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Review

Enablers and barriers to participation in vaccine trials: a narrative synthesis

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ABSTRACT

Objective: To synthesise evidence on barriers and enablers to participation in vaccine clinical trials (2010–2024), with a focus on underserved populations, to support the design of more inclusive vaccine trials.
Materials and methods: A rapid narrative review was conducted using PubMed, identifying 145 peer-reviewed studies published between 2010 and 2024. Data extraction captured study design, participant population, and factors influencing trial enrolment. Findings were thematically analysed, with subgroup synthesis for underserved populations, including pregnant individuals, parents, ethnic minority groups, and LGBTQ+ communities.
Results: Analysis of the 145 included studies identified five themes for enablers and four themes for barriers. Safety concerns were the most frequent deterrent, particularly for proxy decision-makers such as parents and pregnant participants. Institutional mistrust and misinformation were consistent barriers, with the COVID-19 pandemic heightening distrust of governments and pharmaceutical companies and amplifying misinformation through social media. Additional barriers included sociocultural expectations and logistical burdens, particularly in low-resource settings. Enrolment was enabled by altruistic motivations, perceived personal or community benefit, transparent safety communication, logistical ease, and community engagement. Community-led engagement, culturally concordant staff, and proportionate incentives were consistently associated with improved enrolment.
Conclusions: Vaccine trial participation is shaped by a dynamic risk–benefit calculus that manifests differently across populations. Addressing inequities requires sustained community partnerships, culturally competent trial design, proportionate material support, and proactive communication strategies to counter misinformation. These findings provide actionable guidance for designing more inclusive vaccine trials.

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1. Introduction

Clinical trials are necessary for establishing the safety, immunogenicity and efficacy of vaccines, which are estimated to prevent 2 million deaths a year from infectious diseases [1]. The rapid development and deployment of COVID-19 vaccines demonstrated the significant public health impact achievable through successful vaccine trials, contributing to reduced mortality and accelerating pandemic control [2,3]. Similar public health benefits have been achieved in the past through widespread vaccination against diseases like measles, polio, and rubella, as well as the global eradication of smallpox [4]. Yet many high-burden infections remain without any licensed vaccines and global vaccine coverage inequity persists [1,5,6].

Many clinical trials of investigative drugs, including vaccines, experience challenges in meeting initial enrollment targets and timelines [7]. Early phase clinical trials typically enrol healthy volunteers to ensure new vaccines are safe for use. Recruitment of healthy volunteers who are free of the target disease poses unique challenges, as these individuals have different motivations compared to patients seeking a clinical intervention or treatment for a medical condition [8]. Participant dropout after enrolment and during follow-up can compound recruitment shortfalls and trial findings, particularly in larger, later-phase vaccine clinical trials [7]. Failure to reach a specified sample size diminishes the statistical validity of trial endpoints, delays vaccine licensure, increases costs, and reduces public health benefits [9,10]. The factors influencing recruitment are multifaceted and vary across countries and trials, encompassing individual, interpersonal, and structural factors [8].

National vaccine programmes target risk-defined groups rather than individuals by sociodemographic characteristics. Priority groups commonly include age cohorts (for example, pertussis vaccination in pregnant women and infants), occupational exposure (for example, rabies vaccination in bat handlers), underlying health conditions (for example, influenza and pneumococcal vaccination in immunocompromised individuals), or travel (for example, yellow fever vaccination in individuals travelling to endemic countries). However, certain demographic groups, such as ethnic minorities, socioeconomically disadvantaged populations, and LGBTQ+ individuals, are consistently underrepresented in vaccine trials even though they may also fall into an 'at risk' category for a given disease [8,11]. These 'underserved populations' are defined as groups whose inclusion in research is disproportionately low relative to their healthcare needs or disease burden [11]. This category also includes women of childbearing potential, who are often excluded from early-phase trials due to the absence of teratogenicity data from preclinical studies [11,12]. Exclusion of underserved populations limits the generalisability of trial findings [13,14], erodes trust in research among these communities [15], and may contribute to lower vaccine uptake and worsening health disparities [15].

Previous reviews of vaccine trial participation barriers and enablers have been largely disease- or population-specific [16–18]. This narrative review synthesises evidence from 2010 to 2024 to develop a cross-cutting thematic framework of factors influencing vaccine trial participation and to examine how these factors manifest in underserved populations.

2. Materials and methods

2.1. Search strategy

A structured search was conducted in PubMed on 8 November 2024 to identify studies exploring factors influencing participation in vaccine trials. The search strategy combined terms related to vaccine research (e.g. 'vaccine trial', 'vaccine research') with terms relating to trial participation (e.g. 'participation', 'willingness') and attitudinal factors (e.g. 'barriers', 'enablers', 'hesitancy') (Supplementary Table S1). The search string was developed collaboratively with the Patient and Public Involvement and Engagement (PPIE) panel of the NISEC II programme to ensure the relevance and inclusivity of search terms. This review was informed by Cochrane Rapid Review guidance [19], with adaptations reflecting time and resource constraints.

2.2. Eligibility criteria

Studies were eligible for inclusion if they met the following criteria:

- Investigated vaccines targeting infectious diseases.
- Focused on vaccine trial participation, including barriers, enablers, or attitudes.
- Included patients, families, carers, healthcare professionals, or members of the general public, across any age group.
- Reported on real or hypothetical vaccine trials.
- Written in English.
- Published in peer-reviewed journals.

Opinion and editorial pieces were included as they provided relevant conceptual or contextual insights into vaccine trial participation.

Studies published prior to 2010 were excluded to ensure relevance to contemporary vaccine research and social contexts.

2.3. Screening and selection process

All search results were imported into Excel. Titles and abstracts were screened against the eligibility criteria by a single reviewer. Any articles that were unclear or potentially eligible were discussed with the wider study team before final inclusion decisions were made. Full-text review was then conducted on selected articles. Due to the scope and timeline of the project, duplicate screening and formal critical appraisal were not performed.

2.4. Data extraction

Data extraction was carried out by a single reviewer for each study, with the included studies divided among three reviewers. The standardised form used for data extraction included key study characteristics (design, setting, population, and vaccine type), as well as factors associated with willingness or reluctance to participate, classified as barriers or enablers. Populations of interest, including ethnic minority groups, pregnant participants, and other underserved communities, were prespecified based on existing evidence of underrepresentation in clinical research [11]. To ensure consistency, 15 % of extracted studies were independently cross-checked by a second reviewer, with discrepancies resolved by discussion with a third reviewer.

2.5. Data synthesis

Given the heterogeneity of the literature, which included qualitative studies, quantitative surveys, reviews, and opinion-based articles, a narrative synthesis approach was adopted. Thematic categories were developed inductively from the data and reviewed with the lay PPIE panel. A subgroup analysis characterised theme expression in underserved populations (pregnant and postpartum women, parents and guardians, ethnic-minority communities, and LGBTQ+ individuals). Parents and guardians were included because they are decision-makers for children, who are recognised as an underserved group in clinical research [11]. Studies were also coded by publication year (pre- vs post-COVID) and by geographic region (Global North vs Global South) to support narrative comparison of contextual differences. Sex and gender dimensions were assessed during data extraction, including whether studies reported sex-disaggregated findings and whether gendered roles influenced participation; however, most studies did not report disaggregated analyses, limiting further synthesis.

2.6. Public involvement

This review was conducted with input from the Public and Patient Involvement and Engagement (PPIE) panel of the NISEC Consortium. The panel comprised ten lay members (three men and seven women) and eight PPIE Leads from four NISEC national Research Centres and the Centre for Ethnic Health Research, University of Leicester.

The lay members reflected diverse demographic, socio-economic, religious, and cultural backgrounds, and represented the following ethnic groups: White ($n = 1$), Black African/Caribbean (n = 1), South Asian (Indian, Pakistani, Punjabi; $n = 5$), Latino (n = 1), Polish (n = 1), and mixed ethnicity (n = 1). Their ages ranged from the early 20s to the late 60s. Members were based across multiple UK regions, including Leicester, Coventry, Bristol, Southampton, London, Oxford, and Wessex, reflecting a wide range of socio-economic contexts.

Panel members collaborated with the study team through online meetings to refine the review focus, develop search terms, sense-check thematic findings, and provide feedback on manuscript drafts.

3. Results

The database search generated 977 records. Following title and abstract screening, 167 studies were retained for full-text review. After applying the eligibility criteria, a total of 145 studies were included in the final synthesis (Fig. 1).

3.1. Study characteristics

The included literature encompassed a wide variety of study types, participant populations, and geographical regions. Studies ranged from qualitative interviews and focus groups to quantitative surveys, as well as reviews, editorials, and opinion pieces. The characteristics of the included studies are summarized in Table 1. Full details of individual study characteristics are provided in Supplementary Table S2.

A substantial proportion of included publications focused on HIV vaccine trials (63/145; 30 %). These were primarily conducted in sub-Saharan Africa ($n = 45$), with additional studies from North America, Europe, and Asia. Participants were predominantly adults aged 18–49 years, although several studies also included adolescents or young adults. Most cohorts comprised groups at elevated risk of HIV infection, including men who have sex with men, female sex workers, transgender women, and people who use drugs.

3.2. Thematic findings

Analysis of the 145 included studies identified five themes for enablers and four themes for barriers (Table 2). Each theme is summarized below. Full citation lists for studies contributing to each theme are provided in Supplementary Table S3.

3.2.1. Enablers

3.2.1.1. Personal benefits. Direct personal benefits were a prominent enabler across studies, including perceived protection, access to

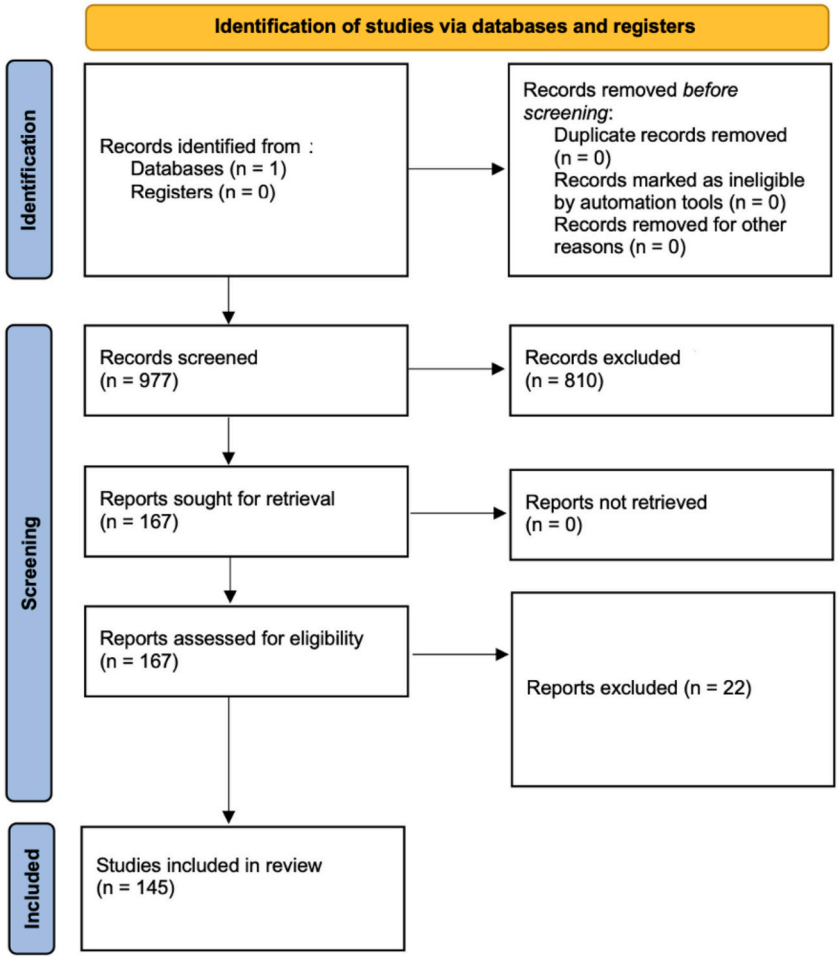

Fig. 1. PRISMA 2020 flow diagram for study selection.

Table 1
Characteristics of the 145 studies included, presented by study design, population focus*, geographic region, and vaccine type*. Values are shown as the total number of studies, with the number of hypothetical trial studies in brackets.

Characteristic	Number of Studies (Hypothetical studies)
Study Type	
Qualitative	64 (21)
Quantitative (surveys)	57 (35)
Clinical trial	8 (1)
Opinion/Editorial/Review	16 (1)
Population Focus* (if multiple populations, studies are counted multiple times in each category)	
General population	52 (15)
Pregnant/postpartum women	14 (7)
Parents and other caregivers	14 (4)
Children and adolescents (<18y)	9 (5)
Men who have sex with men (MSM)	11 (6)
Transgender people	5 (2)
Sex workers	10 (5)
Racial/ethnic minority groups	10 (4)
People who use drugs (PWUD)	7 (6)
Patients with specific medical conditions	9 (4)
Healthcare professionals	8 (7)
Law enforcement and public safety staff	5 (1)
Geographic Region	
North America	49 (16)
Europe	27 (11)
Asia	11 (4)
Africa	45 (13)
Other/Multiple regions	4 (3)
Vaccine Type*	
COVID-19	18 (8)
HIV	63 (30)
General (non-specific or multi-vaccine context)	21 (7)
Ebola	8 (1)
Malaria	4 (0)
TB	3 (1)
Hepatitis C	4 (3)
HPV	3 (2)
Group B Streptococcus (GBS)	3 (3)
Influenza	5 (1)

* Categories with fewer than three studies are not shown in the table.

Table 2
Enablers and barriers to vaccine trial participation identified across the 145 included studies. Values are shown as the total number of studies, with the number of hypothetical trial scenario studies in brackets.

Theme	Number of studies (Hypothetical studies)
Altruism	33 (11)
Personal benefits	32 (15)
Community engagement	13 (3)
Perceived safety	11 (7)
Logistical ease	9 (1)
Institutional distrust and misinformation	43 (14)
Safety concerns	32 (18)
Sociocultural and religious norms	19 (8)
Logistical burdens	19 (7)

healthcare, and financial or material incentives. Perceived protection from disease was frequently cited by participants and extended to close contacts, such as family members, particularly in high risk settings [20,21]. Access to healthcare included routine check-ups [21–23], increased health and disease knowledge [24,25], and short-term insurance [20]. Financial or material incentives such as cash stipends and food packages were frequently cited, particularly in low-resource settings [20,22,26]. Conversely, lack of compensation was identified as a barrier to participation, with participants stating that compensation should match the burden of a trial [23,27,28].

3.2.1.2. Altruism. Participants across studies were consistently driven by altruistic motivations. Participants expressed a desire to protect their local communities [20,23,29], particularly when those communities were at increased risk of the disease targeted by the vaccine trial, such as people who inject drugs or men who have sex with men (MSM) at risk of blood-borne infections [26,30]. Some participants also described a broader commitment to global health [23,31], particularly in the context of pandemics and the aim of returning to pre-pandemic conditions [32–34]. Furthermore, participants were motivated by the opportunity to advance medical science through contributing to vaccine development [31]. Healthcare workers often described participation as part of their professional obligation to promote public health [20,23,33].

3.2.1.3. Community engagement. Community engagement, defined as the continuous and bidirectional sharing of information and resources between scientific and community partners [35], was widely regarded as integral to recruiting diverse participants and providing culturally competent trial designs. Participants valued early and ongoing dialogue between researchers and community leaders, which was seen to build credibility, promote transparency, and improve recruitment [20,22,36]. Participants emphasised the value of engaging with minority-led organisations and decision-making structures [37,38], and highlighted the role of representative healthcare staff in promoting cultural competency [29,39].

3.2.1.4. Perceived safety. Perceived safety of the vaccine was identified as a key enabler for participation in vaccine trials. This was reinforced by transparent communication and educational strategies that targeted participants' specific concerns and levels of health literacy [32,39,40]. Effective messaging included normalising common side effects, explaining the rationale behind accelerated vaccine development, and emphasising adherence to standard safety protocols despite political pressures [32,41]. Accounts from previous trial participants enhanced confidence in the research process [20].

3.2.1.5. Logistical ease. Participants reported that their enrolment and retention would be improved by steps taken to increase convenience and minimise logistical burdens. Travel barriers could be offset through home visits by study staff and providers, reimbursements of travel costs, and provision of transport [20,22]. Time demand on participants could be reduced by remote data collection and fewer total procedures [28,42].

3.2.2. Barriers

3.2.2.1. Safety concerns. Safety considerations were the most frequently cited barrier to vaccine trial enrolment [43,44]. Participants were concerned about both short-term reactions, such as injection-site pain, headaches, and nausea, and unknown long-term consequences, including disability or death [23,45]. Side effects considered minor by researchers, such as headaches or low fever, were viewed as unacceptable by many participants [46,47]. Anxiety about safety concerns was heightened when a vaccine was perceived as new or experimental [48,49]. Safety concerns were exacerbated by high-profile media reports of vaccine harms [50].

3.2.2.2. Institutional distrust and misinformation. Distrust of researchers, government authorities, and the pharmaceutical industry was a key deterrent to vaccine trial participation [18,24]. Participants suspected that researchers were withholding information or not being transparent about vaccine safety, particularly when researchers themselves did not

receive the vaccines [51]. The lack of trust was compounded by inadequate communication: many participants were unclear about trial procedures, feared hidden harms, or misinterpreted minor side effects as signs of serious danger [40,47]. Participants were also concerned about broader political and commercial motives behind vaccine trials, especially in relation to COVID-19 vaccines [34,46]. In Global South contexts, fears of intentional harm were more prominent, such as beliefs that vaccine trials were a means of disease introduction or population control targeting marginalised groups [22,23].

3.2.2.3. Sociocultural and religious norms. Sociocultural and religious norms frequently influenced decisions about vaccine trial participation. Moral and religious objections were particularly common in HIV vaccine trials, which were perceived as linked to unsafe sexual behaviour [37,52]. Decision-making was often collective rather than individual; for example, women deferred to male family members or partners [53], and community leaders were seen as trusted sources whose approval was essential [22]. Participants perceived researchers as insufficiently aware of these sociocultural dynamics, which was cited as a barrier to recruitment, particularly among ethnic minority and marginalised groups [25,29,35].

Conflicts with sociocultural or religious expectations often led to concerns around stigma and discrimination, particularly in HIV vaccine trials [36,37,54]. Participants were concerned that trial participation could imply high-risk behaviour and prompt judgment from others about HIV status or sexual behaviours [22,39]. Concerns about vaccine-induced seropositivity further contributed to fears of being misidentified as HIV-positive [54,55]. Reported consequences included relationship discord, loss of economic support, and the risk of violence [51,55,56].

3.2.2.4. Logistical burdens. Extensive procedural demands were repeatedly identified as a barrier to enrolment and retention. Participants cited insufficient time for frequent clinic appointments, lengthy follow-up schedules, and travel to the vaccine trial centres [20,22,23,43]. Delays in procedures once on-site were reported as amplifying frustration [21]. Repeated or large-volume blood draws were described as painful, vein-damaging, and time-intensive [57]. Additional practical burdens included travel distance and cost [58], the need for official identification documents [59], and remote enrolment via email that reduced comprehension and satisfaction [60]. Behavioural requirements, including continuous condom use, mandated contraception, or strict prohibition on pregnancy, were noted as deterrents in HIV vaccine studies or in trials recruiting volunteers of reproductive age [27,41].

3.3. Population-specific patterns in underserved groups

Pregnant and postpartum participants.

Safety concerns were the predominant barrier among pregnant participants, who prioritised foetal safety over their own, citing miscarriage, congenital abnormalities, and other potential harms as primary barriers [49,61]. Conversely, participants who agreed to enrol in clinical trials were often motivated by a belief that the vaccine would protect their foetus [61,62], or due to anticipated access to enhanced antenatal care during the trial [63]. Familiarity and trust in healthcare professionals also shaped decision-making; many participants preferred to be recruited by their own midwife rather than unfamiliar clinicians [29,61].

Ethnic minority communities.

Among ethnic minority communities in Global North settings, distrust towards researchers was rooted in historical research abuses, particularly among Black populations [25,64]. This distrust was reinforced by contemporary experiences of discrimination and marginalisation within healthcare settings [25,64,65]. Concerns were mitigated when culturally concordant clinicians or faith/community leaders led engagement and when materials were linguistically tailored [66,67].

Parents and guardians.

In studies requiring parental consent for paediatric participation, altruism was reported as an enabler, but was often outweighed by heightened safety concerns for the child [22,68]. Safety concerns were around severe illness and long-term developmental effects, and viewing repeated blood draws as unnecessary and harmful [21,22,48]. Tailored educational support and trusted paediatric clinicians facilitated enrolment [38,69].

LGBTQ+ groups (MSM and transgender women).

Anticipated stigma, fear of vaccine-induced seropositivity, and prior healthcare discrimination were reported barriers among LGBTQ+ groups [39,70,71]. Among MSM in HIV vaccine trials, concerns included behavioural disinhibition due to perceived protection from HIV, potentially leading to reduced condom use and riskier sexual practices [70,71]. Facilitators of participation included peer-led recruitment, inclusive language, LGBTQ+ staff, and testimonials from previous participants [30,71,72].

4. Discussion

This review synthesised data from 145 studies published up to November 2024, examining determinants of participation in vaccine trials. Decisions to enrol were framed by a risk–benefit calculus, incorporating considerations of safety, personal and collective benefits, logistical feasibility, and trust in institutions. Many of these determinants functioned as both enablers and barriers depending on context, and several themes interacted and overlapped with one another. This synthesis highlights shared determinants of participation while also revealing how these factors manifest differently across underserved groups.

Altruism and perceived personal benefit emerged as complementary motivations for trial participation, particularly in settings with a high burden of the disease being targeted by the vaccine [9,32]. In low-resource settings, financial and material incentives helped to offset participation costs and time. However, ethical considerations require that such incentives remain proportionate to the study burden to avoid exploitation of vulnerable participants [73]. Excessive payments have been shown to leave participants feeling unable to decline enrolment despite safety concerns [74]. By contrast, proportionate material support has facilitated recruitment; for example, access to free, high-quality healthcare, as reported in a paediatric malaria vaccine trial, was reported as an appropriate and valued motivator for enrolment [75]. Both inadequate and excessive incentives can undermine inclusivity in trials, highlighting the need for clearer international guidelines to distinguish appropriate support from undue inducement [76]. Given the difficulties recruiting underserved populations to large Phase 3 trials, where financial compensation is not routine, further research is required to clarify the role of financial incentives in enabling or deterring participation.

Safety was both a facilitator and a deterrent to participation, frequently overriding other considerations. Proxy decision makers, such as parents or pregnant individuals, framed risk primarily around the vulnerability of dependents, which amplified hesitancy even when participation offered personal or community benefits [49,61]. Addressing this protective framing requires tailored communication that clearly distinguishes risks to participants from those posed to their dependents.

The COVID-19 pandemic marked a distinct shift in perceptions of vaccine trials. While pre-pandemic mistrust was often rooted in historical and structural inequities among marginalised groups [25,64], post-pandemic studies demonstrated a widespread distrust directed towards pharmaceutical companies, government involvement, and perceived political exploitation [34,46,65]. These concerns were amplified by unfamiliarity with novel vaccine platforms, accelerated development

timelines, and uncertainty about long-term safety [27,66,77]. Participants increasingly reported scepticism towards official narratives, turning instead to social media as a primary source of health information [65,77]. Within social media networks, misinformation spread rapidly, with unverified claims reframing routine adverse event data as evidence of serious harm [78,79]. Evidence from randomised trials indicate that directly addressing rumours and normalising expected side effects improves willingness to participate [78,80]. Proactively leveraging social media for transparent communication and recruitment may therefore be critical to rebuilding trust and enhancing inclusivity in future trials [81].

Perceptions of vaccine trials varied across sociopolitical contexts. In collectivist cultures, which are common in the Global South and among ethnic minority groups in the Global North, group wellbeing is generally prioritised over individual desires and freedoms [82]. In such settings, participation often required collective decision-making or community leader endorsement [53,83]. By contrast, participants in the Global North more frequently prioritised individual autonomy and safety concerns [18,26,49]. These differences highlight the need for context-sensitive trial design; for example, a Kenyan malaria vaccine trial enhanced enrolment through a community-integrated consent process involving elders and social networks, an approach which would conflict with autonomy-centric consent processes in many Global North settings [84]. Logistical barriers such as low literacy, transport costs, and visit frequency were also context-specific [22,27,59], but could be mitigated through strategies including audiovisual consent processes, travel reimbursement, and home visits [20,22]. Actively involving lay representatives from study communities in trial design is essential to ensure cultural and logistical adaptations [85,86].

Legacies of unethical research practices further influenced perceptions of vaccine trials in both the Global South and among ethnic minority communities in the Global North [22,23,56]. Historical abuses, such as the Tuskegee Syphilis Study, alongside experiences of foreign-led research perceived as exploitative in the Global South, created enduring mistrust [22,23,64,87]. Rebuilding trust requires structural changes: establishing long-term partnerships with local institutions to counter perceptions of extractive research [83], employing staff who are representative of the participant community to enhance cultural concordance and inclusion [29,36], and returning findings to communities in accessible formats to demonstrate respect and reciprocity [52,88]. These measures are essential to rebuild confidence in communities historically marginalised within research.

LGBTQ+ communities face distinctive barriers to participation in vaccine research, particularly in HIV trials. Anticipated stigma, whether through disclosure of sexuality, assumptions of high-risk behaviour, or misidentification as HIV-positive due to vaccine-induced seropositivity, has contributed to vaccine trial hesitancy [52,72]. These concerns are compounded by wider patterns of healthcare discrimination and exclusion from research [31,89]. Intersectional identities encounter additional challenges; for example, ethnic minority LGBTQ+ individuals report increased mistrust of institutions and greater stigma within close-knit cultural or religious contexts [54,90]. At the same time, LGBTQ+ communities have a strong tradition of peer advocacy and community mobilisation in HIV prevention and treatment, offering valuable models for inclusive engagement [89,91]. Increasing representation in vaccine trials requires leveraging community networks, addressing stigma, training staff in inclusive practices, and ensuring confidentiality, alongside intersectional strategies that are both culturally and LGBTQ+ competent [92,93].

4.1. Limitations

The results of this study should be interpreted in light of several limitations. In line with Cochrane rapid-review guidance, the search was limited to a single database (PubMed), grey literature was excluded, and screening was conducted by a single reviewer without formal quality appraisal or risk of bias assessment [19]. Opinion and editorial pieces were included, which may not provide objective assessments but were incorporated to provide conceptual or contextual insight and represented only a minor proportion of the dataset (11 %). A substantial proportion of included studies (30 %) focused on HIV vaccine trials, which may bias findings towards HIV-specific barriers such as stigma linked to sexual behaviour and fear of vaccine-induced seropositivity. These barriers are specific to the social context of HIV prevention and may not generalise to other vaccine trials. Hypothetical trials were included and may not fully reflect real-world behaviour [94]; however, no theme was solely derived from hypothetical studies, supporting the stability of thematic conclusions [Table 2].

4.2. Implications for practice, policy, and research

In practice, inclusive trials should provide proportionate financial support, tailored risk communication from trusted clinicians, and proactive use of social media to counter misinformation. Addressing barriers requires multifaceted strategies tailored to specific populations [95]. Mistrust in the Global South and among ethnic minority communities in the Global North should be addressed through long-term community partnerships, recruitment of representative staff, cultural competency training for trial staff, and transparent return of results to participant communities. For LGBTQ+ groups, efforts should focus on stigma reduction, clear communication around sexual health and vaccine-induced seropositivity, and engagement with established advocacy networks. These recommendations reflect strategies that participants across studies described as enablers of participation and align with approaches that have been shown to improve engagement in vaccine trials [85,86].

Policy should reflect the need for sustained investment and accountability in inclusive trial design. Funding bodies such as the NIHR have already prioritised inclusive research, with requirements for patient and public involvement outlined in their Research Inclusion Strategy 2022–27 [96]. However, inclusive recruitment strategies are resource-intensive, and commitments must be matched by dedicated funding to move beyond tokenistic consultation and enable genuine co-design.

Future research should further investigate barriers to vaccine trial participation in underserved populations; within the UK National Immunisation Schedule Evaluation Consortium (NISEC2, NIHR204677), this review will inform a qualitative study investigating barriers to vaccine research participation in underserved populations [97]. Further studies should evaluate pragmatic community-led recruitment strategies and report components, costs, and subgroup effects using standardised frameworks to enable replication and policy translation. Particular attention is needed to intersectional approaches that address overlapping barriers related to ethnicity, sexuality, and social disadvantage.

5. Conclusion

This review synthesises barriers and enablers across populations and highlights concrete directions for more inclusive trial design. In an era of rising vaccine hesitancy, growing numbers of zero-dose children, and widening inequities [98], it is critical that trials embed trust-building, community engagement, and structural adaptations into recruitment through multifaceted strategies. These approaches should be accompanied by clear outcome measurement and follow-up evaluation to ensure that engagement strategies translate into meaningful and sustained improvements in recruitment and retention. Such efforts are particularly urgent given recent cuts to global vaccine funding [99,100], which threaten the sustainability of research at a time when stronger investment is most needed. Strengthening inclusion in vaccine trials is essential not only for scientific validity but also for rebuilding public trust and improving vaccine confidence worldwide.

CRediT authorship contribution statement

Nadia Daniel: Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Data curation, Conceptualization. **Christine Smith:** Writing – review & editing, Methodology, Formal analysis, Data curation, Conceptualization. **Nasima Miah:** Writing – review & editing, Methodology, Data curation, Conceptualization. **Carol Akroyd:** Writing – review & editing, Methodology, Conceptualization. **Tracey Bingham:** Writing – review & editing, Methodology, Conceptualization. **Hannah Brooks:** Writing – review & editing, Methodology, Conceptualization. **Monira Ahmed Chowdhury:** Writing – review & editing, Methodology, Conceptualization. **Gurdeep Kaur:** Writing – review & editing, Methodology, Conceptualization. **Ravinder Kundra:** Writing – review & editing, Methodology, Conceptualization. **Michelle Prendergast:** Writing – review & editing, Methodology, Conceptualization. **Michal Chantkowski:** Writing – review & editing, Methodology, Conceptualization. **Eva Galiza:** Writing – review & editing, Methodology, Conceptualization. **Georgina Nakafero:** Writing – review & editing, Methodology, Conceptualization. **Christina Milton:** Writing – review & editing, Methodology, Conceptualization. **Milena Mejia:** Writing – review & editing, Methodology, Conceptualization. **Denis Murphy:** Writing – review & editing, Methodology, Conceptualization. **Atreya Ramanan:** Writing – review & editing, Methodology, Conceptualization. **Deanna Rex:** Writing – review & editing, Methodology, Conceptualization. **Sophia Wilkinson:** Writing – review & editing, Methodology, Conceptualization. **Susan Owera:** Writing – review & editing, Methodology, Conceptualization. **Kamlesh Khunti:** Writing – review & editing, Methodology, Conceptualization. **Saul N. Faust:** Writing – review & editing, Methodology, Conceptualization. **Maheshi N. Ramasamy:** Writing – review & editing, Supervision, Methodology, Conceptualization.

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Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Eva Galiza reports a relationship with GSK that includes: consulting or advisory and funding grants. Eva Galiza reports a relationship with Moderna that includes: funding grants. Eva Galiza reports a relationship with Janssen that includes: funding grants. Eva Galiza reports a relationship with MSD that includes: funding grants. Kamlesh Khunti reports a relationship with Abbott that includes: consulting or advisory and funding grants. Kamlesh Khunti reports a relationship with AstraZeneca that includes: consulting or advisory and funding grants. Kamlesh Khunti reports a relationship with Bayer that includes: consulting or advisory and funding grants. Kamlesh Khunti reports a relationship with Novo Nordisk that includes: consulting or advisory and funding grants. Reports a relationship with Sanofi Aventis that includes: Kamlesh Khunti reports a relationship with Servier that includes: consulting or advisory and funding grants. Kamlesh Khunti reports a relationship with Lilly that includes: consulting or advisory and funding grants. Kamlesh Khunti reports a relationship with Merck Sharp & Dohme that includes: consulting or advisory and funding grants. Kamlesh Khunti reports a relationship with Boehringer Ingelheim that includes: consulting or advisory and funding grants. Kamlesh Khunti reports a relationship with Oramed Pharmaceuticals that includes: consulting or advisory and funding grants. Kamlesh Khunti reports a relationship with Pfizer that includes: consulting or advisory and funding grants. Kamlesh Khunti reports a relationship with Roche that includes: consulting or advisory and funding grants. Kamlesh Khunti reports a relationship with Daiichi-Sankyo that includes: consulting or advisory and funding grants. Kamlesh Khunti reports a relationship with Applied Therapeutics that includes: consulting or advisory and funding grants. Kamlesh Khunti reports a relationship with Embecta that includes: consulting or advisory and funding grants. Kamlesh Khunti reports a relationship with Nestlé Health Science that includes: consulting or advisory and funding grants. Saul N. Faust reports a relationship with Southampton General Hospital that includes: non-financial support. Saul N. Faust reports a relationship with Janssen that includes: non-financial support. Saul N. Faust reports a relationship with Pfizer that includes: non-financial support. Saul N. Faust reports a relationship with AstraZeneca that includes: non-financial support. Saul N. Faust reports a relationship with GlaxoSmithKline that includes: non-financial support. Saul N. Faust reports a relationship with Novavax that includes: non-financial support. Saul N. Faust reports a relationship with Seqirus Inc that includes: non-financial support. Saul N. Faust reports a relationship with Sanofi that includes: non-financial support. Saul N. Faust reports a relationship with Medimmune that includes: non-financial support. Saul N. Faust reports a relationship with Merck that includes: non-financial support. Saul N. Faust reports a relationship with BioNTech that includes: non-financial support. Saul N. Faust reports a relationship with Cidara that includes: non-financial support. Saul N. Faust reports a relationship with Valneva that includes: non-financial support. Maheshi N. Ramasamy reports a relationship with Iliad Biotechnologies that includes: non-financial support. Maheshi N. Ramasamy reports a relationship with Pfizer that includes: non-financial support. Maheshi N. Ramasamy reports a relationship with Serum Institute of India that includes: non-financial support. Maheshi N. Ramasamy reports a relationship with AstraZeneca that includes: non-financial support. Maheshi N. Ramasamy reports a relationship with VBI Vaccines that includes: non-financial support. Andrea Collins reports a relationship with Sanofi that includes: consulting or advisory and travel reimbursement. Andrea Collins reports a relationship with Pfizer Inc that includes: speaking and lecture fees. The authors have no patents pending to this work. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

All authors attest they meet the ICMJE criteria for authorship.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.vaccine.2025.128183.

Data availability statement

All data analysed in this review are derived from previously published studies. The full list of included studies are provided in the Supplementary Material. No new datasets were generated. Extracted data are available from the corresponding author upon reasonable request.

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