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Factors that impact on recruitment to vaccine trials in the context of a pandemic or epidemic: a qualitative evidence synthesis (Review)

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[Qualitative Review]

Factors that impact on recruitment to vaccine trials in the context of a pandemic or epidemic: a qualitative evidence synthesis

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ABSTRACT

Background

The World Health Organization declared the COVID-19 pandemic on 11 March 2020. Vaccine development and deployment were swiftly prioritised as a method to manage and control disease spread. The development of an effective vaccine relies on people's participation in randomised trials. Recruitment to vaccine trials is particularly challenging as it involves healthy volunteers who may have concerns around the potential risks and benefits associated with rapidly developed vaccines.

Objectives

To explore the factors that influence a person's decision to participate in a vaccine trial in the context of a pandemic or epidemic.

Search methods

We used standard, extensive Cochrane search methods. The latest search date was June 2021.

Selection criteria

We included qualitative studies and mixed-methods studies with an identifiable qualitative component. We included studies that explored the perspectives of adults aged 18 years or older who were invited to take part in vaccine trials in the context of a pandemic or epidemic.

Data collection and analysis

We assessed the title, abstracts and full texts identified by the search. We used a sampling frame to identify data-rich studies that represented a range of diseases and geographical spread. We used QSR NVivo to manage extracted data. We assessed methodological limitations using an adapted version of the Critical Skills Appraisal Programme (CASP) tool for qualitative studies. We used the 'best-fit framework approach' to analyse and synthesise the evidence from our included studies. We then used the Confidence in the Evidence from Reviews of Qualitative research (GRADE-CERQual) assessment to assess our confidence in each finding and develop implications for practice.

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Main results

We included 34 studies in our review. Most studies related to HIV vaccine trials. The other studies related to Ebola virus, tuberculosis, Zika virus and COVID-19. We developed 20 key findings, under three broad themes (with seven subthemes), that described the factors that people consider when deciding whether to take part in a vaccine trial for a pandemic or epidemic disease.

Our GRADE-CERQual confidence was high in nine of the key findings, moderate in 10 key findings and low in one key finding. The main reason for downgrading review findings were concerns regarding the relevance and adequacy of the underlying data. As a result of the over-representation of HIV studies, our GRADE-CERQual assessment of some findings was downgraded in terms of relevance because the views described may not reflect those of people regarding vaccine trials for other pandemic or epidemic diseases. Adequacy relates to the degree of richness and quantity of data supporting a review finding. Moderate concerns about adequacy resulted in a downgrading of some review findings.

Some factors were considered to be under the control of the trial team. These included how trial information was communicated and the inclusion of people in the community to help with trial information dissemination. Aspects of trial design were also considered under control of the trial team and included convenience of participation, provision of financial incentives and access to additional support services for those taking part in the trial.

Other factors influencing people's decision to take part could be personal, from family, friends or wider society. From a personal perceptive, people had concerns about vaccine side effects, vaccine efficacy and possible impact on their daily lives (carer responsibilities, work, etc.). People were also influenced by their families, and the impact participation may have on relationships. The fear of stigma from society influenced the decision to take part. Also, from a societal perspective, the level of trust in governments' involvement in research and trial may influence a person's decision.

Finally, the perceived rewards, both personal and societal, were influencing factors on the decision to participate. Personal rewards included access to a vaccine, improved health and improved disease knowledge, and a return to normality in the context of a pandemic or epidemic. Potential societal rewards included helping the community and contributing to science, often motivated by the memories of family and friends who had died from the disease.

Authors' conclusions

This review identifies many of the factors that influence a person's decision to take part in a vaccine trial, and these reflect findings from reviews that examine trials more broadly. However, we also recognise some factors that become more important in connection with a vaccine trial in the context of a pandemic or epidemic. These factors include the potential stigma of taking part, the possible adverse effects of a vaccine, the added motivation for helping society, the role of community leaders in trial dissemination, and the level of trust placed in governments and companies developing vaccines. These specific influences need to be considered by trial teams when designing, and communicating about, vaccine trials in the context of a pandemic or epidemic.

PLAIN LANGUAGE SUMMARY

What factors influence a person's willingness to take part in a vaccine trial during an epidemic or pandemic?

What is the aim of this review?

Vaccines are important for reducing the spread of infectious diseases during a pandemic such as COVID-19. Clinical trials test these vaccines to make sure that they are safe and effective. But it can be challenging to find enough people who are willing to take part in a vaccine trial for a pandemic or epidemic disease.

The aim of this Cochrane Review of qualitative research (or 'qualitative evidence synthesis') was to find out what influences a person's decision to take part in a vaccine trial in the context of a pandemic or epidemic. Understanding the factors that influence a person's decision to participate in a vaccine trial can inform trial design and development of recruitment strategies that optimise communication, informed consent, and participant inclusion and diversity in vaccine clinical trials. To answer the review question, we analysed 34 studies of people's views and experiences of taking part in a vaccine trial.

Key messages

Many factors influence a person's decision to take part in a vaccine trial during a pandemic or epidemic. People are influenced by the way in which the trial is set up and how information about the trial is communicated. People are also influenced by what they think the possible risks and side effects are. Friends and family may also have influenced their decision. A fear of stigma and distrust in governments may prevent people from taking part in a vaccine trial. People may often see the chance to help others and prevent the spread of disease as a reason to take part in a vaccine trial.

What did we find?

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We included 34 studies that looked at people's views and experiences of being invited to take part in a vaccine trial in the context of a pandemic or epidemic. Most of the studies related to HIV vaccine trials. The other studies related to Ebola virus, tuberculosis, Zika virus and COVID-19. Studies were set in many countries across Africa, Asia, Europe and North America. The studies looked at the views and experiences of adults aged 18 years and over who had been invited to take part in vaccine clinical trials. Some of them had accepted and some had decided not to take part.

Main results

We identified several factors that people consider when deciding whether to take part in a vaccine trial during a pandemic or epidemic. We judged our confidence in these findings to be low, moderate or high depending on how well supported that finding was from the included studies. We had moderate to high confidence in most of the findings.

Some of the factors that influenced people's decisions were under the control of the team setting up the trial. For instance, people were influenced by how trial information was communicated, and whether community members were involved in information delivery. They were also influenced by how easy or convenient it was to take part in the trial, whether they would be paid to take part and whether they would get access to additional support or health services.

Other factors included personal concerns, and the influence of family and friends and wider society. From a personal point of view, people had concerns about vaccine side effects, how well the vaccine works, and how taking part in the trial might impact on their daily lives and responsibilities. People were also influenced by their families and whether taking part might affect their relationships with others. Some people feared stigma from their communities if they took part. People's level of trust in the government's involvement in research and trials could also influence their decisions.

People also considered the possible rewards of taking part in a trial and whether these outweighed the risks. Some of these rewards were personal. People wanted to get faster access to a vaccine, improve their health, improve their understanding of the disease and return to normal life during a pandemic or epidemic. But people were also motivated by wanting to help society and contribute to science. This was often tied to memories of family and friends who had died from the disease.

What are the limitations of the evidence?

We identified 34 studies for this review, but 26 were related to HIV. This raised concerns about the relevance of the data to other diseases. In addition, we had concerns about the quality of the data for some findings. Because of the diversity of the participants in individual studies, we cannot make any inferences by participant types (for example, participants' backgrounds, gender, or social standing or class).

How up-to-date is this evidence?

This review includes studies published before the end of June 2021.

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SUMMARY OF FINDINGS

Summary of findings 1. Factors that impact on recruitment to vaccine trials during a pandemic or epidemic

Theme 1: factors under the control of the vaccine trial teams that influence people's decision to participate			
1.1 Communication of trial information			
Summary of review finding	**Studies contributing to the review finding**	**CERQual assessment of confidence in the evidence**	**Explanation of CERQual assessment**
Finding 1: people appreciated when there was community involvement; including community leaders' involvement, in trial information dissemination. Community leaders themselves valued being involved in trial information dissemination, and developing health literacy within the community, but emphasised the need for clear details of vaccine development and trial processes to be effective in this role.	Brooks 2007; Lesch 2006; Newman 2011a; Newman 2015; Nguyen 2021; Strauss 2001 (2006 study report); Tarimo 2019; Toledo 2014	**Moderate confidence**	No/very minor concerns regarding coherence and minor concerns regarding relevance, methodological limitations. Moderate concerns regarding adequacy.
Finding 2: people considering participating in a vaccine trial for a pandemic or epidemic disease valued the approachability and availability of researchers to answer questions related to the trial.	David 2021; Mbunda 2018; Newman 2011a; Nyamathi 2004; Olin 2006; Slomka 2008; Toledo 2014	**Moderate confidence**	No/very minor concerns regarding coherence and minor concerns regarding relevance and methodological limitations. Moderate concerns regarding adequacy.
Finding 3: people valued information on a vaccine trial for a pandemic or epidemic disease being communicated respectfully and in plain language that could be easily understood. People found leaflets a useful method of conveying information and felt they could be tailored to the information and language needs of specific populations.	Andrasik 2014; Brooks 2007; Chakrapani 2012; Grantz 2019; Newman 2011a; Newman 2015; Olin 2006; Strauss 2001 (2006 study report); Tarimo 2019; Toledo 2014	**Moderate confidence**	No/very minor concerns regarding coherence Minor concerns regarding methodological limitations and adequacy. Moderate concerns regarding relevance.
Finding 4: people emphasised the importance of receiving all the information relating to the vaccine trial for a pandemic or epidemic disease including any potential risks and benefits, together with opportunities to ask questions about anything they do not understand.	Grantz 2019; Jalloh 2019; Lesch 2006; Mbunda 2018; Newman 2011a; Newman 2015; Olin 2006; Strauss 2001 (2006 study report); Tarimo 2010; Tarimo 2019; Toledo 2014	**High confidence**	No/very minor concerns regarding coherence and minor concerns regarding relevance, adequacy and methodological limitations.
Finding 5: people appreciated the availability of information about vaccines, how they were developed and worked, the potential benefits and risks, the implications of participation in a vaccine trial for a pandemic or epidemic disease, and the outcomes of previous studies to inform their decision-making around participation.	Adewoyin 2013; Andrasik 2014; Brooks 2007; Chakrapani 2012; Grantz 2019; Jalloh 2019; Lesch 2006; Mbunda 2018; Newman 2011a; Newman 2015; Nguyen 2021; Nyamathi 2004; Olin 2006; Strauss 2001 (2006 study report); Tarimo 2010; Tarimo 2019; Toledo 2014	**High confidence**	No/very minor concerns regarding coherence Minor concerns regarding relevance, adequacy and methodological limitations.

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1.2 Considerations around trial design			
Summary of review finding	**Studies contributing to the review finding**	**CERQual assessment of confidence in the evidence**	**Explanation of CERQual assessment**
Finding 6: people emphasised the importance of participation being easy, convenient and causing minimal disruption. People were also concerned about possible distress arising from aspects of the trial design.	Adewoyin 2013; Andrasik 2014; Brooks 2007; Chakrapani 2012; Craig 2018; Gobat 2018; Grantz 2019; Lesch 2006; Mbunda 2018; Newman 2006; Newman 2008a; Newman 2008b; Nguyen 2021; Slomka 2008; Toledo 2014; Voytek 2011	**High confidence**	No/very minor concerns regarding coherence and adequacy and minor concerns regarding relevance and methodological limitations.
Finding 7: people described incentives such as money or access to additional support services as an important consideration when deciding whether or not to participate.	Adewoyin 2013; Andrasik 2014; Brooks 2007; Chakrapani 2012; Chin 2016; Craig 2018; David 2021; Gobat 2018; Grantz 2019; Jalloh 2019; Koniak-Griffin 2007; Lesch 2006; Mbunda 2018; Newman 2006; Newman 2008a; Newman 2008b; Nyamathi 2004; Olin 2006; Slomka 2008; Strauss 2001; Strauss 2001 (2006 study report); Tarimo 2019; Tarimo 2010; Tengbeh 2018; Toledo 2014; Voytek 2011; Wentzell 2021	**High confidence**	Minor concerns regarding coherence, relevance and adequacy and methodological limitations.
Theme 2: personal, family and societal factors that influence people's decision to participate in a vaccine trial for a pandemic or epidemic disease			
2.1 Weighing up the risks and benefits			
Summary of review finding	**Studies contributing to the review finding**	**CERQual assessment of confidence in the evidence**	**Explanation of CERQual assessment**
Finding 8: people were hesitant to participate if they had concerns about vaccine side effects, or vaccine efficacy.	Adewoyin 2013; Brooks 2007; Chakrapani 2012; Gobat 2018; Grantz 2019; Jaffe 2020; Jalloh 2019; Lesch 2006; Mbunda 2018; Moutsiakis 2007; Newman 2006; Newman 2008a; Newman 2008b; Newman 2011b; Nyamathi 2004; Olin 2006; Slomka 2008; Tarimo 2010; Wentzell 2021	**Moderate confidence**	Minor concerns regarding adequacy and methodological limitations. Moderate concerns regarding relevance No/very minor concerns regarding coherence.
Finding 9: people were concerned that trial participation could result in adverse outcomes that would impact their ability to fulfil their caring responsibilities or their ability to work or could affect their health insurance.	Adewoyin 2013; Chakrapani 2012; Gobat 2018; Jaffe 2020; Lesch 2006; Newman 2006; Newman 2008a; Newman 2008b; Tarimo 2010; Wentzell 2021	**Moderate confidence**	Moderate concerns regarding relevance and adequacy. Minor concerns regarding methodological limitations No/very minor concerns regarding coherence.

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Finding 10: people did not always understand the difference between being antibody-positive and infected by the disease itself, or the immunity that may or may not be acquired through participation in a vaccine trial for a pandemic or epidemic disease.	Adewoyin 2013; Andrasik 2014; Brooks 2007; Chakrapani 2012; Craig 2018; Jalloh 2019; Koniak-Griffin 2007; Lesch 2006; Mbunda 2018; Newman 2006; Newman 2008a; Newman 2008b; Newman 2011a; Nguyen 2021 Olin 2006; Strauss 2001 (2006 study report); Voytek 2011	**High confidence**	Due to minor concerns regarding coherence, relevance adequacy and methodological limitations.
Finding 11: when making the decision to participate or not, people weighed up the potential harms of trial participation versus the potential harms of the disease.	Brooks 2007; Grantz 2019; Jaffe 2020; Jalloh 2019; Lesch 2006; Newman 2008b; Nguyen 2021; Wentzell 2021	**Moderate confidence**	Moderate concerns regarding adequacy and minor concerns regarding methodological limitations and coherence. No/very minor concerns regarding relevance.

2.2 Influence of other people			
Summary of review finding	**Studies contributing to the review finding**	**CERQual assessment of confidence in the evidence**	**Explanation of CERQual assessment**
Finding 12: people described how the attitudes of family members could influence their willingness to take part in a vaccine trial.	Chakrapani 2012; Craig 2018; Lesch 2006; Mbunda 2018; Nguyen 2021; Tarimo 2011; Voytek 2011; Wentzell 2021	**Moderate confidence**	Minor concerns regarding coherence, relevance and methodological limitations. Moderate concerns regarding adequacy.

2.3 Societal influences			
Summary of review finding	**Studies contributing to the review finding**	**CERQual assessment of confidence in the evidence**	**Explanation of CERQual assessment**
Finding 13: people feared stigma as a result of trial participation where this might carry implications about their sexuality, gender identity or disease status.	Andrasik 2014; Brooks 2007; Chakrapani 2012; Grantz 2019; Lesch 2006; Mbunda 2018; Moutsiakis 2007; Newman 2006; Newman 2008a; Newman 2008b; Nguyen 2021; Nyblade 2011; Strauss 2001 (2006 study report); Toledo 2014	**High confidence**	No/very minor concerns regarding coherence and adequacy. Minor concerns regarding methodological limitations. Moderate concerns around relevance.
Finding 14: people described how their level of trust/distrust in organisations involved in healthcare delivery, medical and scientific research, and governments influenced their decision to participate in a vaccine trial.	Andrasik 2014; Brooks 2007; Chakrapani 2012; Craig 2018; Grantz 2019; Jaffe 2020; Jalloh 2019; Koniak-Griffin 2007; Lesch 2006; Mbunda 2018; Moutsiakis 2007; Newman 2006; Newman 2011a; Newman 2015; Nguyen 2021; Nyamathi 2004; Olin 2006; Strauss 2001 (2006 study report); Tarimo 2011; Tengbeh 2018;	**High confidence**	Minor concerns with methodological limitations and relevance, no/very minor concerns with adequacy and coherence.

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	Toledo 2014; Voytek 2011; Wentzell 2021		
Theme 3: perceived personal and societal rewards that influence people's decision to participate in a vaccine trial for a pandemic or epidemic disease			
3.1 Personal rewards of trial participation			
Summary of review finding	**Studies contributing to the review finding**	**CERQual assessment of confidence in the evidence**	**Explanation of CERQual assessment**
Finding 15: people often viewed trial participation as a way of accessing vaccination with the potential benefit of reduced infection risk; improved knowledge of the disease; and improvements in general health.	Chakrapani 2012; Craig 2018; Jalloh 2019; Koniak-Griffin 2007; Newman 2006; Newman 2011b; Nyamathi 2004; Olin 2006; Strauss 2001; Tengbeh 2018; Voytek 2011; Wentzell 2021	**High confidence**	Minor concerns regarding methodological limitations, relevance and adequacy. No/very minor concerns regarding coherence.
Finding 16: people often considered trial participation as a way of helping society return to its prepandemic or pre-epidemic life.	Chakrapani 2012; Lesch 2006; Wentzell 2021	**Moderate confidence**	Major concerns regarding adequacy. Moderate concerns regarding relevance. Minor concerns regarding methodological limitations and coherence.
3.2 Making a difference: benefits for others			
Summary of review finding	**Studies contributing to the review finding**	**CERQual assessment of confidence in the evidence**	**Explanation of CERQual assessment**
Finding 17: people described their desire to help the community as an important factor in their decision to participate.	Adewoyin 2013; Brooks 2007; Chakrapani 2012; Chin 2016; Craig 2018; David 2021; Gobat 2018; Grantz 2019; Lesch 2006; Newman 2011a; Nguyen 2021; Nyamathi 2004; Slomka 2008; Strauss 2001; Tengbeh 2018; Tarimo 2010; Toledo 2014; Wentzell 2021	**High confidence**	No/very minor concerns regarding coherence. Minor concerns regarding methodological limitations and adequacy and moderate concerns regarding relevance.
Finding 18: people in professional or leadership roles described their perceived duty as part of these roles as an influencing factor in their decision-making.	Chakrapani 2012; Chin 2016; Craig 2018; David 2021; Grantz 2019; Newman 2011a; Newman 2011b; Nguyen 2021; Olin 2006; Tarimo 2010; Tengbeh 2018; Wentzell 2021	**Moderate confidence**	Minor concerns regarding methodological limitations, coherence, and relevance; moderate concerns regarding adequacy.
Finding 19: some people described how their decision to participate in a vaccine trial was influenced by the memory of family	Adewoyin 2013; Brooks 2007; Jaffe 2020; Moutsiakis 2007; Newman 2006; Newman 2011a; Newman	**Low confidence**	Minor concerns regarding methodological limitations and coherence,

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and friends who had died of the disease during the pandemic or epidemic and a desire to protect future generations.	2011b; Tarimo 2019; Toledo 2014; Voytek 2011; Wentzell 2021		moderate concerns regarding relevance and adequacy.
Finding 20: people described how a wish to support the advancement of science and medicine could influence a decision to take part in a vaccine trial in the context of an epidemic or pandemic.	Adewoyin 2013; Chakrapani 2012; David 2021; Gobat 2018; Grantz 2019; Jalloh 2019; Lesch 2006; Newman 2008b; Newman 2011a; Newman 2011b; Slomka 2008; Strauss 2001; Tarimo 2019; Toledo 2014; Wentzell 2021	**Moderate confidence**	Minor concerns regarding methodological limitations, coherence, and adequacy. Moderate concerns regarding relevance.

CER-Qual: Confidence in the Evidence from Reviews of Qualitative research.

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BACKGROUND

Description of the topic

On 11 March 2020, the World Health Organization (WHO) declared a COVID-19 pandemic (WHO 2020a). COVID-19 is a respiratory virus causing a multisystem disease triggered by severe acute coronavirus-2 (SARS-CoV-2) (Li 2020). Amid uncertainties about the spread and severity of the disease and the effectiveness of available interventions, vaccine development was prioritised for managing and controlling the disease spread (Sethi 2020). Consequently, the demand for rapid vaccine development and testing resulted in a large number of vaccine trials (Darzi 2021; Janiaud 2021). However, there is a lack of information on factors influencing recruitment to vaccine trials (Detoc 2019). Recruitment rates for clinical trial participation, more generally, are variable across countries and trials (Darzi 2021; Davis 2020). Recruitment to randomised trials is challenging, and poor recruitment can result in the need for additional time or funding, reduced confidence in results or early trial closure (Kaur 2012; Swan 2009; Treweek 2018). Evidence indicates that around half of all trials fail to recruit the prespecified target number of participants (Bower 2007; McDonald 2006; Sully 2013). Failure to recruit is one of the primary reasons for discontinuation in clinical drug trials (Walters 2017). Recruitment to vaccine trials can be particularly challenging (Cattapan 2019; Harrington 2017). Unlike trials of healthcare treatments, vaccine trials typically involve healthy volunteers who may have concerns about the safety risks associated with enroling in a vaccine trial (Harrington 2017). Potential participants may also have other concerns, and weigh benefits and harms differently (Borobia 2021; Detoc 2017; Gouglas 2018). This can result in recruitment difficulties and subsequent trial discontinuation (Detoc 2019; Petkova 2020).

The COVID-19 pandemic has disproportionately affected Black, Asian, and ethnic minority populations and vulnerable groups (Public Health England 2020; Raisi-Estabragh 2020). Ethnic minority communities, homeless people and vulnerable migrants have a higher mortality risk compared with those of white ethnicity in the UK and USA (Public Health England 2020; Treweek 2020; Yao 2020). Ethnic minority groups and vulnerable populations have been under-represented in COVID-19 vaccine trials (Ekezie 2021; Treweek 2020).

Older people, who are disproportionately affected by COVID-19, are less likely to participate in a vaccine trial and are often not included in the initial vaccine licensure trials (Flores 2021). Vaccine safety and efficacy must be established before public use, and this requires high-quality evidence from well-designed and conducted vaccine trials (Detoc 2019). Evidence suggests that vaccine hesitancy and doubts about vaccine safety may influence the recruitment of participants to vaccine trials (Larson 2016; Wilson 2021).

Pregnant and lactating women are often excluded from vaccine clinical trials because of concerns around administering a vaccine without knowledge of its impact on the foetus and baby (Blehar 2013). Additionally, the physiological complexity of pregnancy added to the fear of legal liability increases the need for additional institutional review before considering including pregnant women in trials (Kons 2022). The decision for the pregnant woman to participate or not is made in cognisance of the fact that she is deciding for her baby as well as herself. In a review of the evidence related to the immunisation safety during pregnancy, the WHO recommended that clinical studies into the effectiveness, safety and outcomes of vaccination in pregnant women in diverse settings should be facilitated (WHO 2014). Others suggest that pregnant women are a vulnerable group and the risks of administering trial drugs without adequate safety data is a significant risk to the woman and foetus (Smith 2020). During the COVID-19 pandemic, guidance for pregnant women concerning vaccine safety in pregnancy was limited, and there were differences in available information and advice causing confusion, which impacted women's decision-making (Kons 2022; Taylor 2021).

Including children in a vaccine trial raises several ethical questions (Atuire 2022). While safe and effective vaccines for children require testing, many countries, particularly low-income and middle-income countries, highlight ethical concerns in relation to clinical trial proposals, especially in the politically charged context of a pandemic (Atuire 2022; Joseph 2015), and where the evidence indicates very low risk from the pandemic disease to children (Ledford 2021). Some ethical questions include whether the vaccine, if approved, will be available in the country where it is tested. In the case of children, it is usual practice to commence trials with children only when the vaccine has been shown to be safe and effective in adults (Gill 2004; Mintz 2021). Vaccines developed during a pandemic have not usually been tested rigorously in adults, therefore the ethics of testing them on children is questionable.

Adults recruited to phase I vaccine clinical trials are healthy volunteers and do not have pre-existing clinical conditions that may be a variable in motivating people to participate in a clinical trial. Healthy volunteers derive no personal therapeutic benefit as they are not directly affected by the disease under study at that point in time. Identified motivational factors can include financial incentives (Lynch 2019), personal gratification or altruistic rewards (Kalbaugh 2021; Wang 2021). Studies on healthy volunteer motivations in vaccine trials have involved particular populations and diseases, such as HIV/AIDS (Kiberd 2009), or Ebola (Cattapan 2019). Cattapan 2019 identified a mix of self-interest and altruism in a study evaluating motivational factors in an Ebola virus epidemic.

Evidence would also suggest that people from non-white backgrounds are less likely to volunteer for research including vaccine trials (Robinson 2021; Razai 2021). Robertson 2021, in a large UK-based survey, identified that vaccine hesitancy was greatest amongst black, Bangladeshi and Pakistani populations in comparison to those with a white ethnic background. In one study exploring vaccine hesitancy across Europe, Stoeckel 2022 identified higher levels of vaccine hesitancy amongst those who do not trust mainstream media. Furthermore, higher social class and higher levels of education were related to lower levels of vaccine hesitancy. These findings underscore the complex and multifaceted nature of vaccine hesitancy, highlighting the need for tailored strategies to address it.

Additionally, people living in rural areas exhibit more vaccine hesitancy than urban dwellers. In the US, mistrust in the health system have been linked to vaccine hesitancy and low vaccination rates amongst some ethnic minority populations, particularly in black communities (Okoro 2021). This mistrust has been linked to previous unethical research studies and experiences of racial discrimination and inequities in healthcare provision (Okoro 2021; Quinn 2019).

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Furthermore, due to the urgent nature of vaccine development for a pandemic or epidemic disease, potential participants might be concerned about the rapidity of vaccine development and perceive that steps in the scientific and regulatory process may have been shortened, which may erode public confidence in participating in trials (Dyer 2020; Langford 2020). Limited timelines for the recruitment stage increase pressures on recruiting staff (Wilson 2021), and this can create tension if potential trial participants do not have sufficient time and information to guide their decision on whether to join a trial (Cattapan 2019).

How the intervention might work and how the health condition might affect people

Vaccine clinical trials depend primarily on the willingness of a diverse group of healthy volunteers to take part in large-scale trials. It is also important that there is representation across all communities to avoid a mismatch between the study population recruited for the trial and the population targeted for the vaccine. Therefore, it is important to identify factors influencing people's decision to take part, in the context of a pandemic or epidemic (Carlsen 2016; O'Callaghan 2020).

It is important to consider the public's support for vaccine trials for a pandemic or epidemic disease (Gobat 2018). Factors such as trust in health professionals, trust and confidence in the government, and knowledge of the disease have been identified as influencing factors (Finset 2020; Gobat 2019; Jaklevic 2020). It has been suggested that people may use an instinctive decision-making style related to decisions around trial recruitment in the context of a pandemic or epidemic (Gobat 2018). A decision to take part in a clinical trial can be influenced by several factors, including: how trial information is communicated; personal factors, such as how other people can influence the decision; and the potential benefit and harm of taking part (Houghton 2020). Specific factors associated with people taking part in vaccine trials can include older age (Hodgson 2021), having heard about vaccine trials through multiple sources and financial incentives (Cattapan 2019; Detoc 2019; Gobat 2018). Taking part in a vaccine trial for a pandemic or epidemic disease may also be influenced by factors such as concerns about the disease prevalence and spread, confidence in the vaccine safety and the impact of restrictive measures in the context of a pandemic or epidemic (Langford 2020). These can influence people's willingness to consider taking part in trials as their concerns for self and family, and the negative psychological effects of quarantine and stress can impact on the decision-making process (Brooks 2020; Wang 2020).

Understanding factors that influence people's decision to participate in trials is likely to help shape future communication between trialists and potential participants and support transparency of information and decision-making to optimise informed choice (Carlsen 2016; O'Callaghan 2020). This communication does not primarily aim to convince the individual to take part in a vaccine trial for a pandemic or epidemic disease but should ideally support the individual's informed choice about participation. In an informed decision-making situation, the person may choose to take part in a vaccine trial or, equally, choose not to.

Why is it important to do this review?

Previous reviews about recruitment to trials have considered barriers from the participant's perspective (Prescott 1999), and from the perspective of recruiting clinicians (Fletcher 2012; Prescott 1999). Other reviews have focused on recruitment to trials for specific therapeutic indications (e.g. oncology; Fayter 2007), or specific vulnerable populations (Glover 2015). In one qualitative evidence synthesis (QES), Houghton 2020 reviewed the barriers to and facilitators of recruitment to clinical trials across different healthcare settings from the perspective of both trial participants and decliners. Whilst this body of work offers valuable insight into potential factors associated with trial recruitment, such as perceived risk, treatment preference and trial burden, it falls short of providing specific insights for decision-making for taking part in vaccine trials in the context of a pandemic or epidemic.

To gain a comprehensive understanding of the factors associated with recruitment to pandemic- or epidemic-related vaccine trials requires exploration of the barriers and facilitators that guide decision-making amongst potential trial participants.

Qualitative research explores how people perceive and experience the world in which they live. Through synthesising qualitative studies exploring people's attitudes, views and decisions about pandemic or epidemic vaccine trial participation, we can identify factors that trialists should consider when developing strategies to inform and support public decision-making processes about recruitment to pandemic or epidemic vaccine trials. The findings from this review will inform current and future vaccine trials conducted in similar circumstances in the future.

OBJECTIVES

To explore the factors that influence a person's decision to participate in a vaccine trial in the context of a pandemic or epidemic.

METHODS

When preparing this review, we used the Cochrane Effective Practice and Organisation of Care Group's Protocol and Review Template v1.3 for QES (Glenton 2022).

Studies considered for this review

Types of studies

We included primary studies that used recognised methods of qualitative data collection and data analysis including ethnography, phenomenology, case studies, grounded theory studies and qualitative process evaluations. We included studies that used qualitative methods for data collection (e.g. focus group discussions, individual interviews, observation, diaries, document analysis, open-ended survey questions) and qualitative methods for data analysis (e.g. thematic analysis, framework analysis, grounded theory approaches).

We included mixed methods studies where it was possible to extract the data collected and analysed using qualitative methods.

We excluded studies that collected data using qualitative methods but did not analyse them using qualitative analysis methods (e.g. open-ended survey questions where the response data were analysed using descriptive statistics only).

We included both published and unpublished studies and studies published in any language.

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We included studies regardless of whether they were conducted alongside studies of the effectiveness of interventions to improve vaccination uptake for a pandemic or epidemic disease.

We did not exclude studies based on our assessment of methodological limitations as these may have contributed insights into particular contexts or circumstances as well as to the overall phenomenon (Carroll 2013). We instead used the information about methodological limitations to assess our confidence in the review findings.

Topic of interest

We included studies with a primary focus on people's experiences of, and attitudes to, participating in a vaccine trial in the context of a pandemic or epidemic.

We included studies that reported the views and experiences of adults aged 18 years and older. This included adults who had been invited to participate in trials as well as adults who had not received an invitation, those who accepted an invitation to participate and those who did not accept an invitation to participate.

By "vaccine trials in the context of a pandemic or epidemic" we referred to prophylactic or therapeutic vaccine trials related to the disease caused by the pandemic or epidemic and in which the trial was being conducted in response to, and during, the pandemic or epidemic. We included studies conducted in any setting that was experiencing a pandemic or epidemic.

We considered an epidemic to be a widespread disease outbreak within a region and a pandemic as an epidemic that spread over multiple regions or continents.

We considered a prophylactic or therapeutic vaccine as one that induced an immune response in an individual intended to prevent disease spread by reducing development of symptoms and severity of disease.

Search methods for identification of studies

Electronic searches

The Effective Practice and Organisation of Care Information Specialist developed the search strategies in consultation with the review authors (Cochrane (EPOC)).

We searched the following electronic databases on 28 June 2021: Ovid MEDLINE, EBSCOhost CINAHL, Scopus, Ovid PsycINFO, Epistemonikos and ORRCA (Online Resource for Research in Clinical triAls).

We developed search strategies for each database. We did not apply any limits on language or publication date. We included the MEDLINE filter for qualitative studies, which is a modified version of the University of Texas filter described at libguides.sph.uth.tmc.edu/search_filters/ovid_medline_filters ((("semi-structured" or semistructured or unstructured or informal or "in-depth" or indepth or "face-to-face" or structured or guide) adj3 (interview* or discussion* or questionnaire*))).ti,ab. or (focus group* or qualitative or ethnograph* or fieldwork or "field work" or "key informant").

This filter was used in the searches on Ovid MEDLINE, EBSCOhost CINAHL, Scopus and PsycINFO. It was chosen as it performed with the best balance of sensitivity and precision in a review by Wagner 2020. We provided all strategies used in the review in Appendix 1.

We searched the Cochrane COVID-19 Study Register for any qualitative study relating to COVID-19 vaccine trials because that was an ongoing pandemic at the time the searches were conducted. The Cochrane COVID-19 Study Register includes preprint material.

Searching other resources

We reviewed the reference lists of all the included studies and key references (i.e. relevant systematic reviews) (Horsley 2011), and conducted a cited reference search for all included studies in Web of Science Core Collection, Clarivate Analytics and Google Scholar.

We checked the reference lists of studies included in linked intervention reviews to identify any qualitative studies associated with these studies. We selected the included studies that exactly fulfilled the eligibility criteria.

In addition to searching the databases outlined, we conducted a search of theses on 24 June 2021 via Ethos, the DART E-theses portal and ProQuest Dissertations & Theses Abstract & Index.

Selection of studies

After removing duplicates, two review authors (PM, LB, MD, KR, EM, CH) independently assessed each title and abstract of the identified records to evaluate eligibility. We used Covidence software for title and abstract screening. We excluded references that did not meet the eligibility criteria. After this, we retrieved the full text of all the papers identified as potentially relevant by both review authors. Two review authors (PM, LB, MD, KR, EM, CH) independently assessed these full-text papers for inclusion. We resolved disagreements by discussion or, when required, by involving a third review author. Where appropriate, we contacted the study authors to request information.

Language translation

We designed our search strategy to include studies in any language and planned to use translation services if studies were in languages none of the review team were proficient in. We used open-source software in the screening phase for initial translation on any abstract in that category (Google Translate). However, following screening all included studies were in English.

Sampling of studies

QES aims for conceptual richness and contextual comparisons, rather than an exhaustive sample, and large amounts of study data can impair the quality of the analysis (Ames 2017; Suri 2011). We identified 45 studies that met our inclusion criteria. Due to the number of studies eligible for inclusion, we decided to sample the studies for more meaningful analysis, we chose the following three-step sampling frame (Ames 2017).

- First, in order to ensure that we captured diverse diseases classed as epidemic or pandemic that had a vaccine developed, we included all 45 studies that examined a range of pandemics or epidemics: tuberculosis (TB), HIV, Ebola, Zika and COVID-19.
- Second, we assessed the data richness of the studies focusing on TB, HIV, Ebola, Zika and COVID-19. To do this we used a simple 1 to 5 scale (Table 1), with permission from Cochrane (EPOC).

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- Third, from these studies, we sampled 36 papers of 35 studies that scored 3 or higher for data richness; but we also ensured spread across different geographical areas with different income levels.

Data extraction

We used QSR NVivo Version R1.6 to manage data extraction and the synthesis process. This enabled six review team members to work effectively and transparently on the synthesis (Houghton 2017). We extracted information about the first author, publication date, study language, country, setting, type of pandemic or epidemic, type of vaccine, whether participants were acceptors or decliners, whether the scenario presented to participants was real or hypothetical, gender and any other relevant information. We extracted information about how the studies were designed and conducted. Finally, we extracted all data relevant to the review's objective, including descriptions of themes and categories as well as illustrative quotes. Six review authors (PM, LB, MD, KR, EM and CH) extracted the data on all included studies with ongoing discussion and moderation to ensure consistency. Information about design, setting and methods were extracted from all the sampled studies. The data extraction form and process were pilot tested initially, and the revisions were agreed amongst review authors.

Assessing the methodological limitations of included studies

At least two review authors (from PM, LB, MD, KR, EM and CH) independently assessed the methodological limitations for each study using a quality assessment tool for qualitative studies that has been used in previous Cochrane Reviews (Ames 2017; Ames 2019; Houghton 2020). This tool was based on the CASP tool (CASP 2018), but has since gone through several iterations. We resolved any disagreements by discussion or, when required, by involving a third review author.

We assessed methodological limitations according to the following domains.

- Were the settings and context described adequately?
- Was the sampling strategy described, and is this appropriate?
- Was the data collection strategy described and justified?
- Was the data analysis described, and is this appropriate?
- Were the claims made/findings supported by sufficient evidence?
- Was there evidence of reflexivity?
- Did the study demonstrate sensitivity to ethical concerns?
- Any other concerns?

Once we assessed methodological limitations using the domains outlined above at individual study level, we assessed overall concerns regarding methodological limitations for each study. We reported our assessments in a Methodological Limitations table, using a 'Yes', 'No', 'Could not determine' rating (Table 2). We used these assessments to support our GRADE-CERQual (Confidence in the Evidence from Reviews of Qualitative research) assessment of our confidence in the review findings (Lewin 2018).

Data management, analysis and synthesis

We used the 'best-fit framework approach' to identify a 'lens' to analyse and synthesise the evidence from our included studies (Booth 2015). The best-fit framework synthesis method requires identification and subsequent modification of an existing (a priori) model or framework from a similar yet different phenomenon of interest (Carroll 2013). Our choice of the best fit method acknowledges that the context-specific nature of vaccine trials in a pandemic or epidemic may require further thematic synthesis, either external to, or within, the proposed framework.

The 'best fit' a priori framework synthesis involves several stages: 1. Identify a pre-existing conceptual model or framework; 2. Include all relevant qualitative studies satisfying criteria; 3. Code evidence from included studies against the a priori framework; 4. Use a thematic synthesis approach to generate new themes on any evidence that cannot be coded against the framework to supplement the framework's themes; 5. Create a new framework consisting of a priori themes and new themes supported by the evidence; 6. Revisit the evidence to explore the relationships between the themes and create a new model. We used all stages of the a priori framework synthesis to synthesise our findings (Booth 2015). Our final choice of framework was determined after familiarising ourselves with the data in the included studies. We opted to use a *thematic framework* based on themes from the previously published Cochrane QES that explored what influences people's decision to take part in trials in general (Houghton 2020). The original framework includes three themes with a further six subthemes (Table 3).

Coding consisted of six review authors (PM, CH, LB, MD, KR and EM) rereading the studies and applying the framework, moving between the data and the developing themes. Creating themes involved rearranging data according to relationships and then finally developing themes and interpretation, where we revisited the evidence to explore the relationships between the themes and considered how the themes addressed the review question and aim.

All the evidence could be coded against the three broad domains of the framework. However, we revised the wording of some of the main themes and subthemes to better reflect the synthesis findings. We included an additional subtheme in Theme 2 to reflect societal influences. The changes in the three themes and related subthemes are reflected in Table 4.

During all stages of data synthesis, the review team held regular meetings to facilitate critical discussion and interrogation of the data. Peer review of synthesised findings facilitated trustworthiness, coherence and relevance of the findings.

Developing implications for practice

When we had prepared the review findings, we examined each finding, identified factors that could have influenced recruitment for pandemic or epidemic vaccine trials, and developed prompts for future trialists. These prompts are presented in the 'Implications for practice' section. These prompts are not intended to be recommendations but are framed as questions to help trialists consider the implications of the review findings within their context. We obtained feedback from a selection of stakeholders including trialists, clinicians and potential trial participants from

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different countries about the relevance of these prompts and how they were framed and presented. We revised the prompts based on that feedback.

Assessing our confidence in the review findings

Five review authors (PM, LB, MD, KR and EM) used the GRADE-CERQual approach to assess our confidence in each finding (Lewin 2018). GRADE-CERQual assesses confidence in the evidence based on the following four key components.

- Methodological limitations of included studies: the extent to which there were concerns about the primary study's design or conduct that contributed evidence to an individual review finding.
- Coherence of the review finding: an assessment of how clear and cogent the fit was between the data from the primary studies and a review finding that synthesises those data. By cogent, we mean well-supported or compelling.
- Adequacy of the data contributing to a review finding: an overall determination of the degree of richness and quantity of data supporting a review finding.
- Relevance of the included studies to the review question: the extent to which the body of evidence from the primary studies supporting a review finding applies to the context (perspective or population, phenomenon of interest, setting) specified in the review question.

After assessing each of the four components, we judged the overall confidence in the evidence supporting the review finding. We judged confidence as high, moderate or low. The final assessment was based on consensus amongst the review authors. All findings started as high confidence and were then downgraded if there were important concerns regarding any GRADE-CERQual components.

Review author reflexivity

Author reflexivity considers any influences or biases that may impact the review process (Flemming 2021). The core review team includes researchers who had received health-specific professional training and those who had not. All review authors are researchers within health care. Some are focusing on trial methodology, and others on qualitative research in trials (PM, LB, MD and CH). All review authors have training and expertise in qualitative research and QES. Most were involved in a previous Cochrane QES reporting on the factors that influence people's decision whether to take part in a trial (Houghton 2020).

The review team have varying views on vaccine development and vaccination programmes. This variety will minimise the risk of one perspective dominating the review. These views have arisen from different personal and professional experiences, such as, but not exclusive to: practising as an infectious diseases doctor in a pandemic (XHC); conducting research in the areas of pandemic vaccine trials (RC), infectious diseases (XHC), recruitment to trials (PM, CH, LB, MD and DD), public health and health services research (KR, EM, CG and AB). All review authors believe that trial participation, both in the context of a pandemic or epidemic and otherwise, should be voluntary. Moreover, all review authors believe in the importance of easy access to evidence-based information about the potential benefits and harms of trial participation, including information about potential adverse effects and uncertainties.

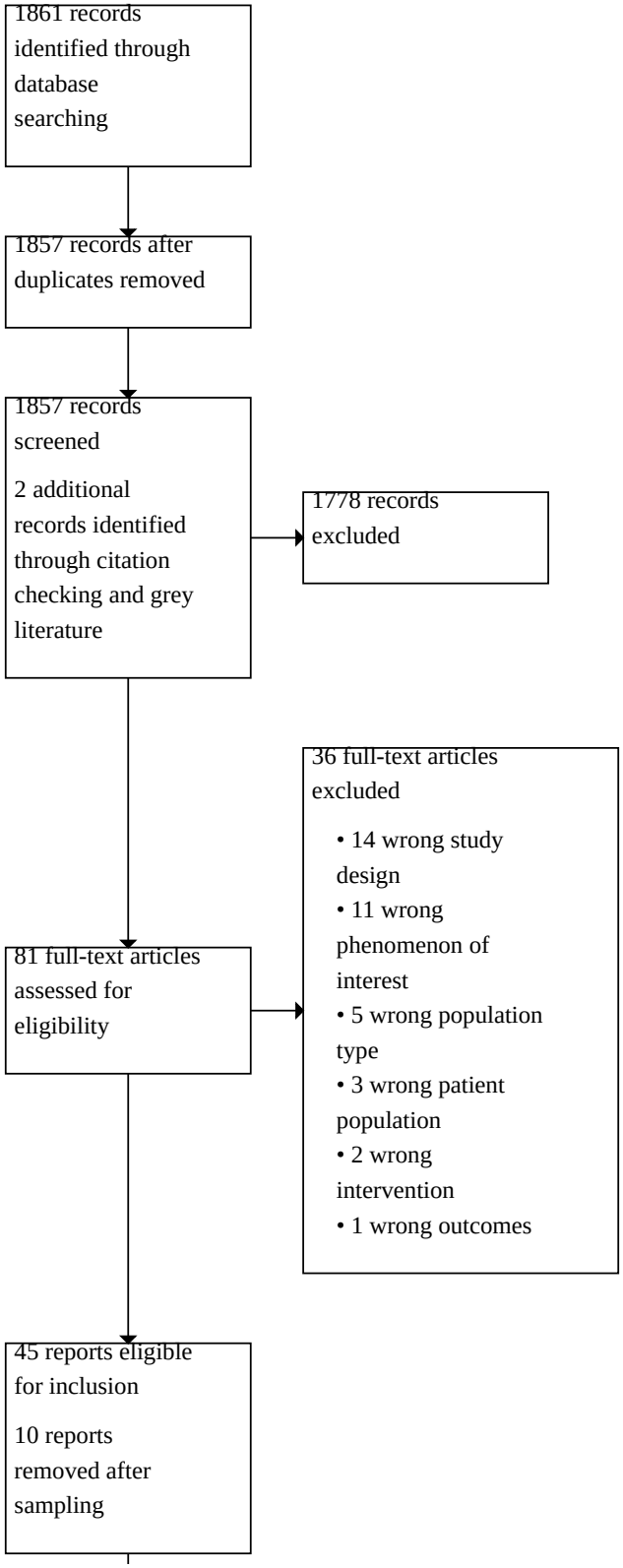
Central to reflexivity is remaining open to any viewpoints that may influence decision-making. This was achieved through regular team meetings at each stage of the review process where the team critically discussed personal views and experiences of vaccine development and vaccination programmes. Six primary review authors (PM, LB, MD, KR, EM and CH) conducted the synthesis, and provided feedback on their findings and interpretations to the whole review team. This involved sending drafts of the work to all the team and obtaining feedback and occasional meetings with members of the wider team. As different review authors approached the synthesis from different perspectives, this collaborative effort facilitated a richer, more nuanced understanding of a complex situation while allowing opportunities to highlight and discuss any preconceptions, values or beliefs held by individual review authors. The principal review author (PM) maintained a reflective diary to capture key discussions and decisions reached at team meetings. Memos on stages of synthesis were maintained in NVivo to provide a transparent account of the interpretation process and the development of themes.

RESULTS

We included a PRISMA flow diagram of our search results and the process of screening and selecting studies for inclusion (Figure 1). We identified 1861 records through database searching and, following screening, reviewed 81 full-text articles for eligibility. Forty-five reports were eligible for inclusion and after sampling 35 reports of 34 studies were included in the review. Where the same study (i.e. using the same sample and methods) was presented in different reports, we collated these reports so that each study (rather than each report) was the unit of interest in our review. There were two reports from one study (Strauss 2001). We included all unique data from all related study reports.

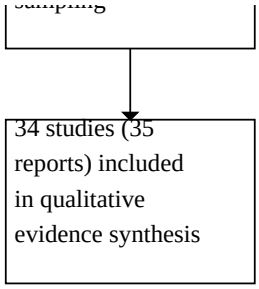
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Figure 1.



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Figure 1. (Continued)



We included 34 studies (35 papers) in our review (Adewoyin 2013; Andrasik 2014; Brooks 2007; Chakrapani 2012; Chin 2016; Craig 2018; David 2021; Gobat 2018; Grantz 2019; Jaffe 2020; Jalloh 2019; Koniak-Griffin 2007; Lesch 2006; Mbunda 2018; Moutsiakis 2007; Newman 2006; Newman 2008a; Newman 2008b; Newman 2011a; Newman 2011b; Newman 2015; Nguyen 2021; Nyamathi 2004; Nyblade 2011; Olin 2006; Slomka 2008; Strauss 2001; Tarimo 2010; Tarimo 2011; Tarimo 2019; Tengbeh 2018; Toledo 2014; Voytek 2011; Wentzell 2021). Findings of Strauss 2001 were first published in 2001 and then in 2006, involving the same study population. All the other papers were from different studies. Studies were published between 2001 and 2021 and were all published in English. The study authors gathered data via individual semi-structured interviews and focus group interviews that were analysed using a variety of qualitative analysis methodologies. See Summary of findings 1; Characteristics of included studies table, and Characteristics of excluded studies table, for further details on included and excluded studies.

Disease type

A total of 25 studies focused on invitation to take part in HIV vaccine trials (Adewoyin 2013; Andrasik 2014; Brooks 2007; Chakrapani 2012; Chin 2016; Koniak-Griffin 2007; Lesch 2006; Mbunda 2018; Moutsiakis 2007; Newman 2006; Newman 2008a; Newman 2008b; Newman 2011a; Newman 2011b; Newman 2015; Nyamathi 2004; Nyblade 2011; Olin 2006; Slomka 2008; Strauss 2001; Tarimo 2010; Tarimo 2011; Tarimo 2019; Toledo 2014; Voytek 2011). Of the remaining studies, five focused on Ebola (David 2021; Grantz 2019; Jalloh 2019; Nguyen 2021; Tengbeh 2018), one on TB (Craig 2018), one on Zika (Jaffe 2020), one on COVID-19 (Wentzell 2021), and one on participation in vaccine trials in general (Gobat 2018).

Study participants

There was a diverse range of study participants, with most studies involving people from various backgrounds, regardless of their sexual/gender identity or socioeconomic status. In terms of the studies focused on willingness to partake in HIV vaccine trials, eight studies included a diverse sample in participant type to include; men who have sex with men (two studies) (Adewoyin 2013; Chakrapani 2012), transgender women (one study) (Andrasik 2014), and minority groups (five studies) (Brooks 2007; Koniak-Griffin 2007; Nyamathi 2004; Toledo 2014; Voytek 2011). The study of Zika vaccine trials included females who were pregnant or recently pregnant. The participants from the other studies were a mix of gender and socioeconomic backgrounds (Jaffe 2020).

Of 34 studies, seven included people who accepted participation in a vaccine trial for a pandemic or epidemic disease (Chin 2016; Newman 2011b; Nguyen 2021; Slomka 2008; Tengbeh 2018; Wentzell 2021), and two included only people who had declined (Newman 2008a; Tarimo 2011). One study asked participants about their willingness to hypothetically take part in a vaccine trial (Olin 2006). The other included studies involved people who had either accepted or declined participation in vaccine trials.

Study settings

Sixteen studies were situated in the US (Adewoyin 2013; Andrasik 2014; Brooks 2007; Chin 2016; Craig 2018; Jaffe 2020; Koniak-Griffin 2007; Moutsiakis 2007; Newman 2006; Newman 2008b; Nyamathi 2004; Slomka 2008; Strauss 2001; Toledo 2014; Voytek 2011; Wentzell 2021); four in Canada (David 2021; Newman 2008a; Newman 2011a; Newman 2011b); four in Tanzania (Mbunda 2018; Tarimo 2010; Tarimo 2011; Tarimo 2019); two in Sierra Leone (Jalloh 2019; Tengbeh 2018); one in India (Chakrapani 2012); one in Guinea (Grantz 2019); one in South Africa (Lesch 2006); one in Kenya (Nyblade 2011); one in the Democratic Republic of Congo (Olin 2006); one in Belgium, Spain, Poland and the UK (Gobat 2018); one in Thailand, India, South Africa and Canada (Newman 2015); and one in Sierra Leone, Guinea and Liberia (Nguyen 2021).

Review findings

We organised our 20 findings under three broad themes and seven subthemes based on, but adapted from, an original framework (Houghton 2020), and outlining the factors that impact on recruitment to vaccine trials in the context of a pandemic or epidemic (Table 4).

Theme 1: factors under the control of the vaccine trial teams that influence people's decision to participate

This theme describes how the manner in which trialists design, conduct and communicate trials can influence people's decision to participate in a vaccine clinical trial for a pandemic or epidemic disease. These factors are described within two subthemes; communication of trial information and considerations around trial design.

Subtheme 1.1: communication of trial information

Finding 1: people appreciated when there was community involvement, including community leaders' involvement, in trial information dissemination. Community leaders themselves valued being involved in trial information

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dissemination, and developing health literacy within the community, but emphasised the need for clear details of vaccine development and trial processes to be effective in this role (moderate confidence finding).

Six studies highlighted collaborative partnerships and community involvement, including community liaison or leaders' involvement in information dissemination in vaccine trials as important (Brooks 2007; Lesch 2006; Nguyen 2021; Strauss 2001; Tarimo 2019; Toledo 2014). Being able to identify with someone and "*follow role models* (F, DBN)" (Lesch 2006, p.750) was shared as a motivator for listening to details around trial participation, and a research team with "*strong personal ties to the community*" was given a hearing because of those community links (2006 study report of Strauss 2001, p.567).

People who decided to participate in vaccine trials also spoke of the value they placed in the opinions of those who had previously lived through the experience of taking part in a vaccine trial (Tarimo 2019; Toledo 2014). "*Former volunteers*" were considered "*the correct people to impart knowledge, and these volunteers may be impactful in disseminating the knowledge given their previous experience*" (Tarimo 2019, p.9). In one study, the inclusion of ethnic minorities in HIV vaccine trials was seen as important by some participants but others "*noted the importance of not singling out particular ethnic and racial groups*" (Toledo 2014, p.e88). One trial reported that community groups in HIV vaccine trials in particular "*want to feel empowered: they want to feel engaged. Engage them in the actual setting up of the trial. Include them in every aspect*" (injecting drug user) (Newman 2011a, p.1754).

One HIV vaccine study that terminated early because of recruitment issues suggested that to effectively disseminate information about a trial "*you want the whole community, everyone should be involved … there should be every race, every class*" (Newman 2011a, p.1754). In contrast, other authors spoke of the benefit of concentrating the planning and rolling out information dissemination to community liaison individuals or community leaders in order to provide the community with confidence in the information available (Lesch 2006; Newman 2011a; Newman 2015; Strauss 2001).

Vaccine trial literacy was identified as a key component of community stakeholder engagement in information dissemination (Newman 2011a; Newman 2015). Achieving vaccine trial literacy could be influenced by several factors including language differences "*completely different vernacular vocabularies across multiple languages (even within country)*" (Newman 2015, p.6), educational standards, cultural beliefs and research naivety amongst communities (Newman 2011a; Newman 2015). Community leaders spoke of eagerness to be effective at vaccine trial information dissemination and helping to educate their communities and increasing trial literacy. To do this they needed to have a clear understanding of how the trial vaccine was developed and how the trial was being conducted. One participant in the trial commented: "*At least tell us what it is, a vaccine and then we can participate effectively, and be willing to support the trial*" (Newman 2015, p.6). Using the knowledge as a power concept, Newman 2015 highlighted the importance of equal power relationships in relation to information access between community leaders and researchers and an imbalance in this resulted in community leaders not having sufficient knowledge of the vaccine and the trial conduct to adequately impart information to potential trial participants (Lesch 2006; Newman 2015; Strauss 2001). "*Community advocates perceived their effectiveness in this role was constrained by unequal power dynamics and limited communication with research teams*" (Newman 2015, p.6).

On some occasions, disclosure of information related to vaccine development or the vaccine trial itself was not forthcoming, and this had a negative impact on community leaders' sense of involvement and value to the process (Strauss 2001). Community leaders expected appropriate inclusive information sharing rather than being party to limited information that served the researcher's purpose. "*Participants expressed a need for information and ongoing education programmes for community members and stated that this lack of education and information about vaccines stood in the way of trial participation*" (Lesch 2006, p.743). Being poorly informed of important aspects of the trial, such as vaccine development issues, trial conduct plans and issues, ongoing recruitment challenges such as potential trial cessation when recruitment was not adequate adversely affected community leaders' engagement with the process and reduced their willingness to promote trial participation (Brooks 2007; Lesch 2006; Nguyen 2021; Strauss 2001 (2006 study report); Tarimo 2019; Toledo 2014).

Overall, across studies people valued the involvement of those who had been prior volunteers, or current respected members of the local community or community leaders (or both) in the dissemination of information on vaccine trial recruitment (Brooks 2007; Lesch 2006; Newman 2011a; Newman 2015; Nguyen 2021; Strauss 2001 (2006 study report); Tarimo 2019; Toledo 2014). Those community members and leaders involved in trial recruitment highlighted the need for ongoing information updates from the researchers on the trial to facilitate their communication of trial information to the local community (Lesch 2006; Newman 2011a; Newman 2015).

Finding 2: people considering participating in a vaccine trial for a pandemic or epidemic disease valued the approachability and availability of researchers to answer questions related to the trial (moderate confidence finding).

Participants across seven studies highlighted the importance of the approachability and availability of researchers to answer questions and thus allay fears and misconceptions of potential trial participants (David 2021; Mbunda 2018; Newman 2011a; Nyamathi 2004; Olin 2006; Slomka 2008; Toledo 2014). This was particularly evident in HIV vaccine trials where a high level of concern existed amongst potential participants around the potential adverse effects of the vaccine.

Mbunda 2018 highlighted the importance of the trial team in informing participants about the trial and being available to '*settle qualms, doubts and myths*' about HIV vaccine clinical trials, one participant stated: "*The trial team taught us very well, made us understand the whole issue, helped me to overcome my fear*" (Mbunda 2018, p.29).

Participants regularly reported the importance of trialists having time to talk and explain the complexities of the study (Olin 2006; Slomka 2008; Toledo 2014), with some suggesting that this helped them feel less like "*guinea pigs*" who "*the scientists were using as part of their data to move a product forward*" (Nyamathi 2004, p.376).

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Three studies reported the positive impact of promised interaction with research staff "*that were open and upfront about potential risks could influence participation interest*" (Toledo 2014, p.e86) (Mbunda 2018; Nyamathi 2004; Toledo 2014).

Finding 3: people valued information on a vaccine trial for a pandemic or epidemic disease being communicated respectfully and in plain language that could be easily understood. People found leaflets a useful method of conveying information and felt they could be tailored to the information and language needs of specific populations (moderate confidence finding).

Participants in several studies highlighted the importance of communicating information about vaccine trials in a clear understandable way to facilitate a person's decision-making around trial participation (Andrasik 2014; Brooks 2007; Chakrapani 2012; Grantz 2019; Newman 2011a; Newman 2015; Newman 2015; Strauss 2001 (2006 study report); Tarimo 2019; Toledo 2014). As one participant (sex worker) indicated when discussing motivators to participate in an HIV vaccine clinical trial: "*You must first explain what the vaccine is and the effects it produces in the human body, and after having been informed, we will judge if is necessary to have it or not, but people have to be informed correctly*" (Olin 2006, p.536).

Participants highlighted the importance of using plain language in any documentation related to trial information. Participants across several studies acknowledged that many communities have their own subculture which brings with it nuances in language that may be difficult to understand by those outside that specific subculture (Chakrapani 2012; Grantz 2019; Newman 2015; Strauss 2001 (2006 study report); Tarimo 2019; Toledo 2014). They felt that using plain language made it more likely that it would be understood and would speak to '*the dialect of the population*' (Newman 2015). Participants in some studies who advocated using community liaison people in information dissemination as previously outlined, suggested that these community liaisons would be familiar with local language and cultural contexts and could advise on adaptation of documentation to optimise effectiveness (Lesch 2006; Newman 2015; Strauss 2001 (2006 study report)).

Several studies highlighted the importance of targeted information for specific groups of the population (Andrasik 2014; Brooks 2007; Newman 2015; Tarimo 2019; Toledo 2014). For example, Andrasik 2014 identified that transwomen had particular concerns as a group and would be reluctant to participate in an HIV vaccine trial without specific information related to their particular information needs; as one transwoman said: "*You can't get us (transwomen) into something if we know nothing about it*" (Andrasik 2014, p.8). In a similar vein, Grantz 2019 concluded from their findings that tailoring information to address the diverse backgrounds and experiences of the target population improved understanding and participation. Participants in some studies suggested that flyers were a useful method of conveying trial information in a manner that addressed local population needs in terms of language and cultural complexities (Tarimo 2019, p.9; Toledo 2014).

Participants in several studies spoke of the importance of how communication was relayed and considered it a key element that information that was communicated respectfully, as this increased the likelihood of a positive reception for that information (Chakrapani 2012). In one study evaluating willingness to participate in HIV vaccine trials amongst men who have sex with men, one participant noted: "*Doctors behaviour is the main, if he talks respectfully then it will obviously make a difference, if doctors behaviour is good then we will take part in the study. The main thing is how you talk*" (Panthi, FG5, Mumbai) (Chakrapani 2012, p.2).

Finding 4: people emphasised the importance of receiving all the information relating to the vaccine trial for a pandemic or epidemic disease including any potential risks and benefits, together with opportunities to ask questions about anything they do not understand (high confidence finding).

Participants in 13 studies highlighted the importance of open honest communication of trial information to ensure that people contemplating taking part in the vaccine trial had been given all the available information and also provided with opportunities to ask questions about anything they did not understand (Grantz 2019; Jalloh 2019; Lesch 2006; Mbunda 2018; Newman 2008a; Newman 2011a; Newman 2015; Nguyen 2021; Olin 2006; Strauss 2001 (2006 study report); Tarimo 2010; Tarimo 2019; Toledo 2014). Participants felt they would then be able to make an informed decision about participation when they had all the details.

Participants across 11 studies consistently spoke of the importance of providing those considering taking part in a trial with details of any potential risks of taking the vaccine (Grantz 2019; Jalloh 2019; Lesch 2006; Mbunda 2018; Newman 2011a; Newman 2015; Olin 2006; Strauss 2001 (2006 study report); Tarimo 2010; Tarimo 2019; Toledo 2014). When asked to identify what would encourage Hispanic people to participate in HIV clinical trials, one participant explained: "*The research team should tell the person who is going to participate about all of the risks that they run by getting the vaccine, if they could get sick or if there aren't any risks. The researchers need to be completely frank with the person who is going to participate in the study*" (Toledo 2014, p.e87).

Participants in some studies were concerned that they had inadequate information provided or that some of the details of the vaccine such as potential adverse effects had not been shared possibly because of the need to increase recruitment to the trial (Mbunda 2018; Newman 2011a; Newman 2015; Olin 2006). One participant in an HIV vaccine trial suggested: "*They never actually said that anything like this could possibly happen, but of course if they did nobody would take the trial. So, it was in the back of my mind, wondering, did they know that this was ever a possibility? Because of course if they told anybody nobody would take it*" (Newman 2015, p.453).

In one Ebola vaccine trial, participants highlighted feelings of concern about the adequacy of information provided, together with a lack of opportunity to engage in open communication with researchers around details of the Ebola vaccine (Jalloh 2019). Similarly, a nurse participant in another Ebola vaccine trial commented: "*The answers to my questions were lacking. The staff were not well placed to give me answers. They should have started with teaching and do a better job at convincing people to participate*" (Nguyen 2021, p.44).

Finding 5: people appreciated the availability of information about vaccines, how they were developed and worked, the potential benefits and risks, the implications of participation in a vaccine trial for a pandemic or epidemic disease, and the outcomes of previous studies to inform their decision-making around participation (high confidence finding).

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People across 17 studies expressed an interest in knowing more about vaccines and how they worked. They identified the type of information they thought people considering taking part in a vaccine trial in the context of a pandemic or epidemic wanted to have so that they could make an informed choice about participation (Adewoyin 2013; Andrasik 2014; Brooks 2007; Chakrapani 2012; Grantz 2019; Jalloh 2019; Lesch 2006; Mbunda 2018; Newman 2011a; Newman 2015; Nguyen 2021; Nyamathi 2004; Olin 2006; Strauss 2001 (2006 study report); Tarimo 2011; Tarimo 2019; Toledo 2014). This included information about how the vaccine was developed, its contents and potential adverse effects, and information about the trial results to date and what taking part in a trial would mean for them.

Participants across several studies felt that the provision of detailed information on the development of the vaccine was important when considering participation (Jaffe 2020; Newman 2008a; Newman 2011a; Olin 2006). In one HIV vaccine trial, participants in five of the study's six focus groups highlighted their limited knowledge and uncertainties regarding specifics about the vaccine was as a barrier to their participation (Newman 2006). One participant asked: "*where will they find the virus? Will they take it from a HIV positive person or are they just simply making it?*" (Newman 2006, p.213). In one study, the most frequently cited barrier by potential participants to HIV trial participation was a lack of sufficient information around the vaccine and the trial (Andrasik 2014). Ongoing HIV education as well as information on the trial was reported to promote participation in some HIV vaccine clinical trials (Lesch 2006; Slomka 2008; Toledo 2014).

Many participants across studies had specific concerns around adverse effects related to the vaccine (Brooks 2007; Grantz 2019; Lesch 2006; Nguyen 2021; Nyamathi 2004; Olin 2006; Tarimo 2010). These concerns were particularly evident in people considering participation in HIV vaccine trials. Lack of adequate information was reported as leading to misinterpretation which could lead to people declining to participate in trials. Participants expressed that they wished to be informed around all aspects particularly adverse effects, so they could weigh up the risks of participation to them. Participants in several studies were concerned at the limited information available on how safe it was to take the vaccine (Brooks 2007; Grantz 2019; Lesch 2006; Nguyen 2021; Nyamathi 2004; Olin 2006; Tarimo 2010). While they knew the purpose of the trial was to determine safety and efficacy, they wanted to have some knowledge of these aspects to help them decide around participation (Grantz 2019; Nguyen 2021).

People across several studies wanted information on aspects of the trial such as: the content of the vaccine, the stage of the trial, the results to date, who might benefit, credibility of the researchers conducting the trial and outcomes of previous studies (Andrasik 2014; Brooks 2007; Chakrapani 2012; Grantz 2019; Newman 2011a; Newman 2015; Strauss 2001 (2006 study report); Tarimo 2019; Toledo 2014). Clear transparent information particularly in relation to HIV vaccine clinical trials and potential risks to participants was highlighted by participants as fundamental to informed decision-making. Studies reported participants expressed interest in knowing how the vaccine trial had turned out '*what they hoped to achieve and information after the trial to know if it has been successful or not*' (Nyamathi 2004, p.376). Understanding the implication of participation in a vaccine trial was identified by participants in one study as critical to informed decision-making (Strauss 2001, 2006 study report). The information content was considered more useful by participants in some studies if it was targeted at a specific need of a particular group, for example a woman looking to start a family may have information needs around how being on an HIV vaccine trial may impact on when she can become pregnant: "*I didn't have that worry of being infertile because of the vaccine … I may get another child if I wish … but my worry is that I don't know what will be the side effects of that vaccine in the body!*" (Informant 14, woman) (Tarimo 2011, p.e14619).

Subtheme 1.2: considerations around trial design

Finding 6: people emphasised the importance of participation being easy, convenient and causing minimal disruption. People were also concerned about possible distress arising from aspects of the trial design (high confidence finding).

Participants in several studies highlighted the importance of convenience as a factor in trial participation (Brooks 2007; Craig 2018; Lesch 2006; Newman 2008b; Toledo 2014, Voytek 2011), with some studies reporting specific factors such as practical and simple in design (Brooks 2007; Lesch 2006; Nguyen 2021), a time commitment that was not prohibitive (Craig 2018; Gobat 2018; Grantz 2019; Newman 2008a; Newman 2008b; Slomka 2008; Toledo 2014), reasonable travel expenses and distance to travel (Grantz 2019; Lesch 2006; Newman 2006; Slomka 2008), and preferably located in a familiar centre (Newman 2006; Newman 2008b; Toledo 2014; Voytek 2011). Logistical demands imposed by a vaccine trial, such as the required number and frequency of study visits, and the duration of the trial, location of the trial centre and cost of getting there were considered by many as potential barriers to participation. Participants across studies indicated a preference for minimal attendance, as one suggested: "*I would prefer going once* [clinic visit] *and getting it all*" (Brooks 2007, p.54), within easy to access facilities "*… would be concerned about the hassle of getting to the trial headquarters*" (Newman 2006, p.214), and financial support to attend the trial site. One participant considering participation in an HIV vaccine trial suggested: "*I must be going to the clinic, where will I get the money to go to the clinic, because I must get the taxi, and all that? I don't have money to go to the trial site*" (F, KOSH) (Lesch 2006, p.746).

Frequency of attendance had a direct impact on availability for work, as one participant in a study looking at HIV vaccine trial motivators indicated: "*If I take too much time off of work and tell them that, 'Oh, I have another appointment' … what would my potential employer think*" (Newman 2008a, p.6).

The time commitment was a concern for participants with caring responsibilities for family members (Toledo 2014; Voytek 2011). In addition, delays in starting a trial "*opened up the possibility for participants to change their minds*" (Nguyen 2021, p.44).

Concerns around possible distress were important considerations for participants in several studies when deciding to participate. The route of administration was a barrier to participation (e.g. injection or oral) (Newman 2006) based on fear of needles and blood collection (Grantz 2019; Voytek 2011).

Having a confirmatory test for HIV before participation in an HIV vaccine trial was a major concern for participants (Adewoyin 2013; Lesch 2006; Tarimo 2010). Some worried that being on the trial would suggest they were HIV positive by virtue of their participation

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(Andrasik 2014; Lesch 2006). As one woman invited to an HIV vaccine trial stated: "*Testing for HIV is not a joke — I get freaked out every time I do it. Even though I know I have not done anything crazy or whatever, you know? The bottom line if I've had sex anything is possible … testing for my status willingly for this thing is gonna be a problem for me and for a lot of other people as well*" (F, CT) (Lesch 2006, p.746).

The follow-ups and routine HIV-testing associated with participating in the HIV vaccine trial inform participants if they are infected earlier than if they were not on the trial and this was a cause of distress (Tarimo 2010). Also, specific to HIV vaccine trials was participants' desire for full assurances of privacy and confidentiality (Chakrapani 2012; Lesch 2006).

Abstinence from penetrative sex during an HIV vaccine trial period was a deterrent to participation (Mbunda 2018; Tarimo 2011). For instance, a newly married man postponed enroling to give priority to having a child: "*First, it was the vaccine on trial, and we were told that if we accept to participate in that program we are not supposed to engage in penetrative sexual intercourse with any woman for a year to avoid its effects in pregnancy. At that time, I was doing another attempt in order to get a child!*" (Informant 12, man) (Tarimo 2011, p.e14620).

Finding 7: people described incentives such as money or access to additional support services as an important consideration when deciding whether or not to participate (high confidence finding).

Participants in many studies considered monetary incentives a motivating factor in reaching a decision to participate in vaccine trials in the context of a pandemic or epidemic across numerous disease types; HIV (Brooks 2007; Chakrapani 2012; Chin 2016; Koniak-Griffin 2007; Lesch 2006; Newman 2006; Newman 2008a; Newman 2008b; Nyamathi 2004; Slomka 2008; Strauss 2001; Toledo 2014; Voytek 2011; Wentzell 2021), TB (Craig 2018), Ebola (David 2021; Grantz 2019), and COVID-19 (Wentzell 2021). Monetary incentives were important for different reasons, for example, those living in poverty or homelessness needing compensation, and those taking time away from their work to participate in a trial needing compensation for loss of earnings.

The importance of a financial incentive was particularly evident in trials recruiting participants who were living in poverty, on low incomes or undergraduate students. In the COVID-19 vaccine trial, a minority of participants were aged in their 20s and enroled for the money (Wentzell 2021). Moreover, in an HIV vaccine trial recruiting men who have sex with men in India, a participant stressed that: "*If kothis in dhandha [sex work] need to participate, then some money other than travel allowance has to be given, since their earnings depend on their sex work*" (KI1, Chennai) (Chakrapani 2012). In addition, a homeless participant in another HIV vaccine trial revealed that: "*For me it would have to be monetary compensation. I don't care what the side effects are, as long as I know I'm going to be taken care of* " (Koniak-Griffin 2007, p.691). Moreover, in an Ebola vaccine trial, a participant revealed: "*If they had not given me any money, I wouldn't have done the study.*" (David 2021, p.4).

However, participants in some studies viewed financial incentives suspiciously (Craig 2018; David 2021; Newman 2008a; Newman 2011a; Slomka 2008; Wentzell 2021). A perception amongst older participants in a COVID-19 trial was that compensation raised an ethical concern (Wentzell 2021). For example, one participant recalled that when she was contacted by the trial team to volunteer: "*they were like, 'you will be compensated' and I was like, 'Well that's not why I'm doing it*'" (Wentzell 2021, p.2449). Additionally, in an HIV trial, participants highlighted that excessive payment "*may be tantamount to coercion*" (Newman 2008a, p.1094).

The provision of resources, supports and services were considered important in helping people decide on participating in vaccine trials. In one HIV vaccine trial, assistance with 'basic needs' would help transwomen participate in HIV vaccine trials because they had little time left for other activities such as research participation (Andrasik 2014).

For many HIV vaccine trials where vaccine-induced infection was a concern, participants worried about who would take care of their medical care and associated costs (Adewoyin 2013; Brooks 2007; Koniak-Griffin 2007; Newman 2006; Newman 2008b; Slomka 2008; Strauss 2001 (2006 study report)), financial compensation for any physical or social harm (Chakrapani 2012; Strauss 2001 (2006 study report)), the need for health and life insurance and compensation for family members (Chakrapani 2012; Nyamathi 2004; Olin 2006; Tarimo 2010), financial survival of their family if they lost employment (Lesch 2006), and support with dealing with insurance (Newman 2008a). Prompt quality care and compensation for their family in the event of serious adverse events was also a concern for participants in an Ebola vaccine trial (Jalloh 2019). A male participant in a study exploring HIV vaccine trial participation suggested that: "*There has to be some kind of help, support. You have to be sure someone will take care of you and your family if something happens*" (Gay Latino man) (Newman 2006). A police officer participant in an HIV vaccine trial study in Tanzania asked: "*Will I be insured if I die after introducing the virus? What will I leave my children with? We have African families … One thinks that if I die after being vaccinated; won't I leave them* [the family] *in difficulties?*" (Tarimo 2010).

As one participant in an Indian-based study of HIV vaccine trial participation amongst men who have sex with men stated: "*If the vaccine fails, if after taking the vaccine I become 'positive,' then what about me after that? If the company [trialists] is giving me some policy … some budget for me … either they give money or they give a job that remains a lifetime … then we can take part in that study*" (Panthi, FG5, Mumbai) (Chakrapani 2012).

In some of the included studies, potential trial participants reported being more likely to agree to participate in a vaccine trial in the context of a pandemic or epidemic if they were to experience quicker access to free health care for the duration of the trial (Brooks 2007; David 2021; Gobat 2018; Grantz 2019; Mbunda 2018; Newman 2006; Slomka 2008; Tarimo 2019; Tengbeh 2018). This was particularly common amongst low-income populations with limited or no health insurance (Brooks 2007; Grantz 2019).

This improved access to health care was reported by many individuals as being a means of accessing regular check-ups and health screening that they would not otherwise have access to (Mbunda 2018; Slomka 2008; Tarimo 2019; Tengbeh 2018). One participant in an HIV vaccine trial reported: "*There were so many advantages because to participate in these studies [HIV vaccine trials], you first have to undergo a medical check-up. The act of being checked for your health status is one of the greatest benefits of participation. Another benefit is to know that your health is safe, and*

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another benefit we got by participating was that for those of us who were found with some problems [unhealthy status], we were treated. Those were the benefits we got" (Tarimo 2019). Access to such healthcare was voiced by some participants in an Ebola vaccine trial as being of higher value than the vaccine itself (Tengbeh 2018). In one study of individuals who participated in a Phase II Ebola vaccine clinical trial in Canada, this was referred to as "VIP care", with trial participants experiencing "*easier access to nurses and doctors, closer follow-up and better access to care*" (Tengbeh 2018).

Other participants expressed the view that contacts they made through participation in a vaccine trial could increase access to social services and offer opportunities for employment (Strauss 2001; Tengbeh 2018; Voytek 2011). One woman who participated in an HIV vaccine trial said: "*I have gotten a lot out of it … because I was in a (study) before … they had assisted me in getting clean before I relapsed … They helped me with my housing … And then … I still benefit from it as far as … if there was something going on, I could just ask anybody in here for assistance. I really believe that if I were in need, they would assist to the best of their capability*" (Voytek 2011). For participants of some HIV vaccine trials, the availability of condoms at the trial centres was an additional perceived benefit (Mbunda 2018).

Theme 2: personal, family and societal factors that influence people's decision to participate in a vaccine trial for a pandemic or epidemic disease

This theme describes personal, family and societal factors that influence people's decision to participate in a vaccine trial in the context of a pandemic or epidemic. Personal factors are described as *weighing up the risks and benefits*; the influence of family is presented under *Influence of others*; *and societal influences* describes fear of stigma and issues around trust.

Subtheme 2.1: weighing up the risks and benefits

Finding 8: people were hesitant to participate if they had concerns about vaccine side effects, or vaccine efficacy (moderate confidence finding).

Many studies identified reasons why individuals were reluctant to take part in a vaccine trial for a pandemic or epidemic related to concerns about vaccine adverse effects or vaccine efficacy (or both) (Adewoyin 2013; Brooks 2007; Chakrapani 2012; Gobat 2018; Grantz 2019; Jaffe 2020; Jalloh 2019; Lesch 2006; Mbunda 2018; Moutsiakis 2007; Newman 2006; Newman 2008a; Newman 2008b; Newman 2011b; Nyamathi 2004; Olin 2006; Slomka 2008; Tarimo 2010; Wentzell 2021).

Some individuals expressed concerns about the newness of the vaccine and they did not want to feel "*like a guinea pig*" by taking part in a trial (Moutsiakis 2007; Newman 2011b). For instance, one participant invited to an HIV vaccine trial stated: "*Guinea pigs are considered expendable*", with another adding, "*I don't want to be the guinea pig!*" (Moutsiakis 2007, p.256). For individuals in many studies, fear of both short- and long-term vaccine adverse effects reportedly influenced their decision to participate in a vaccine trial for a pandemic or epidemic disease (Adewoyin 2013; Andrasik 2014; Brooks 2007; Chakrapani 2012; Craig 2018; Grantz 2019; Jalloh 2019; Lesch 2006; Newman 2006; Newman 2008a; Mbunda 2018; Nguyen 2021; Nyamathi 2004; Slomka 2008; Voytek 2011). Specifically related to HIV vaccine trials included in the review, no previous awareness or knowledge about HIV vaccines and HIV vaccine trials fuelled "*Fear of the unknown*" and enroling was viewed "*riskier than you might think*" (Newman 2008a, p.1094).

This fear was also captured by a participant in an Ebola vaccine trial: "*Supposed you take the [experimental] vaccine and it results in Ebola … what if there are serious reactions to the vaccine, or any other medical complication as a result of the vaccination requiring medical treatment? What happens? These are big issues*" (Jalloh 2019, p.6).

The fear associated with the risk of long-term adverse effects was expressed as a major concern for participants in many studies (Adewoyin 2013; Brooks 2007; Chakrapani 2012; Grantz 2019; Jalloh 2019; Lesch 2006; Mbunda 2018; Newman 2006). This fear is illustrated in one Ebola vaccine trial participant's view that the three-month observation window was: "*not enough to study the side effects; they could happen three, five, ten years later*" (Grantz 2019, p.7168). Participants worried about the risk of impotence or insanity (Chakrapani 2012), impact on future fertility (Lesch 2006; Mbunda 2018), effects on bone marrow and possible kidney failure (Brooks 2007), liver and heart damage (Nyamathi 2004), and damage to liver and kidneys and hair loss (Newman 2006). This fear is illustrated in the following HIV vaccine trial participant comment: "*I mean with the vaccine, your liver, your kidneys can be harmed.*" "*Will it make me lose my hair?*" (Newman 2006, p.213). Potential negative interactions with hormone therapy or sexual reassignment surgery may have influenced participation amongst male-to-female transgender participants in an HIV vaccine trial (Andrasik 2014).

In terms of fertility, women in the study by Newman 2008a raised concerns about possible teratogenic effects of both experimental and approved HIV vaccines, and how that would impact on fertility and breastfeeding. This was echoed in Tarimo 2010 where women had concerns about fertility. All participants were female police officers. As outlined by one female participant: "*Is there any possibility for me to get a child? Won't they [the researchers] just destroy my gametes!*" (p.6). Furthermore, in this study, male participants had concerns about impotence following receipt of the HIV vaccine. Some participants in the same study were concerned about having to postpone pregnancy while participating in the trial (Tarimo 2010). Specifically, in relation to a Zika vaccine trial, Grantz 2019 and Jaffe 2020 found that some women felt it was worth the risk to receive the vaccine, whereas others did not. As one female participant stated: "*The risks of having a baby born with Zika are so much, are so far greater than the risk of any type of vaccine that they would have developed*" (Jaffe 2020, p.6925).

Short-term adverse effects of concern were expressed to a lesser degree and included allergy or vaccine-induced infection (Chakrapani 2012), headaches or nausea (Grantz 2019). In one Ebola vaccine trial, short-term adverse effects influencing participants' decision to participate were fever, headache, vomiting, muscle soreness, sweats and dizziness, because these were the symptoms present in early Ebola virus disease (Nguyen 2021).

For some, their energy and intent were focused on staying healthy and avoiding "*adding anything unnecessary*" to their body (Craig 2018, p.6), caring for their "*own self and health and protection*" (Newman 2011b, p.456), and they would "*rather just stay healthy*" (Adewoyin 2013, p.22). Two studies reported views of participants not concerned about adverse effects. In a COVID-19 vaccine trial, one participant noted: "*I don't really have any side*

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effects, but if they come, it's just part of the research. That's why they're paying me" (Wentzell 2021, p.2449). Similarly, in an HIV vaccine trial, a participant believed that the risk of adverse effects was not a major concern, adding: "*The health concerns were minor; I mean, they weren't negligible but they were minor. I know that if I had any side effects, I don't think they would be life threatening—not from a vaccine … unlikely*" (Newman 2008a, p.1094).

Evidence of a vaccine's efficacy was an important factor in deciding to participate in some studies (Jaffe 2020; Jalloh 2019; Newman 2006; Newman 2008a; Newman 2008b). Newman 2008b outlined that "*concerns about efficacy were expressed in regard to both experimental and approved HIV vaccines. Respondents stated, albeit paradoxically, that they would be hesitant to participate in a trial of an HIV vaccine that had uncertain efficacy*' (p. 4). Having "*more proof*" on results from earlier trials affected the decision-making of one public health leader participant in an Ebola vaccine trial: "*The only thing that will affect my decision in participating is to have more proof on the sample cases conducted [in earlier trials] and the successful results [of those trials], the lab [results], historical background, and the agency involved [in the trial] especially on their responsibilities and reliability*" (Jalloh 2019, p.7). However, in one trial, some participants reported not being influenced by the vaccine's efficacy, understanding that: "*the efficacy is still not established … so that's why they have this trial*" (Newman 2008a, p.1095)

Finding 9: people were concerned that trial participation could result in adverse outcomes that would impact their ability to fulfil their caring responsibilities or their ability to work or could affect their health insurance (moderate confidence finding).

Many studies identified several perceived risks to participation beyond the possible adverse effects from receiving the vaccine itself (Adewoyin 2013; Chakrapani 2012; Gobat 2018; Jaffe 2020; Lesch 2006; Newman 2006; Newman 2008a; Newman 2008b; Tarimo 2010; Wentzell 2021).

Individuals who already had children, or had caring responsibilities, voiced concerns for their dependent's wellbeing should something adverse occur because of trial participation (Chakrapani 2012; Gobat 2018; Wentzell 2021). In the context of an HIV vaccine trial, one focus group member outlined: "*Many kothis have dependent parents to take care [of]. More than any other person, kothis love their parents very much. Hence, I do not know whether they will participate in this vaccine trial*" (Chakrapani 2012, p.4).

In addition, participants in some studies reported concerns about employability, or losing their employment, following enrolment in a vaccine trial (Adewoyin 2013; Lesch 2006). Furthermore, participants in some studies had concerns about the impact of participation in the trial on their health insurance eligibility (Adewoyin 2013; Newman 2006; Newman 2008a). One participant discussing possible enrolment in an HIV vaccine trial stated: "*Employers cannot hire you or give you medical insurance for pre-existing conditions … Like one of my friends, he, gorgeous, gorgeous guy, he got hired by El Al Airlines which is based out of Dubai and they give you HIV tests and he was positive and they said sorry, we don't want you … God, if, if my blood showed up this positive you know, for the rest of my life, I think that creates problems with careers; whether you are changing jobs, changing underwriters, changing insurers*" (Adewoyin 2013, p.23–24). In another HIV vaccine trial, one participant outlined: "*the biggest worry would be your disability policy and you are disqualified and you might not be able to qualify for insurance after that*" (Newman 2006, p.214).

Finding 10: people did not always understand the difference between being antibody-positive and infected by the disease itself, or the immunity that may or may not be acquired through participation in a vaccine trial for a pandemic or epidemic disease (high confidence finding).

Across many trials, a perceived risk of taking part was developing the disease or testing positive to an antibody test as a result of vaccination. This belief was reported by participants in HIV trials (Adewoyin 2013; Andrasik 2014; Brooks 2007; Chakrapani 2012; Koniak-Griffin 2007; Lesch 2006; Mbunda 2018; Newman 2006; Newman 2008a; Newman 2008b; Newman 2011a; Olin 2006; Strauss 2001 (2006 study report); Voytek 2011), two Ebola trials (Jalloh 2019; Nguyen 2021), and one TB trial (Craig 2018).

There was reported lack of understanding of the difference between being antibody-positive rather than infected by the pandemic disease itself (Olin 2006), and this caused fear. For example, one man in reference to an HIV vaccine trial in New York outlined: "*And, like, who wants to go through that mental anguish, you doing something good, putting yourself through vaccine trial and then all of a sudden when you do get tested, oh, your test came back positive. You know how, nobody know how that is going to affect you mentally*" (Adewoyin 2013, p.23). Even when individuals understood the difference of being falsely HIV-positive after vaccination, there was a fear of being perceived by others as HIV positive (Mbunda 2018).

In one HIV vaccine trial, respondents mostly understood that a false-positive result did not signify HIV infection; however, they worried about dealing with others' reactions to this and having to prove they are really negative (Newman 2008a). Moreover, there was a concern for risks to wives in one HIV vaccine study including men who have sex with men, fearing the virus might "*jump from him to her*" (Chakrapani 2012, p.e51081).

Conversely, there was a belief that the HIV vaccine offered protection encouraging risky sexual behaviours (Chakrapani 2012; Newman 2006; Newman 2011a; Newman 2015). Some believed that having the HIV vaccine would protect them and those engaged in sex work would do so without condoms, "*they will start engaging [in sex work] without condoms*" (Kothi, FG7, Chennai) (Chakrapani 2012, p.e51081). In one HIV vaccine study, one participant made reference to being like 'superman' after having the vaccine: "*The understanding of vaccine to the general public means I am immune: you have given me the invisible cloak; you've given me the Superman suit. I'm all good*" (African/Caribbean key informant) (Newman 2011a, p.1753). Similarly, engaging in risky sexual behaviour believing to be protected against HIV because of trial participation whereas they could have received a placebo was a concern raised in a trial involving ethnic minority groups (Newman 2006). There was a lack of understanding amongst participants in some studies on the implications in being in either the intervention or the control group (Chakrapani 2012; Newman 2006; Newman 2011a; Newman 2015).

Finding 11: when making the decision to participate or not, people weighed up the potential harms of trial participation versus the potential harms of the disease (moderate confidence finding).

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Participants in some of the included studies weighed up the perceived risk of the vaccine trial versus the risk of getting the disease. Some felt that any risk as a result of partaking in a vaccine trial for a pandemic or epidemic disease was preferable to the risk of getting the disease that the vaccine had been developed for (Brooks 2007; Grantz 2019; Jaffe 2020; Jalloh 2019; Lesch 2006; Newman 2008b; Nguyen 2021; Wentzell 2021).

This was particularly noted in front-line workers who experienced increased exposure to a particular pandemic or epidemic (Grantz 2019; Jalloh 2019; Nguyen 2021; Wentzell 2021). This was outlined by medical workers during the Ebola epidemic, as they "referenced the unknown risks and dangers" they faced. As one participant suggested: "*We don't know who we're dealing with in our job*", and "*anybody and everybody comes to the hospital*" said another participant (Grantz 2019, p.7167). In relation to a vaccine trial for the COVID-19 pandemic, some participants were motivated by the hope of receiving a potentially effective vaccine. As one participant reported: "*I usually don't participate in any other trials, but this one I decided [to] because I really want to be vaccinated*" (Wentzell 2021, p.2448). In contrast to the earlier finding that individuals may be less likely to participate if they had caring responsibilities, participants in Wentzell 2021 hoped that by receiving a potentially effective vaccine they could protect their family members, particularly those considered vulnerable. One participant stated: "*I felt like if it kept me from getting it, I wouldn't be able to give it to my wife or children*"*;* while another suggested "*I knew I would have a chance of getting a real vaccine before everybody else and as a caregiver for an elderly person, that would be a good thing*" (p.2449).

Conversely, in two studies related to HIV vaccine trials, some participants did not feel at risk of contracting the virus and, therefore, did not see the value in taking part in the vaccine trial (Newman 2006; Tarimo 2010).

Subtheme 2.2: influence of other people

Finding 12: people described how the attitudes of family members could influence their willingness to take part in a vaccine trial (moderate confidence finding).

Many of the studies highlighted the importance of family attitudes on willingness to participate in a vaccine trial (Chakrapani 2012; Craig 2018; Lesch 2006; Mbunda 2018; Nguyen 2021; Tarimo 2011; Voytek 2011; Wentzell 2021).

The role of family in willingness to participate was discussed by several participants across studies with many explicitly stating that they did not participate or would not participate because of family attitudes. Family concerns that were discussed included concerns of both parents and significant others around potential adverse effects: one HIV-negative participant, a healthcare provider himself whose parents are both physicians in his country of birth, said that when he mentioned the possibility of his participation, they tried to dissuade him. "*They were just fearful that there would be some side effects*" (Craig 2018, p.6).

Within HIV vaccine trials and the context of relationships, the issue of obtaining a false-positive result was given as a reason for resistance from significant others with one respondent reporting his partner's discomfort about him possibly testing false-positive influenced his decision not to enrol: "*the false-positive was always a sticky issue and even with my partner, because I did ask him about it*" (Newman 2008a, p.1093). Another individual in the same study identified the dramatic effect that a false-positive could have on a relationship: "*If a partner turned up HIV positive it would certainly have a drastic effect on our lives together for sure …*" (Newman 2008a, p.1093). Some participants in studies looking at HIV vaccine trial participation identified concerns that partners or significant others may presume by virtue of trial participation that they were HIV positive as a result infidelity (Craig 2018; Tarimo 2011). Both male and female participants expressed fears that an intent to take part could signal to their respective partners that they have an HIV infection and that this would create conflict within the relationship. Young men, in particular, expressed concern about their intimate relationships with one saying: "*The fiancée won't trust you from the moment you plan to get the vaccine. She will think that by taking part you are infected straight away … She will believe that you have been given her the virus and so she will also be infected*" (young police officer 2, Group 4) (Tarimo 2010, p.5).

Some individuals who chose to participate in the vaccine trial regardless of their family's objections, decided not to disclose their participation to their family with one HIV-negative participant explaining: "*It would just be too much to explain and they'd be worried or tell me not to do it because it's not good for me*" (Craig 2018, p.6).

In contrast, Chin 2016 identified that an altruistic outlook often influenced by family members was instrumental in motivating people to consider taking part in a vaccine trial for a pandemic or epidemic disease. As one participant identified: "*It's really important that everybody does something to give back to the community, which is something my mother always kind of instilled in me*" (#7, W) (Chin 2016, p.6).

Subtheme 2.3: societal influences

Finding 13: people feared stigma as a result of trial participation where this might carry implications about their sexuality, gender identity or disease status (high confidence finding).

Several studies identified fear of being stigmatised or discriminated against as a factor in not participating in a vaccine trial (Andrasik 2014; Brooks 2007; Chakrapani 2012; Grantz 2019; Lesch 2006; Mbunda 2018; Moutsiakis 2007; Newman 2006; Newman 2008a; Newman 2008b; Nguyen 2021; Nyblade 2011; Strauss 2001 (2006 study report); Toledo 2014). Individuals voiced concerns that being known as having participated in a trial would lead to discrimination based on sexuality, gender non-conformity or disease status. Members of groups that already experience stigmatisation expressed fear of additional stigma as a result of their participation in a vaccine trial with one transwoman explaining: "*That's a very stigma on the trans girls because we are very much stigmatized anyway. I have a whole lot of girlfriends that want to know about the vaccine, that's trans, but they too scared to go into certain places to learn about it because they don't want no one to think that they have it [HIV], which they don't have it*" (Andrasik 2014, p.5).

Another reported fear was that trial participation could possibly lead to participants being identified as members of a particular cohort that experiences discrimination. Chakrapani 2012 identified such barriers in willingness to participate in vaccine trials amongst men who have sex with men but live with their parents or wives.

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As one key respondent noted: "*Since MSM [men who have sex with men] are hidden in this society, I don't know how MSM will accept to participate in this trial since that might reveal their sexuality to others*" (Kothi, FG5, Chennai) (Chakrapani 2012, p.4).

Newman 2008a reported that the intersection of HIV vaccine trial enrolment with assumptions of HIV status or sexuality could be a potential source of fear of stigma or discrimination: one participant in the study highlighted this concern: "*That would be a nasty thing to have to deal with just because I know what U.S. immigration border guards are like … and I think if they even have a whiff or an idea that you might be gay, I think that they would dig deep to see if they could find that HIV distinction so that they can discriminate against you*" (Newman 2008a, p.1094).

Participation in a trial leading to being identified as a person who engages in high-risk activities and being discriminated against on that basis was also reported as a reason for non-participation in a vaccine trial for a pandemic or epidemic disease. This issue is identifiable across many of the included studies that particularly focus on HIV vaccine trials with participants voicing concerns that others may see their decision to participate in a vaccine trial as evidence of seeking out an HIV vaccine in order to potentially engage in high-risk behaviours (i.e. men who have sex with men, intravenous or injecting drug users and sex workers) (Brooks 2007; Chakrapani 2012; Lesch 2006; Mbunda 2018; Moutsiakis 2007; Newman 2008a; Newman 2008b; Nyblade 2011; Toledo 2014).

Participants in one vaccine trial spoke about additional stigma related to inaccurate perceptions by some people around linkages in diseases. For example, it was sometimes presumed that because people participated in a vaccine trial for TB, they were positive for TB, and it was also presumed those that had TB also were also usually positive for HIV. "*Another individual described how her nephew died of TB and her family was affected by the stigma. She explained that despite the knowledge that TB is curable, 'there can be whole areas of the hospital that are under quarantine but also deeply marked by stigma related to TB. People assume that if you have TB, you also have HIV.' Even though her nephew was HIV-negative, 'nobody would come visit him in the hospital.'*" (Craig 2018, p.5).

Finding 14: people described how their level of trust/distrust in organisations involved in healthcare delivery, medical and scientific research, and governments influenced their decision to participate in a vaccine trial (high confidence finding).

Trust in organisations involved in the delivery of healthcare services, medical and scientific research and government involvement was identified as an important factor that may influence people's decision to take part in a vaccine trial for a pandemic or epidemic disease across numerous studies (Andrasik 2014; Brooks 2007; Chakrapani 2012; Craig 2018; Grantz 2019; Jaffe 2020; Jalloh 2019; Koniak-Griffin 2007; Lesch 2006; Mbunda 2018; Moutsiakis 2007; Newman 2006; Newman 2011a; Newman 2015; Nguyen 2021; Nyamathi 2004; Olin 2006; Strauss 2001 (2006 study report); Tarimo 2010; Tengbeh 2018; Toledo 2014; Voytek 2011; Wentzell 2021).

A lack of trust or suspicion of the motives of medical researchers was reported by many of the studies (Andrasik 2014; Brooks 2007; Chakrapani 2012; Craig 2018; Grantz 2019; Jaffe 2020; Jalloh 2019; Koniak-Griffin 2007; Lesch 2006; Mbunda 2018; Moutsiakis 2007; Newman 2006; Newman 2011a; Newman 2015; Nguyen 2021; Nyamathi 2004; Olin 2006; Strauss 2001 (2006 study report); Tarimo 2010; Tengbeh 2018; Toledo 2014; Voytek 2011; Wentzell 2021). One study commented: "*All of them – the vaccine, the shots. All of them. It's just like can you really trust what's inside of it? Like, is your doctor really telling you the truth that's inside of it?*" (Andrasik 2014, p.6). Another participant echoed this lack of trust and stated: "*I don't like doctors and they mess up a lot and so I really wouldn't want to take the risk or whatever*" (Koniak-Griffin 2007, p.693).

Beyond trust in medical professionals, a lack of trust in the process of medical research itself was also given by individuals as a reason for declining to participate. One study reported that some participants voiced concerns around the trustworthiness of researchers, and their capacity to trust the scientists' involvement in vaccine trials when pharmaceutical companies were sponsoring the trial (Strauss 2001 (2006 study report)).

Alongside these expressions of distrust, individuals from lower-income countries had further concerns around the rationale behind the higher proportion of trials being conducted in poorer countries. They also queried whether safety protocols were being followed, and whether testing was equally being conducted in rich countries. One participant in an Indian HIV vaccine trial reported: "*I even doubt whether a Phase I trial [in India] among normal human volunteers was actually conducted*" (Service provider, KI, India) (Newman 2015, p.8).

Another participant who declined to participate in a TB vaccine trial voiced disappointment and frustration at the imbalance between richer countries where research usually originates and poorer countries where the research is often conducted: "*In most cases, when the funding dries up or the project winds up, that [is] it. The Europeans and the Americans just walk out and are fine. Essentially, you've utilized [our] bodies, you've gained knowledge, personal, professional, and academic advancement. And, in return, [you've] hired a few people and built a few buildings, but [you] haven't really given [us] anything*" (Craig 2018, p.8).

Some participants across studies expressed a lack of trust of international organisations and voiced circulating negative information as a reason not to participate in an Ebola vaccine trial (Grantz 2019). The information was frequently referred to as 'conspiracy theories' and dismissed by the international organisations as having no basis in fact. Amongst the conspiracy theories identified by participants was a suggestion that Ebola was introduced by "the whites" to eliminate the native African population, and that the Ebola epidemic was "a ploy" by pharmaceutical companies in order to profit by forcing accelerated and possibly substandard vaccine trials. Front-line workers were reported as referring to the "*Ebola industry*" where "*the whites*" would potentially benefit from eventual vaccine production. Concerns were also reported that the collection of blood as part of the trial process was not being used to determine vaccine performance but was instead being used to screen people with Ebola for quarantine. (Grantz 2019).

Conversely, some participants expressed a positive disposition towards organisations involved in trials as an influencing factor in the decision to participate (Chakrapani 2012; Craig 2018; Jaffe 2020; Jalloh 2019; Mbunda 2018; Newman 2015; Tengbeh 2018; Wentzell 2021). Some participants within these studies considered scientific healthcare research, and government involvement in research

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in a trusting positive manner for the most part. Furthermore, trial endorsement by a community-based organisation (CBO) was perceived as being a factor in positively influencing willingness to participate in a vaccine trial for a pandemic or epidemic disease.

Referring to a government-led crackdown in India on the sale of expired medications, one focus group member commented on a government-led HIV vaccine trial: "*These days government has awakened and located all drugs that were expired; so in such a situation … if bravely it [trial] is implemented through organizations like [CBO name], we will very well welcome the trial*" (Chakrapani 2012, p.4). However, another focus group member on the same study clarified that in order to support or participate in a vaccine trial transparency was a requirement: "*All information about vaccine trials including previous experiences should be shared with us and if awareness is created by the government then we will trust the government*" (Chakrapani 2012, p.4).

A participant in a COVID-19 vaccine trial while expressing trust in the scientific community felt that government should not be involved as it then politicised the situation: "*I think that people need to trust science and learn from authority, from scientists. And I don't think politics and the other political movement should be involved in vaccine acceptance or usage or trial or decisions*" (Wentzell 2021, p.2448).

Trial endorsement by a relevant CBO was commonly viewed positively by individuals: "*The government is here today, gone tomorrow; government can change anytime. But if [CBO name] is with us … then we will do it*" (Chakrapani 2012, p.3). This trust in the CBO was voiced more positively by another individual in the same study: "*If the [CBO] project manager calls us, all of us will participate. We will participate in the study purely for them. We will come for the organization; if they tell us to go, then we will go*" (Chakrapani 2012, p.3).

Theme 3: perceived personal and societal rewards that influence people's decision to participate in a vaccine trial for a pandemic or epidemic disease

This theme explores the perceived personal and societal rewards that influence people's decision to participate in a vaccine trial in the context of a pandemic or epidemic. This theme focuses on two subthemes; *personal rewards of trial participation* and *making a difference: benefits for others.*

Subtheme 3.1: personal rewards of trial participation

Finding 15: people often viewed trial participation as a way of accessing vaccination with the potential benefit of reduced infection risk; improved knowledge of the disease and improvements in general health (high confidence finding).

For many individuals in the included studies the potential to receive an effective vaccine and to be protected from, or at a reduced risk of, the pandemic or epidemic disease was viewed as one of the greatest benefits of participating in a vaccine trial (Chakrapani 2012; Craig 2018; Jalloh 2019; Koniak-Griffin 2007; Newman 2006; Newman 2011b; Nyamathi 2004; Olin 2006; Strauss 2001; Tengbeh 2018; Voytek 2011; Wentzell 2021). This motivation to participate in vaccination trials was evidenced by participants in a study focusing on COVID-19, as evidenced in one participant's comment: "*I usually don't participate any other trials, but this one I decided [to] because I really want to be vaccinated*" (Wentzell 2021, p.2448), or a participant in an HIV vaccine trial: "*I've dated guys that have shot drugs … and … who knows? I may come up with the virus couple of years from now … (I'd participate) I guess just so I won't get the virus*" (Voytek 2011, p.4).

The acquired knowledge of the disease gained through trial participation, and the sense of confidence and empowerment associated with this, was a perceived benefit of trial participation by participants across some studies (Mbunda 2018; Nyamathi 2004; Slomka 2008; Tarimo 2019; Voytek 2011). Amongst participants of HIV vaccine trials in particular, "*knowledge made the participants confident and resilient*", with one female participant saying that through education related to the trial: "*I got a lot of self-confidence as opposed to the time before trial when it came to testing for HIV, but now I am full of confidence*" (Mbunda 2018, p.24). One study reported that for some, this new knowledge gained through trial participation incentivised them to improve their health through reducing risky behaviours (Voytek 2011).

For some potential participants, there was also a perception that participation in a vaccine trial would offer them some protection against other health conditions and lead to improvements in their general health (Gobat 2018; Strauss 2001; Tarimo 2019; Tengbeh 2018). One participant of an Ebola vaccine trial said: "*To me the vaccine does not only prevent Ebola, it also prevents some minor illnesses like rash etc. I have experienced it*" (Tengbeh 2018, p.40). For others, the perceived benefits to one's general health were due to the additional healthcare offered to trial participants (Tarimo 2019).

Finding 16: people often considered trial participation as a way of helping society return to its prepandemic or pre-epidemic life (moderate confidence finding).

For some individuals, participation in a vaccine trial in the context of a pandemic or epidemic brought with it some hope for the future. Unprecedented lockdowns were introduced in response to the COVID-19 pandemic. Participants of one COVID-19 vaccine trial viewed the potential for the vaccine to allow society to return to "*normalcy*" and for the pandemic to "*go away*" as their primary incentives for participating (Wentzell 2021). One participant commented: "*If the vaccine works, we're probably back to normal*", while another hoped that her participation: "*gets us one step closer to going back to normal. Once we're able to figure out this vaccine and once we're able to mass produce it and get it out to people, I'm just hoping that this [pandemic] will go away*" (Wentzell 2021).

For the participants of one HIV vaccine trial, the ability to engage in risky sexual behaviours was a perceived benefit of the protection offered by the vaccine (Chakrapani 2012). For others, participation in an HIV vaccine trial was viewed as an enabler of full participation in society (Lesch 2006).

Subtheme 3.2: making a difference: benefits for others

Finding 17: people described their desire to help the community as an important factor in their decision to participate (high confidence finding).

Across a number of studies, and in different pandemic and epidemic contexts, people were motivated by their willingness to help the community by participating in vaccine trials (Adewoyin 2013; Brooks 2007; Chakrapani 2012; Chin 2016; Craig 2018; Craig 2018; David 2021; Gobat 2018; Grantz 2019; Lesch 2006; Lesch 2006;

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Newman 2011a; Nguyen 2021; Nyamathi 2004; Nyamathi 2004; Slomka 2008; Strauss 2001; Tarimo 2010; Tengbeh 2018; Toledo 2014; Wentzell 2021). Those who choose to participate in trials made reference to their desire to "*save others*" (Grantz 2019), to "*help others*" (Adewoyin 2013; Craig 2018; Wentzell 2021), and to be a "*good Samaritan*" (Brooks 2007) in the wider community. Others viewed their trial participation as something that would contribute specifically to their community (Chin 2016; David 2021; Gobat 2018; Grantz 2019; Lesch 2006; Newman 2011a). One participant in an HIV vaccine trial commented: "*On a community level, individuals may also be more likely to participate if they can easily recognize the value or contribution that their participation makes to the 'greater good' of Latinos or their local community*" (Brooks 2007). While primarily related to studies of HIV vaccination, as noted in Newman 2011b "*The social meaning of HIV vaccine trials as a vital community undertaking emerged as an element of continued support for HIV vaccine trials, more so than individual motivations for protection against HIV infection. Participants invoked altruism and giving back to one's community under the rubric of this communitarian construction of an HIV vaccine trial*"; this was also noted in the context of Ebola vaccine trials.

The benefits for others were held as more important than any personal harms (Brooks 2007; Chin 2016; Craig 2018; Nyamathi 2004; Toledo 2014), or personal gains that may be associated with the vaccine trial participation (Chakrapani 2012; Newman 2011a): "*I will participate in the trial. It is okay if the vaccine has no effect on me or something not so good happens to me; at least I would have done some good work like how there are some patriots who become martyrs for their country*" (Kothi, FG1, Mumbai) (Chakrapani 2012).

Others echoed this sense that any risks of participation in the study were outweighed by the potential to contribute to "*overcoming a huge disease burden*" as another enroled HIV-negative participant put it (Craig 2018). One HIV-infected individual said: "*The danger is minimal, the benefit is tremendous*" (Craig 2018). Trial participation, for some people, gave a sense of contributing to something, for the good of others, that was bigger than themselves (Chin 2016; Grantz 2019; Newman 2011a; Nguyen 2021; Wentzell 2021).

By participating in vaccine trials some people viewed themselves as heroes (Tengbeh 2018), as making a sacrifice (Grantz 2019; Tengbeh 2018), and took personal pride as a result of their trial participation (Tarimo 2010; Tengbeh 2018). Recognition was also important for some as identified in one HIV trial; participants wanted to "show off" that they had helped to make the HIV vaccine (Tarimo 2010), others wanted some public acknowledgement (Tengbeh 2018). For others, this duty to participate in vaccine trials was everyone's duty: '*Some saw doing this duty as everyone's job, like P5 who noted, "I think everybody should contribute to a positive outcome, and I thought this was my way of contributing." Others attributed their desire to help others to their life experiences or histories. For instance, P6 explained that he came from a long line of veterans and like his Normandy-survivor uncle used to say, "Somebody has to be the first one out of the plane"*'(Wentzell 2021).

Finding 18: people in professional or leadership roles described their perceived duty as part of these roles as an influencing factor in their decision-making (moderate confidence finding).

A sense of duty and an obligation was highlighted as a reason individuals participated in vaccine trials (Chin 2016; Craig 2018; David 2021; Grantz 2019; Newman 2011a; Newman 2011b; Nguyen 2021; Olin 2006; Tarimo 2010; Tengbeh 2018; Wentzell 2021). This duty was born from different sources, an obligation that may have been aligned to professional status, if individuals were professionals with a tradition of protecting the public – for example, nurses, police officers, medics and scientists (Grantz 2019; Nguyen 2021; Tarimo 2010; Wentzell 2021). A police officer in Tarimo 2010 stated: "*In addition, they referred to their obligation as police officers, that the role of protecting civilians could motivate them to take part in the trial. So, they included, fulfilling moral principles and self-sacrifice to save lives of millions of people who are dying of HIV infection: I think this [taking part in the trial] is part of motivation in my duty because if I get vaccinated and make it successful, I will save the civilians whom I protect. And to work as a police officer, there must be people to protect. No police force without people. I think this is one of the moral principles that I should do*" (low-ranking female police officer 10, Group 3) (Tarimo 2010). Participants working in medical or scientific fields in Wentzell 2021 on COVID-19 vaccine trial proposed that because they worked in public health, they had to be a champion for trial participation: "*I think I have to be a champion for causes like this. Practice what I preach*" others in this study viewed it as their responsibility '*Similarly, P16 noted, "I do biomedical research, and whenever there is an opportunity to participate, I try to participate. I feel it's my responsibility as somebody who enrolls people to do clinical research, to do the same, when somebody else is trying to advance science"*' (Wentzell 2021).

A duty to one's community was also seen as a reason for trial participation, this sense of duty was often associated with people's standing as a leader in their community (Olin 2006; Tengbeh 2018); that they needed to lead by example (Grantz 2019). For others, vaccine trial participation was influenced by obligation a sense of duty that they had to give back to their community (Chakrapani 2012; Chin 2016; Craig 2018; David 2021; Grantz 2019). Participants in Chin 2016 highlighted that they were obliged to "*do good*" as an atonement for their own actions, "*Participation in the HVT (HIV Vaccine Trials) can itself represent an explicit form of atonement: I've been part of negative stuff all my life. I ran the streets for a long time. I did drugs so many years. I tore down my community. I sold and did a lot of drugs. I hurt a lot of people. So eventually, I mean: I don't do nothing negative no more, so I'm going to be part of something positive. Now I want to help*" (#9, AA) (Chin 2016, p.8).

Participants of other studies suggested they had a duty to elevate the stigma associated with their community that may have been caused by the pandemic or epidemic and needed to show that they (as members of the community) were willing to participate in activities to find a cure (Chakrapani 2012; Craig 2018; Grantz 2019). Kothis further expressed that participation in trials might help to combat stigma: "*We should definitely participate; not just for us, but also for the general public. They will appreciate us when they come to know that we [MSM] participated in the trials and that was why a vaccine is available now*" (Kothi, FG1, Chennai) (Chakrapani 2012).

Finding 19: some people described how their decision to participate in a vaccine trial was influenced by the memory of family and friends who had died of the disease during the pandemic or epidemic and a desire to protect future generations (low confidence finding).

People invited to participate in vaccine trials in the context of a pandemic and epidemic may be more willing to participate if they had lost a relative because of the disease (Moutsiakis 2007; Newman 2011b; Voytek 2011), or if they were concerned of the

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impact of the disease on the wellbeing of people in the future (Adewoyin 2013; Brooks 2007; Jaffe 2020; Newman 2006; Newman 2011a; Tarimo 2019; Toledo 2014; Wentzell 2021). This finding relates particularly to participation in HIV vaccination trials.

The memory of family members and friends dying with HIV was shared as a motivator to trial participation of Newman 2011b; Moutsiakis 2007; and Voytek 2011. Trial participation was viewed as their opportunity to remember and honour their relative or friend, to try and stop the death that they have been exposed to and loss they had experienced: *'V3 stated: "For me, [the HIV vaccine trial] is a memorial to my friends who died from the disease … to do something to help eradicate the disease." V2 stated: "I thought about my brother who died with AIDS." Those who participated identified several persons who had died of HIV/AIDS. V3 stated: "I certainly had lots of friends who died of AIDS." V2 reported at least one brother and his male partner both died of HIV/AIDS*' (Moutsiakis 2007). A male participant in an HIV vaccine study commented: "*I've had so many people, so many friends of mine die; I've watched so many people die. I used to volunteer at Casey House, at Bruce House (hospice and supportive housing for people living with HIV). I've seen so much and anything that I can do to help try and stop it, why wouldn't I?*" (41-year-old gay man) (Newman 2011b).

People who decided to participate in vaccine trials, also spoke of the future: "*I feel like if I'm participating in a HIV vaccine trial, possibly to help someone in the future; that's why I would do it*" (Newman 2006), and how their contribution to trials could benefit their families and their communities in the future and the generations yet to come (Adewoyin 2013; Brooks 2007; Jaffe 2020; Newman 2006; Newman 2011a; Tarimo 2019; Toledo 2014; Wentzell 2021).

Although most of these related to HIV vaccination trials (Adewoyin 2013; Brooks 2007; Newman 2006; Newman 2011a; Tarimo 2019; Toledo 2014), being mindful in relation to the potential benefits for future generations, was also noted in studies focusing on Zika virus (Jaffe 2020) and COVID-19 vaccine (Wentzell 2021) trials. As one person suggested: "*I'm doing this for your kids and your grandkids*" (Wentzell 2021).

Finding 20: people described how a wish to support the advancement of science and medicine could influence a decision to take part in a vaccine trial in the context of an epidemic or pandemic (moderate confidence finding).

Supporting and contributing to the enterprise of science and medicine [vaccine] development were also voiced by people as reasons to participate in vaccine trials for a pandemic or epidemic disease (Adewoyin 2013; Chakrapani 2012; David 2021; Gobat 2018; Grantz 2019; Jalloh 2019; Lesch 2006; Newman 2011b; Slomka 2008; Tarimo 2019; Toledo 2014; Wentzell 2021).

Some people offered a pragmatic rationale that their support, and so their likelihood to participate in trials, was grounded in the value they placed in scientific knowledge and their desire to contribute to the development of scientific knowledge: '*Interviewees frequently identified "supporting" or "believing in" science and vaccines as key to their self-identity and participation. In a representative comment, P13 stated, "I just believe in science"*' (Wentzell 2021). Participants in other studies elaborated on how they viewed the advancement of science and medicine and were very clear that their participation had the potential to impact specifically on pharmacological development: "*If I can participate in research for drugs like Ebola. If I can participate in making a change for the medication*" (David 2021).

People willing to participate in vaccine trials suggested that trials [research] were the only way to "find" a cure, and so end the epidemic or pandemic (Adewoyin 2013; Chakrapani 2012; Jalloh 2019; Lesch 2006; Newman 2008b; Newman 2011a; Strauss 2001).

Ending the HIV epidemic, or at least "*minimise the disease from being spread*" (Lesch 2006); "*advancing research to end the AIDS epidemic"* (Newman 2008b); ending Ebola "*I would be comfortable to do so [accept an experimental Ebola vaccine] in the context of trying to solve a problem, reduce the risk to humanity and give our people the chance to end a disease that has had catastrophic effects on our lives*" (medical doctor, Western Area) (Jalloh 2019) would provide an historical change (Lesch 2006) that would bring back "*normal life*".

The ability to represent their specific community in medical advancement was also noted as an important reason to participate in vaccine trials (Chakrapani 2012; Grantz 2019; Lesch 2006; Newman 2008b; Newman 2011a; Tarimo 2019; Toledo 2014; Wentzell 2021). Trials were seen to need participants from people of all groups, across countries, with different wellness and illness related to the disease. One Hispanic participant in an HIV vaccine trial commented: "*Not that you would necessarily need a vaccine for white people and one for people of color…but it's really important that … everybody, children, every walk of life, be a part of the research for the vaccine because you need to know how it works in different people, different races*" (Toledo 2014, p.e86).

By contributing to science and vaccine development some participants suggested they were not just advancing science and eradicating/limiting the spread of the disease but also, as stated by participants in one COVID-19 vaccine trial, limiting the misinformation surrounding science and vaccine safety. '*Some participants hoped their participation could demonstrate vaccine safety specifically for members of the groups with which they identified, especially minoritized racial or ethnic groups. For example, P22 identified as South Asian and said he hoped to lead by example for his and other minority "ethnic groups," "some of whom have been deliberately mistreated with respect to vaccination in the past." He hoped his example would make people "a little more comfortable with getting vaccinated, and trusting science and good medical advice and NIH and CDC and all of that." Others hoped to allay concerns within their age cohort, like P13 who wanted "to show that people in my age group don't have to be worried about it, that I have a good experience with it. And so then they should feel like they would have a good experience with it*"' (Wentzell 2021, p.2448).

Confidence in the findings

Based on the GRADE-CERQual assessment, we graded the findings in theme one: factors under the control of the vaccine trial teams that influence people's decision to participate, as either moderate or high confidence. There were four findings with this theme graded as high confidence and three findings graded as moderate. Findings in theme two: personal, family and societal factors that influence people's decision to participate were also graded from moderate to high. There were three findings with high confidence and four with moderate confidence. Theme three: perceived personal and societal rewards that influence people's decision to participate had

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six findings: one graded at low confidence (Finding 19), two at moderate confidence and three at high confidence. Summary of findings 1 presents a summary of the GRADE-CERQual assessment and the full evidence profiles including justifications are detailed in Appendix 2.

DISCUSSION

Summary of findings

This review sought to explore people's views, perspectives and experiences of the factors that influence a person's decision to take part in a vaccine trial in the context of a pandemic or epidemic. Our review included 34 studies (35 papers) that met the inclusion criteria. Across the included studies, there was a good balance between gender, ethnicity and participants who did or did not choose to participate in a vaccine trial for a pandemic or epidemic disease. Most studies focused on participating in HIV vaccine trials, but other pandemic or epidemic diseases such as TB, Ebola, Zika and COVID-19 were represented to a lesser degree.

Some factors were considered to be under the control of the trial team. These included how trial information was communicated and the inclusion of people in the community to help with trial information dissemination. Aspects of trial design were also considered under control of the trial team and included convenience of participation, provision of financial incentives and access to additional support services for those taking part in the trial.

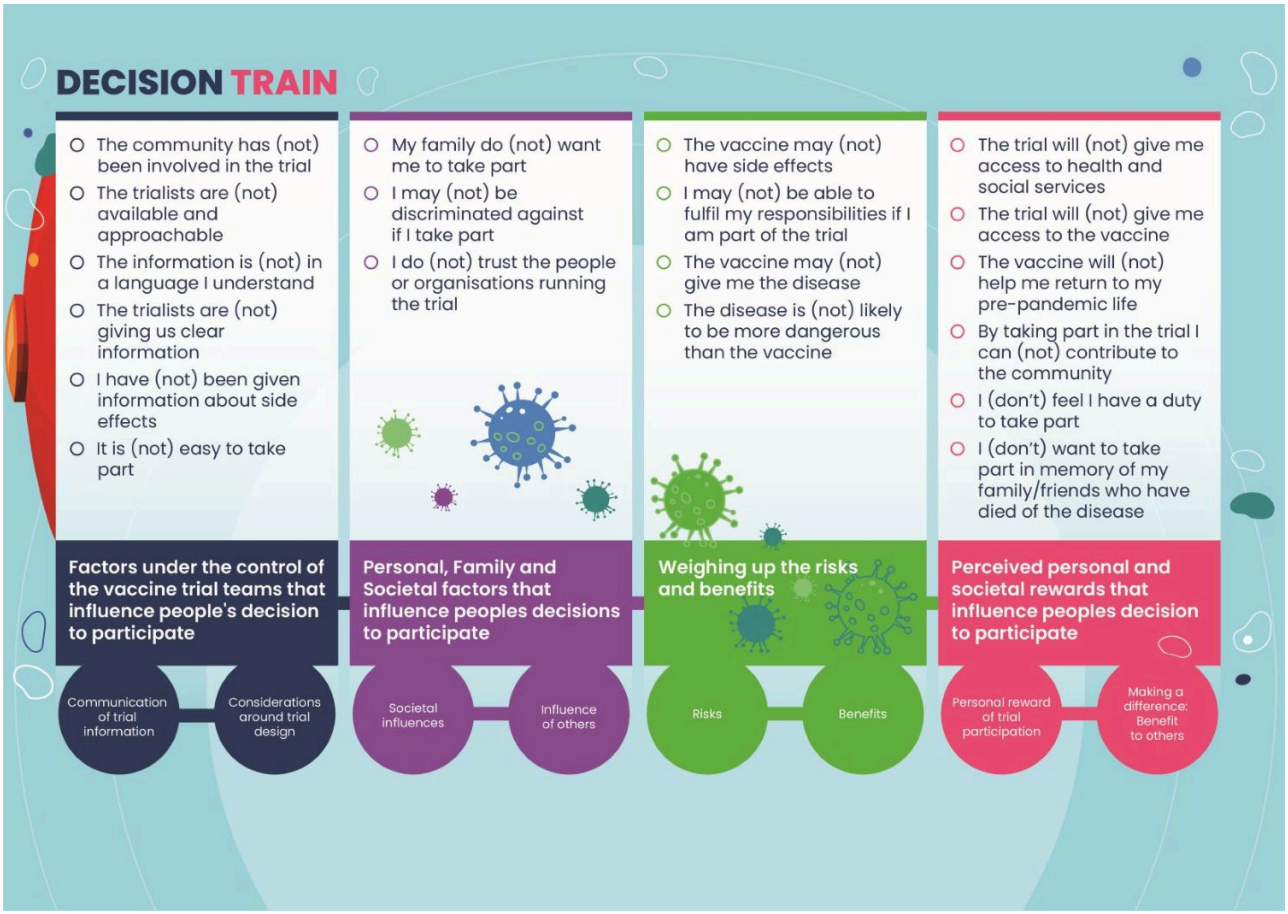
Other factors influencing people's decision to take part could be personal, from family, friends or from wider society. From a personal perceptive, people had concerns about vaccine adverse effects, vaccine efficacy and possible impact on their daily lives (caring responsibilities, work, etc.). People were also influenced by their families, and the impact participation may have on relationships. The fear of stigma from society influenced the decision to take part. Also, from a societal perspective, the level of trust in governments' involvement in research and trials may influence a person's decision.

Finally, the perceived rewards, both personal and societal, were influencing factors on the decision to participate. Personal rewards included access to a vaccine, improved health and improved disease knowledge; and a return to normality in the context of a pandemic or epidemic. Potential societal rewards included helping the community and contributing to science; often motivated by the memories of family and friends who had died from the disease.

As in the Houghton 2020 review, we developed a conceptual model to reflect a person's decision process around whether to take part in a vaccine trial for pandemic or epidemic disease based on the concept of a decision train (Figure 2). An individual's thought processes around whether or not to participate in a vaccine trial in the context of a pandemic or epidemic were likened to a journey on a decision train. Trains of thought or considerations could be compartmentalised reflecting factors that were related to the main themes. The themes are inter-related as the carriages reflecting those considerations can be linked.

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Figure 2. Figure 2 Decision Train



The decision train includes a variety of factors that influence people's decisions to participate in a vaccine trial. The factors under the control of the vaccine trial team can be seen as a series of steps not always in sequence, starting with how the trial itself is designed and how the trial information is communicated. Societal influences and the influence of others follow. Various factors might influence the decision, these include the influence of family or friends, the fear of possible stigma or discrimination and the level of trust in those involved in the trial. This can lead to a shift in thinking or a review of trial information and requirements.

The risks and benefits, such as potential adverse effects of the vaccine or of the disease itself, also play a role in vaccine trial participation. The potential rewards an individual values may influence their view of vaccine trial participation and the ultimate destination of the decision train (Figure 2).

Comparison with other reviews

Factors under the control of the vaccine trial teams that influence people's decision to participate included how adequate trial information was, how it was communicated and by whom. People within our review described the inclusion of trusted people in the community being involved with trial information dissemination as a positive influencing factor in decisions to take part in a vaccine trial.

Our review found that the availability of information on the trial vaccine was a key determinant in individuals' informed decision-making. Easily accessible and understandable information on all aspects of the pandemic vaccine trial was seen as fundamental to informed decision-making by stakeholders from both community leader recruiters and potential participants themselves (Lesch 2006; Nguyen 2021; Tarimo 2019; Toledo 2014). This review identified that trust in trial information was increased when community leaders were involved in information dissemination; however, this is less evident in other reviews (Mills 2006; Naidoo 2020; Sheridan 2020). This suggests that community leader involvement could be related to the high number of HIV studies within this review as building trust amongst potential participants is a challenge in these studies for a variety of reasons (McCann 2013). In relation to COVID-19, Razai 2021 suggests that building trust is key to addressing concerns around vaccines and creating an opportunity for dialogue that will allow people generally trusted by the community and held in high regard, such as general practitioners, to address any concerns or questions people may have.

In one overview of QES examining the psychosocial determinants of research participation amongst patients and the public, Sheridan 2020 identified that potential participants' knowledge of the trial and the quality of the study information had a mixed impact on decision to take part. Complexity of information was a barrier to a decision to take part in some cases (Fayter 2007; Forcina

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2018; Limkakeng 2013), but conversely vague information was a deterrent in others (Nievaard 2004). Additionally, in one review, distrust was linked to poor quality of information leading to a lack of knowledge and understanding (Limkakeng 2013). In one QES examining the burden of trial participation, Naidoo 2020 also highlighted complexities around getting an appropriate balance of trial information, where participants could be overwhelmed with too much, or too complex or poorly formatted information, or could be distrustful of the trial if essential information related to potential risks were considered insufficient.

Across several reviews, there is adequate information as a prerequisite to informed decision-making for people considering taking part in any research study (Mills 2006; Naidoo 2020; Sheridan 2020). This is arguably a factor for a pandemic or epidemic disease when vaccine development can be considered to have occurred faster than normal, without the same opportunity to test vaccine safety and efficacy before vaccine roll out. Similar reports of the importance of adequate accurate information have been highlighted in reviews exploring vaccine trial recruitment in non-pandemic or non-epidemic times (Stangl 2019; Villa 2020). The lack of adequate information around COVID-19 vaccination for perinatal women, challenges discussing vaccination with their healthcare provider and the impact of family members opinions were reported as factors that impacted on pregnant and lactating women's decision-making in relation to COVID-19 vaccination (Craig 2020; Huang 2022).

Within this review, limited or sketchy information negatively impacted trust of potential participants and increased levels of concern around the reason for the information gap (e.g. Mbunda 2018; Newman 2011a; Newman 2015; Nguyen 2021; Wentzell 2021). Evidence suggests that minority ethnic communities would be willing to participate in research if it was relevant to them, and if they were provided with sufficient information to allow them to make an informed decision on participation (Ekezie 2021; Gill 2013).

Within our review, people described personal, family and societal factors that influence their decision to participate similar to reports from other qualitative syntheses of trial participation (Houghton 2020; McCann 2013; Nielsen 2019). We found that the decision to take part in a vaccine trial for a pandemic or epidemic disease was influenced by personal implications of trial participation with important considerations being how practical, convenient or potentially disruptive the trial was and what level of trust the potential participants had in the recruiters or indeed the organisations involved in vaccine development or roll out.

Participants across the studies in our review described the importance of family members' influence in their decision-making particularly related to the risks involved in vaccine trial participation. This influence could either encourage or discourage participation and was a key determinant in their final decision. Our finding of encouragement or discouragement from others has also been highlighted elsewhere as an influencing factor for trial participation (Gregersen 2019; Houghton 2020; Hughes-Morley 2015; Nalubega 2015; Nielsen 2019). Minorities have been disproportionately affected by COVID-19, and have higher mortality rates than the general population, yet are amongst the groups with the lowest vaccination rates (Kalbaugh 2021; Public Health England 2020; Wang 2021). Involvement of high-risk groups in vaccine trials is important to ensure that safety data are available for all populations (Raisi-Estabragh 2020). Therefore, it is important to explore perceptions towards participation in vaccine trials for all populations, including ethnic minorities (Ekezie 2021; Raisi-Estabragh 2020).

We found that stigma, both for potential participants and for their families, was an influencing factor in willingness to participate in a vaccine trial in the context of a pandemic or epidemic. Stigma was frequently related to incorrect presumption of the participant having the disease and looking for a cure or assumptions of risky behaviour that meant the individual was at high risk for the disease, possibly influenced by the number of HIV vaccine trials in our study sample. Sheridan 2020 also identified that perceived stigma is a commonly reported barrier to recruitment to trials in HIV (Dhalla 2013; Nalubega 2015) or mental health (Hughes-Morley 2015; Woodall 2010).

Historically there is an association between stigma and pandemic or epidemic outbreaks up to and including COVID-19 (Villa 2020), with the cause of the stigma generally accepted to be fear of infection (Stangl 2019). Stigma can manifest as blame when infection is associated with behavioural contexts, such as infection prevention and control practices, and engaging in high-risk behaviours such as intravenous drug use (Hargreaves 2020). However, stigma associated with infectious disease occurs even when there is evidence that there is no longer, or never was, an infection risk to others (Smith 2011). A 2020 QES examining non-pharmaceutical interventions for infectious diseases found that the associated stigma can persist after the intervention, in this case quarantine, had ceased (Sopory 2022). Stigma was also identified in the COVID-19 pandemic particularly towards people of Asian descent, health workers, people with COVID-19 and marginalised populations (Bagcchi 2020; Mukumbang 2020; Sotgiu 2020; WHO 2020b). Anticipated stigma related to COVID-19 has been reported as impacting people's willingness to undergo testing (Earnshaw 2020). This suggests that as well as providing clear, coherent and accurate information for trial participants in the context of a pandemic or epidemic, trialists should consider engaging in broader information programmes thereby reducing the potential for trial participants to be stigmatised.

Within this review the level of trust of institutions, organisations or governments involved in vaccine development or roll out emerged as significant factors that influenced decision-making and motivations to participate in vaccine trials for a pandemic or epidemic disease. Studies that included participants from low- or middle-income areas reported lower levels of trust and also identified a perceived overuse of their minority or ethnic population for vaccine trials as a concern (Craig 2018; Grantz 2019). Some participants considered that governments should not be involved in vaccine trials in an epidemic or pandemic as it politicised the situation and was a potential conflict of interest (Wentzell 2021). While trust in researchers is a reported feature in participants' decision-making process generally (Naidoo 2020; Sheridan 2020; Stangl 2019; Villa 2020), trust in organisations or governments highlights a unique consideration for recruitment to vaccine trials for a pandemic or epidemic disease not evident in recruitment to trials generally.

Within this review perceived personal and societal rewards that influence people's decision to participate related to personal rewards such as access to a vaccine, improved health and improved disease knowledge, and a return to normality in the context of a pandemic or epidemic. Potential societal rewards included

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helping the community and contributing to science, which could be motivated by the memories of family and friends who died from the disease.

People in our review described potential improvements to their health such as being protected from getting the disease in question or other health benefits beyond the disease, as a motivating factor to take part in a vaccine trial. These improvements were often due to the improved access to health care and monitoring that comes with trial participation.

For many potential trial participants, the routine screening and free health care that are offered to those that participate in a trial were commonly expressed to be a significant motivator to take part. Previous reviews have reported similar findings in relation to incentives to participate in health research and clinical trials in general (Houghton 2020; Hughes-Morley 2015; Nielsen 2019; Sheridan 2020).

People in our review also described making a difference to others as a factor that could influence their decision-making in relation to vaccine trial participation. Previous explorations of people's motivation to participate in clinical trials have identified both self-interest and altruistic motivations as two primary drivers for trial participation (Houghton 2020; Locock 2011; McCann 2010; McCann 2013; Olsen 2020). Whilst these two stimuli for trial participation are often intertwined and mutually dependent (Olsen 2020), our review highlighted that participants across 17 studies identified a willingness to help the community as their main motivation without the need for any immediate personal gain. This could be reflective of the potential perceived impact of the prevailing pandemic or epidemic infectious disease on society at large.

Some people in our review described taking part in a vaccine trial because of feeling a sense of duty to their future generations or feeling that they had an opportunity to honour the memory of family and friends who had died as a result of the pandemic or epidemic. These motivating factors have been described across other trial settings (Bidad 2016; Canvin 2006), and, whilst not influenced by self-interest, they can reflect a sense of personal responsibility grounded in a perception of personal contribution.

Overall completeness and applicability of evidence

The included studies encompassed a wide range of countries; however, 17 were based in the US, and were predominately based on people of both genders, in rural and urban settings across different socioeconomic groups. All the studies were published in English since the early 2000s.

Twenty-six studies focused on people's perceptions of taking part in HIV vaccine trials, five focused on Ebola, one on TB, one on Zika and one on COVID-19. As a result of the over-representation of HIV studies, the views described may not reflect those of people regarding vaccine trials for other pandemic or epidemic diseases. However, given how widespread reactions to pandemics or epidemics are, the findings of this review make a significant contribution to understanding how people perceive taking part in a vaccine trial for a pandemic or epidemic disease.

Limitations of the review

Following sampling, we only included nine studies that dealt with vaccine trials for a pandemic or epidemic disease outside of HIV. However, there was a disproportionate number of HIV vaccine-related studies prior to sampling also, so our intention was to ensure we included studies that related to other pandemic and epidemic diseases.

We did not have a Patient Public Involvement (PPI) contributor on the review team. However, we asked a PPI representative, with experience in reviewing plain language summaries, to review the findings and plain language summaries. We received feedback from the PPI representative on the review content and readability and revised some aspects based on that feedback.

In terms of the concepts used for our review, we found it challenging to clearly define what a pandemic or epidemic was. The definition of both is open to interpretation and the WHO definition has been altered over the past 10 years and may change again in the future. Changes in definition can lead to altered classifications of what diseases are considered epidemic or pandemic.

AUTHORS' CONCLUSIONS

Implications for practice

Based on the key findings of our review we have developed a series of questions and prompts that may aid trialists in the planning of their recruitment strategies for vaccine trials in the context of a pandemic or epidemic. Some of these questions also align with the implications arising from a review on recruitment to randomised trials in health care (Houghton 2020), but differ in that they reflect some factors identified in this review specific to recruitment to vaccine trials in the context of an epidemic or pandemic that were not evidenced in general trial recruitment.

Communicating about the trial

- Has the trial team talked to potential participants to find out what they want and need in terms of information? Are the trial team aware of **specific fears and concerns** or possible misunderstandings that potential participants may have about the benefits and harms of trial participation?
- Has the trial team considered **how community leaders could be involved** in the planning and design of the trial and in the dissemination of trial information to potential participants?
- Do potential participants have easy access to **information about potential adverse effects**, including risks of infection and false-positive results and **information about vaccine efficacy**? And do they have information about the risk of vaccine adverse effects compared to the risk of disease infection?
- Is the trial team addressing potential participants' information needs in an **honest and sensitive** manner? And do potential participants regard this communication as open and honest?
- Are trial team members **approachable and available** to answer any queries participants might have after the trial has begun?
- Has the trial team considered whether **information to family and friends** of participants should also be made available?
- Has the trial team given potential participants information about the **potential benefits** of the trial to **science and to the community**?
- Has the trial team given potential participants **information** not only about the **benefits and harms** of the vaccine, but also about the possible benefits and harms of being in a trial?

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- Is all information written in **plain language** that is **culturally specific** to the target population?

Offering relevant incentives and support

- Has the trial team considered how trial participation can be made **easy and convenient** for participants? For instance, how can trial participation involve as little time, travel and expenses as possible?
- Has the trial team considered the types of **expenses** that trial participants may need compensation for, including for travel, time off work or childcare?
- Has the trial team considered any negative impacts that trial participation could have on **employability or health insurance qualification**?
- Does the trial team possess a good understanding of the expectations of potential participants with regard to type of **remuneration, support and acknowledgement**? For instance, will participants be provided with additional access to health care and social services during trial participation? And is this important to them?
- Has the trial team considered whether trial participation carries any **risk of stigma**, for instance because of what participation may imply about participants' sexuality, gender identity or disease status? If so, has the team explored, in collaboration with future participants, how this risk could be minimised?

Funding, collaboration and transparency

- Is it clear to potential participants **who the trial team are**, who they collaborate with and who they receive funding from?
- Has the trial team considered how **collaboration with certain organisations** or governments could influence trial recruitment? And has the trial team tried to avoid collaboration with organisations that could negatively impact recruitment?

Directions for further research in this field

There is a clear need to better understand the factors that impact decision-making around recruitment to vaccine clinical trials in a pandemic or epidemic. Future research around recruitment to clinical trials in a pandemic or epidemic could be incorporated as a study within a trial (SWAT) in vaccine clinical trials.

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Editorial and peer-reviewer contributions

The following people conducted the editorial process for this article.

- Sign-off Editor (final editorial decision): Lisa Bero, Cochrane Editorial Board.
- Managing Editor (selected peer reviewers, collated peer-reviewer comments, provided editorial guidance to authors, edited the article): Helen Wakeford, Central Editorial Service.
- Editorial Assistant (conducted editorial policy checks and supported editorial team): Leticia Rodrigues, Central Editorial Service.
- Copy Editor (copy editing and production): Anne Lawson, Central Production Service, Cochrane.
- Peer-reviewers (provided comments and recommended an editorial decision): Shaun Treweek, University of Aberdeen, UK (content review); Professor Caroline Wroe, Newcastle Hospitals NHS Foundation Trust, UK (clinical review); Toby Lasserson, Deputy Editor-in-Chief, Cochrane Library (consumer review); Professor Jane Noyes, School of Medical and Health Sciences, Bangor University, UK (methods review); Irma Klerings, Cochrane Austria, Cochrane Public Health, Department for Evidence-based Medicine and Evaluation, University for Continuing Education Krems, Austria (search review). One additional peer reviewer provided content peer review but chose not to be publicly acknowledged.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Adewoyin 2013

Study characteristics	
Notes	**Aim:** (quote) "to better understand their *(MSM or men who have sex with men)* attitudes towards getting involved in biomedical HIV prevention research."
	Country and income classification level: US, high income
	Participants: male
	Participants' SES: variety of SES backgrounds

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Adewoyin 2013 *(Continued)*

Type of disease: HIV

Method of data collection and analysis: focus groups, thematic analysis

Funding: no funding directly reported; however it was noted that: (quote) "this study was a supplement to HVTN505, a phase IIb vaccine trial recruiting MSM *(men who have sex with men)* in the US."

Notes: *unpublished Master of Public Health thesis, University of Washington

Andrasik 2014

Study characteristics	
Notes	**Aim:** (quote) "to explore barriers and facilitators to male to female (MTF) transgender participation in preventive HIV vaccine clinical trials." **Country and income classification level:** US, high income **Participants:** female **Participants' SES:** variety of SES backgrounds **Type of disease:** HIV **Method of data collection and analysis:** focus groups, thematic analysis **Funding:** not reported

Brooks 2007

Study characteristics	
Notes	**Aim:** (quote) "it explores concerns and motivators regarding participation in HIV vaccine trials among Spanish-speaking Latinos." **Country and income classification level:** US, high income **Participants:** female and male **Participants' SES:** variety of SES backgrounds **Type of disease:** HIV **Method of data collection and analysis:** focus groups, grounded theory **Funding:** (quote) "this research was supported by the University wide AIDS Research Program through a grant to the UCLA California AIDS Research Center (CC99-LA-002) and the UCLA AIDS Institute and Pallotta Teamworks AIDS Vaccine Rides and by grant P30MH58107 from the National Institutes of Mental Health."

Chakrapani 2012

Study characteristics	
Notes	**Aim:** (quote) "we explored multi-level factors associated with willingness to participate among men who have sex with men in India."

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Chakrapani 2012 *(Continued)*

Country and income classification level: India, lower middle

Participants: male

Participants' SES: low income

Type of disease: HIV

Method of data collection and analysis: focus groups, interviews, thematic analysis

Funding: (quote) "this study was funded by the Canadian Institutes of Health Research, the Social Sciences and Humanities Research Council, and the Canada Research Chairs program. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript."

Chin 2016

Study characteristics

Notes

Aim: (quote) "we examined motivations for entering an HVT *(HIV Vaccine Trial)* using in-depth qualitative interviews – how, and to what relative degree participants see altruism, personal benefits, and compensation as motivators."

Country and income classification level: US, high income

Participants: male

Participants' SES: not reported

Type of disease: HIV

Method of data collection and analysis: interviews, content analysis

Funding: (quote) "this research was supported by a center grant from the National Institute of Mental Health to the HIV Center for Clinical and Behavioural Studies at New York State Psychiatric Institute and Columbia University (P-30-MH43520; Principal Investigator: Anke A. Ehrhardt, Ph.D.) and by a training grant from the National Institute of Mental Health (T32-MH19139, Behavioural Sciences Research in HIV Infection; Principal Investigator: Theodorus Sandfort, Ph.D.) This content is solely the responsibility of the authors and does not necessarily represent the official views of NIHM or the NIH."

Craig 2018

Study characteristics

Notes

Aim: (quote) "to qualitatively examine why foreign-born adults living in the United States decide to participate, or not, in *a tuberculosis vaccine* clinical trial."

Country and income classification level: US, high income

Participants: female and male

Participants' SES: variety of SES backgrounds

Type of disease: TB

Method of data collection and analysis: the parent trial was funded by Aeras. This interview analysis of potential subject motivation to participate in a phase I TB vaccine trial was funded by SYNERGY, The Dartmouth Clinical and Translational Science Institute, a program of the National Institutes of Health

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Craig 2018 *(Continued)*

	(NIH) Clinical and Translational Science Award (CTSA) program, (quote) "phase I trial of DAR-901 in foreign-born HIV positive subjects: safety and volunteerism."

David 2021

Study characteristics	
Notes	**Aim:** (quote) "we ethnographically explore the motivations of Canadian HIV immunocompromised participants to engage in a Phase II Ebola clinical trial." **Country and income classification level:** Canada, high income **Participants:** female and male **Participants' SES:** low income **Type of disease:** Ebola **Method of data collection and analysis:** (quote) "semi-structured interviews employing situational and discursive analysis were conducted and analysed using critical qualitative interpretivist thematic analytical techniques." **Funding:** Canadian Institutes of Health Research Grant PJT-148908, Global Vaccine Logics. This is academic funding and the funder had no influence in the design of the study and collection, analysis, interpretation of data and writing the manuscript.

Gobat 2018

Study characteristics	
Notes	**Aim:** (quote) "we aimed to identify public views regarding provision of information and consent to participate in primary and critical care clinical research during a future influenza-like illness pandemic." **Countries and income classification level:** Belgium, Spain, Poland, UK, high income **Participants:** female and male **Participants' SES:** not reported **Type of disease:** pandemics generally **Method of data collection and analysis:** focus groups, interviews, framework analysis **Funding:** this work was conducted as part of a programme of work undertaken by Platform foR European Preparedness Against (Re-) emerging Epidemics (PREPARE), funded by the European Union Seventh Framework Programme for Research and Technological Development (FP-7) (grant agreement 602525). We received additional funds from Health and Care Research Wales through their funding of PRIME Centre Wales.

Grantz 2019

Study characteristics

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Grantz 2019 *(Continued)*

Notes	**Aim:** (quote) "alongside the clinical aspects of the immunogenicity and safety trial of an Ebola vaccine deployed among front-line workers, a qualitative study was conducted to describe motivations behind individuals' decisions to participate – or not to participate – in the study." **Country and income classification level:** Guinea, low income **Participants:** female and male **Participants' SES:** variety of SES backgrounds **Type of disease:** Ebola **Method of data collection and analysis:** focus groups, interviews, thematic analysis **Funding:** Médecins Sans Frontières – Operational Center Brussels. Epicentre received core funding from Médecins Sans Frontières.

Jaffe 2020

Study characteristics	
Notes	**Aim:** (quote) "to examine women's decision-making processes around vaccine research participation during infectious disease outbreaks." **Country and income classification level:** US, high income **Participants:** female (pregnant or recently pregnant) **Participants' SES:** variety of SES backgrounds **Type of disease:** Zika **Method of data collection and analysis:** interviews, thematic analysis **Funding:** supported in part by the National Institute of Allergy and Infectious Diseases of the National Institutes of Health under award number R01AI108368 (PI, Lyerly).

Jalloh 2019

Study characteristics	
Notes	**Aim:** (quote) "to obtain rich understanding and subjective interpretations regarding nuances and complexities related to ethical considerations for a potential experimental Ebola vaccine trial in the context of an unprecedented and ongoing outbreak." **Country and income classification level:** Sierra Leone, low income **Participants:** female and male **Participants' SES:** variety of SES backgrounds **Type of disease:** Ebola **Method of data collection and analysis:** interviews, focus groups, qualitative content analysis **Funding:** (quote) "CDC Foundation provided financial support to FOCUS 1000."

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Koniak-Griffin 2007

Study characteristics	
Notes	**Aim:** (quote) "this qualitative study explores factors that might affect future participation of homeless 18- to 24-year-olds of diverse racial/ethnic backgrounds in HIV vaccine trials (HIVVTs)." **Country and income classification level:** US, high income **Participants:** female and male **Participants' SES:** low income **Type of disease:** HIV **Method of data collection and analysis:** focus groups, content analysis **Funding:** (quote) "this study was supported by grants from the UCLA AIDS Institute and the UCLA School of Nursing."

Lesch 2006

Study characteristics	
Notes	**Aim:** (quote) "a qualitative investigation into the factors that may enable or inhibit participation among persons eligible to enrol in a future HIV vaccine trial." **Country and income classification level:** South Africa, upper middle **Participants:** female and male **Participants' SES:** not reported **Type of disease:** HIV **Method of data collection and analysis:** interviews, focus groups, grounded theory analytic coding **Funding:** (quote) "funded by the European Union."

Mbunda 2018

Study characteristics	
Notes	**Aim:** (quote) "the overall aim for this thesis was to increase knowledge of factors contributing to recruitment and participation of young people in preventive HIV vaccine trials." **Country and income classification level:** Tanzania, lower middle **Participants:** female and male **Participants' SES:** not reported **Type of disease:** HIV **Method of data collection and analysis:** focus groups, thematic analysis **Funding:** (quote) "my studies were made possible by the generous financial support from The Swedish International Development Cooperation Agency, SIDA."

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Mbunda 2018 *(Continued)*

Notes: *PhD thesis, Karolinska Institutet, Stockholm

Moutsiakis 2007

Study characteristics	
Notes	**Aim:** (quote) "to learn why, in a city conducting HIV vaccine trials and attempting to address barriers to minority recruitment, blacks still do not take part in HIV vaccine trials. The paper also seeks to identify steps to increase their participation." **Country and income classification level:** US, high income **Participants:** female and male **Participants' SES:** variety of SES backgrounds **Type of disease:** HIV **Method of data collection and analysis:** ethnographic interviews, thematic analysis **Funding:** (quote) "provided by research grant #5-R25-CA89396-02 from the National Institute of Health for a radiology cancer research training curriculum."

Newman 2006

Study characteristics	
Notes	**Aim:** (quote) "the purpose of this study was to explore perceived barriers that may limit HIV vaccine trial participation as well as motivations for participation from the perspectives of low socioeconomic Latino and African-American communities at elevated risk for HIV." **Country and income classification level:** US, high income **Participants:** female and male **Participants' SES:** variety of SES backgrounds **Type of disease:** HIV **Method of data collection and analysis:** focus groups, narrative thematic analysis **Funding:** (quote) "supported by the University wide AIDS Research Program through a grant to the UCLA California AIDS Research Center (CC99-LA-002) and the UCLA AIDS Institute and Palotta Teamworks AIDS Vaccine Rides."

Newman 2008a

Study characteristics	
Notes	**Aim:** (quote) "the purpose of the present study was to explore in depth the perspectives and concerns of persons who screened into a Phase IIb HIV vaccine trial but subsequently declined to enroll, in order to discern implications for improving trial recruitment and for better addressing the needs of potential trial participants." **Country and income classification level:** Canada, high income

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Newman 2008a *(Continued)*

Participants: male

Participants' SES: variety of SES backgrounds

Type of disease: HIV

Method of data collection and analysis: interviews, narrative thematic analysis

Funding: (quote) "this study was funded by the Ontario HIV Treatment Network."

Newman 2008b

Study characteristics

Notes

Aim: (quote) "the purpose of this investigation is to identify commonalities and differences in barriers and motivators to HIV vaccine trial participation, and acceptability of future U.S. Food and Drug Administration (FDA)-approved HIV vaccines, respectively, in order to identify implications of clinical trials for future HIV vaccine dissemination."

Country and income classification level: US, high income

Participants: female and male

Participants' SES: variety of SES backgrounds

Type of disease: HIV

Method of data collection and analysis: focus groups, narrative thematic analysis

Funding: (quote) "this study was supported by the University wide AIDS Research Program (UARP) through a grant to the UCLA California AIDS Research Center (CC99-LA-002), The UCLA AIDS Institute and Pallotta Teamworks AIDS Vaccine Rides, the Ontario HIV Treatment Network, and NIMH R01 MH069087."

Newman 2011a

Study characteristics

Notes

Aim: (quote) "we investigated how persons from key populations at higher risk of HIV exposure interpreted the process and outcomes of the Step Study HIV-1 vaccine trial, which was terminated early, and implications for willingness to participate in and community support for HIV vaccine research."

Country and income classification level: Canada, high income

Participants: female and male

Participants' SES: variety of SES backgrounds

Type of disease: HIV

Method of data collection and analysis: focus groups, narrative thematic techniques based on grounded theory

Funding: (quote) "this research was supported in part by the Ontario HIV Treatment Network (grant ROGB169) and the Canada Research Chairs Program."

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Newman 2011b

Study characteristics	
Notes	**Aim:** (quote) "the purpose of this mixed methods investigation was to explore in depth participant experiences and reactions." **Country and income classification level:** Canada, high income **Participants:** female and male **Participants' SES:** not reported **Type of disease:** HIV **Method of data collection and analysis:** mixed methods, interviews, thematic analysis **Funding:** (quote) "this research was supported in part by funding from The Ontario HIV Treatment Network (OHTN), the Social Sciences and Humanities Research Council of Canada, and the Canada Research Chairs program."

Newman 2015

Study characteristics	
Notes	**Aim:** (quote) "our aim was to assess and deepen the empirical foundation for priorities included in the *Good Participatory Practice* (GPP) *Guidelines for Biomedical HIV Prevention Trials* and to highlight challenges in implementation that may merit further attention in subsequent GPP iterations." **Countries and income classification level:** Thailand, India, South Africa, Canada, mixed **Participants:** female and male **Participants' SES:** variety of SES backgrounds **Type of disease:** HIV **Method of data collection and analysis:** interviews, focus groups, thematic analysis **Funding:** (quote) "this research was supported in part by grants from: Canadian Institutes of Health Research (THA-118570; PAN, GL, VC) http://www.cihr-irsc.gc.ca, Canadian Institutes of Health Research (MOP-102512; PAN, VC) http://www.cihr-irsc.gc.ca, Social Sciences and Humanities Research Council (861080042; PAN) http://www.sshrc-crsh.gc.ca Canada Research Chairs Program (PAN) http://www.chairs-chaires.gc.ca and Canada Foundation for Innovation (PAN) www.innovation.ca."

Nguyen 2021

Study characteristics	
Notes	**Aim:** (quote) "to our knowledge no study has explored frontline nurses' experiences of their decision-making process when partaking in clinical trials using unproven agents during the Ebola crisis, which is the aim of this qualitative descriptive study." **Countries and income classification level:** Sierra Leone, Guinea, Liberia, low income **Participants:** female and male **Participants' SES:** not reported **Type of disease:** Ebola

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Nguyen 2021 *(Continued)*

Method of data collection and analysis: interviews, thematic analysis

Funding: (quote) "Elrha's Research for Health in Humanitarian Crises, Grant/Award Number: 19852; Wellcome Trust; DFID."

Nyamathi 2004

Study characteristics	
Notes	**Aim:** (quote) "the purpose of this study was to conduct community-based participatory research (CBPR), using a qualitative design, focused on assessing factors that might impact future participation of high-risk homeless and impoverished adults of primarily racial/ethnic minorities in HIVVTs (HIV Vaccine Trials)." **Country and income classification level:** US, high income **Participants:** female and male **Participants' SES:** low income **Type of disease:** HIV **Method of data collection and analysis:** focus groups, ethnographic analysis **Funding:** (quote) "funded by the UCLA Center for Vulnerable Populations Research award and the UCLA Intramural Grant Award."

Nyblade 2011

Study characteristics	
Notes	**Aim:** (quote) "this study expands current knowledge of stigma and discrimination related to participation in HIV vaccine research in sub-Saharan Africa by exploring the perception of stigma and discrimination as a barrier to participation in HIV vaccine research in Kenya." **Country and income classification level:** Kenya, lower middle **Participants:** female and male **Participants' SES:** not reported **Type of disease:** HIV **Method of data collection and analysis:** focus groups, iterative coding process **Funding:** (quote) "this study was made possible by the generous support of the American people through the United States Agency for International Development (USAID)."

Olin 2006

Study characteristics	
Notes	**Aim:** (quote) "the present study provides qualitative data on knowledge and attitudes about vaccines, HIV/AIDS, and sexual behaviour from a potential cohort in DR Congo, and on factors which may determine willingness or unwillingness of high-risk persons to volunteer for clinical trials of a cross-clade HIV vaccine."

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Olin 2006 *(Continued)*

Country and income classification level: Democratic Republic of Congo, low income

Participants: female and male

Participants' SES: variety of SES backgrounds

Type of disease: HIV

Method of data collection and analysis: focus groups, interviews, thematic analysis*

Funding: (quote) "this research was made possible by NIH/CFAR grant #P30A142855-01 and the CFAR programme at the Johns Hopkins School of Public Health."

Notes: *data analysis methodology not explicitly stated

Slomka 2008

Study characteristics	
Notes	**Aim:** (quote) "this paper examines views of African American drug users about decisions to participate in research." **Country and income classification level:** US, high income **Participants:** female and male **Participants' SES:** variety of SES backgrounds **Type of disease:** HIV **Method of data collection and analysis:** interviews, content analysis **Funding:** (quote) "partial funding for this study was provided by the National Institute on Drug Abuse."

Strauss 2001

Study characteristics	
Notes	From the 2001 study report **Aim:** (quote) "this paper examines factors impacting willingness to volunteer in phase III preventative HIV vaccine trials." **Country and income classification level:** US, high income **Participants:** female and male **Participants' SES:** variety of SES backgrounds **Type of disease:** HIV **Method of data collection and analysis:** interviews, freelisting, thematic analysis **Funding:** (quote) "this study was supported by funds from the Centers for Disease Control and Prevention (CDC)." From the 2006 study report **Aim:** (quote) "we elicited recommendations regarding how vaccine efficacy trials should be conducted from members of communities that have been disproportionately affected by HIV/AIDS."

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Strauss 2001 *(Continued)*

Country and income classification level: US, high income

Participants: female and male

Participants' SES: mixed

Type of disease: HIV

Method of data collection and analysis: interviews, analysis method not specified

Funding: (quote) "this research was supported by CDC cooperative agreements to the University of California, San Francisco (U64/CCU910851), University of North Carolina at Chapel Hill (U48/CCU409660), and University of Pennsylvania (U64/CCU310867). Dr. Johnson's effort was funded by NIMH Grant K08MH01995."

Tarimo 2010

Study characteristics

Notes

Aim: (quote) "the purpose of this study among police officers in Dar es Salaam, Tanzania, was to explore the underlying reasons that induce people to enrol in an HIV vaccine trial."

Country and income classification level: Tanzania, lower middle

Participants: female and male

Participants' SES: middle income

Type of disease: HIV

Method of data collection and analysis: focus groups, thematic content analysis

Funding: (quote) "the work was supported by financial aid from Sida / SAREC."

Tarimo 2011

Study characteristics

Notes

Aim: (quote) "the purpose of this study was to understand why some individuals who were randomized in a Phase I and II HIV vaccine trial (HIVIS03) in Dar es Salaam, Tanzania, subsequently declined."

Country and income classification level: Tanzania, lower middle

Participants: female and male

Participants' SES: not reported

Type of disease: HIV

Method of data collection and analysis: interviews, content analysis

Funding: (quote) "the study was supported with funding from the Swedish International Agency for Development Cooperation (SIDA)."

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Tarimo 2019

Study characteristics	
Notes	**Aim:** (quote) "this study describes perceptions of the participating communities at five years post completion of Phase I/II HIV vaccine trials in Dar es Salaam, Tanzania." **Country and income classification level:** Tanzania, lower middle **Participants:** female and male **Participants' SES:** variety of SES backgrounds **Type of disease:** HIV **Method of data collection and analysis:** focus groups, thematic analysis **Funding:** (quote) "this work was supported by local institution (MUHAS) capacity building section under Sida funds."

Tengbeh 2018

Study characteristics	
Notes	**Aim:** (quote) "is to analyse participant motivations for volunteering for an Ebola vaccine study, and to consider the implications of such motivations for clinical research ethics and community engagement in trials in low-resource settings." **Country and income classification level:** Sierra Leone, low income **Participants:** female and male **Participants' SES:** not reported **Type of disease:** Ebola **Method of data collection and analysis:** ethnographic observation, focus groups, interviews **Funding:** (quote) "this project has received funding from the Innovative Medicines Initiative 2 Joint Undertaking under grant agreement No 115854. This Joint Undertaking receives support from the European Union's Horizon 2020 research and innovation programme and the European Federation of Pharmaceutical Industries and Association."

Toledo 2014

Study characteristics	
Notes	**Aim:** (quote) "this qualitative study explored how African-Americans and Hispanics living in the San Francisco Bay area perceived HIV disease and phase -I HIV vaccine clinical trials and solicited information on motivators and barriers to participation." **Country and income classification level:** US, high income **Participants:** female and male **Participants' SES:** not reported **Type of disease:** HIV **Method of data collection and analysis:** interviews, thematic analysis

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Toledo 2014 *(Continued)*

	Funding: (quote) "funding for this research was provided by U.S. Centers for Disease Control and Prevention under Grant No. U65 CCU923369."

Voytek 2011

Study characteristics	
Notes	**Aim:** (quote) "this study examines factors associated with participation in an actual HIV vaccine trial among African-American women in Philadelphia." **Country and income classification level:** US, high income **Participants:** female **Participants' SES:** low income **Type of disease:** HIV **Method of data collection and analysis:** interviews, thematic analysis **Funding:** (quote) "preparation of this manuscript was supported in part by the following grants: U01-AI-048014, Penn Prevention Clinical Trials Unit (Metzger, PI) and 6-P30-AI-45008 (Hoxie, PI)."

Wentzell 2021

Study characteristics	
Notes	**Aim:** (quote) "to use COVID-19 vaccine trial participants' experiences to identify key themes in the lived experience of vaccination early in the vaccine approval and distribution process." **Country and income classification level:** US, high income **Participants:** female and male **Participants' SES:** not reported **Type of disease:** COVID-19 **Method of data collection and analysis:** interviews, thematic analysis **Funding:** not reported

CFAR: Center for AIDS Research; COVID-19: coronavirus disease 2019; MSM: men who have sex with men; NIH: National Institutes of Health; NIHM: National Institute of Mental Health; SES: socioeconomic status; TB: tuberculosis; UCLA: University of California, Los Angeles.

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Cattapan 2019	Not sampled as limited data for extraction
Doshi 2017	Not sampled as scored 2 on data richness scale
Ekezie 2021	Not sampled as limited data for extraction

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Study	Reason for exclusion
Enria 2016	Not sampled as limited focus of the review aims and objectives
Hays 1999	Not sampled as scored 1 on data richness scale
Liamputtong 2015	Not sampled as scored 2 on data richness scale
Lindegger 2007	Not sampled as scored 1 on data richness scale
Nyamathi 2007	Not sampled as limited data for extraction
Nyaoke 2017	Not sampled as scored 2 on data richness scale
Ryan 1995	Not sampled as scored 1 on data richness scale

ADDITIONAL TABLES

Table 1. Purposeful Sampling Frame

	Measure	Example
1	Very little qualitative data presented that relate to the synthesis objective. Those findings that are presented are fairly descriptive.	A mixed-methods study using open-ended survey questions or a more detailed qualitative study where only part of the data relate to the synthesis objective
2	Some qualitative data presented that relate to the synthesis objective	A limited number of qualitative findings from a mixed-methods or qualitative study
3	A reasonable amount of qualitative data that relate to the synthesis objective	A typical qualitative research article in a health services journal
4	A good amount and depth of qualitative data that relate to the synthesis objective	A qualitative research article in a social sciences journal with more context and setting descriptions
5	A large amount and depth of qualitative data that relate in depth to the synthesis objective	From a detailed ethnography or a published qualitative article with the same objectives as the synthesis

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Table 2. Assessment of methodological limitations

Study ID	Was there a clear statement of the aims of the research?	Is a qualitative methodology appropriate?	Was the research design appropriate to address the aims of the research?	Was the recruitment strategy appropriate to the aims of the research?	Were the data collected in a way that addressed the research issue?	Has the relationship between researcher and participants been adequately considered?	Have ethical issues been taken into consideration?	Was the data analysis sufficiently rigorous?	Is there a clear statement of findings?	How valuable is the research?	Overall assessment
Adewoyin 2013	Yes	Yes	Yes	Yes	Yes	Could not determine	Yes	Could not determine	Yes	Yes	Minor concerns
Andrasik 2014	Yes	Yes	Could not determine	Yes	Yes	Yes	Could not determine	Yes	Yes	Yes	Minor concerns
Brooks 2007	Yes	Yes	Could not determine	Could not determine	Could not determine	Could not determine	Could not determine	Yes	Yes	Yes	Moderate concerns
Chakrapani 2012	Yes	Could not determine	Could not determine	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Minor concerns
Chin 2016	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No concerns
Craig 2018	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Minor concerns
David 2021	Yes	Yes	Yes	Yes	Yes	Could not determine	Yes	Could not determine	Yes	Yes	Minor concerns
Gobat 2018	Yes	Yes	Yes	Yes	Yes	Could not determine	No	Could not determine	Yes	Yes	Minor concerns
Grantz 2019	Yes	Yes	Yes	Yes	Yes	Could not determine	Yes	Yes	Could not determine	Could not determine	Minor concerns

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Table 2. Assessment of methodological limitations *(Continued)*

Jaffe 2020	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Could not determine	Yes	Yes	Minor concerns
Jalloh 2019	Yes	Yes	Could not determine	Yes	Yes	Could not determine	Yes	Yes	Yes	Yes	Minor concerns
Koniak-Griffin 2007	Yes	Yes	Could not determine	Yes	Yes	Could not determine	Yes	Yes	Yes	Yes	Minor concerns
Lesch 2006	Yes	Yes	Could not determine	Yes	Yes	Yes	Could not determine	Yes	Yes	Yes	Minor concerns
Mbunda 2018	Yes	Yes	Yes	Yes	Yes	Yes	Could not determine	Could not determine	Yes	Yes	Minor concerns
Moutsiakis 2007	Yes	Could not determine	Yes	Yes	Yes	Could not determine	Could not determine	Could not determine	Yes	Could not determine	Moderate concerns
Newman 2006	Yes	Yes	Yes	Yes	Yes	Could not determine	Yes	Yes	Yes	Yes	Minor concerns
Newman 2008a	Yes	Yes	Yes	Yes	Yes	Could not determine	Could not determine	Yes	Yes	Yes	Minor concerns
Newman 2008b	Yes	Could not determine	Could not determine	Yes	Yes	Could not determine	Yes	Yes	Yes	Yes	Minor concerns
Newman 2011a	Could not determine	Could not determine	Could not determine	Yes	Yes	Could not determine	Yes	Yes	Yes	Yes	Minor concerns
Newman 2011b	Yes	Yes	Yes	Yes	Yes	Could not determine	Could not determine	Yes	Yes	Yes	Minor concerns
Newman 2015	Yes	Yes	Yes	Yes	Yes	Yes	Could not determine	Yes	Yes	Yes	Minor concerns
Nguyen 2021	Yes	Yes	Yes	Yes	Yes	Could not determine	Yes	Could not determine	Yes	Could not determine	Minor concerns

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Table 2. Assessment of methodological limitations *(Continued)*

Nyamathi 2004	Yes	Yes	Yes	Yes	Yes	Could not determine	Could not determine	Yes	Yes	Yes	Minor concerns
Nyblade 2011	Yes	Yes	Yes	Yes	Yes	Could not determine	Could not determine	Yes	Yes	Yes	Minor concerns
Olin 2006	Yes	Yes	Yes	Yes	Yes	Could not determine	Yes	Could not determine	Yes	Yes	Minor concerns
Slomka 2008	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Minor concerns
Strauss 2001 (2001 and 2006 study reports)	Yes	Yes	Yes	Yes	Yes	Could not determine	Could not determine	Yes	Yes	Yes	Minor concerns
Tarimo 2010	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Could not determine	Yes	Minor concerns
Tarimo 2011	Yes	Yes	Yes	Could not determine	Yes	Could not determine	Yes	Yes	Yes	Yes	Minor concerns
Tarimo 2019	Yes	Yes	Yes	Could not determine	Yes	Could not determine	Yes	Yes	Yes	Yes	Minor concerns
Tengbeh 2018	Yes	Yes	Yes	Could not determine	Yes	Could not determine	Yes	Could not determine	Yes	Yes	Minor concerns
Toledo 2014	Yes	Yes	Could not determine	Yes	Yes	Could not determine	Yes	Yes	Yes	Yes	Minor concerns
Voytek 2011	Yes	Could not determine	Could not determine	Could not determine	Could not determine	Could not determine	Yes	Could not determine	Could not determine	Could not determine	Moderate concerns
Wentzell 2021	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No concerns

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Table 3. Thematic Framework factors that influence recruitment to trials (Houghton 2020)

Theme	Subtheme
Trial influences on decision to participate	• Communication of trial information • Significant trial components
Personal influences on the decision to participate	• Influence of other people • Weighing up the risks and benefits
The impact of potential outcomes on the decision to participate	• Personal benefits of trial participation • Making a difference: benefits for others

Houghton 2020.

Table 4. Conceptual framework factors that impact decision to take part in a vaccine trial for a pandemic or epidemic disease

Theme	Subtheme
Factors under the control of the vaccine trial teams that influence people's decision to participate	• Communication of trial information • Considerations around trial design
Personal, family and societal factors that influence people's decisions to participate	• Weighing up the risks and benefits • Influence of other people • Societal Influences
Perceived personal and societal rewards that influence people's decision to participate	• Personal rewards of trial participation • Making a difference: benefit to others

APPENDICES

Appendix 1. Search strategies

MEDLINE (Ovid MEDLINE Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE Daily and Ovid MEDLINE) from 1946 (searched 28 June 2021)

#	Searches	Results
1	patient selection/	**67374**
2	patient participation/	**27250**
3	motivation/	**71002**
4	exp volunteers/	**32957**
5	or/1-4	**195378**
6	exp vaccines/	**240756**

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(Continued)

7	exp immunization/	**184271**
8	or/6-7	**337201**
9	5 and 8	**2011**
10	((participat* or recruit* or enrol* or non-particip* or nonparticip* or selection) adj6 (epidemic* or pandemic*)).ti,ab,kf.	**713**
11	((participat* or recruit* or enrol* or non-particip* or nonparticip* or selection) adj6 (vaccin* trial* or vaccin* research or vaccin* clinical trial* or vaccin* clinical stud* or vaccin* clinical research or vaccin* stud* or immuni*)).ti,ab,kf.	**2952**
12	((barrier? or motivat* or facilitat* or decision? or decline? or refuse? or refusal or experience? or attitude?) adj6 (trial* or research or study or studies) adj6 (vaccin* or immuni* or pandemic* or epidemic*)).ti,ab,kf.	**1600**
13	or/9-12	**6984**
14	((participat* or recruit* or enrol* or non-particip* or nonparticip* or selection) and vaccin* and (trial* or research or study or studies)).ti.	**345**
15	((("semi-structured" or semistructured or unstructured or informal or "in-depth" or indepth or "face-to-face" or structured or guide) adj3 (interview* or discussion* or questionnaire*)) or (focus group* or qualitative or ethnograph* or fieldwork or "field work" or "key informant")).ti,ab. or interviews as topic/ or focus groups/ or narration/ or qualitative research/	**428988**
16	px.fs.	**1115064**
17	15 or 16	**1424278**
18	13 and 17	**1166**
19	14 or 18	**1398**

CINAHL from 1980, EBSCOhost (searched 28 June 2021)

#	Query	Results
S1	(MH "Patient Selection") OR (MH "Consumer Participation")	**45,580**
S2	(MH "Motivation") OR (MH "Volunteer Experiences")	**42,554**
S3	S1 OR S2	**87,284**
S4	(MH "Vaccines+") OR (MH "Immunization+")	**62,851**
S5	S3 AND S4	**580**
S6	TI ((participat* or recruit* or enrol* or non-particip* or nonparticip* or selection) N6 (epidemic* or pandemic*)) OR AB ((participat* or recruit* or enrol* or non-particip* or nonparticip* or selection) N6 (epidemic* or pandemic*))	**278**

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(Continued)

S7	TI ((participat* or recruit* or enrol* or non-particip* or nonparticip* or selection) N6 (vaccin* trial* or vaccin* research or vaccin* clinical trial* or vaccin* clinical stud* or vaccin* clinical research or vaccin* stud* or immuni*)) OR AB ((participat* or recruit* or enrol* or non-particip* or nonparticip* or selection) N6 (vaccin* trial* or vaccin* research or vaccin* clinical trial* or vaccin* clinical stud* or vaccin* clinical research or vaccin* stud* or immuni*))	**741**
S8	TI ((barrier? or motivat* or facilitat* or decision? or decline? or refuse? or refusal or experience? or attitude?) N6 (trial* or research or study or studies) N6 (vaccin* or immuni* or pandemic* or epidemic*)) OR AB ((barrier? or motivat* or facilitat* or decision? or decline? or refuse? or refusal or experience? or attitude?) N6 (trial* or research or study or studies) N6 (vaccin* or immuni* or pandemic* or epidemic*))	**674**
S9	S5 OR S6 OR S7 OR S8	**2,138**
S10	((("semi-structured" or semistructured or unstructured or informal or "in-depth" or indepth or "face-to-face" or structured or guide) N3 (interview* or discussion* or questionnaire*)) or (focus group* or qualitative or ethnograph* or fieldwork or "field work" or "key informant"))	**303,208**
S11	(MH "Interviews+") OR (MH "Narratives") OR (MH "Focus Groups") OR (MH "Qualitative Studies+")	**317,010**
S12	S10 OR S11	**406,631**
S13	S9 AND S12	**410**
S14	TI ((participat* or recruit* or enrol* or non-particip* or nonparticip* or selection) and vaccin* and (trial* or research or study or studies))	**128**
S15	S13 OR S14	**511**

PsycINFO from 1806 (date searched 28 June 2021)

#	Search terms	Results
1	patient selection/	**255**
2	client participation/	**2482**
3	motivation/	**55917**
4	exp volunteers/	**5301**
5	or/1-4	**63400**
6	immunization/	**4975**
7	5 and 6	**58**
8	((participat* or recruit* or enrol* or non-particip* or nonparticip* or selection) adj6 (epidemic* or pandemic*)).ti,ab.	**88**

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(Continued)

9	((participat* or recruit* or enrol* or non-particip* or nonparticip* or selection) adj6 (vaccin* trial* or vaccin* research or vaccin* clinical trial* or vaccin* clinical stud* or vaccin* clinical research or vaccin* stud* or immuni*)).ti,ab.	**176**
10	((barrier? or motivat* or facilitat* or decision? or decline? or refuse? or refusal or experience? or attitude?) adj6 (trial* or research or study or studies) adj6 (vaccin* or immuni* or pandemic* or epidemic*)).ti,ab.	**294**
11	or/7-10	**573**
12	((participat* or recruit* or enrol* or non-particip* or nonparticip* or selection) and vaccin* and (trial* or research or study or studies)).ti.	**70**
13	((("semi-structured" or semistructured or unstructured or informal or "in-depth" or indepth or "face-to-face" or structured or guide) adj3 (interview* or discussion* or questionnaire*)) or (focus group* or qualitative or ethnograph* or fieldwork or "field work" or "key informant")).ti,ab.	**297781**
14	exp qualitative methods/	**17476**
15	13 or 14	**301222**
16	11 and 15	**124**
17	12 or 16	**188**

Scopus, Elsevier (searched 28 June 2021)

((TITLE-ABS-KEY ((participat* OR recruit* OR enrol* OR non-particip* OR nonparticip* OR selection) W/6 (epidemic* OR pandemic* OR trial* OR research OR study OR studies) W/6 (vaccin* or immuni*)) OR (TITLE-ABS-KEY ((barrier* OR motivat* OR facilitat* OR decision* OR decline* OR refuse* OR refusal OR experience* OR attitude*) W/6 (trial* OR research OR study OR studies) W/6 (vaccin* OR immuni* OR pandemic* OR epidemic*))) AND (TITLE-ABS-KEY (interview* OR discussion* OR questionnaire* OR focus AND group* OR qualitative OR ethnograph* OR fieldwork OR field AND work OR key AND informant))) OR (TITLE ((participat* OR recruit* OR enrol* OR non-particip* OR nonparticip* OR selection) AND vaccin* AND (trial* OR research OR study OR studies)))) OR ((KEY (((selection OR participation OR volunteer* OR motivation) AND (vaccine* OR immuni*))) AND TITLE-ABS-KEY ((interview* OR discussion* OR questionnaire* OR focus AND group* OR qualitative OR ethnograph* OR fieldwork OR field AND work OR key AND informant))))

Epistemonikos, Epidemonikos Foundation: www.epistemonikos.org/ (searched 28 June 2021)

Title: ((participat* OR recruit* OR enrol* OR non-particip* OR nonparticip* OR selection) AND vaccin* AND (trial* OR research OR study OR studies))

ORRCA Online Resource for Research in Clinical triAls www.orrca.org.uk/ (searched 28 June 2021)

Title/Abstract: vaccine OR vaccination OR epidemic OR pandemic

EThOS (ethos.bl.uk/Home.do) (searched 28 June 2021)
Search terms
vaccin* AND recruit*, OR vaccin* AND epidemic OR vaccin* AND recruit* AND epidemic OR Vaccin* AND Recruit* AND pandemic

Cochrane COVID-19 Study register (searched 28 June 2021)

participat* or recruit* or enrol* or non-particip* or nonparticip* or selection or barrier* or motivat* or facilitat* or decision* or decline* or refuse* or refusal or experience* or attitude*

vaccin* + Study type: Qualitative + Study type: Other

ProQuest Dissertations and Theses Global and UK & Ireland (searched 28 June 2021)

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(TI,AB,SU((participat* OR recruit* OR enrol* OR non-particip* OR nonparticip* OR selection) NEAR/6 (epidemic* OR pandemic* OR trial* OR research OR study OR studies) NEAR/6 (vaccin* or immuni*)) OR TI,AB,SU((barrier* OR motivat* OR facilitat* OR decision* OR decline* OR refuse* OR refusal OR experience* OR attitude*) NEAR/6 (trial* OR research OR study OR studies) NEAR/6 (vaccin* OR immuni* OR pandemic* OR epidemic*)) OR SU((selection OR participation OR volunteer* OR motivation) AND (vaccine* OR immuni*))) AND TI,AB,SU(interview* OR discussion* OR questionnaire* OR focus group* OR qualitative OR ethnograph* OR fieldwork OR field work OR key informant*)

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Appendix 2. GRADE-CERQual evidence profile

Theme 1: factors under the control of the vaccine trial teams that influence people's decision to participate.

1.1 Communication of trial information

Summary of review finding	Studies contributing to the review finding	Methodological limitations	Coherence	Relevance	Adequacy	CERQual assessment of confidence in the evidence	Explanation of CERQual assessment
Finding 1: people appreciated when there was community involvement, including community leaders' involvement, in trial information dissemination. Community leaders themselves valued being involved in trial information dissemination, and developing health literacy within the community, but emphasised the need for clear details of vaccine development and trial processes to be effective in this role.	Brooks 2007; Lesch 2006; Newman 2011a; Newman 2015; Nguyen 2021; Strauss 2001 (2006 study report); Tarimo 2019; Toledo 2014	**Minor concerns** regarding methodological limitations, based on the assessment of 1 study with no concerns, 6 studies with minor concerns and 1 study with moderate concerns.	**No/very minor concerns** regarding coherence with data in primary studies clearly representing the finding. No ambiguities.	**Moderate concerns** regarding relevance as 5 studies were hypothetical. No concerns regarding geography Mix of low, middle and high-income countries. Vaccine for diseases mostly HIV and Ebola.	**Moderate concerns** regarding adequacy with 8 qualitative studies contributing with rich data.	**Moderate confidence**	Due to no/very minor concerns regarding coherence and minor concerns regarding relevance, methodological limitations. Moderate concerns regarding adequacy.
Finding 2: people considering participating in a vaccine trial for a pandemic or epidemic disease valued the approachability and availability of researchers to answer questions related to the trial.	David 2021; Mbunda 2018; Newman 2011a; Nyamathi 2004; Olin 2006; Slomka 2008; Toledo 2014	**Minor concerns** regarding methodological limitations, based on the assessment of 7 studies with minor concerns.	**No/very minor concerns** regarding coherence with data in primary studies clearly representing the finding. No ambiguities.	**No/very minor concerns** regarding relevance as 2 studies were hypothetical. No concerns regarding geography. Mix of low, middle and high-income countries. Vaccine for diseases mostly HIV and Ebola.	**Moderate concerns** regarding adequacy with 7 qualitative studies contributing with rich data.	**Moderate confidence**	Due to no/very minor concerns regarding coherence and minor concerns regarding relevance and methodological limitations. Moderate concerns regarding adequacy.

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Finding 3: people valued information on a vaccine trial for a pandemic or epidemic disease being communicated respectfully and in plain language that could be easily understood. People found leaflets a useful method of conveying information and felt they could be tailored to the information and language needs of specific populations.	Andrasik 2014; Brooks 2007; Chakrapani 2012; Grantz 2019; Newman 2011a; Newman 2015; Olin 2006; Strauss 2001 (2006 study report); Tarimo 2019; Toledo 2014	**Minor concerns** regarding methodological limitations, based on the assessment of 1 study with no concerns, 8 studies with minor concerns and 1 study with moderate concerns.	**No/very minor concerns** regarding coherence with data in primary studies clearly representing the finding. No ambiguities.	**Moderate concerns** regarding relevance as most studies were hypothetical. No concerns regarding geographical spread. Mix of low, middle and high-income countries. Vaccine for diseases all HIV.	**Minor concerns** regarding adequacy with 10 qualitative studies only contributing with rich data.	**Moderate confidence**	No/very minor concerns regarding coherence Minor concerns regarding methodological limitations and adequacy. Moderate concerns regarding relevance.
Finding 4: people emphasised the importance of receiving all the information relating to the vaccine trial for a pandemic or epidemic disease including any potential risks and benefits, together with opportunities to ask questions about anything they do not understand.	Grantz 2019; Jalloh 2019; Lesch 2006; Mbunda 2018; Newman 2011a; Newman 2015; Olin 2006; Strauss 2001 (2006 study report); Tarimo 2010; Tarimo 2019; Toledo 2014	**Minor concerns** regarding methodological limitations, based on the assessment of 1 study with no concerns and 10 studies with minor concerns and 1 study with moderate concerns.	**No/very minor concerns** regarding coherence with data in primary studies clearly representing the finding. No ambiguities.	**Moderate concerns** regarding relevance as most studies were hypothetical. No concerns regarding geography Mix of low, lower middle, upper middle and high-income countries. Vaccine for diseases mostly HIV and Ebola.	**Minor concerns** regarding adequacy with eleven qualitative studies contributing with rich data.	**High confidence**	Due to no/very minor concerns regarding coherence. Minor concerns regarding relevance, adequacy and methodological limitations.
Finding 5: people appreciated the availability of information about vaccines, how they were developed and worked, the potential benefits and risks, the implications of participation in a vaccine trial for a pandemic or epidemic disease, and the outcomes of previous studies to inform their decision-mak-	Adewoyin 2013; Andrasik 2014; Brooks 2007; Chakrapani 2012; Grantz 2019; Jalloh 2019; Lesch 2006; Mbunda 2018; Newman 2011a; Newman 2015; Nguyen 2021; Nyamathi 2004; Olin 2006; Strauss 2001 (2006 study report); Tarimo 2010; Tarimo 2019; Toledo 2014	**Minor concerns** regarding methodological limitations, based on the assessment of 1 study with no concerns, fifteen studies with minor concerns and 1 study with moderate concerns.	**No/very minor concerns** regarding coherence with data in primary studies clearly representing the finding. No ambiguities.	**Moderate concerns** regarding relevance as most studies were hypothetical. No concerns geography /income level. Mix of low, lower middle, upper middle and high-income countries.	**Minor concerns** regarding adequacy 17 studies contributing with rich data.	**High confidence**	No/very minor concerns regarding coherence. Minor concerns regarding relevance, adequacy and methodological limitations.

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ing around participation.				Vaccine for diseases mostly HIV and Ebola.			

1.2 Considerations around trial design

Summary of review finding	Studies contributing to the review finding	Methodological limitations	Coherence	Relevance	Adequacy	CERQual assessment of confidence in the evidence	Explanation of CERQual assessment
Finding 6: people emphasised the importance of participation being easy, convenient and causing minimal disruption. People were also concerned about possible distress arising from aspects of the trial design.	Adewoyin 2013; Andrasik 2014; Brooks 2007; Chakrapani 2012; Craig 2018; Gobat 2018; Grantz 2019; Lesch 2006; Mbunda 2018; Newman 2006; Newman 2008a; Newman 2008b; Nguyen 2021; Slomka 2008; Toledo 2014; Voytek 2011	**Minor concerns** regarding methodological limitations, based on the assessment 14 studies with minor concerns and 2 studies with moderate concerns.	**No/very minor concerns** regarding coherence with data in primary studies clearly representing the finding. No ambiguities.	**Moderate concerns** regarding relevance as most studies were hypothetical. No concerns geography /income level. Mostly high-income countries but the samples were mostly from lower socioeconomic groups. Good range of disease type.	**No/very minor concerns** regarding adequacy with 13 qualitative studies and 3 mixed methods studies and most contributing with rich data.	**High confidence**	No/very minor concerns regarding coherence and adequacy. Minor concerns regarding relevance and methodological limitations.
Finding 7: people described incentives such as money or access to addition support services as an important consideration when deciding whether or not to participate.	Adewoyin 2013; Andrasik 2014; Brooks 2007; Chakrapani 2012; Chin 2016; Craig 2018; David 2021; Gobat 2018; Grantz 2019; Jalloh 2019; Koniak-Griffin 2007; Lesch 2006; Mbunda 2018; Newman 2006; Newman 2008a; Newman 2008b; Nyamathi 2004; Olin 2006; Slomka 2008; Strauss 2001; Strauss 2001 (2006 study report); Tarimo 2019; Tarimo 2010; Tengbeh 2018; Tole-	**Minor concerns** regarding methodological limitations, based on the assessment of 2 studies with no concerns, 19 studies with minor concerns and 2 studies with moderate concerns.	**Minor concerns** regarding coherence with some concerns about the fit between the data from primary studies where monetary incentives were viewed suspiciously. Being recognised and acknowledged	**Minor concerns** regarding relevance as most studies were hypothetical. No concerns geography/income level. Mixture of high-, upper- to middle-, low- to middle- and low-income countries. Good range of disease type.	**Minor concerns** regarding adequacy with 21 qualitative studies and 2 mixed methods studies. Many contributing with rich data.	**High confidence**	Minor concerns regarding coherence, relevance and adequacy and methodological limitations.

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	do 2014; Voytek 2011; Wentzell 2021		for participation was a feature of 2 studies undertaken in Africa only.				

Theme 2: personal, family and societal factors that influence people's decision to participate in a vaccine trial for a pandemic or epidemic disease.

2.1 Weighting up the risks and benefits

Summary of review finding	Studies contributing to the review finding	Methodological limitations	Coherence	Relevance	Adequacy	CERQual assessment of confidence in the evidence	Explanation of CERQual assessment
Finding 8: people were hesitant to participate if they had concerns about vaccine side effects, or vaccine efficacy.	Adewoyin 2013; Brooks 2007; Chakrapani 2012; Gobat 2018; Grantz 2019; Jaffe 2020; Jalloh 2019; Lesch 2006; Mbunda 2018; Moutsiakis 2007; Newman 2006; Newman 2008a; Newman 2008b; Newman 2011b; Nyamathi 2004; Olin 2006; Slomka 2008; Tarimo 2010; Wentzell 2021	**Minor concerns** regarding methodological limitations, based on the assessment of 1 study with no concerns, 16 studies with minor concerns and 2 with moderate concerns.	**No/very minor concerns** regarding coherence with data in primary studies clearly representing the finding. No ambiguities.	**Moderate concerns** regarding relevance as studies mainly based on hypothetical scenarios for HIV studies. Good geographic and income level spread.	**Minor concerns** regarding adequacy with 19 studies contributing to the finding.	**Moderate confidence**	Minor concerns regarding adequacy and methodological limitations. Moderate concerns regarding relevance. No/very minor concerns regarding coherence.
Finding 9: people were concerned that trial participation could result in adverse outcomes that would impact their ability to fulfil their caring responsibilities or their ability to work or could affect their health insurance.	Adewoyin 2013; Chakrapani 2012; Gobat 2018; Jaffe 2020; Lesch 2006; Newman 2006; Newman 2008a; Newman 2008b; Tarimo 2010; Wentzell 2021	**Minor concerns** regarding methodological limitations, based on the assessment of 1 study with no concerns and studies with minor concerns and 1 study with moderate concerns.	**No/very minor concerns** regarding coherence with data in primary studies clearly representing the finding. No ambiguities.	**Moderate concerns** regarding relevance as studies mainly based in high income countries. 8 studies were hypothetical. 5 studies based in US and most studies were related to HIV.	**Moderate concerns** regarding adequacy with 10 studies contributing.	**Moderate confidence**	Moderate concerns regarding relevance and adequacy. Minor concerns regarding methodological limitations. No/very minor concerns regarding coherence.

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Finding 10: people did not always understand the difference between being antibody-positive and infected by the disease itself, or the immunity that may or may not be acquired through participation in a vaccine trial for a pandemic or epidemic disease.	Adewoyin 2013; Andrasik 2014; Brooks 2007; Chakrapani 2012; Craig 2018; Jalloh 2019; Koniak-Griffin 2007; Lesch 2006; Mbunda 2018; Newman 2006; Newman 2008a; Newman 2008b; Newman 2011a; Nguyen 2021 Olin 2006; Strauss 2001 (2006 study report); Voytek 2011	**Minor concerns** regarding methodological limitations, based on the assessment of 15 studies with minor concerns and 2 studies with moderate concerns.	**Minor concerns** regarding coherence with data in primary studies clearly representing the finding but with some ambiguities.	**Minor concerns** regarding relevance as studies included a diversity of geography, and disease type. Most contributing studies based on hypothetical scenarios and based in high income countries.	**Minor concerns** regarding adequacy with 17 studies contributing with rich data.	**High confidence**	Minor concerns regarding coherence, relevance adequacy and methodological limitations.
Finding 11: when making the decision to participate or not, people weighed up the potential harms of trial participation versus the potential harms of the disease.	Brooks 2007; Grantz 2019; Jaffe 2020; Jalloh 2019; Lesch 2006; Newman 2008b; Nguyen 2021; Wentzell 2021	**Minor concerns** regarding methodological limitations, based on the assessment of 1 study with no concerns, 6 studies with minor concerns and 1 study with moderate concerns.	**Minor concerns** regarding coherence as finding reflects mix of front-line workers who may be at higher risk and individuals.	**No/very minor concerns** regarding relevance as studies included a diversity of geography, income level of country of origin and disease type.	**Moderate concerns** regarding adequacy with 8 contributing studies.	**Moderate confidence**	Moderate concerns regarding adequacy. Minor concerns regarding methodological limitations and coherence. No/very minor concerns regarding relevance.
2.2 Influence of other people							
Summary of review finding	**Studies contributing to the review finding**	**Methodological limitations**	**Coherence**	**Relevance**	**Adequacy**	**CERQual assessment of confidence in the evidence**	**Explanation of CERQual assessment**
Finding 12: people described how the attitudes of family members could influence their willingness to take part in a vaccine trial.	Chakrapani 2012; Craig 2018; Lesch 2006; Mbunda 2018; Nguyen 2021; Tarimo 2011; Voytek 2011; Wentzell 2021	**Minor concerns** regarding methodological limitations, based on the assessment of 1 study with no	**Minor concerns** regarding coherence based on variations within the data with different stud-	**Minor concerns** regarding relevance as studies included diversity of disease type. Good geographical although participant income only reported in 3 studies.	**Moderate concerns** regarding adequacy with 8 studies contributed to this finding	**Moderate confidence**	Minor concerns regarding coherence, relevance and methodological limitations.

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		concerns, 6 studies with minor concerns and 1 study with moderate concerns.	ies reporting different aspects of family attitudes.		however the richness of the data in the contributing studies is high.		Moderate concerns regarding adequacy.

2.3 Societal influences

Summary of review finding	Studies contributing to the review finding	Methodological limitations	Coherence	Relevance	Adequacy	CERQual assessment of confidence in the evidence	Explanation of CERQual assessment
Finding 13: people feared stigma as a result of trial participation where this might carry implications about their sexuality, gender identity or disease status.	Andrasik 2014; Brooks 2007; Chakrapani 2012; Grantz 2019; Lesch 2006; Mbunda 2018; Moutsiakis 2007; Newman 2006; Newman 2008a; Newman 2008b; Nguyen 2021; Nyblade 2011; Strauss 2001 (2006 study report); Toledo 2014	**Minor concerns** regarding methodological limitations, based on the assessment of twelve studies with minor concerns and 2 studies with moderate concerns.	**No/very minor concerns** regarding coherence with data in primary studies clearly representing the finding. No ambiguities.	**Moderate concerns** regarding relevance as studies were primarily related to HIV which has additional stigma to other diseases 2 studies of Ebola.	**No/very minor concerns** regarding adequacy with 14 studies contributed to this finding with good data richness.	**High confidence**	No/very minor concerns regarding coherence and adequacy. Minor concerns regarding methodological limitations. Moderate concerns around relevance.
Finding 14: people described how their level of trust/distrust in organisations involved in healthcare delivery, medical and scientific research, and governments influenced their decision to participate in a vaccine trial.	Andrasik 2014; Brooks 2007; Chakrapani 2012; Craig 2018; Grantz 2019; Jaffe 2020; Jalloh 2019; Koniak-Griffin 2007; Lesch 2006; Mbunda 2018; Moutsiakis 2007; Newman 2006; Newman 2011a; Newman 2015; Nguyen 2021; Nyamathi 2004; Olin 2006; Strauss 2001 (2006 study report); Tarimo 2011; Tengbeh 2018; Toledo 2014;	**Minor concerns** regarding methodological limitations, based on the assessment of 2 studies with no concerns, 18 studies with minor concerns and 3 studies with moderate concerns.	**No/very minor concerns** regarding coherence with data in primary studies clearly representing the finding. No ambiguities.	**Minor concerns** regarding relevance as studies represented good diversity amongst disease type (and geographical spread). There was a mix of income levels and mix of real and hypothetical scenarios.	**No/very minor concerns** regarding adequacy with 23 studies contributing to this finding with good data richness.	**High confidence**	Minor concerns with methodological limitations and relevance. No/very minor concerns with adequacy and coherence.

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	Voytek 2011; Wentzell 2021						
Theme 3: perceived personal and societal rewards that influence people's decision to participate in a vaccine trial for a pandemic or epidemic disease.							
3.1 Personal rewards of trial participation							
Summary of review finding	**Studies contributing to the review finding**	**Methodological limitations**	**Coherence**	**Relevance**	**Adequacy**	**CERQual assessment of confidence in the evidence**	**Explanation of CERQual assessment**
Finding 15: people often viewed trial participation as a way of accessing vaccination with the potential benefit of reduced infection risk; improved knowledge of the disease; and improvements in general health.	Chakrapani 2012; Craig 2018; Jalloh 2019; Koniak-Griffin 2007; Newman 2006; Newman 2011b; Nyamathi 2004; Olin 2006; Strauss 2001; Tengbeh 2018; Voytek 2011; Wentzell 2021	**Minor concerns** regarding methodological limitations, based on the assessment of 1 study with no concerns, 10 studies with minor concerns and 1 study with moderate concerns.	**Minor concerns** regarding coherence with a few concerns about the fit between the data and the finding.	**Moderate concerns** regarding relevance as studies due to the lack of participants from higher socio-economic backgrounds, the limited geographic spread of studies – none from Europe. Good spread of disease type.	**No/very minor concerns** regarding adequacy with 12 qualitative studies reporting with rich data.	**High confidence**	Minor concerns regarding methodological limitations, relevance and adequacy. No/very minor concerns regarding coherence.
Finding 16: people often considered trial participation as a way of helping society return to its pre-pandemic or epidemic life.	Chakrapani 2012; Lesch 2006; Wentzell 2021	**Minor concerns** regarding methodological limitations, based on the assessment of 2 studies with minor concerns and 1 study with no concerns.	**Minor concerns** regarding coherence with a few concerns about the fit between the data and the finding.	**Moderate concerns** regarding relevance as studies due to the lack of participants from higher socioeconomic backgrounds, the limited geographic spread of studies – none from Europe, and the limited number of diseases represented (HIV and COVID-19).	**Major concerns** regarding adequacy with 3 studies with sparse data relating to this finding.	**Moderate confidence**	Major concerns regarding adequacy. Moderate concerns regarding relevance. Minor concerns regarding methodological limitations and coherence.
3.2 Making a difference: benefits for others							
Summary of review finding	**Studies contributing to the review finding**	**Methodological limitations**	**Coherence**	**Relevance**	**Adequacy**	**CERQual assessment of**	**Explanation of CERQual assessment**

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					confidence in the evidence	
Finding 17: people described their desire to help the community as an important factor in their decision to participate.	Adewoyin 2013; Brooks 2007; Chakrapani 2012; Chin 2016; Craig 2018; David 2021; Gobat 2018; Grantz 2019; Lesch 2006; Newman 2011a; Nguyen 2021; Nyamathi 2004; Slomka 2008; Strauss 2001; Tengbeh 2018; Tarimo 2010; Toledo 2014; Wentzell 2021	**Minor concerns** regarding methodological limitations, based on the assessment of thirteen studies with minor concerns, 1 study with moderate concerns and 2 studies with no concerns.	**No/very minor concerns** regarding coherence with data in primary studies clearly representing the finding. No ambiguities.	**Moderate concerns** regarding relevance as studies had limited geographical spread/income level. Studies included a reasonable range of diseases (e.g. Ebola, COVID-19 and TB) but focused more on HIV. Studies were situated in both hypothetical and lived experiences and included those who had/would participate and those who had/would decline trial participation.	**Minor concerns** regarding adequacy with fifteen qualitative studies and 1 mixed methods study contributing reasonably thick data.	**High confidence**	No/very minor concerns regarding coherence. Minor concerns regarding methodological limitations and adequacy. Moderate concerns regarding relevance.
Finding 18: people in professional or leadership roles described their perceived duty as part of these roles as an influencing factor in their decision-making.	Chakrapani 2012; Chin 2016; Craig 2018; David 2021; Grantz 2019; Newman 2011a; Newman 2011b; Nguyen 2021; Olin 2006; Tarimo 2010; Tengbeh 2018; Wentzell 2021	**Minor concerns** regarding methodological limitations, based on the assessment of 10 studies with minor concerns and 2 studies with no concerns.	**Minor concerns** regarding coherence with a few concerns about the fit between the data and the finding.	**Minor concerns** regarding relevance as studies had a moderate geographical spread / income level. Studies included a reasonable range of diseases. Studies were situated in both hypothetical and lived experiences and included those who had/would participate and those who had/would decline trial participation.	**Moderate concerns** regarding adequacy with twelve qualitative studies contributing moderately thick data.	**Moderate confidence**	Minor concerns regarding methodological limitations, coherence, and relevance. Moderate concerns regarding adequacy.
Finding 19: some people described how their decision to participate in a vaccine trial was influenced by the memory of family and friends who had died of the disease during the pandemic or epidemic and a desire	Adewoyin 2013; Brooks 2007; Jaffe 2020; Moutsiakis 2007; Newman 2006; Newman 2011a; Newman 2011b; Tarimo 2019; Toledo 2014; Voytek 2011; Wentzell 2021	**Minor concerns** regarding methodological limitations, based on the assessment of 7 studies with minor concerns, 3 studies with	**Minor concerns** regarding coherence with a few concerns about the fit between the data and the finding.	**Moderate concerns** regarding relevance as studies had limited geographical spread/income level. Studies included did not provide reasonable range of diseases but focused more on HIV. Studies were	**Moderate concerns** regarding adequacy with 10 qualitative studies and 1 mixed methods study contributing	**Low confidence**	Minor concerns regarding methodological limitations and coherence. Moderate concerns regarding relevance and adequacy.

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to protect future generations.		moderate concerns and 1 study with no concerns.		situated in both hypothetical and lived experiences and included those who had/would participate and those who had/would decline trial participation.	moderately thick data.		
Finding 20: people described how a wish to support the advancement of science and medicine could influence a decision to take part in a vaccine trial in the context of an epidemic or pandemic.	Adewoyin 2013; Chakrapani 2012; David 2021; Gobat 2018; Grantz 2019; Jalloh 2019; Lesch 2006; Newman 2008b; Newman 2011a; Newman 2011b; Slomka 2008; Strauss 2001; Tarimo 2019; Toledo 2014; Wentzell 2021	**Minor concerns** regarding methodological limitations, based on the assessment of 14 studies with minor concerns and 1 study with no concerns.	**Minor concerns** regarding coherence with a few concerns about the fit between the data and the finding.	**Moderate concerns** regarding relevance as studies had limited geographical spread/income level. Studies included a range of diseases but focused more on HIV. Studies were situated in both hypothetical and lived experiences and included those who had/would participate, however, those who had/would decline trial participation were focused mainly on hypothetical situations.	**Minor concerns** regarding adequacy with 14 qualitative studies and 1 mixed methods study contributing reasonably thick data.	**Moderate confidence**	Minor concerns regarding methodological limitations, coherence, and adequacy. Moderate concerns regarding relevant

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HISTORY

Protocol first published: Issue 1, 2022

CONTRIBUTIONS OF AUTHORS

The protocol was drafted by PM, LB, MD and CH.

All the review team reviewed several drafts of the protocol and offered comments and suggestions (PM, LB, MD, KR, EM, CG, DD, AB, SS, RC, XHC, CH).

PM, CH, LB, MD, KR and EM conducted study selection and data extraction.

PM, CH, LB, MD, KR and EM conducted analysis, assessment of methodological limitations and the GRADE-CERQual assessment of confidence in the review findings.

CG revised the plain language summary.

PM, CH, LB, MD and KR drafted the manuscript.

All review authors provided feedback on the initial review draft.

All review authors read and approved the final manuscript.

DECLARATIONS OF INTEREST

PM: none.

LB: none.

MD: none.

KR: none.

EM: none.

CG: is a Cochrane editor but was not involved in the editorial process of this review.

DD: Cochrane Pregnancy and Childbirth Group Editor but was not involved in the editorial process of this review.

SS: is a Cochrane editor but was not involved in the editorial process of this review.

AB: is a Cochrane editor but was not involved in the editorial process of this review.

RC: none.

XHC: none.

CH: none.

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Internal sources

- No sources of support provided

External sources

- Horizon 2020, Ireland

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

When we became familiar with the evidence in the eligible studies it became clear that recruitment to vaccine trials does not just occur during a pandemic or epidemic. Recruitment can continue after the acute phase has passed, therefore it was more accurate to refer to recruitment to vaccine trials in the context of a pandemic or epidemic, and we altered the title slightly.

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- The protocol title was: factors that impact on recruitment to vaccine trials during a pandemic or epidemic: a qualitative evidence synthesis.
- The review title was: factors that impact on recruitment to vaccine trials in the context of a pandemic or epidemic: a qualitative evidence synthesis.

The aim of the protocol was to explore the factors associated with a person's decision to take part in a pandemic or epidemic vaccine trial. We changed the wording to reflect the title change to explore the factors that influence a person's decision to participate in a vaccine trial in the context of a pandemic or epidemic.

In the searching phase we included MEDLINE filter for qualitative studies, which is a modified version of the University of Texas filter described at libguides.sph.uth.tmc.edu/search_filters/ovid_medline_filters. We had not described this in the protocol. This filter was used in the searches on Ovid MEDLINE, EBSCOhost CINAHL, Scopus and PsycINFO. It was chosen as it performed with the best balance of sensitivity and precision in a review by Wagner 2020. We provided all strategies used in the review (Appendix 1).

In the protocol, we had indicated that we would use QSR NVivo Version 12 to manage data extraction and synthesis. NVivo had updated its software as we began the review, and we managed the date extraction and synthesis process using the new version, QSR NVIVO V. R1.6.

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