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Equality, Diversity and Inclusion in Early Phase Trials – a Qualitative Study

RESEARCH PROTOCOL

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Final Protocol

Sheffield Clinical Trials Research Unit (CTRU)

Equality, Diversity and Inclusion in Early Phase Trials – a Qualitative Study

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Abbreviations

CTU – Clinical Trials Unit

EDI – Equality, diversity, and inclusion

INCLUDE - INnovations in CLinical trial design and delivery for the UnDEr-served

MHRA – Medicines and Healthcare products Regulatory Agency

NHS - National Health Service

PIS – Participant Information Sheet

ScHARR – School of Health and Related Research

UKCRC – United Kingdom Clinical Research Collaboration

General information

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Protocol amendments since version

Not applicable

1. Lay person summary

Representation (also known as "EDI" - Equality, diversity and inclusion) is important in clinical trials as trial results should be relevant to all populations that might benefit from the treatment being studied, and all individuals should have equal access to potentially beneficial trial treatments. Early phase trials are small studies undertaken in humans to understand aspects of a new drug: their safety, how much is safe to give and how the body deals with the treatment, etc before testing the drug further. The importance of EDI in early phase trials is not understood. This is partly because these early phase trials are usually quite small (often less than 20 participants); making it challenging to include multiple patient groups (e.g. ethnicities) in a given study. There may also be barriers faced by patients in being aware of, or participating in, early phase trials, which may be made worse by the high-risk nature of these trials.

In this study, we will interview around 10 individuals that are involved in early phase trials, including clinicians and researchers. The interviews will explore their views on the value and relevance of EDI in early phase trials, if (and how) they have incorporated EDI into early phase trials, and any challenges of doing so. We will also interview patients and research participants from ethnic minorities to explore their views on the value of and the challenges of taking part in early phase trials. The interviews will be analysed and themes identified. The findings from this study will help those undertaking early phase trials to decide if, when, and how, to include EDI in their research.

2. Introduction

Equality, diversity and inclusion (EDI) concerns the inclusion of underserved groups in research. Equality relates to to ensuring individuals are not treated less favourably due to their characteristics and have equal opportunities to take part in early phase trials, and are provided with equal opportunities if they decide to take part in a trial. Diversity concerns recognising and respecting differences in individuals who are approached to take part, and decide to take part, in early phase trials. Inclusion relates to creating an environment where everyone feels welcomed and valued. The importance of equality, diversity and inclusion (EDI) in late phase trials (i.e. phases III

and IV) is widely accepted as treatments may affect diverse subsets of the population differently [1], with efforts ongoing to improve the representation of underserved groups [2,3].

Little attention has been paid to EDI in early phase trials that are undertaken in humans (i.e., studies with a phase I component). These explanatory trials help us understand treatment aspects such as the correct dose, how it should be administered, side effects, early signals of efficacy or activity, and how the body deals with the treatment. They hugely influence the further development and testing pathway of treatments but pose unique EDI challenges, as they are much smaller than later phase trials and are higher risk. Recently, regulators and funders globally have promoted wider inclusion of underrepresented groups [4–8].

EDI in early phase trials is important for equal access to research and healthcare, but impact on results on excluding certain groups might differ across trials. It may be the case, for certain conditions or treatments, a focus on EDI does not impact on the outcomes; for example, due to a lack of variation in how individuals may react to the treatment under investigation. In other cases there may be differences in outcomes according to ethnicity, for example. Directly or indirectly excluding certain subsets of the population from such trials may lead to an inequitable health policy stacked against underrepresented subpopulations.

The challenges associated with incorporating EDI into early phase trials also warrants exploration. There is a lack of related literature that specifically relates to early phase studies – most of the limited evidence that exists relates to later phase trials. In these late phase studies, a range of challenges have been identified, including study participants' lack of interest in research, lack of trust in trials, language barriers, communication barriers, poor access to and knowledge of trials, and trial burden [1,3]. A few studies have been published that specifically relate to early phase trials [9,10], including a qualitative meta-synthesis of the factors that may influence involvement in early phase cancer trials, identifying factors such as fear and uncertainty of the new treatment and patients' perceptions of their relatives views towards their involvement in the research being important as to whether or not a patient takes part in an early phase trial [9].

3. Overview

This cross-sectional, one-to-one qualitative study will undertake a broad exploration of the current practice, importance, experiences, and difficulties associated with incorporating EDI into early phase trials. Experts in early phase trials and patient and research participants will be sought to discuss these topics within qualitative semi-structured interviews.

When discussing EDI with participants, we will refer to "underserved groups". We will use the National Institute for Health Research's (NIHR's) guidance from the INnovations in CLinical trial design and delivery for the UnDEr-served (INCLUDE) project to define an underserved group, which states that:

> "The work of the NIHR-INCLUDE project shows that there is no single definition for an under-served group."

> "A key finding from our work is that the definition of 'under-served' is often very context and study specific. An under-served group for one disease or type of study may be the opposite to that of another."

Generally, when discussing underserved groups within the study, a broad definition of such groups will be used.

4. Aims and objectives

Research question

What are the perceptions of key stakeholders (both patients/research participants and professionals (clinicians and researchers)) on EDI in such trials?

Ethnic minorities have been selected as a group of interest as this attribute is consistency cited as one being underrepresented in clinical trials [11,12]. However, if we struggle to recruit ethnic minorities, those from non-ethnic minorities may be recruited in order to seek their views.

Aims and objectives

Our specific objectives are to explore the perceptions of patients and research participants, researchers and clinicians who have experience of early phase trials on:

1. Their understanding of EDI in early phase trials;

2. The aims and value of EDI in early phase trials;
3. When EDI in early phase trials is less or more important (if applicable and with reasons);
4. If and how EDI has been previously incorporated in early phase trials;
5. The challenges and enablers in incorporating EDI in early phase trials

5. Study design

Justification of number of interviews

The number of interviews is based on feasibility considerations due to funding constraints. As such, the number of interviews undertaken will be limited to around ten stakeholders. Target stakeholders of interest are clinicians from both oncology and non-oncology specialities, trial methodologists, and patient and research participants. A diverse sample of interviewees will be sought, with possibly only one or two individuals from each of these stakeholder groups interviewed. We will try to ensure a diverse group of patient and research participants are interviewed (e.g. various ages), whilst concentrating on those from ethnic minorities. Unfortunately, given the funding constraints, we will not have the resources to interview other stakeholders, including regulatory representatives and research ethics committee members.

Identification of participants

We will purposefully identify potential interviewees by:

a) Searching institution webpages or registries for those that are involved in early phase trials. For example, Medicines Healthcare and products Regulatory Agency (MHRA) registered phase 1 units, or those that are listed on the UK Clinical Research Collaboration (UKCRC) clinical trials unit (CTU) website as having expertise in phase 1 studies;
b) Asking our co-applicants and other contacts for any other individuals they are aware of who may be experienced in conducting early phase trials;
c) Approaching patients / research participants, whom we will identify via our co-applicants, or by asking those that are involved in early phase trials to identify individuals who may be interested;
d) In order to identify individuals we may email an individual (or generic email address) within a department or research group and ask if they can identify anyone that may be interested in participating.

e) By reaching out using social media and research platforms, including Twitter and 'People in Research' NIHR webpages. The information provided via these channels will be very clear about the participants we are interested in interviewing (see *'Participant eligibility'*) avoid lots of interest from ineligible participants.

In order to select participants for interview, a simple registration questionnaire will be used to enable potential participants to express their interest in participation. The basic information that will be collected will include – age, gender, ethnicity, experience in early phase trials (years), speciality (oncology or non-oncology, professionals only). Those participants that are invited via a social media or research platform will be provided with a link to the survey on the social media entry itself. Other participants, who are invited via email, will be sent the link via email in the initial email invitation. An email reminder may be sent one week after the initial email is sent in the case of no response.

Study co-applicants may be invited to an interview if they have not been closely involved in the development of the semi-structured interview topic guide.

Participant eligibility

Eligible 'professional' participants (i.e. clinicians, researchers) will be those who are closely involved in undertaking or regulating early phase trials . We will prioritise those involved in non-commercial studies (in the UK) as it is likely that commercial studies studies may have different pressures or motivations to include EDI in early phase trials.

We will aim to recruit patient and research participants who are either from ethnic minorities, and/or have experience of taking part in early phase trials (or being approached to participate in them). Ideally participants will meet both criteria. We will collect which ethnic group the individual aligns with in the survey outlined above.

Those who have not previously taken part in early phase trials may also be interviewed, although priority will be given to interviewing those that are from ethnic minorities and/or have experience in early phase trials.

Patient and research participants may be healthy volunteers (as early phase trials may involve such individuals), or those with a health condition.

Professional interviewees will not necessarily be from underserved groups.

Recruitment of interviewees

Those individuals that are selected for interview will be emailed a copy of the and consent form, with a reminder email 1 week after the initial email if no response, and a telephone call or email 1 week further on if still no response. A 'response' will constitute completing the registration questionnaire, or emailing/calling to say the participant is/is not interested. If the participant agrees to participate (either via the survey, or via email), a convenient time and date for the interview will be scheduled. Individuals who are sent the survey (without a direct invitation to participate in an interview) may later be reminded via email to complete the survey.

Some participants who seem particularly suitable for interview may be invited to interview without having to complete the survey first. Such individuals will still be requested to complete the survey in order for basic demographic details about them to be collected.

Participants who complete the survey will be able to access the PIS through a link on the survey itself.

Consent to participate in the qualitative study will be gained via a consent form, which will be completed by the participant prior to the interview, and sent back, via email or post, to the researcher. The participant will sign the consent form using an electronic, or wet ink, signature. The form will then be countersigned by the researcher, and a copy of the completed consent form emailed or posted back to the participant. Willingness to take part in the interview (i.e., consent) will be verbally reaffirmed directly prior to the interview.

Data collection

One to one semi-structured interviews will be carried out either in-person or via Google Meet with approximately 10 individuals. This is likely to consist of:

- Three patient and research participants

- Four clinicians (two from oncology, two from non-oncology specialities)*
- Three clinical trial methodologists

Prior to the interview, the researcher will reconfirm that the participant consents to participate and will talk the participant through pertinent aspects of the participant information sheet. The participant will be sent definitions of key terms being used in this study (e.g. EDI, early phase trial and underserved groups) for discussion within the interview.

Interviews will be undertaken in-person (if the participant is based in Sheffield, the interview will be undertaken in a meeting room within ScHARR) or via video call will be semi structured, with a topic guide which will evolve throughout the study. The topic guide will be tested first on members of the project team in order to check face validity and the flow of the interview. Interviews will last around 45 minutes to one hour.

The qualitative interviews with professionals are expected to cover:

- The participant's perceptions of the definition of EDI in the context to early phase trials. In order to enable this, the interviewee will be presented with a definition of EDI, and will be asked to discuss its relevance and validity in relation to early phase trials.
- The participant's perceived value and aim of incorporating EDI in early phase trials. For example, are there specific scientific implications of including (or not including) EDI in early phase trials.
- If, and how, EDI has been incorporated into early phase trials that the participant has undertaken.
- Any difficulties of incorporating EDI into early phase trials

The interviews with patient and research participants will cover:

- The participant's perceptions of the definition of EDI in relation to early phase trials. In order to enable this, the interviewee will be presented with a definition of EDI, and will be asked to discuss its relevance and validity in relation to early phase trials.
- The participant's perceptions of an early phase trial.
- Their views regarding the barriers and enablers for underserved groups participating in early phase trials.

- Their views on how the inclusion and accessibility of early phase trials to underserved groups could be improved.

If applicable, patient and research participants will be encouraged to discuss their own experience of being involved in early phase trials, and therefore, the experience of the interviewee's ethnic minority group may take focus. However, across the study, we will broadly discuss underserved groups (encompassing the broad definition as stated above) where possible.

All interviews will be digitally recorded (with consent) on an encrypted Dictaphone and transcribed for in-depth analysis. Transcripts will be anonymised prior to analysis.

Analysis

Data will be analysed using inductive thematic analysis within NVivo software. If possible (where there is a member of staff available), a second person will also assist with analysis by also undertaking coding, and themes across the two sets of codes compared in order to increase the reliability of the analysis. However, due to funding constraints, this may not be possible.

Themes and sub-themes will be discussed by the project management group (see *section 7, oversight* section). Data saturation will not be considered due to the small numbers interviewed; rather we will look to achieve "information power", as conceived by Malterud et al, where the size of the study is determined by the amount of information the sample holds [13]. Emphasis will be on collecting detailed data from experienced participants.

5. Patient and Public Involvement

We will seek input from our PPI representative (DO) into the study, including this protocol, the semi-structured interview guide, dissemination materials, and other associated documents. DO will be renumerated for her time in line with guidance provided by the NIHR, which includes £25 for attendance at a one-hour meeting, £50 for a two hour activity, and £75 for an activity that involves half a day of work [14]. Patient and research participants that take part in an interview will be provided with £50 to renumerate their time, plus travel expenses (if appropriate).

6. Participant withdrawals

Individuals will be able to withdraw at any point prior to the end of the qualitative interview. After this point, the data will be incorporated into the analysis and will not be withdrawn.

7. Oversight

The central team (co-applicants CC, MD and RC) will undertake the day-to-day implementation of the study.

Other list co-applicants will meet with regularly with the central team to oversee and provide input into the running of the study. The oversight group will provide input into the study protocol, semi-structured interview topic guide, results, and write-up of the study within a peer-reviewed journal.

8. Dissemination

Publication

The results of the study will be published within a peer reviewed journal. Confidentiality will be ensured by anonymising participant's identities. Due to the likelihood of individuals being identifiable from the name of the trial they work on and disease area, this information will not be used in reports or in the direct quotations included within them.

Participants

Patient and research participants will be provided with a lay-person summary of the findings from this study.

9. Data storage and sharing

Data storage

Transcripts will be pseudo-anonymised, with both unedited and pseudo-anonymised versions stored on the University file store (X drive).

All files will be stored within folders with restricted access rights. Only those who have the need to access the data (i.e. those staff undertaken day-to-day work or qualitative analysis on the study within Sheffield CTU) will have access to these folders.
The survey will be undertaken and stored on Qualtrics, with data also downloaded to an X drive folder with restricted access rights.

Data retention
Identifiable data (interview transcripts, survey responses, contact details) will be retained until the end of the project (defined as publication in a peer reviewed journal). Pseudo-anonymised interview transcripts and anonymised survey responses will be retained for 5 years after the end of the project.

Data sharing
Whole transcripts will not be shared with other researchers, due to the risk of identification from the qualitative transcripts.

10. Finance

Research funding has been obtained from the Research England Participatory Research Fund.

11. Ethics approval

Ethical approval will be sought from the ScHARR ethics committee.

Ethical approval will not be sought from an NHS research ethics committee, which means that individuals with only NHS contracts (who are not contracted to a University) will not be able to participate in this study.

12. Timetable

	March	April	May	June	July
Develop key documents					
Ethics approvals					

Recruitment participants and collect data					
Analysis and write-up					

13. References

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