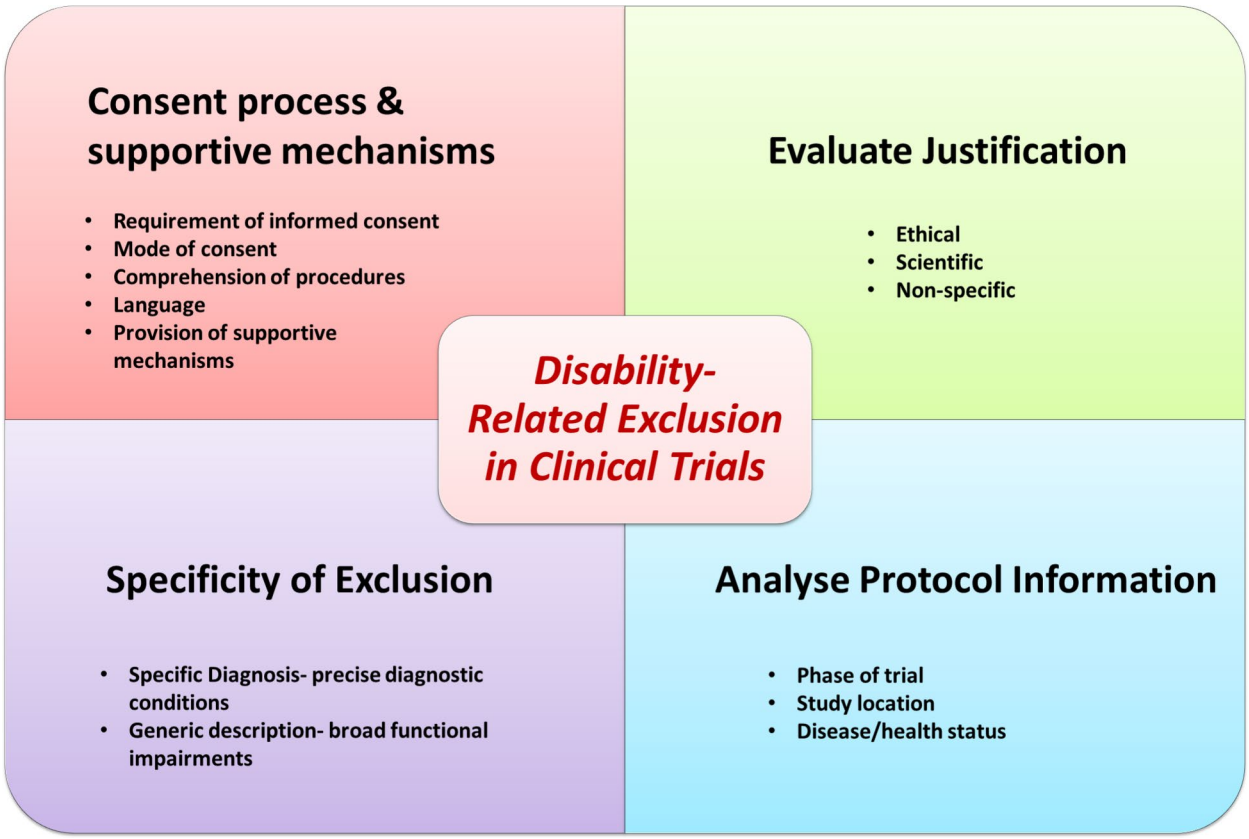

Fig. 1 Methodological framework for assessing disability-related exclusion

Three reviewers worked on the coding of the disability domains. A panel of disability experts and researchers were involved in collectively resolving the disagreements or conflicts between the reviewers and ensuring coding consistency using qualitative discussion and feedback. We calculated the proportions of different disability-related exclusions found in clinical trial protocols relevant to India, both with and without specific diagnoses and/or justifications. We also assessed exclusions based on intellectual disability separately since the consent process for study participation requires a certain level of understanding regarding procedures, risks, and benefits, which could conflate exclusions based on intellectual disability.

Furthermore, we conducted a sub-analysis of the consent requirements and reviewed the exclusion criteria related to intellectual disability, aiming to avoid conflating disability status with the ability to provide informed consent. Exclusions related to disability were categorized by country, trial phase, and disease focus, and presented as proportions, and juxtaposed with disability-related exclusions to identify trends and patterns. All quantitative analyses were conducted using Microsoft Excel.

Qualitative analysis

All protocols that potentially excluded participants due to disability-related language (in eligibility criteria) were considered for qualitative analysis. We extracted text related to the exclusion of persons with disabilities, the justifications provided for these exclusions, and the investigators' discretion in excluding participants. We used an inductive approach to analyze the text phrases reflecting disability-related justifications and discretion to understand the underlying reasons. Text patterns were retrieved and classified into disability-related themes and interpreted with input from the study team. Phrases that best reflected the themes and provided context for the quantitative findings were synthesized. Three authors conducted qualitative analysis using Microsoft Excel, and manual coding was used. Differences in coding were resolved with a panel of disability experts and researchers.

Results

Our search strategy yielded a total of 11,975 publications published between January 2017 and December 2024 from the listed data sources. From high-impact journals (impact factor > 10, $n = 176$) listed in the Web of Science,

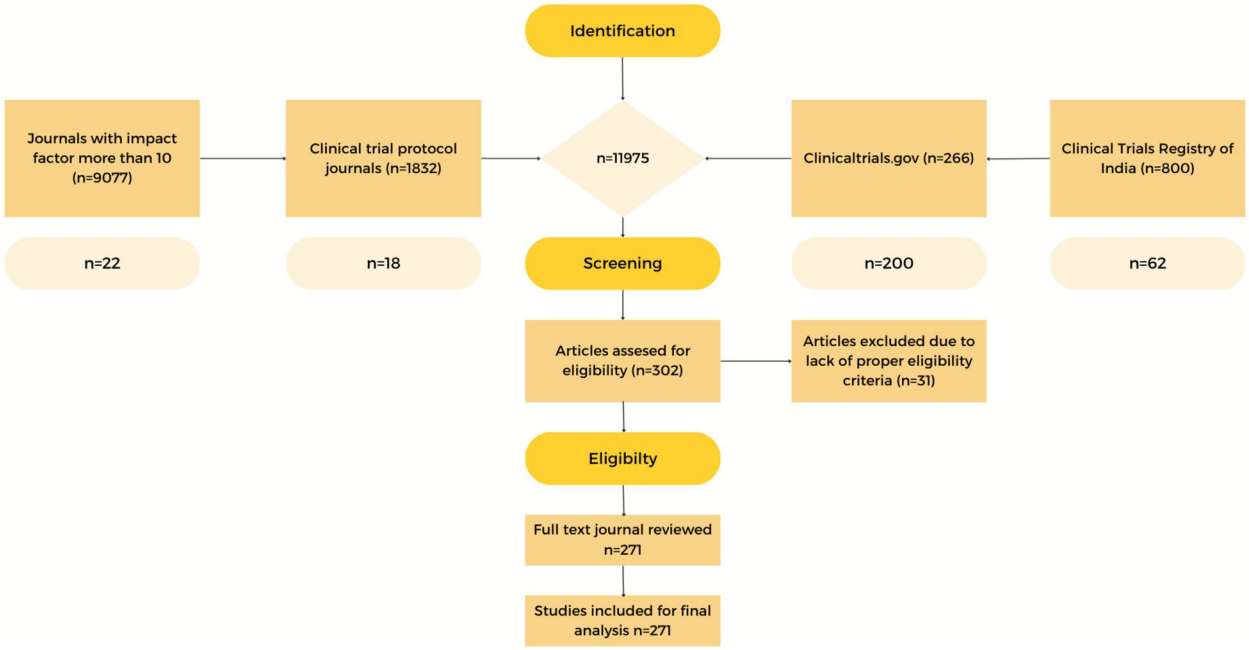

Fig. 2 Flow chart on screening and inclusion of trials

9077 articles were retrieved, of which 22 protocols pertaining to clinical trials in India were shortlisted. From medical journals known for publishing study protocols, we retrieved 1832 articles, of which 18 protocols were shortlisted. A search on ClinicalTrials.gov yielded 266 protocols relevant to biomedical research, of which 200 met our inclusion criteria. Searches in the CTRI database and PubMed yielded 800 publications, of which 62 were relevant (Fig. 2).

After eliminating redundancies and rejecting protocols with insufficient qualifying requirements in the text, 271 protocols from the final list of 302 were shortlisted. These selected protocols were categorized under seven therapeutic areas: non-communicable diseases ($n=85$, 31%), infectious/immunity-related diseases ($n=62$, 22.9%), genetic/reproductive health issues ($n=28$, 10.3%), mental health conditions ($n=17$, 6.3%), skin disorders ($n=19$, 7%), gastrointestinal and nutrition-related conditions ($n=23$, 8.5%), and critical or rare health conditions ($n=26$, 9.6%). Eleven protocols (4.1%) failed to identify a specific disease or health condition.

Of the 271 protocols, 117 (43.2%) included 126 instances of disability-related exclusions within the inclusion and exclusion criteria (Supplementary Table 1). The majority of disability-related exclusions were for neurological disabilities (69.8%), followed by speech and language-related disabilities (16.6%), blood disorders (9.5%), locomotor disabilities (3.1%), and hearing and vision-related disabilities (1%). Other disabilities, including leprosy-cured persons, dwarfism, and acid attack victims, were not excluded (Table 1). Of the 126 disability-related exclusions, our qualitative analysis of the relevant text revealed that only 11.9% were based on specific diagnoses related to the disability, while the remaining 88.3% were based on vague and broad descriptions that did not specify the condition. Exclusions for speech and language disabilities and neurological disorders were not based on specific diagnoses in 100% and 97% of cases, respectively. Contrastingly, exclusions related to blood disorders were entirely (100%) based on specific diagnoses.

Only 17.4% of protocols that excluded persons with disabilities provided some form of study-related justification; others offered none. Twenty-five percent of exclusions related to neurological disabilities included some form of justification in the protocol (Table 1). On evaluating the justifications provided for the exclusion of people with neurological disabilities (within the eligibility criteria), the reasons most commonly cited were not related to specific trial risk or mechanism but generic concerns about the "risk of study participation" or "participant safety." Other justifications included terms such as "inappropriateness for participation," "interference with study participation or compliance," and "interference with study implementation" due to neurological or associated conditions. In a few protocols, the exclusion rationale was defined as "potential influence or interference with result interpretation" or "confounding of study efficacy" associated with neurological conditions.

Table 1 Disability-based exclusions in clinical trial protocols by type, diagnosis specificity, and justification

Disability type	Exclusions based on disability % (*n*)	Exclusion without specific diagnosis % (*n*)	Exclusion without justification % (*n*)
Locomotor	3.1 (4)	3.6 (4)	3.8 (4)
Blood disorders	9.5 (12)	0.0 (00	11.5 (12)
Neurological	69.8 (88)	76.5 (85)	63.4 (66)
Speech and language	16.6 (21)	18.9 (21)	20.1 (21)
Vision/hearing	0.8 (1)	0.9 (1)	0.9 (1)
Total (*n*)	126	112	105

Note: Exclusions related to intellectual disability were assessed separately, as the consent process for study participation inherently requires a certain level of understanding regarding study procedures, risks, and benefits. This factor could confound exclusion patterns specific to intellectual disability

Persons with disabilities were excluded at a relatively higher rate in phase 3 trials (49.2%) than in phase 1 (3.1%), phase 2 (11.1%), and phase 4 trials (9.5%). The proportion of disability-related exclusions in Indian study protocols (44.4%) differed moderately from that of foreign/multicentric protocols (54.76%) (Table 2). With respect to research areas, 37.3% of the disability-related exclusions were observed in protocols related to non-communicable diseases, followed by infectious diseases or immunity-related conditions (26.2%) (Fig. 3).

An analysis of investigator discretion regarding the exclusion of persons with disabilities revealed a range of underlying reasons. Of the 126 disability-related exclusions identified in the protocols, 76.9% ($n=97$) included some form of investigator discretion. From these, we identified five broad categories of discretion, each offering varying levels of latitude for investigators to exclude persons with different disabilities. Most forms of discretion were based on the perceived vulnerability of participants due to specific underlying medical conditions that could affect study participation. In some cases, blanket terms were used to describe medical conditions, allowing a broader scope for exclusion. Some exclusions were also based on vague conditions that were neither medical nor grounded in specific criteria. Certain forms of discretion positioned investigators as "surrogate decision-makers," enabling subjective judgments about participant exclusion. Additionally, the perceived ability to participate in the study (e.g., to comply with or adhere to study requirements) was also used as a discretionary criterion in some studies (Table 3).

Textual analysis of the consent process described in the protocols revealed that 46 out of 271 protocols (16.9%) did not mention any consenting process within their inclusion or exclusion criteria. Among the remaining 225 protocols, 30 (11.1%) referred to consent merely as a requirement for study inclusion, without detailing specific procedures or requirements. The remaining 195 protocols included some form of consent procedure, such as written, verbal, or oral consent, thumb impression, or parental assent. Of these, 179 protocols (66.0%) specifically required written or verbally informed consent. Notably, 16 protocols (5.9%) explicitly required participants to possess a relatively high level of comprehension regarding study purpose, procedures, risks, side effects, and regulatory requirements. This requirement may implicitly be a barrier for individuals with intellectual disabilities, unless appropriate support mechanisms are provided. However, upon review, many protocols did not include any form of provisions for enabling supported decision-making (Supplementary Table 2).

Discussion

This study attempted to assess their inclusion of persons with disabilities in clinical research pertaining to India using a broader social model of disability. Our findings show that one-third of clinical trial protocols (40%) had vague or non-specific language in the exclusion criteria text, which could potentially exclude persons with disabilities from participating in clinical research. Most of the protocols did not describe any supportive mechanisms to assist persons with disabilities during the recruitment. Affirmation of supportive mechanisms within the eligibility criteria text will thus be essential to avoid exclusion by default. Half of the disability-related exclusion text was observed in protocols of phase 3 trials, compared to phase 1 and 2 trials. This could be attributed to the inclusion needs of early phase trials restricted mostly toward healthy volunteers.

People with neurological and mental health conditions, along with speech and language disabilities, were most frequently excluded by the language used in the eligibility criteria, followed by those with blood disorders. Notably, the exclusion rates for people with neurological and mental disorders were disproportionately high, reflecting global patterns documented in prior studies [10,

Table 2 Distribution of studies by disability type, study location, and research phase

Disability type	Total cases	Phase 1 % (*n*)	Phase 2 % (*n*)	Phase 3 % (*n*)	Phase 4 % (*n*)	Phase 2 and 3% (*n*)	Phase 1 and 2 % (*n*)	India % (*n*)	Multicentric % (*n*)	NA % (*n*)
Locomotor	4	0.0 (0)	25.0 (1)	25.0 (1)	0.0 (0)	25.0 (1)	0.0 (0)	75.0 (3)	25.0 (1)	0.0 (0)
Blood disorder	12	16.6 (2)	16.6 (2)	58.3 (7)	0.0 (0)	8.3 (1)	0.0 (0)	41.6 (5)	50.0 (6)	8.3 (1)
Neurological	88	2.2 (2)	12.5 (11)	51.1 (45)	10.2 (10)	4.5 (4)	2.2 (2)	39.7 (35)	60.2 (53)	0.0 (0)
Speech and language	21	0.0 (0)	0.0 (0)	42.8 (9)	9.5 (2)	0.0 (0)	4.7 (1)	57.1 (12)	42.8 (9)	0.0 (0)
Vision/hearing	1	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	100 (1)	0.0 (0)	0.0 (0)

Note: Exclusions related to intellectual disability were assessed separately, as the consent process for study participation inherently requires a certain level of understanding regarding study procedures, risks, and benefits. This factor could confound exclusion patterns specific to intellectual disability

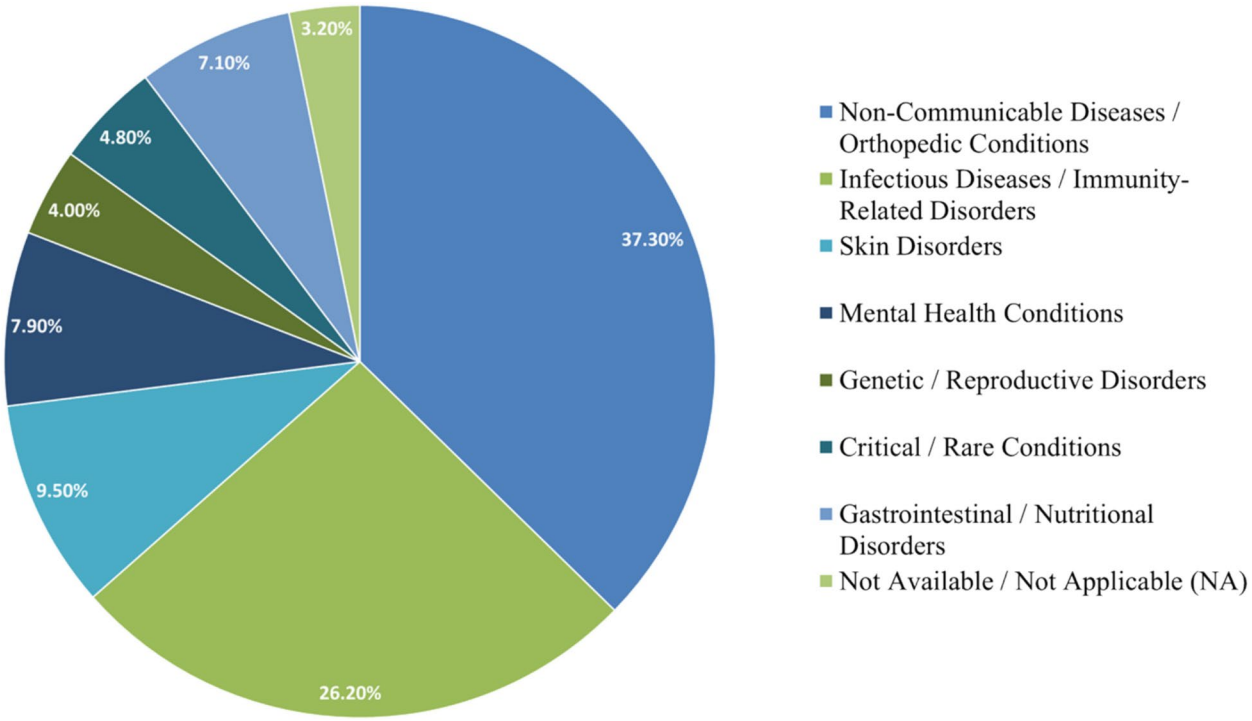

Fig. 3 Categorization of clinical trials based on the type of health condition

11]. Conversely, exclusions based on locomotor, visual, and hearing disabilities were comparatively rare, especially when assessed against protocols from developed countries.

Most exclusions in eligibility criteria are based on neurological disabilities that lacked specific diagnostic criteria and were instead framed using broad, non-specific terms spanning multiple disability domains. This ambiguity in exclusionary language may provide investigators with considerable discretion in excluding individuals with neurological or mental health conditions. For instance, the term "psychiatric disorders" was frequently cited as an exclusion criterion, despite the absence of a standard definition. The term encompasses a wide spectrum of conditions ranging from mild to severe including highly prevalent mental health conditions in India such as alcohol use disorder and clinical depression. The use of such vague criteria suggests that, within the Indian clinical trial landscape, the presence of any mental health condition, regardless of its severity or specific diagnosis, is potentially viewed as a barrier to participation [4].

Similarly, exclusions for speech and language disabilities were predominantly based on generic descriptions of functional limitations in communication skills and language proficiency [12]. Such imprecisely defined eligibility criteria could inadvertently exclude individuals facing any form of language barrier. Our analysis revealed that intellectual disability was not explicitly cited in exclusion criteria across protocols. However, a number of protocols required participants to demonstrate an understanding of study procedures without specifying any supportive measures to assist individuals with intellectual, speech, or language disabilities. To ensure equitable participation, protocols could proactively outline an accessible consent process, including multiple modes of consent (e.g., multilingual, visual, audio, video, and Braille), supported decision-making (involving family or friends), and adequate time, space, and tools to facilitate the consent process and comprehension. Such provisions are essential to uphold ethical standards and ensure the inclusion of persons with disabilities in clinical research.

The absence of explicit references to supports and accommodations in study protocols may contribute to the potential exclusion of persons with disabilities, as those responsible for screening participants may assume such measures are unnecessary. Our analysis found that the majority of studies did not provide any justification for the exclusion of persons with disabilities [13, 14]. Where justifications were offered, they were often ambiguous and lacked scientific or ethical grounding. Among the most frequently cited reasons were concerns related to participant safety or risk, yet these were rarely defined or substantiated. Some investigators also justified exclusions based on factors such as "study implementation,"

Table 3 Categories of investigator discretion and their interpretive rationale for participant exclusion

Investigator discretion as in protocol	Interpretive rationale
Other severe acute or chronic medical or psychiatric conditions, including recent (within the past year) or active suicidal ideation or behavior, or laboratory abnormality that may increase the risk associated with study participation or investigational product administration or may interfere with the interpretation of study results and, in the judgment of the investigator, would make the participant inappropriate for entry into this study	Perceived vulnerability of the participants due to the underlying specific medical conditions
Subject has a clinically significant medical, psychiatric, or cognitive illness, or recreational drug/alcohol use that, in the opinion of the investigator, would affect the subject's safety or compliance	Perceived vulnerability of the participants due to the underlying non-specific blanket medical terms
In the opinion of the investigator, there are other issues that would interfere with compliance with the study requirements and completion of evaluations required for this study	Perceived vulnerability of the participants due to the underlying conditions, which were neither medical nor any other specific criteria
Any other condition that, in the opinion of the investigator, would jeopardize the safety or rights of a volunteer participating in the trial or would render the subject unable to comply with the protocol	Perceived vulnerability of the participants due to the underlying conditions, which were neither medical nor any other specific criteria
Judgment by the investigator that the patient should not participate in the study if the patient is unlikely to comply with study procedures, restrictions, and requirements	Surrogate decision by the investigator
Subjects' parent(s)/LAR(s) who, in the opinion of the investigator, can and will comply with the requirements of the protocol (e.g., completion of the diary cards, return for follow-up visits)	Perceived ability to participate in the study (to comply or adhere to)

"interference with result interpretation," or "confounding of study efficacy."

Therefore, supportive accommodation for persons with disabilities must extend beyond the consenting phase and continue throughout the entire study process, including trial procedures, implementation, and data collection. Measures such as transportation support, assisted data collection, alternative test formats, virtual visits/virtual participation options, sign language interpretation, and accessible study materials can help uphold the individuality, agency, autonomy, and dignity of participants with disabilities. These measures play a critical role in engaging meaningful participation and ensuring that research environments are disability-friendly.

Most protocols relied heavily on the investigator's discretion to exclude persons with disabilities. Investigators often used vague medical terminology that granted broad leeway to determine eligibility. For instance, while certain psychiatric conditions, such as schizophrenia or severe depression, would have a justifiable impact on study participation, the use of broad phrases like "any neurological or psychiatric disorder" enabled the exclusion of individuals even with mild mental health conditions. Additionally, some of the protocols also allowed investigators to exclude participants based on non-medical criteria, further expanding the scope for subjective judgment and potentially reinforcing implicit biases. Such investigator's discretion should be interpreted from a biased perspective of recruiters. Clinical trials are often resource-intensive and time-consuming which makes the investigators prone to selection bias [15].

Such broad criteria potentially encompassing functional impairments, socio-economic status, or gender can result in trials that are exclusive and unrepresentative of persons with disabilities and other marginalized groups [11, 16, 17]. Surprisingly, a few protocols exhibited even higher levels of investigator discretion, which we refer to as surrogate decision-making on behalf of participants. These protocols included language such as "judgment of the investigator," effectively diminishing participant agency. Although such instances were relatively few, they underscore the need for closer scrutiny of ambiguous, unscientific, and potentially exclusionary language in clinical trial protocols.

This review underscores that the use of vague or open-ended language in clinical trial protocol's exclusion criteria may inadvertently result in the exclusion of persons with disabilities, irrespective of the investigators' specific intent. To mitigate this risk, inclusion and exclusion criteria in clinical trial protocols must be critically assessed for the use of ambiguous language, such as "etc." or "any other conditions," which lacks specificity and invites subjective interpretation. Ethics and scientific committees must establish clear standards for the precise, appropriate, and inclusive language in eligibility criteria to promote equitable participation and uphold the integrity of clinical research.

Overall, the language used in defining the eligibility criteria in clinical trial protocols must evolve from

an exclusionary perspective and language to one that actively fosters inclusive research participation, particularly for persons with disabilities [4, 11, 12]. As clinical trials become increasingly expensive and time-constrained, investigators may tend to enroll participants who are most likely to contribute to sample size goals within limited timeframes. This pragmatic selection approach, when combined with the limited resources for providing necessary accommodation and the absence of robust ethical oversight, creates significant barriers to the inclusion of persons with disabilities. Addressing these systematic challenges requires deliberate structural reforms [18, 19]. Inclusion of persons with disabilities in research committees could be a constructive step toward promoting their representation in clinical research [20]. Furthermore, protocol language that is ambiguous, open-ended, or subject to individual interpretation must be critically reviewed. Every eligibility criterion should be accompanied by a clear, scientifically or ethically justified rationale to ensure transparency, fairness, and accountability in participant selection.

Clinical trial registries could adopt and enforce guidelines that mandate the use of inclusive language in all registered protocols. Biomedical research institutions and bodies which are involved in formulating biomedical research guidelines could take active steps to address the adequate representation of diverse populations in clinical research even at the stage of protocol development. The National Ethical Guidelines for Biomedical and Health Research, 2017 involving human participants could add specific clauses to promote the inclusionary language toward persons with disabilities in clinical trials and other health research studies in India. Inclusivity guidelines must also consider other inherent factors like age, gender, geographical, and socio-economic status which may mediate exclusion through disability status. Ensuring such inclusion is not merely a matter of regulatory compliance but an ethical imperative. Excluding persons with disabilities from research by default restricts their access to the potential benefits of participation, undermines principles of equity, and compromises both generalizability and societal relevance of research outcomes.

Limitations

This study has few limitations. First, we focused only on language pertaining to the eligibility criteria of clinical trial protocols in India from January 2017 onward; this could have led to missing of supports/accommodations that could have been documented elsewhere in protocols. Because of this, we might have overlooked pertinent research that was released prior to 2017 or those not indexed in the selected sources. We limited our search to biomedical journals with an impact factor greater than 10 indexed in the Web of Science; however, we included low-impact journals known to publish trial protocols. Second, the possibility of underreporting in the coded eligibility criteria cannot be ruled out. In few (3) cases, for unknown reasons, one or more eligibility criteria were censored (i.e., blacked out) in the publicly available study protocols. Our study findings must be interpreted only in the context of the language which could potentially exclude persons with disabilities in trials and may not reflect or measure actual research participation.

Conclusion

Stakeholders involved in clinical trials have a critical responsibility to ensure that persons with disabilities are not excluded through non-inclusive language or criteria when defining eligibility. It is essential to sensitize the investigators to the principles of non-exclusionary language, reasonable accommodation, and supportive measures. This may include use of accessibility and mobility devices, audio-visual aids, and sign language interpreters to support persons with disabilities during the research process. Systemic challenges such as limited awareness of legal and ethical obligations toward persons with disabilities, inadequate institutional advocacy for research equity, the absence of standardized guidelines and best practices for disability-inclusive research and its language, and under-representation of persons with disabilities on research oversight committees could be addressed.

Supplementary Information

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Supplementary Material 1.
Supplementary Material 2.
Supplementary Material 3.
Supplementary Material 4.

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Authors' contributions

This study was conceptualized by KN, MM, AVJ, and YS. The original draft of the manuscript was written by KN, AVJ, SM, and NR and critical revisions for important intellectual content were conducted by all authors. All authors had full access to all the data in the study, and the corresponding author had final responsibility for the decision to submit for publication.

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Data availability
The paper contains the actual research findings and further inquiries can be directed to the corresponding author.

Declarations

Ethics approval and consent to participate
This study was performed based on secondary data; the study did not require ethics approval.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

Author details
[1]Department of Socio-Behavioural Research, ICMR-National Institute for Research in Tuberculosis, Chennai, Tamil Nadu, India. [2]Academy of Scientific & Innovative Research, CSIR-HRDC Campus, Postal Staff College Area, Sector 19, Kamla Nehru Nagar, Ghaziabad, Uttar Pradesh, India. [3]Department of Health Economics, ICMR-National Institute for Research in Tuberculosis, Mayor Sathyamoorthy Road, Chetpet, Chennai, Tamil Nadu 600031, India. [4]SRM School of Public Health, SRM Institute of Science and Technology, Kattankulathur, Tamil Nadu, India. [5]Indian Institute of Management, Bangalore, Karnataka, India. [6]Department of Biochemistry, ICMR-National Institute for Research in Tuberculosis, Chennai, Tamil Nadu, India. [7]Department of Bacteriology, ICMR-National Institute for Research in Tuberculosis, Chennai, Tamil Nadu, India.

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