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Review article

# Why do people take part in vaccine trials? A mixed methods narrative synthesis

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ABSTRACT

*Objectives:* To understand why individuals do or do not take part in vaccine trials, exploring the motivators and barriers to identify effective strategies to optimise recruitment in vaccine research.
*Methods:* Qualitative studies and quantitative surveys capturing data on reasons for trial participation/decline were included. Six databases were searched from 1996 to October 2021. Two reviewers independently screened and assessed risk of bias. Results were reported narratively and analysed using thematic analysis.
*Results:* We included 32 studies (17 qualitative; 12 quantitative; 3 mixed-methods) that covered a wide range of populations, geographical areas and disease types. Eight themes were identified 1) altruism; 2) potential for personal benefit; 3) perceived risks; 4) trust or distrust; 5) social networks; 6) stigma; 7) practical implications; 8) research vanguard.
*Conclusion:* Our findings provide a detailed description of how potential participants weigh up their decisions to participate in vaccine trials, which could inform the planning and implementation of studies to enhance recruitment.
*Practice implications:* Clinical trial researchers should consider a patient-centered approach to recruitment, tailoring promoting material and attempt to understand fears, stigma and perceived risks. In addition, recognising the importance of trust and the key role friends, communities, family, and those in supervisory positions play in decisions.

## 1. Introduction

Clinical trials often suffer from recruitment difficulties, leading to early study termination or underpowered studies: 44–69% of UK publicly-funded trials do not recruit to target [1,2]. As well as wasting time and money, this poses ethical concerns for recruited participants [3] and affects completion speed and results dissemination.

A range of reasons for poor recruitment have been reported including individual concerns around intervention safety, treatment preference and time investment; and factors at recruitment sites (e.g. communication about the study, staff resourcing and lack of equipoise) [4,5]. Recruitment and participation in research have been the subject of both secondary [6] and tertiary reviews [7], but this work identified a lack of reviews on participation in vaccine trials [6]. This is significant, especially in a period when infectious diseases and pandemics appear to be increasing [8] and particularly in the shadow of COVID-19.

There are two key differences between treatment intervention trials and vaccine trials: (i) participants in vaccine trials are free of the target disease, and (ii) vulnerable populations are often involved from as early as phase II [9], including young children aged 5–12 [10], older adults [10], and pregnant women [11]. Adverse event reporting is often more stringent than in other Clinical Trials of an Investigational Medicinal Product and volunteers may need to be monitored in specialised centres [9,12]. Additionally, when vaccines are being developed in a pandemic, some trial phases may be accelerated or enhanced, (e.g. phase I human studies may be started before animal studies, and large-scale product manufacturing may happen before all safety data are obtained [13]). Vaccine trials, if effective, may also have a public health benefit

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compared to other clinical trials i.e., (i) vaccinated people not only reduce their personal risk, but they contribute to lowering the population risk by reducing disease transmission; (ii) and may be different for communicable or chronic disease prevention. As such, there may be different motivations for taking part in vaccine trials than other clinical trials.

Vaccine hesitancy grew significantly during the COVID-19 pandemic, in response to the rapid development and implementation of the vaccine [14,15]; potentially building on previous health scares, including the spurious link between the Measles Mumps Rubella (MMR) vaccine and autism [16]. A growth in 'vaccine deniers' or 'anti-vaxxers' can limit the pool of potential trial participants.

This review aimed to understand why individuals do or do not take part in vaccine trials, exploring the motivators and barriers to identify effective strategies to optimise recruitment in vaccine research. In addition, identifying any key relationships between participant demographics, disease and trial groups.

## 2. Methods

The review was registered with PROSPERO (CRD42020222396) and conducted and reported in accordance with relevant guidance [17,18].

### 2.1. Search strategy

The search strategy was developed from a previous overview of reviews [7]and adapted to vaccine-specific research. Six databases (MEDLINE, Embase, CINAHL, PsycINFO, Cochrane Library, OpenGrey) were searched from 1996 to October 2021. The full search strategy is reported in Supplementary Material 1. Results were imported to EndNote X9 and de-duplicated. Backwards and forwards-citation searching was completed by examining references from included papers and Google Scholar, respectively.

### 2.2. Eligibility criteria

We included qualitative, quantitative, or mixed methods studies reporting facilitators and/or barriers to participation in real (rather than hypothetical) vaccine trials following an invitation to participate. Studies were restricted to English. To reflect the publication of the International Conference on Harmonization Good Clinical Practice: Consolidated Guidance [19,20] searches were started in 1996.

### 2.3. Study Selection

Two researchers (AD; FR) independently screened titles and abstracts and undertook full text screening, recording reasons for exclusion. Discrepancies were resolved by consensus or discussion with a third researcher (AS).

### 2.4. Data extraction and analysis

Data extraction used a pre-designed form, and included: study aims, target population, population characteristics, study design and participation barriers/facilitators. One researcher independently extracted data with a second researcher independently checking forms. Means and percentages were collected or calculated from reported data where available. We checked studies to ensure that data from participants were not included twice.

Given the variety of included study designs, a narrative synthesis was conducted [21]. This textual allowed us to summarise the findings from included studies and, in addition, to consider any relationships between study types on a variety of measures [22]. Thus, providing a thorough and critical overview, identifying gaps and formulating meaningful summaries of previously published research.

The reasons presented for vaccine trial participation or decline in the included papers were mapped onto existing themes identified from previous reviews on research participation [23,24]. For any data that did not fit within these existing frameworks, new themes were developed. Data from both quantitative and qualitative studies were tabulated under each theme allowing for data integration from different study types [25]. This approach provided the scope to compare the factors associated with vaccine trial participation to those identified in other types of research. Themes were then cross tabulated according to disease type, population group and vaccine trial phase:

- Phase I: First time in human studies with primary aim of ensuring no major safety issues.
- Phase II: Aims to identify effectiveness in treatment or prevention and identify dosing levels.
- Phase III: Aims to confirm effectiveness and safety, confirm dosing, identify side effects, and compare to known or standard treatments. Often a blind trial.
- Phase IV: Post-marketing surveillance or monitoring to determine long term effects.

Planned synthesis on individuals who declined trial participation was not possible due to insufficient studies. Findings were presented narratively.

### 2.5. Quality assessment

Two researchers (AD; FR) independently assessed the validity and methodological rigor of studies. The Critical Appraisal Skills Programme tool [26] was used for qualitative and mixed-methods studies and the Joanna Briggs Institute Critical Appraisal Checklist for Analytical Cross-Sectional Studies tool [27] was used for quantitative surveys. Discrepancies were resolved by consensus or discussion with a third researcher (AS).

## 3. Results

The searches generated 6718 potentially eligible articles, and 5010 studies after the exclusion of duplicates. Of these, 4841 were excluded based on the title and abstract, leaving 175 full-text articles to be assessed for eligible. After full text screening 32 met the inclusion criteria (see Fig. 1 and Supplementary Material 2).

### 3.1. Characteristics of included studies

The thirty-two studies (Table 1) were published 1999–2021 and included 17 qualitative, 12 quantitative and 3 mixed-methods studies. Studies covered a broad range of geographical locations, trial stages, populations, and disease areas; most common were US trials (n = 11), phase two trials (n = 14) and in adults (n = 24). A large focus of trials were targeted around HIV vaccines (n = 12), which may be explained by a number of factors including the global prevalence of HIV and AIDS [28], the lack of vaccine success to date, and commercial and socio-political influences on research funding. The A total of 11,650 participants were involved, excluding one study not reporting participant numbers [29]. Only two studies included individuals who declined trial participation (non-consenters), seven included trial consenters and non-consenters, the large majority (n = 25) included only consenters (see Supplementary Material 3).

### 3.2. Quality of evidence

Nearly all (19/20) qualitative studies were rated low or some concerns (Supplementary Material 4), the latter particularly evident in the role of the researcher, which was unclear or unreported. All studies gave valuable insights into the topic of interest, often exploring views from under-researched communities and giving good accounts of the settings

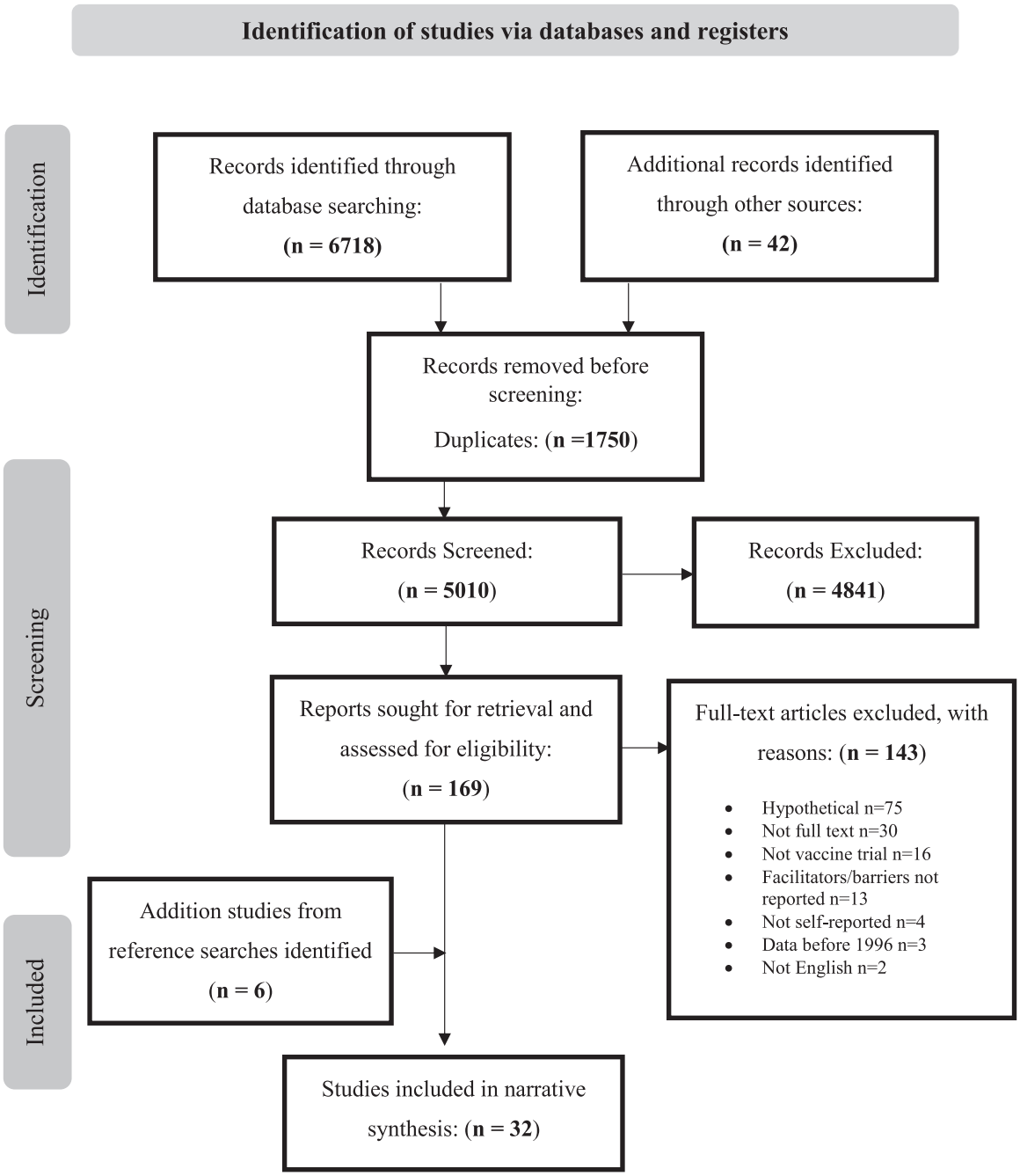


**Fig. 1.** PRISMA flow diagram of literature search and study selection phases; n, number.

of interest.

Only 1 out of 12 cross-sectional studies scored 100% in quality [33] (Supplementary Material 5): in 7/12 studies potential confounders were not addressed and outcome measures were either not validated or not reliable.

Narrative Synthesis.

Table 2 shows the themes identified from the narrative synthesis that influenced decision making on trial participation. Supporting quotes can be found in Supplementary Material 6.

### 3.3. Research vanguard

A finding not reported in previous reviews of the influences on research participation was that some healthcare professionals stated a professional responsibility or obligation to participate in research [34, 42,52,61], partly to be consistent with their advice to other potential trial participants [45]. Furthermore, others reported that they wished to set an example by '*promoting the common good*' [52] and demonstrate vaccine safety to promote the trial or vaccine approval.

### 3.4. Altruism

Altruism was consistently highlighted as a strong motivator for participation and central to many participants' decisions [30,31,33,35, 38,41,46]. Respondents overwhelmingly [32,34,35,38,40,42,53,61] recognised the importance of participation for vaccine advancement, and its contribution to scientific progress [30,31,33,35,38,41,43,46], societal health [43–45,49,56,61], safety to others and return to "*normalcy*" [61]. In contrast, altruistic motivates were not influential in paediatric or later phase trials.

**Table 1**
Characteristics of Included Studies.

| First Author | Year | Country | Vaccine target | Trial Phase | Methods |
|---|---|---|---|---|---|
| Abrams[30] | 2011 | South Africa | Tuberculosis | 1 | Qualitative |
| Brown[31] | 2015 | Peru | HPV | 4 | Qualitative |
| Buchbinder[32] | 2004 | USA | HIV | 2 | Quantitative survey |
| Cattapan[33] | 2019 | Canada | Ebola, Influenza | 1 | Quantitative survey |
| Chantler[34] | 2007 | UK | Diptheria, meningitis (pneumococcal) | Not reported | Qualitative |
| Chin[35] | 2016 | USA | HIV | 2b | Qualitative |
| Colfax[36] | 2005 | USA, Canada, Netherlands | HIV | 3 | Quantitative survey |
| Costas[37] | 2012 | Spain | H5N1 influenza vaccine | 3 | Quantitative survey |
| Craig[38] | 2018 | USA | Tuberculosis | 1 | Qualitative |
| David[39] | 2021 | Canada | Ebola | 2 | Qualitative |
| Detoc[40] | 2019 | France | Clostridium Difficile,<br>Streptococcus Pneumoniae,<br>Staphylococcus Aureus,<br>Respiratory Syncytial Virus,<br>Ebola,<br>Pneumococcal,<br>Malaria,<br>Shigella Sonnei | 3<br>2b<br>2b<br>2<br>2<br>2b<br>1<br>1 | Quantitative survey |
| Diemert[41] | 2017 | USA, Brazil | Hookworm | 1 | Quantitative survey |
| Drapkin[42] | 2012 | USA | Influenza | 2 | Qualitative |
| Fowler[43] | 2006 | USA | Genital herpes (HSV) | Not reported | Quantitative survey |
| Gikonyo[44] | 2008 | Kenya | Malaria | 2b | Qualitative |
| Grantz[45] | 2019 | Guinea | Ebola | 3 | Qualitative |
| Gray[46] | 2008 | UK | HIV | 2 | Quantitative survey |
| Johnson[47] | 1999 | USA | HIV | 1 | Quantitative survey |
| Moutsiakis[48] | 2007 | USA | HIV | Not reported | Qualitative |
| Newman[49] | 2011 | Canada | HIV | 2b | Mixed methods |
| Newman[50] | 2008 | Canada | HIV | 2b | Mixed methods |
| Nguyen[51] | 2021 | Sierra Leone | Ebola | Not reported | Qualitative |
| Nieminen[52] | 2015 | Finland | Pneumococcal disease | 3, 4 | Quantitative survey |
| Nyaoke[53] | 2017 | Kenya | HIV | 1 | Qualitative |
| Nyblade[54] | 2011 | Kenya | HIV | 1 | Qualitative |
| Pell[55] | 2010 | Papua New Guinea | Malaria | Not reported | Mixed methods |
| Sanga[56] | 2021 | Tanzania | HIV | 1, 2 | Qualitative |
| Stratton[57] | 2015 | USA | HPV | 1 | Quantitative survey |
| Sur[58] | 2009 | India | Typhoid Fever | 3b | Quantitative survey |
| Tarimo[59] | 2011 | Tanzania | HIV | 1, 2 | Qualitative |
| Tengbeh[29] | 2018 | Sierra Leone | Ebola | 2 | Qualitative |
| Van den Berg[60] | 2019 | Uganda, Tanzania, Kenya | Malaria | 2b, 3 | Qualitative |
| Wentzell[61] | 2021 | USA | COVID-19 | 3 | Qualitative |
| Wolters[62] | 2014 | Netherlands | Nicotine addiction | 2 | Qualitative |

Key: HIV, Human Immunodeficiency Virus; HPV, Human Papillomavirus; COVID-19, Coronavirus disease

### 3.5. Conditional altruism

Whilst altruism was often mentioned, there was also a need for potential personal benefit (i.e. 'conditional altruism')[6]. Some individuals hoped that through participation they would gain recognition, achieve a sense of purpose [29,35,41,48] or further their education [29,30,46,47,61]. In addition, a motivation was the potential to preserve personal health through disease protection [29,42,47,52,61,62]. Protection [29,34,42,58,61] extended to family members [34,43,45,55,56], future partners [43] and *"other vulnerable individuals in their lives"*[61]. For example, pregnant participants noted the benefits of conferred immunity [42]. These motivations were particularly apparent for those in high-risk settings [36,40,43,45,49,51,56,58] or who thought themselves high risk [36,40,43,49,58]. Early access to vaccination was particularly appealing to some participants [42].

Compensation for participation could be offered in the form of medical care (e.g. a check-up) or throughout the trial [31,34,36,38,40,44,45,47,52,53,56,60,62], particularly in countries where access to high quality healthcare is not universal [29,34,42,44,46,56–58,60,62]. Financial benefits were often reported [30,33,35–38,40,41,43,46,47,53,61], albeit not always the primary determinant of participation. However, a lack of financial incentive was sometimes cited to explain non-participation [29,43,48,54]. Some indicating *"time is money"* [45] and feeling offended and *"insulted"* [50] at insignificant compensation for participation, e.g. comparing it to *"a miserable soda can"* [45]. This was particularly the case in trials in which blood samples were required, where participants mentioned compensation was inadequate for *"all they took out"* [45] and suggested *"they should be given food supplements to replace the blood drawn"* [56].

### 3.6. Perceived risks

In contrast, many participants were attuned to vaccine risks [29,32,34,38,40,42,44,45,50,52,56,58,59] particularly unknown side effects in the short- or long-term with one study noting the observation period was *"not enough to study the side effects; they could happen three, five, ten years later"* [45]. Many *"were suspicious of the vaccine safety"*[52], expressing concerns that protection was *"not guaranteed"* [45] and that potential lack of effectiveness was risky [40,45,50]. Others speculated that participation could heighten disease exposure [38].

Media coverage was also influential, particularly in paediatric trials where parents declined participation after recalling negative vaccination outcomes and vaccine controversy that heightened anxieties. However, knowledge and understanding of the trial phase was also important in processing their trial participation safety with several participants mentioning the low risks associated with phase III trials [61].

Concerns were also raised around timing, with some refusing participation because a routine vaccine would be given a few weeks later, therefore parents believed would result in *"too many chemicals"* [34] put in their child's body at once. Especially significant in Ebola vaccination trials, blood drawing was mentioned relating to

**Table 2**
Overview of Themes.

| Theme | Studies referring to theme | Description |
|---|---|---|
| Research Vanguard | [34,42,45,52,61] | • Professional responsibility<br>• To be consistent with own advice<br>• Encouraging others to be vaccinated<br>• Setting example to the general population, colleagues, patients or to friends and family |
| Altruism | [30–35,38,40–46, 53,56,61] | • Helping others<br>• Contributing to community or society<br>• Benefits to science |
| Conditional Altruism | [29–31,33–37, 40–58,60–62] | • Early access to vaccine<br>• Closer monitoring<br>• Protection<br>• Gain knowledge<br>• Financial benefits |
| Perceived Risks | [29,32,34,38,40, 42,44,45,50,52, 56,58,59,61] | • Adverse effects<br>• Experimental treatment<br>• Media coverage<br>• Risks associated with trial procedures such as blood drawing |
| (Dis)trust | [29,32,35,37,40, 43,45,51,56,58] | • (Dis)trust and confidence in various bodies<br>• Suspicions of intent |
| Social Networks | [29,32,35,37,40, 44,45,47,51,60, 62] | • Influence of others; healthcare professionals, family or friends<br>• Direct dissuasion from others<br>• Rumours |
| Stigma Relating to the Underlying Condition/ Research Participation | [31,32,38,44,45, 50,51,54] | • Potential fear of reactions/ rejection from others<br>• Associated with the disease of interest |
| Practical Implications | [32,34,38,40,44, 45,50,52,55,59] | • Problematic trial design such as intervention blinding<br>• Burden of research requirements such as time and effort |

participation in some trials [29,34,44,45,56], particularly pediatric trials [34,44,52]. However, whilst blood drawing was mainly a disincentive to participation, for others a lack of blood drawing was problematic, as this was seen as a means to confirm the vaccine was working [42].

### 3.7. (Dis)trust in research

Confidence or trust in the research or clinician was important [35,37, 40] for vaccine trial participation. Distrust of government and/or pharmaceutical companies [32,40] was highlighted as a disincentive. Distrust of vaccine research appeared heightened when research groups and research populations were from different contexts [29,43] and included fears of blood stealing [29], that researchers were benefiting from disease outbreaks [45,51,56,58] and resentment of becoming 'guinea pigs' [45,56,58]. Distrust in healthcare professionals was not mentioned in any paediatric trial.

### 3.8. Social networks

The opinions of friends, family, colleagues, communities and trial participants were heavily influential on participation decisions [35,37, 40,45,47,60,62] and worked in both directions. For example, some healthcare professionals had been influenced by work supervisors *"he's actually the one who gave us the courage [to participate]"* [45]. However, linked to research distrust, negative vaccine rumours deterred participation [29,32,44,45,51,60].

### 3.9. Stigma relating to the underlying condition/research participation

The stigma of association with a vaccine trial was a concern when it was feared others would associate them with the disease, particularly evident in HIV trials and those in high-risk groups [31,50,51,54]. The trial location was also closely associated with stigma *"…their office [trial site] being on Church Street doesn't help. I mean you go into a clinic like that, people see you walk in and think, 'Oh, that person, I just saw him go into that AIDS clinic;' the community isn't that big"* [50]. However, this was not always a barrier with some citing a desire to reduce stigma as a motivator for participation [38].

In addition, there was a stigma around research participation itself. Some expressed fears they would encounter negative community responses, such as being accused of collusion [32,44,45], especially in communities where research is distrusted.

### 3.10. Practical implications of participation

Further influence were the time, effort and procedures required, with many considering these were not outweighed by direct and indirect benefits of participation [32,34,38,40,45,50,55,59]. Blinded of treatment was problematic in several studies as respondents were anxious to know what they received, regardless of whether or not they preferred the active vaccine [32,44,50,52].

## 4. Discussion and conclusion

### 4.1. Discussion

The review included a total of 32 studies: 17 that were qualitative; 12 quantitative surveys and 3 mixed-methods studies. The studies were undertaken in a wide range of countries, and the vaccines were focused on a wide range of target diseases. To our knowledge, this is the first narrative synthesis highlighting the reasons why people participate or decline participation in vaccine trials, including only real, rather than hypothetical trials. Eight key themes were identified from the primary studies as barriers or facilitators of vaccine trial participation. One new theme not identified previously is 'research vanguard'. Remaining themes were mapped onto key existing themes [6,7]: altruism, conditional altruism, personal benefit, perceived risk, (dis)trust, social networks, stigma and practical implications.

The theme 'research vanguard' has not been reported before but it was prominent here. Healthcare workers indicated that trial participation was driven by a sense of responsibility or a wish to set an example, and they stressed the importance of wanting to act consistently with their own advice. Some also stated that they were influenced to participate in a trial by a supervisor, although not always with a positive outcome. This raises some ethical considerations around pressures to participate, confidentiality and bias. Researchers should consider healthcare workers are safeguarded, that their participation has scientific value, scientific validity and they are selected fairly, rather than a mere convenience.

Altruistic motives remain a strong motivator for participation, with individuals recognising their contribution to scientific advancement, public safety and societal health. However, altruistic motives were not influential in paediatric or later phase vaccination studies, contrasting with previous reports [7]; the difference is potentially explained by the greater emphasis reported in vaccine studies on 'conditional altruism', such as personal benefit, additional protection and a greater desire for their child to receive enhanced and accessible medical care. Furthermore, the potential personal benefits of early vaccine access and closer health monitoring were particularly apparent in biofluid disease trials, those in high-risk settings or thought themselves high risk and trials involving pregnant women.

Attitudes towards financial compensation were highlighted, firstly the lack of financial incentive and secondly as an adequate amount for

their time and samples. A balance between reasonable compensation and inducement needs to be considered, achieved through engagement with patient and public involvement and advisory groups [63]. In addition, to reduce burden, postal questionnaires and remote interventions may be implemented.

Uncertainties around vaccine safety, side effects, vaccine 'effectiveness', blood drawing and risk of unguaranteed protection were identified, as noted previously [7]. This was particularly evident in paediatric trials where parents considered the safety and invasiveness of the study, suggesting that parental decisions on child participation may depend on their familiarity with healthcare, research and science. It is notable that the barrier 'distrust in clinicians or healthcare professionals' was not reported in any paediatric vaccine trial, suggesting the potential for doctors and other clinicians to offer support and independent advice about a trial. In this review blood drawing for trial purposes was found to be a disincentive to participation, however the lack of blood drawing to monitor vaccine effectiveness was also found to be a problem. Interestingly, later phase trials were shown to be an important element for participants in processing whether they deemed the trial safe, as a result of knowing more about the treatment being offered [50,61]. While obtaining bloods may be unavoidable in some vaccine trials, researchers could consider explaining the trial phase particularly if at a later stage.

The spread of misinformation, largely through media coverage, heightened these uncertainties negatively affecting understanding, and influencing trial participation decisions. However, the media has been shown as a successful promoting tool for vaccine trials [64–67]. The type of media coverage and promotional materials used in vaccination trials warrants future research to explore the potential differences in the pattern among health and age groups, trial phases and paediatric settings which may illustrate the need to tailor promoting tools [68].

Trusting the opinions of clinicians and researchers was important for adults when considering participation. However, a more influential effect came from the trust in friends, family members, colleagues, communities and other trial participants. The 'community vanguard' seems to be a crucial source of information and advice, but it also poses challenges: researchers need to consider how to engage with community groups, potentially through shared-decision meetings, vaccination promotion campaigns, or the co-design of information, which is a current area of research [69].

Fear of blood theft or misuse was a reason for declining participation, particularly in Ebola vaccine trials. Fears, misconceptions and mistrust must be taken seriously, and attempts made to understand the reasoning behind these concerns. This could be achieved through one-to-one discussions, community engagement and clear information provision to ensure that concerns are addressed [70].

Societal expectations were found to be a barrier to participation, as previously reported [7,40,71], usually in the form of stigma. Respondents reported a fear of stigma, personally or by association, and discrimination associated with trial participation; these fears were more common in HIV trials or lower income countries, but not exclusively so. The challenges for trials are to address the associated stigma and rumours faced by high-risk groups and ensure participant anonymity. Trial personnel need to consider engaging with rumours and sharing narratives to understand how these could be addressed. It is clear from this review that there are many parallels between the literature on vaccine trial participation and vaccine uptake. For example, reasons for the significant variation in rates of uptake of Covid-19 vaccines are reflected in our themes partly explained by societal and cultural norms around trust, personal freedoms and altruism (including protecting others and societal protection) [72].

Study processes have consistently been reported as a deciding factor for trial participation in a range of settings and have been the subject of interventions [3,73]. Unlike previous trial settings [3,6,7] randomisation was not reported as a concern. Conversely, blinding of treatment was reported as a reason for refusing to participate with participants expressing concerns over 'mistrust', the lack of protection and side effects of the placebo. Every effort should be made to providing clear transparent information on both study arms and ensure concerns are addressed.

This review has several strengths. Firstly, the use of recent mixed methods systematic reviews [6,7] as a framework for reporting findings, enabling us to place the findings in the context of existing evidence and the use of a replicable search strategy, entry criteria and quality appraisal. While the inclusion of vaccine trials based solely on real trial invitations may be viewed as a strength, due to having a greater validity than hypothetical trial invitations, it may be argued this is also a limitation. If decision making on hypothetical trial invitations were very similar to decisions on real trials, the size of the evidence base would be greatly increased by their inclusion. There has been limited research assessing the validity of hypothetical decisions but the relevant published research suggests differences between real and hypothetical decisions, including participation in biobank studies [74,75]. However, hypothetical trial invitations may provide useful valid and meaningful information that influence participation in vaccine trials and therefore future reviews may want to consider reviewing hypothetical trials to optimise recruitment in vaccine research.

There are also several possible limitations. Although the database search was extensive, we were able to include only English language articles, which may have limited the volume of included research and introduced bias. The findings were limited to the data and results reported by primary study authors and their interpretation, which may have influenced the review findings. In particular, the primary study results were based on sample responses, and it is possible that some individual respondents may have placed greater emphasis on some themes over others. Very few studies included the views of trial non-consenters, and when non-consenter data were available, they tended to be merged with the views of consenters, reducing their usefulness. This is a recurrent problem in methodological research about research recruitment and retention, and in research about healthcare uptake, and possible solutions are not simple. However, evidence from primary studies is that some non-consenters are willing to discuss their experiences; therefore, an opportunity has been missed by some of the included studies.

### 4.2. Conclusion

Overall, this review has provided important insights for understanding how potential participants weigh up decisions about vaccine trial participation. The findings of this review may be used to inform future vaccine trial conduct and design when planning and implementing recruitment strategies.

### 4.3. Practice implications

This review has demonstrated that significant others such as friends, communities, family, and those in supervisory positions play a key role in decisions. There was a greater emphasis on personal protection than in previous research and this warrants further clarification in trial settings. It is clear, that decision making around vaccine trial participation is situated within social norms and cultural values and linked to perceptions relating to vaccines more generally. Research to explore in more detail the social and cultural differences in response to vaccine trials and vaccines – according to trial phase, disease type and patient group would inform the type of media coverage and promotional materials used in vaccine trials. There may be a need to tailor promoting tools to the intended audience in order to optimise trial recruitment.

Clinical trial researchers should consider engaging with potential participants and sharing narratives in order to understand fears, stigma and perceived risks. Financial compensation should be offered, however it is also important to establish a reasonable compensation amount particularly in trials where blood samples are obtained, which will

require trial-specific discussion. Evidence from this review is that non-financial benefits (e.g., free, accessible health care) may also contribute to individual decisions to take part.

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## CRediT authorship contribution statement

**Rose Fi:** Formal analysis, Investigation, Validation, Writing – review & editing. **Dean Alex:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Writing – review & editing. **Scantlebury Arabella:** Conceptualization, Methodology, Supervision, Writing – review & editing. **Jones Katherine:** Formal analysis, Validation, Visualization, Writing – original draft. **Knapp Peter:** Writing – original draft, Conceptualization, Methodology, Supervision, Visualization. **Adamson Joy:** Conceptualization, Methodology, Supervision, Visualization, Writing – original draft.

## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.pec.2023.107861.

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