



Deposited via The University of Sheffield.

White Rose Research Online URL for this paper:

<https://eprints.whiterose.ac.uk/id/eprint/214356/>

Version: Published Version

Article:

Meskell, P., Biesty, L.M., Dowling, M. et al. (2022) Factors that impact on recruitment to vaccine trials during a pandemic or epidemic: a qualitative evidence synthesis. *Cochrane Database of Systematic Reviews*, 2022 (1). MR000065. ISSN: 1465-1858

<https://doi.org/10.1002/14651858.mr000065>

This review is published as a Cochrane Review in the Cochrane Database of Systematic Reviews [2022, Issue 1]. Cochrane Reviews are regularly updated as new evidence emerges and in response to comments and criticisms, and the Cochrane Database of Systematic Reviews should be consulted for the most recent version of the Review.' + '[Meskell P, Biesty LM, Dowling M, Meehan E, Glenton C, Devane D, Shepperd S, Booth A, Cox R, Chan XHS, Houghton C.]. [Factors that impact on recruitment to vaccine trials during a pandemic or epidemic: a qualitative evidence synthesis (Protocol)]. *Cochrane Database of Systematic Reviews* 2022, Issue 1. Art. No.: MR000065. DOI: <http://dx.doi.org/10.1002/14651858.MR000065>

Reuse

Items deposited in White Rose Research Online are protected by copyright, with all rights reserved unless indicated otherwise. They may be downloaded and/or printed for private study, or other acts as permitted by national copyright laws. The publisher or other rights holders may allow further reproduction and re-use of the full text version. This is indicated by the licence information on the White Rose Research Online record for the item.

Takedown

If you consider content in White Rose Research Online to be in breach of UK law, please notify us by emailing eprints@whiterose.ac.uk including the URL of the record and the reason for the withdrawal request.



Cochrane
Library

Cochrane Database of Systematic Reviews

Factors that impact on recruitment to vaccine trials during a pandemic or epidemic: a qualitative evidence synthesis (Protocol)

Meskell P, Biesty LM, Dowling M, Meehan E, Glenton C, Devane D, Shepperd S, Booth A, Cox R, Chan XHS, Houghton C

Meskell P, Biesty LM, Dowling M, Meehan E, Glenton C, Devane D, Shepperd S, Booth A, Cox R, Chan XHS, Houghton C.
Factors that impact on recruitment to vaccine trials during a pandemic or epidemic: a qualitative evidence synthesis (Protocol).
Cochrane Database of Systematic Reviews 2022, Issue 1. Art. No.: MR000065.
DOI: [10.1002/14651858.MR000065](https://doi.org/10.1002/14651858.MR000065).

www.cochranelibrary.com

Factors that impact on recruitment to vaccine trials during a pandemic or epidemic: a qualitative evidence synthesis (Protocol)

Copyright © 2022 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

WILEY

TABLE OF CONTENTS

ABSTRACT	1
BACKGROUND	2
OBJECTIVES	3
METHODS	3
ACKNOWLEDGEMENTS	6
REFERENCES	7
APPENDICES	9
CONTRIBUTIONS OF AUTHORS	10
DECLARATIONS OF INTEREST	10
SOURCES OF SUPPORT	11

[Qualitative Protocol]

Factors that impact on recruitment to vaccine trials during a pandemic or epidemic: a qualitative evidence synthesis

Pauline Meskell¹, Linda M Biesty², Maura Dowling², Elaine Meehan³, Claire Glenton⁴, Declan Devane⁵, Sasha Shepperd⁶, Andrew Booth⁷, Rebecca Cox⁸, Xin Hui S Chan⁹, Catherine Houghton⁵

¹Department of Nursing and Midwifery, University of Limerick, Limerick, Ireland. ²School of Nursing and Midwifery, National University of Ireland, Galway, Galway, Ireland. ³Ageing Research Centre, School of Allied Health, University of Limerick, Limerick, Ireland. ⁴Norwegian Institute of Public Health, Oslo, Norway. ⁵School of Nursing and Midwifery, National University of Ireland Galway, Galway, Ireland. ⁶Nuffield Department of Population Health, University of Oxford, Oxford, UK. ⁷School of Health and Related Research, University of Sheffield, ScHARR, Sheffield, UK. ⁸Department of Clinical Sciences, University of Bergen, Bergen, Norway. ⁹Centre for Tropical Medicine and Global Health, University of Oxford, Oxford, UK

Contact: Pauline Meskell, pauline.meskell@ul.ie.

Editorial group: Cochrane Methodology Review Group, Cochrane Effective Practice and Organisation of Care Group.

Publication status and date: New, published in Issue 1, 2022.

Citation: Meskell P, Biesty LM, Dowling M, Meehan E, Glenton C, Devane D, Shepperd S, Booth A, Cox R, Chan XHS, Houghton C. Factors that impact on recruitment to vaccine trials during a pandemic or epidemic: a qualitative evidence synthesis (Protocol). *Cochrane Database of Systematic Reviews* 2022, Issue 1. Art. No.: MR000065. DOI: [10.1002/14651858.MR000065](https://doi.org/10.1002/14651858.MR000065).

Copyright © 2022 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

ABSTRACT

Objectives

This is a protocol for a Cochrane Review (qualitative). The objectives are as follows:

This is a protocol for a Cochrane Review (qualitative). The review aims to explore the factors associated with a person's decision to take part in a pandemic or epidemic vaccine trial.

BACKGROUND

Description of the topic

In March 2020, the World Health Organization (WHO) declared a COVID-19 pandemic (WHO 2020). COVID-19 is a multi-system disease caused 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 pandemic (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 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 treatment trials, vaccine trials typically involve healthy volunteers who may have concerns about the risks associated with enrolling 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). Older people, who are disproportionately affected by COVID-19, are less likely to participate in a vaccine trial (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).

Furthermore, due to the urgent nature of vaccine development in a pandemic or epidemic, potential participants might be concerned about the rapidity of vaccine development and perceive that steps in the scientific process have been shortened, which may erode public confidence in participating in trials (Dyer 2020; Langford 2020). Limited timelines for recruitment increase recruitment pressures (Wilson 2021), and this can create a 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 trials depend primarily on the willingness of a diverse group of healthy volunteers to take part in large-scale trials. Hence, it is important to identify factors influencing people's decision to take part, including during a pandemic or epidemic, and support transparency of information and decision-making to optimise informed choice (Carlsen 2016; O'Callaghan 2020).

Support from the public for trials overall, and even more so during a pandemic or epidemic, is evident (Elliot 2019; 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 during 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 in a pandemic or epidemic is also influenced by factors such as concerns about the disease prevalence and spread, confidence in the vaccine safety and the impact of restrictive measures during 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 decisions to participate in trials is likely to help shape future communication between trialists and potential participants. However, this communication does not simply aim to convince the individual to take part in a pandemic or epidemic vaccine trial. It has the further objective of supporting 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 a recent qualitative evidence synthesis, 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 a pandemic or epidemic.

To gain a comprehensive understanding of the factors associated with recruitment to vaccine trials during a pandemic or epidemic requires exploration of the barriers and facilitators that guide decision-making among 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 COVID-19 vaccine trials and, more broadly, inform vaccine trials conducted in similar circumstances in the future.

OBJECTIVES

This is a protocol for a Cochrane Review (qualitative). The review aims to explore the factors associated with a person's decision to take part in a pandemic or epidemic vaccine trial.

METHODS

Criteria for considering studies for this review

Types of studies

We will include primary studies that use recognised methods of qualitative data collection and data analysis, including: ethnography, phenomenology, case studies, grounded theory studies and qualitative process evaluations. We will include studies that use 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). For mixed-method studies, we will include them if it is possible to extract the data collected and analysed using qualitative methods. Studies will be eligible regardless of whether they were conducted alongside studies of the effectiveness of interventions to improve vaccination uptake in a pandemic or epidemic. We will include both published and unpublished studies and studies published in any language.

We will exclude studies that collect data using qualitative methods but do not analyse them using qualitative analysis methods (e.g. open-ended survey questions where the response data are analysed using descriptive statistics only). We will not exclude studies based on our assessment of methodological limitations, because these may contribute insights into particular contexts or circumstances as well as to the overall phenomenon. We will use the information about methodological limitations to assess our confidence in the review findings.

Topic of interest

We will include studies with a primary focus on people's experiences of, and attitudes to, participating in a vaccine trial during a pandemic or epidemic. Eligible studies will report the views and experiences of adults (≥ 18 years). This includes adults who have been invited to participate in trials as well as adults who have not received an invitation.

By 'vaccine trials in a pandemic or epidemic' we refer to prophylactic or therapeutic vaccine trials related to the disease that caused the pandemic or epidemic, and in which the trial is being conducted in response to, and during, the pandemic or epidemic. We will include studies conducted in any setting that is experiencing a pandemic or epidemic. We consider an epidemic to be a large disease outbreak within a region and a pandemic as an epidemic that spreads over multiple regions or continents. We consider a prophylactic or therapeutic vaccine as one that builds immunity in an individual and is intended to prevent disease spread, prevent development of symptoms and reduce severity of disease.

Search methods for identification of studies

Electronic searches

The [Cochrane \(EPOC\)](#) Effective Practice and Organisation of Care Information Specialist will develop the search strategies in consultation with the review authors.

We will search the following electronic databases.

- MEDLINE, Ovid
- CINAHL (Cumulative Index to Nursing and Allied Health Literature), EbscoHost
- Scopus
- PsycINFO
- Epistemonikos
- ORRCA (Online Resource for Research in Clinical trials)

We will develop search strategies for each database. We will not apply any limits on language or publication date. Where appropriate, we will include a methodological filter for qualitative studies. See [Appendix 1](#) for the MEDLINE search strategy, which we will adapt for other databases. We will provide all strategies used in the final review.

Grey literature

In addition to searching the databases outlined, we will conduct a grey literature search of theses via Ethos, the DART-Europe E-theses portal and ProQuest Dissertations & Theses Abstract & Index.

Searching other resources

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

We will search the Cochrane COVID-19 Study Register for any qualitative study relating to COVID-19 vaccine trials, because that is an ongoing pandemic at the time the searches will be conducted. The Cochrane COVID-19 Study Register includes pre-print material.

We will check the reference lists of studies included in linked intervention reviews to identify any qualitative studies associated with these studies. We will also contact researchers with expertise relevant to the review topic to request studies that might meet our inclusion criteria. We will select the included studies that exactly match the eligibility criteria.

Selection of studies

Two review authors will independently assess each title and abstract of the identified records to evaluate eligibility. We will use [Covidence](#) software for title and abstract screening. We will exclude references (at title and abstract screening) that do not meet the eligibility criteria. After that, we will retrieve the full text of all the papers identified as potentially relevant by either or both review authors. Two review authors will then assess these papers independently. We will resolve disagreements by discussion or, when required, by involving a third review author. Where appropriate, we will contact the study authors for further information. Where review authors are also authors of any of the studies identified in the searches, they will not assess these studies for inclusion.

Language translation

For titles and abstracts published in a language beyond the proficiencies of the team, we will carry out an initial translation through open source software (Google Translate). If this translation indicates possible inclusion, or if the translation is insufficient to decide, we will retrieve the paper's full text. We will then ask Cochrane networks or other networks proficient in that language to assist us in assessing the full text of the paper for inclusion. We will consider asking the original authors to assist in the provision of translation of the full text of the paper. If this cannot be achieved for a paper in a particular language, the paper will be listed under 'Studies awaiting classification' to ensure transparency in the review process. We will use professional translation services if needed.

Sampling of studies

Qualitative evidence synthesis aims for conceptual richness and contextual comparisons, and large amounts of study data can impair the quality of the analysis. Depending on the number of studies eligible for inclusion, we may need to sample the studies for more meaningful analysis.

To allow for the broadest possible variation within the included studies, we will use maximum variation purposive sampling to select from the eligible studies (Ames 2017; Suri 2011). Potential sources of variation may include the characteristics of the participants such as age and gender, the type of vaccine and associated disease it aims to prevent, the year in which the trial was conducted and the country income level. We will also assess the data richness of eligible studies, for instance by using the approach used by Ames 2019. Once we have determined suitable variables, we will create a sampling frame and map all eligible studies onto the frame. We will then review the studies within each cell of the frame and decide how many studies to include in the review. We will also purposely seek additional studies that address characteristics not previously identified as important, but that are identified during the initial analysis.

We will include a PRISMA flow diagram to show the results of our search and of screening and selecting studies for inclusion. Where the same study (i.e. using the same sample and methods) has been presented in different reports, we will collate these reports so that each study (rather than each report) is the unit of interest in our review. We will include all unique data from all related study reports. We will include a table listing studies that we excluded from our review at the full-text stage and the main reasons for exclusion.

Data extraction

We will use Qualitative Data Analysis Software (QSR) NVivo Version 2020/R1 to manage data extraction and synthesis (Nvivo 2020). We will extract information about the first author, publication date, study language, country, setting, type of pandemic or epidemic, type of vaccine, participants' age, gender, socioeconomic status, ethnicity and any other information relevant for any planned subgroup analyses. We will extract information about how the study was designed and conducted. Finally, we will extract all data relevant to the review's objective, including descriptions of themes and categories as well as illustrative quotes. PM, CH, LB, EM and MD will individually extract pertinent information about design, setting and methods, and the data from all the sampled studies. We will

pilot test the data extraction form and process initially, and review authors will agree on any revisions.

Assessing the methodological limitations of included studies

At least two review authors (from PM, LB, MD, CH, EM) will independently assess methodological limitations for each study using a quality assessment tool for qualitative studies used in previous Cochrane Reviews (Ames 2017; Ames 2019; Houghton 2020). Where any of the review authors are also authors of included studies, they will not be involved in assessing the study's methodological limitations. We will resolve disagreements by discussion or, when required, by involving a third review author.

We will assess methodological limitations according to the following domains.

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

We will report our assessments in a Methodological Limitations table, using a 'yes/no/can't tell' rating. We will use 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 will use 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 model 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 four stages:

1. identify a pre-existing conceptual model or framework;
2. include all relevant qualitative studies satisfying criteria;
3. map data from included studies onto framework;
4. use a thematic synthesis approach to generate completely new themes to supplement the framework's themes.

We will determine our final choice of framework after familiarising ourselves with the data in the included studies. We are currently considering using a thematic framework based on themes from the previously published Cochrane qualitative evidence synthesis that has explored what influences people's decision to take part in trials in general (Houghton 2020). This framework includes three themes with a further six subthemes, described below.

- 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

We will code the evidence from the included studies against the proposed framework. We will create new or revised themes using thematic synthesis on any evidence that cannot be coded against the framework. We will then produce a new framework combining existing framework and new themes supported by the evidence.

We will manage this process using QSR NVIVO V2020/R1. This will enable four review team members to work effectively and transparently on the synthesis. We will use the attributes function in NVivo to generate 'queries', which will facilitate potential subgroup analysis, such as age, geographical location, or income setting.

Developing implications for practice

When we have finished preparing the review findings, we will examine each finding, identify factors that could influence recruitment for pandemic or epidemic vaccine trials and develop prompts for future trialists. We will present these prompts in the implications for practice section. These prompts are not intended to be recommendations, but will be phrased as questions to help trialists consider the implications of the review findings within their context. We will send these implications for practice to a selection of stakeholders from different countries and COVID-19 vaccine trialists to gather their feedback about the relevance of these prompts and how they are phrased and presented.

Assessing our confidence in the review findings

At least five review authors (PM, LB, MD, EM, CH) will use 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.

1. Methodological limitations of included studies: the extent to which there are concerns about the primary study's design or conduct that contributed evidence to an individual review finding.
2. Coherence of the review finding: an assessment of how clear and cogent the fit is between the data from the primary studies and a review finding that synthesises those data. By cogent, we mean well-supported or compelling.
3. 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.
4. 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 will judge the overall confidence in the evidence supporting the review finding.

We will judge confidence as high, moderate, low, or very low. The final assessment will be based on consensus among the review authors. All findings start as high confidence and will then be graded down if there are important concerns regarding any GRADE-CERQual components.

Summary of qualitative findings table and evidence profile

We will present summaries of the findings and our assessments of confidence in these findings in a summary of qualitative findings table. We will present detailed descriptions of our confidence assessment in an evidence profile.

Integrating the review findings with other Cochrane Reviews

We will integrate our key review findings with the Cochrane Review by Houghton 2020, which explores factors influencing people's decisions to participate in healthcare trials. We are particularly interested in the extent to which our findings reflect or differ from the Houghton 2020 review, as well as comparing our confidence in the evidence in the context of pandemic or epidemic vaccine trials.

We will also explore how we can integrate the findings from both qualitative reviews with those of a related Cochrane Review of the effectiveness of recruitment interventions (Trewick 2018), to explore how the interventions assessed in the review could be better designed or implemented in the context of pandemic or epidemic vaccine trials. We will consider using the proposed framework from Houghton 2020 as an integration tool to compare the findings across the two qualitative evidence syntheses and the intervention review. We will consider several possible approaches, including a logic model approach (Ames 2020), or a matrix approach (Harden 2018), depending on the nature of our findings.

Review author reflexivity

Author reflexivity considers any influences or biases that may impact the review process (Flemming 2021). The core review team includes researchers with and without a healthcare background. All review authors are researchers within health care. Some are focusing on trial methodology, and others on qualitative research in trials (PM, LB, MD, PM, LB). All review authors have training and expertise in qualitative research and qualitative evidence synthesis. Most were involved in a previous Cochrane qualitative evidence synthesis 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: practicing 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 (CH, MD, PM, LB, DD), public health and health services research (AB, CG, EM); and as the recipient of vaccinations due to a chronic health condition (AB). All authors believe that trial participation, both in the context of a pandemic or epidemic and otherwise, should be voluntary. Moreover, all 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 side effects and uncertainties.

Central to reflexivity is remaining open to any viewpoints that may influence decision-making. This will be achieved through regular team meetings at each stage of the review process where the team will critically discuss personal views and experiences of vaccine development and vaccination programmes. In addition, the lead author (PM) will maintain a reflexive journal to capture key discussions and decisions reached at team meetings.

ACKNOWLEDGEMENTS

Paul Miller, Cochrane Information Specialist, for his work on topic refinement and support in developing the search strategy.

When preparing this protocol, we used EPOC's Protocol and Review Template for Qualitative Evidence Synthesis ([Glenton 2020](#)).

This review is part of a larger study being undertaken by the VACCELERATE consortium.

REFERENCES

Additional references

Ames 2017

Ames HM, Glenton C, Lewin S. Parents' and informal caregivers' views and experiences of communication about routine childhood vaccination: a synthesis of qualitative evidence. *Cochrane Database of Systematic Reviews* 2017, Issue 2. Art. No: CD011787. [DOI: [10.1002/14651858.CD011787.pub2](https://doi.org/10.1002/14651858.CD011787.pub2)]

Ames 2019

Ames H, Glenton C, Lewin S. Purposive sampling in a qualitative evidence synthesis: a worked example from a synthesis on parental perceptions of vaccination communication. *BMC Medical Research Methodology* 2019;**19**(1):26. [DOI: [10.1186/s12874-019-0665-4](https://doi.org/10.1186/s12874-019-0665-4)]

Ames 2020

Ames H, Glenton C, Leon N. Using a matrix analysis to integrate findings from a qualitative evidence synthesis and a review of effectiveness: a worked example. *Advances in Evidence Synthesis: special issue, Cochrane Database of Systematic Reviews* 2020;**9** (Suppl 1):447. [DOI: [10.1002/14651858.CD202001](https://doi.org/10.1002/14651858.CD202001)]

Booth 2015

Booth A, Carroll C. How to build up the actionable knowledge base: the role of 'best fit' framework synthesis for studies of improvement in healthcare. *BMJ Quality & Safety* 2015;**24**:700-8. [DOI: [10.1136/bmjqs-2014-003642](https://doi.org/10.1136/bmjqs-2014-003642)]

Borobia 2021

Borobia AM, García-García I, Díaz-García L, Rodríguez-Mariblanca A, Martínez de Soto L, Monserrat Villatoro J, et al. Health care workers' reasons for choosing between two different COVID-19 prophylaxis trials in an acute pandemic context: single-center questionnaire study. *Journal of Medical Internet Research* 2021;**23**(2):e23441. [DOI: [10.2196/23441](https://doi.org/10.2196/23441)]

Bower 2007

Bower P, Wilson S, Mathers N. Short report: how often do UK primary care trials face recruitment delays? *Family Practice* 2007;**24**(6):601-3. [DOI: [10.1093/fampra/cmm051](https://doi.org/10.1093/fampra/cmm051)]

Brooks 2020

Brooks SK, Webster RK, Smith LE. The psychological impact of quarantine and how to reduce it: rapid review of the evidence. *Lancet* 2020;**395**(10227):912-20. [DOI: [10.1016/S0140-6736\(20\)30460-8](https://doi.org/10.1016/S0140-6736(20)30460-8)]

Carlsen 2016

Carlsen B, Glenton C. The swine flu vaccine, public attitudes, and researcher interpretations: a systematic review of qualitative research. *BMC Health Service Research* 2016;**16**:203. [DOI: [10.1186/s12913-016-1466-7](https://doi.org/10.1186/s12913-016-1466-7)]

Carroll 2013

Carroll C, Booth A, Leaviss J, Rick J. "Best fit" framework synthesis: refining the method. *BMC Medical Research Methodology* 2013;**13**:37. [DOI: [10.1186/1471-2288-13-37](https://doi.org/10.1186/1471-2288-13-37)]

Cattapan 2019

Cattapan A, Browne K, Halperin D, Castri A, Fullsack P, Graham J, et al. Motivation for participating in phase 1 vaccine trials: comparison of an influenza and an Ebola randomised control trial. *Vaccine* 2019;**37**(2):289-95. [DOI: [10.1016/j.vaccine.2018.11.014](https://doi.org/10.1016/j.vaccine.2018.11.014)]

Cochrane (EPOC)

Cochrane Effective Practice and Organisation of Care (EPOC). Qualitative Evidence Syntheses guidance on when to sample and how to develop a purposive sampling frame. Available at: epoc.cochrane.org/resources/epoc-resources-review-authors (accessed after 2 December 2021).

Covidence [Computer program]

Veritas Health Innovation Covidence. Version accessed after 2 December 2021. Melbourne, Australia: Veritas Health Innovation. Available at covidence.org.

Darzi 2021

Darzi A, Goddard A, Henderson K, Mahajan R, Marx C, Mortensen N, et al. Increasing recruitment into covid-19 trials. *BMJ* 2021;**372**:n235. [DOI: [10.1136/bmj.n235](https://doi.org/10.1136/bmj.n235)]

Davis 2020

Davis J, Ferreira D, Denholm JT, Tong S. Clinical trials for the prevention and treatment of COVID-19: current state of play. *Medical Journal of Australia* 2020;**213**:86-93. [DOI: [10.5694/mja2.50673](https://doi.org/10.5694/mja2.50673)]

Detoc 2017

Detoc M, Gagneux-Brunon A, Lucht F, Botelho-Nevers E. Barriers and motivations to volunteers' participation in preventive vaccine trials: a systematic review. *Expert Review of Vaccines* 2017;**16**(5):467-77. [DOI: [10.1080/14760584.2017.1297706](https://doi.org/10.1080/14760584.2017.1297706)]

Detoc 2019

Detoc M, Launay O, Dualé C, Mutter C, Le Huec J-C, Lenzi N, et al. Barriers and motivations for participation in preventive vaccine clinical trials: experience of 5 clinical research sites. *Vaccine* 2019;**37**:6633-9. [DOI: [10.1016/j.vaccine.2019.09.048](https://doi.org/10.1016/j.vaccine.2019.09.048)]

Dyer 2020

Dyer O. Covid-19: Eli Lilly pauses antibody trial for safety reasons. *BMJ* 2020;**371**:m3985. [DOI: [10.1136/bmj.m3985](https://doi.org/10.1136/bmj.m3985)]

Elliot 2019

Elliott LK, Bami H, Gelkopf MJ, Yee RC, Feldman BM, Goh YI. Patient and caregiver engagement in research: factors that influence co-enrollment in research. *Pediatric Rheumatology Online Journal* 2019;**17**(1):85.

Fayter 2007

Fayter D, McDaid C, Eastwood A. A systematic review highlights threats to validity in studies of barriers to cancer trial participation. *Journal of Clinical Epidemiology* 2007;**60**(10):990-1001. [DOI: [10.1016/j.jclinepi.2006.12.013](https://doi.org/10.1016/j.jclinepi.2006.12.013)]

Finset 2020

Finset A, Bosworth H, Butow P, Gulbrandsen P, Hulsman RL, Pieterse AH, et al. Effective health communication - a key factor in fighting the COVID-19 pandemic. *Patient Education and Counseling* 2020;**103**(5):873-6. [DOI: [10.1016/j.pec.2020.03.027](https://doi.org/10.1016/j.pec.2020.03.027)]

Flemming 2021

Flemming K, Noyes J. Qualitative evidence synthesis: where are we at? . *International Journal of Qualitative Methods* 2021;**20**:1. [DOI: [10.1177/1609406921993276](https://doi.org/10.1177/1609406921993276)]

Fletcher 2012

Fletcher B, Gheorghe A, Moore D, Wilson S, Damery S. Improving the recruitment activity of clinicians in randomised controlled trials: a systematic review. *BMJ Open* 2012;**2**(1):e000496. [DOI: [10.1136/bmjopen-2011-000496](https://doi.org/10.1136/bmjopen-2011-000496)]

Flores 2021

Flores L, Frontera W, Andrasik M. Assessment of the inclusion of racial/ethnic minority, female and older individuals in vaccine trials. *JAMA Network Open* 2021;**4**(2):e2037640. [DOI: [10.10001/jamanetworkopen.2020.37640](https://doi.org/10.10001/jamanetworkopen.2020.37640)]

Glenton 2020

Glenton C, Bohren MA, Downe S, Paulsen EJ, Lewin S, on behalf of Effective Practice and Organisation of Care (EPOC). EPOC Qualitative Evidence Syntheses: Protocol and review template. Version 1.1. EPOC Resources for review authors. Oslo: Norwegian Institute of Public Health; 2020. Available at: epoc.cochrane.org/epoc-specific-resources-review-authors.

Glover 2015

Glover M, Kira A, Johnston V, Walker N, Thomas D, Chang AB, et al. A systematic review of barriers and facilitators to participation in randomized controlled trials by Indigenous people from New Zealand, Australia, Canada and the United States. *Global Health Promotion* 2015;**22**(1):21-31. [DOI: [10.1177/1757975914528961](https://doi.org/10.1177/1757975914528961)]

Gobat 2018

Gobat NH, Gal M, Butler CC, Webb SA, Francis NA, Stanton H, et al. Talking to the people that really matter about their participation in pandemic clinical research: a qualitative study in four European countries. *Health Expectations* 2018;**21**(1):387-95. [DOI: [10.1111/hex.12634](https://doi.org/10.1111/hex.12634)]

Gobat 2019

Gobat N, Butler CC, Mollison J, Francis NA, Gal M, Harris V, et al. What the public think about participation in medical research during an influenza pandemic: an international cross-sectional survey. *Public Health* 2019;**177**:80-94. [DOI: [10.1016/j.puhe.2019.07.005](https://doi.org/10.1016/j.puhe.2019.07.005)]

Gouglas 2018

Gouglas D, Thanh Le T, Henderson K, Kaloudis A, Danielsen T, Hammersland NC, et al. Estimating the cost of vaccine development against epidemic infectious diseases: a cost minimisation study. *Lancet Global Health* 2018;**6**:e1386-96. [DOI: [10.1016/S2214-109X\(18\)30346-2](https://doi.org/10.1016/S2214-109X(18)30346-2)]

Harden 2018

Harden A, Thomas J, Cargo M, Harris J, Pantoja T, Flemming K, et al. Cochrane Qualitative and Implementation Methods Group guidance series—paper 5: methods for integrating qualitative and implementation evidence within intervention effectiveness reviews. *Journal of Clinical Epidemiology* 2018 ;**97**:70-8. [DOI: [10.1016/j.jclinepi.2017.11.029](https://doi.org/10.1016/j.jclinepi.2017.11.029)]

Harrington 2017

Harrington L, Van Damme P, Vandermeulen C, Mali S. Recruitment barriers for prophylactic vaccine trials: a study in Belgium. *Vaccine* 2017;**35**(48 Pt B):6598-603. [PMID: 29074202]

Hodgson 2021

Hodgson SH, Mansatta K, Mallett G, Harris V, Emary KR, Pollard AJ. What defines an efficacious COVID-19 vaccine? A review of the challenges assessing the clinical efficacy of vaccines against SARS-CoV-2. *Lancet Infectious Diseases* 2021;**21**(2):e26-e35. [DOI: [10.1016/S1473-3099\(20\)30773-8](https://doi.org/10.1016/S1473-3099(20)30773-8)]

Horsley 2011

Horsley T, Dingwall O, Sampson M. Checking reference lists to find additional studies for systematic reviews. *Cochrane Database of Systematic Reviews* 2011, Issue 8. Art. No: MR000026. [DOI: [10.1002/14651858.MR000026.pub2](https://doi.org/10.1002/14651858.MR000026.pub2)]

Houghton 2020

Houghton C, Dowling M, Meskell P, Hunter A, Gardner H, Conway A, et al. Factors that impact on recruitment to randomised trials in health care: a qualitative evidence synthesis. *Cochrane Database of Systematic Reviews* 2020, Issue 10. Art. No: MR000045. [DOI: [10.1002/14651858.MR000045.pub2](https://doi.org/10.1002/14651858.MR000045.pub2)]

Jaklevic 2020

Jaklevic MC. Researchers strive to recruit hard-hit minorities into COVID-19 vaccine trials. *Journal of the American Medical Association* 2020;**324**(9):826-8. [DOI: [10.1001/jama.2020.11244a](https://doi.org/10.1001/jama.2020.11244a)]

Janiaud 2021

Janiaud P, Axfors C, Ioannidis J, Hemkens L. Recruitment and results reporting of Covid-19 randomized clinical trials registered in the first 100 days of the pandemic. *JAMA Network Open* 2021;**4**(3):e210330. [DOI: [10.1001/jamanetworkopen.2021.0330](https://doi.org/10.1001/jamanetworkopen.2021.0330)]

Kaur 2012

Kaur G, Smyth R, Williamson P. Developing a survey of barriers and facilitators to recruitment in randomized controlled trials. *Trials* 2012;**13**:218.

Langford 2020

Langford AT. Health communication and decision making about vaccine clinical trials during a pandemic. *Journal of Health Communication* 2020;**25**(10):780-9. [DOI: [10.1080/10810730.2020.1864520](https://doi.org/10.1080/10810730.2020.1864520)]

Larson 2016

Larson H, de Figueiredo A, Xiahong Z, Schulz W, Verger P, Johnston I, et al. The state of vaccine confidence 2016:

global insights through a 67-country survey. *EBioMedicine* 2016;**12**:295-301. [DOI: [10.1016/j.ebiom.2016.08.042](https://doi.org/10.1016/j.ebiom.2016.08.042)]

Lewin 2018

Lewin S, Booth A, Glenton C, Munthe-Kaas H, Rashidian A, Wainwright M, et al. Applying GRADE-CERQual to qualitative evidence synthesis findings: introduction to the series. *Implementation Science* 2018;**13**(1):2. [DOI: [10.1186/s13012-017-0688-3](https://doi.org/10.1186/s13012-017-0688-3)]

Li 2020

Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. *New England Journal of Medicine* 2020;**382**(13):1199-207. [DOI: [10.1056/NEJMoa2001316](https://doi.org/10.1056/NEJMoa2001316)]

McDonald 2006

McDonald AM, Knight RC, Campbell MK, Entwistle VA, Grant AM, Cook JA, et al. What influences recruitment to randomised controlled trials? A review of trials funded by two UK funding agencies. *Trials* 2006;**7**:9. [DOI: [10.1186/1745-6215-7-9](https://doi.org/10.1186/1745-6215-7-9)]

Nvivo 2020

Nvivo. NVivo qualitative data analysis software; [NVivo qualitative data analysis software;]. NVivo qualitative data analysis software; QSR International Pty Ltd. Version R1, 2020. 2020.

O'Callaghan 2020

O'Callaghan KP, Blatz AM, Offit PA. Developing a SARS-CoV-2 vaccine at warp speed. *Journal of the American Medical Association* 2020;**324**(5):437-8. [DOI: [10.1001/jama.2020.12190](https://doi.org/10.1001/jama.2020.12190)]

Petkova 2020

Petkova E, Antman EM, Troxel AB. Pooling data from individual clinical trials in the COVID-19 era. *Journal of the American Medical Association* 2020;**324**(6):543-5. [DOI: [10.1001/jama.2020.13042](https://doi.org/10.1001/jama.2020.13042)]

Prescott 1999

Prescott RJ, Counsell CE, Gillespie WJ, Grant AM, Russell IT, Kiauka S, et al. Factors that limit the quality, number and progress of randomised controlled trials. *Health Technology Assessment* 1999;**3**(20):iii-139. [DOI: [10.1016/s0895-4356\(99\)00141-9](https://doi.org/10.1016/s0895-4356(99)00141-9)]

Sethi 2020

Sethi BA, Sethi A, Ali S, Aamir HS. Impact of Coronavirus disease (COVID-19) pandemic on health professionals. *Pakistan Journal of Medical Science* 2020;**36**(COVID19-S4):S6-S11. [DOI: [10.12669/pjms.36.COVID19-S4.2779](https://doi.org/10.12669/pjms.36.COVID19-S4.2779)]

Sully 2013

Sully BG, Julious SA, Nicholl J. A reinvestigation of recruitment to randomised, controlled, multicenter trials: a review of trials funded by two UK funding agencies. *Trials* 2013;**14**:166. [DOI: [10.1186/1745-6215-14-166](https://doi.org/10.1186/1745-6215-14-166)]

Suri 2011

Suri H. Purposeful sampling in qualitative research synthesis. *Qualitative Research Journal* 2011;**11**(2):63-75.

Swan 2009

Swan J, Robertson M, Evans S. Managing clinical research in the UK: summary of finding; 2009. Available at: qmro.qmul.ac.uk/xmlui/bitstream/handle/123456789/1014/Robertson%20managing%20clinical%20research%202010%20Published.pdf.

Treweek 2018

Treweek S, Pitkethly M, Cook J, Fraser C, Mitchell E, Sullivan F, et al. Strategies to improve recruitment to randomised trials. *Cochrane Database of Systematic Reviews* 2018, Issue 2. Art. No: MR000013. [DOI: [10.1002/14651858.MR000013.pub6](https://doi.org/10.1002/14651858.MR000013.pub6)]

Walters 2017

Walters SJ, Bonacho dos Anjos Henriques-Cadby I, Bortolami O, Flight L, Hind D, Jacques RM, et al. Recruitment and retention of participants in randomised controlled trials: a review of trials funded and published by the United Kingdom Health Technology Assessment Programme. *BMJ Open* 2017;**7**:e015276. [DOI: [10.1136/bmjopen-2016-015276](https://doi.org/10.1136/bmjopen-2016-015276)]

Wang 2020

Wang C, Pan R, Wan X. Immediate psychological responses and associated factors during the initial stage of the 2019 coronavirus disease (COVID-19) epidemic among the general population in China. *International Journal of Environmental Research and Public Health* 2020;**17**(5):1729. [DOI: [10.3390/ijerph17051729](https://doi.org/10.3390/ijerph17051729)]

WHO 2020

World Health Organization . WHO Director-General's opening remarks at the media briefing on COVID-19 - 11 March 2020; 2020. Available at: www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020 .

Wilson 2021

Wilson B, Wright K, Taylor R, Higgs E. Beyond recruitment: good participatory practice enhances the impact of research in a pandemic. *Nature Medicine* 2021;**27**:367-71. [DOI: [10.1038/s41591-021-01271-3](https://doi.org/10.1038/s41591-021-01271-3)]

APPENDICES

Appendix 1. Draft for MEDLINE Search strategy

1 patient selection/

(Continued)

2	patient participation/
3	motivation/
4	exp volunteers/
5	or/1-4
6	exp vaccines/
7	exp immunization/
8	or/6-7
9	5 and 8
10	((participat* or recruit* or enrol* or non-particip* or nonparticip* or selection) adj6 (epidemic* or pandemic*)).ti,ab,kf.
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.
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.
13	or/9-12
14	((participat* or recruit* or enrol* or non-particip* or nonparticip* or selection) and vaccin* and (trial* or research or study or studies)).ti.
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/
16	px.fs.
17	15 or 16
18	13 and 17
19	14 or 18

CONTRIBUTIONS OF AUTHORS

The protocol was drafted by PM, LB, MD, CH. All the review team reviewed several drafts of the protocol and offered comments and suggestions (PM, LB, MD, EM, CG, DD, AB, SS, RC, XHC, CH). The search strategy was developed by Paul Miller and reviewed by an Information Specialist in Cochrane Norway.

DECLARATIONS OF INTEREST

Pauline Meskell: none known
 Linda Biesty: none known
 Maura Dowling: none known

Elaine Meehan: none known
Claire Glenton: none known
Declan Devane: none known
Sasha Shepperd: none known
Andrew Booth: none known
Rebecca Cox: none known
Xin-Hui Chan: none known
Catherine Houghton: none known

SOURCES OF SUPPORT

Internal sources

- No sources of support provided

External sources

- Horizon 2020, Ireland

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 101037867