REcruitment in Mental health trials: broadening the 'net', opportunities for INclusivity through online methoDs (RE-MIND)

Acronym:
RE-MIND

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ABBREVIATIONS

CI	Chief Investigator
CRN	Clinical Research Network
CTU	Clinical Trials Unit
HTA	Health Technology Assessment
NIHR	National Institute for Health Research
PIS	Participant Information Sheet
PPI	Patient and Public Involvement
UoN	University of Nottingham

STUDY BACKGROUND INFORMATION AND RATIONALE

Lack of diversity in trial recruitment is a moral, ethical and scientific issue (1). Homogenous groups can skew findings and impact generalisability to the wider population (2). Greater inclusivity would result in more robust data to inform decisions in healthcare, potentially reducing disparity in health outcomes. Health inequalities have come to the forefront during the COVID-19 pandemic, where older adults, those with existing health conditions, and ethnic minorities are disproportionately affected (3).

Despite being the gold standard of research to determine effectiveness, randomised controlled trials (RCTs) often struggle with participant recruitment, engagement and retention. Attaining these key targets is undoubtedly critical for trial success, however, it is important to ensure that the recruited patients are representative of the wider population (4). Evidence indicates that ethnic minority populations are significantly under-represented in clinical trials (5). Bower et al (6) demonstrated that recruitment to research trials is not aligned with disease prevalence rates in England, with historically low recruitment rates in geographical areas of high prevalence of mental health conditions. Although these issues are relevant to all clinical trials, they may be specifically exacerbated when recruiting vulnerable populations, such as participants with mental health issues. The added difficulties of recruiting to mental health trials in general have been well cited, with issues including “gatekeeping” clinicians who seek to protect perceived ‘vulnerable’ participants, symptom-profiles of some mental health disorders adding further complexity to engaging participants (7), and stigma surrounding mental health. The concerns around stigma are compounded within ethnic minority populations by feelings of mistrust and skepticism of mental health research (8). The issue of poor ethnic diversity in mental health trials is particularly concerning given that black and ethnic minorities experience unduly high levels of adverse mental health (9), which may in part reflect systemic racism (10).

In recognition of the need to reduce disparities in participation in research, the National Institute for Health Research (NIHR) Clinical Research Network commissioned “INCLUDE” to provide a framework for researchers and funders when developing research protocols. The framework also includes examples of how to broaden inclusivity (11).

Whilst clinical trials have been traditionally conducted in a clinical face-to-face setting, since the late 1990s, there has been an increasing trend towards online or ‘digital’ trials (12) using web-based approaches and other multi-media. Online recruitment strategies including social media and website campaigns offer researchers the opportunity to modify their recruitment materials and strategies based on feedback/engagements with the adverts to allow a targeted strategy to reach specific target audiences (13,14). In comparison to more traditional recruitment strategies via National Health Service (NHS) clinics and specialist services, online recruitment may reach communities who are not currently under the care of specialist mental health services. This may be particularly important for conditions where specialist care is only offered at centers typically in large cities (15), or when widening recruitment to black, and minority ethnic communities (16). In addition, online recruitment through multi-media platforms (web, Facebook, twitter etc.) has been shown to potentially cost less than off-line (face-to-face) recruitment therefore providing more efficient trial delivery (17).

Despite these advantages, there is notable concern about the “digital divide”, which in its simplest terms reflects those connected to the internet and those who are not, but more recently also is considered to reflect differences in usage (usage gap) and technical skills (18). Thus, shifting to online delivery of trial procedures (such as recruitment or the intervention itself) may further exacerbate health inequalities and skew trial participation away from under-served populations. Existing research on online trial delivery has focused on attainment of overall trial recruitment targets and perceived barriers, rather than sample characteristics. There is mixed evidence regarding issues of recruitment and engagement with online trials. Whereas some trials have

reported particularly good recruitment and engagement (19), other evidence indicates that online trials may be particularly susceptible to poor recruitment and limited engagement with the intervention (20). Some known possible barriers to the delivery of online trials include poor technology skills, interfaces that are not user-friendly, concerns around data security and a lack of support from healthcare professionals (20,21).

A recent study looked at data from NIHR Health Technology Assessment (HTA) trials of mental health and found 60% failed to reach their original recruitment target. The authors reflected on how online recruitment and consent may navigate some of these issues (15), however, they did not conduct a formal comparison between online and offline conducted trials. Brogger-Mikkelsen et al1 (7) found that 12/23 (52%) of studies that used an online recruitment strategy had a better recruitment rate when compared to offline recruitment strategies. However, it is not clear what demographic characteristics may influence this and the number of papers examined were limited due to the authors' inclusion criteria. This study proposes to build on this existing evidence base to better understand the use of online recruitment in clinical trials in mental health.

STUDY OBJECTIVES AND PURPOSE

PURPOSE

The purpose of this study is to identify and provide evidence and guidance for use of online methods in the recruitment of participants into mental health trials, with a focus on whether online methods can enhance inclusivity.

SECONDARY OBJECTIVES

- To determine the proportion of trials using online recruitment methods who recruit to target.
- To assess whether online recruitment methods are associated with a more representative sample.
- To identify which techniques in online recruitment improve representativeness.
- To develop guidance for clinical trial groups.

STUDY DESIGN

STUDY CONFIGURATION

This study involves three work packages (WPs):

WP1: Evidence review of recently published randomised trials in mental health to assess the impact of online recruitment versus off-line recruitment in clinical trials.

WP2: A qualitative study will investigate the experiences, opinions and ideas of key stakeholders on use of online recruitment as an approach.

WP3: Combining the results of WP1 and WP2 to produce guidance and a list of recommendations about the use of online recruitment of participants into mental health clinical trials.

STUDY MANAGEMENT

The Co-Chief Investigators have overall responsibility for the study and shall oversee all study management.

DURATION OF THE STUDY AND PARTICIPANT INVOLVEMENT

Location of study:
Nottingham Clinical Trials Unit, School of Medicine
University of Nottingham, Nottingham, NG7 2RD
Start date: February 2022
End date: July 2023
Length of study: 18 months

Data collection, analysis and the study output are planned to be completed within 12 months. The timescale below gives a brief overview of the project plan.

0-3 months	***Study set-up*** WP1: Development of the literature review search strategy and design bespoke data extraction tool. WP2: Design the topic guide for the focus groups/interviews, develop supporting documents e.g., participant information sheet, invitation letter and consent form, and submit for relevant ethics approvals.
4-6 months	***Conduct of evidence review and prepare for qualitative work package*** WP1: Conduct all literature searches and carry out data extraction. WP2: Identify and send invitations to potential participants to join focus groups/interviews after ethical approval has been received.
7-10 months	***Conduct of qualitative work package*** WP1: Conduct analysis from the data extraction (descriptive data and evidence synthesis of any qualitative data reported). WP2: Conduct focus groups/interviews and analyse data.
11-12 months	***Triangulation of data*** Data from the evidence review (descriptive and evidence synthesis) and the qualitative focus groups/interviews (themes) triangulated to inform guidance development.
13-16 months	***Development of guidance documents*** Drafting of guidance documents and papers for publication.
15-18 months	**Dissemination** All outputs finalised and dissemination strategy agreed.

STUDY METHODS

WPI: EVIDENCE REVIEW

This part of the study will assess the impact of online recruitment versus off-line recruitment in clinical trials. We will compare the outcomes of recently published NIHR Health Technology Assessment (HTA) funded randomised controlled trials in mental health, as well as published RCTs in the top Mental Health Journals according to search engine and expert team.

Sample

Filters will be set from 2018 in order to select the most recent evidence using the latest online recruitment methods. The number of Journals searched, up to a maximum of five, will be dependent on the number of searches returned in order to manage the quantity of data. Journals will be prioritised from the number one journal onwards. Utilising the HTA cohort and focussing on published RCTs will ensure methodological quality of the trials included in the review.

Eligibility criteria

Inclusion criteria:

1) Studies used an RCT design (including feasibility and pilot RCTs and any qualitative analysis)
2) Studies used offline, online or both methods for participant recruitment/identification
3) Be delivered in healthcare, community or secure settings (we anticipate most being in healthcare)
4) Patients must be mental health patients identified as reaching a pre-defined cut-off on a mental health scale as defined by the study authors or for meeting DSM or ICD criteria
5) Participants will include all ages
6) Studies trialling an intervention aimed at improving mental health as defined by the study authors
7) Studies published in either a peer review journal or HTA monograph

Exclusion criteria:

1. Prevention studies
2. Articles with a main focus on another condition (not mental health)
3. Articles on interventions for ADLs, self-care, independence, or lifestyle
4. Non-patient studies e.g., healthcare providers

Recruitment method definitions

We will specify online recruitment methods as social media advertisements, Google search engine advertisements, and other website campaigns. (22)

We will specify offline recruitment methods as in-clinic recruitment, soliciting subjects through mail and telephone using health records and registers, media campaigns, newspaper advertisements, and input during radio and television talks. (22)

Data collection

Data will be extracted using a bespoke tool focussing on:

a) Study design, year, and location by country
b) Whether the trial reached the planned sample size within time and to target
c) Participant baseline characteristics (i.e. age, gender, ethnicity, occupation, socio-economic status, first language – to be guided by INCLUDE) to identify inclusivity and diversity and assess whether the trial was representative of the clinical and wider populations represented
d) Type of recruitment strategies used (e.g. Webpage or via social media)
e) Recruitment rates (the average number of patients enrolled in the study per month and per day of active recruitment) and conversion rates (the percentage of participants screened who proceed to enrol into the clinical trial).

Where this information is not clear in the published work, we will contact the authors. As open reporting of this information is an important outcome in itself, we will report which papers did not provide this information in their published work.

Analysis

The team will present descriptive data on the published trials that meet the eligibility criteria. The data extraction tool will be refined and further developed in months 0-2. However, broadly, the quantitative data extrapolated will be guided by the INCLUDE list of under-served groups.

Qualitative data extracted will include barriers and facilitators to use of the different online recruitment methods as well as efficiency and cost of methods. A thematic evidence synthesis will be conducted independently to identify any trends in the findings (23). Thematic evidence

synthesis is recognised as an important contributor to guidance development through its ability to bring together different and contradictory perspectives to produce an in-depth understanding of experiences and priorities (24).

WP2 – QUALITATIVE STUDY

The qualitative study will investigate the experiences, opinions and ideas of key stakeholders on use of online recruitment as an approach. This will include Patient and Public Involvement (PPI), Clinical Research Network (CRN) as well as those working in trial design, conduct and delivery.

Sample

The team will identify participants via the following groups; INCLUDE, Trial Forge (https://www.trialforge.org) the CRN network, and the UK Trial Managers Network (UKTMN). For PPI we will approach existing groups through MindTech (https://www.institutemh.org.uk/research/national-and-regional-research-networks/nihr-mindtech) and the "Sprouting Minds" Young Persons Advisory Group (YPAG), which includes representation from ethnic minority communities across England. Local ethnic minority communities working with the Centre for BME Health Leicester will also be approached.

Methods

Focus groups or interviews will be used to collect data from a diverse stakeholder population, to maximise time and resources and to identify and clarify views in relation to others who have a similar lived experience and support sharing of their ideas and similar or different opinions (25). A schedule of topics and questions will be developed to help guide discussion (26).

We will aim to conduct approx. 5 role specific focus groups of 5-6 participants where possible to encourage engagement and support discussion, however mixed groups may be undertaken where numbers of participants are limited for a given role. Roles will include trial management staff, those involved in recuriting participants (PIs, RNs), CIs as well as patients and members of the public. In addition, interviews may also be conducted to capture key stakeholders who may find it difficult to attend a group.

Although we don't anticipate any safety issues, talking about mental health and clinical trial participation may be a sensitive subject for some individuals, particularly for those representing the patient and public groups, the team will be able to offer one-to-one interviews if preferred on advice from our PPI collaborators.

Recruitment and informed consent

The research team will send an invitation email, to potential participants, or to organisations to share with their membership lists, including a participant information sheet outlining the purpose of the study and a consent form If required reminder emails will be sent after seven days following the invitation email. Due to the impact of COVID on continued 'ways of working' remaining online or at least a hybrid approach it is anticipated that most focus groups and interviews will take place online via videoconference software such as Microsoft TEAMS. Consent therefore will be accepted as a return of email (to the invitation email) stating the participant has read and understood the consent form and agrees to participate. This correspondence will be filed as the record of consent.

Consent to audio-record the focus groups and take field notes to record discussions will be sought from participants along with acceptance for anonymous direct quotes, phrases and terminology to be used in any dissemination activity such as publications, reports and presentations.

The researcher(s) will explain to potential participants that entry into the study is entirely voluntary and that they can withdraw at any time. In the event of their withdrawal, it will be explained that

their data collected so far cannot be erased and will be used in the final analyses where appropriate.

Analysis

Audio-recorded data will be transcribed for both focus groups and interviews by the research team and/or a UoN authorised transcriber. At least two researchers will analyse the transcripts.

Thematic analysis will be conducted in accordance with Braun and Clarke's standard methods (27). Two researchers will independently conduct initial open coding and categorisation with the aid of NVivo12, a qualitative data management software. The researchers will anonymise participant's information by using unique participant identification numbers and removing identifiable information. Differences in interpretation will be resolved through discussion between coders and then if required, a third person (someone from the research team) will be involved. Categories and themes will be developed by constantly refining the coding scheme and master themes will be identified.

WP3 - GUIDANCE DEVELOPMENT

Data from WP1 and WP2 will be triangulated for convergence, discrepancy or complementary information. The research team will also endeavour to map the findings to those of published evidence on barriers to face-to- face recruitment of under-served groups to inform our guidance. Findings will be used to identify factors that impact online recruitment to mental health trials, these factors will inform the development of the guidance document and recommendations for future research.

ETHICAL AND REGULATORY ASPECTS

ETHICS AND APPROVALS

The qualitative study will not be initiated before the protocol and relevant supporting documents have received relevant approval.

All focus group participants will be provided with a consent form and information sheet (which includes a detailed description of the nature of the study, why the research is being conducted, why they have been chosen to participate, and the nature of the questions that will be asked), and the researcher(s) will answer any questions before consenting. All participants will have time to decide if they wish to participate in the study.

Participants will be asked for their permission to video and/or audio record the focus groups. Focus groups transcripts will not contain names or other details that might identify the participant. Instead, non-identifiable codes will be used, and other identifiable information will be removed. To avoid identification of participants through quotes in published research, all participants will be assigned non-identifiable codes.

RECORDS

Source documents

Source documents will be filed at the Nottingham Clinical Trials Unit and may include but are not limited to, consent forms, study records, field notes, focus group/interview transcriptions and audio and video records. Only the research team will have access to the study documentation.

DATA PROTECTION

The research team will endeavour to protect the rights of the study's participants to privacy and informed consent, and will adhere to the Data Protection Act, 2018. All source documents will be held securely on the University of Nottingham secure dedicated web server. Access will be restricted by user identifiers and passwords (encrypted using a one-way encryption method).

Confidentiality and privacy will be ensured for all participants. The information gathered will only be used for scientific purposes for example presentations, research purposes, publications and using anonymous direct quotes, phrases and terminology in the analysis and report.

The research team will video and audio record focus groups/interviews. Recordings will be transferred to the secured project shared drive as soon as possible by the research team.

The research team will de-identify transcripts of focus groups/interviews. These transcripts will be assigned a code. An encrypted document showing the link between the code and the corresponding transcript will be kept separately and preserved until the end of the study.

Complete anonymity of participants amongst other members cannot be guaranteed in focus groups. To address this, the participant information sheet states that participation is voluntary and reminds participants to respect the privacy of their colleagues and not repeat what is said in the discussions to others. Participants will be asked to sign a statement in the consent form that states they will not reveal any information that is shared in confidence in the focus groups. The researcher(s) will also remind participants about confidentiality of participants and information shared in the focus groups.

RECORD RETENTION AND ARCHIVING

In accordance with the University of Nottingham Code of Research Conduct and Research Ethics, the Chief Investigator will maintain all records and documents regarding the conduct of the study. These will be retained for at least 7 years or for longer if required. If the responsible investigator is no longer able to maintain the study records, a second person will be nominated to take over this responsibility.

The study documents held by the Chief Investigator will be finally archived at the Nottingham Clinical Trials Unit at the University of Nottingham. This archive will include all anonymised transcripts, study databases and associated data encryption codes.

STATEMENT OF CONFIDENTIALITY

Individual participant information obtained as a result of this study are considered confidential and disclosure to third parties is prohibited with the exceptions noted above.

Participant confidentiality will be further ensured by utilising identification code numbers to correspond to treatment data in the computer files.

PUBLICATION AND DISSEMINATION POLICY

Any reports or publications resulting from this work can be accessed through the University of Nottingham hosted webpage. To ensure that the findings from the research inform practice, the findings will be disseminated by presenting the results at national and international conferences and seminars, holding workshops with key stakeholders, publishing in a peer reviewed journals and sharing the results with key groups accessed through our co-applicants e.g. UKTMN, TrialForge and INCLUDE.

Study participants will receive a thank you email from the Chief Investigator. The guidance document along with any final reports or publications of key study findings will also be provided.

STUDY FINANCES

Funding source

This study is funded by NIHR CTU Support Funding supporting efficient innovative delivery of NIHR research.

Participant stipends and payments

Participants will not be paid to participate in the study. No travel expenses will be offered as focus groups will be conducted virtually.

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