ANNUAL EFFICIENT STUDIES FUNDING CALLS FOR CTU PROJECTS FINAL REPORT

Section 1: Title of Project

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

Section 2: Abstract

Background: Barriers to mental health research participation are well documented including distrust of services and research, and stigma surrounding mental health. These barriers contribute to a lack of diversity amongst participants in mental health research, which threatens the generalisability and applicability of research findings. Given the recent widespread use of technology in medical research, this study aimed to explore the perspectives of key partners on the use of online (e.g., social media) and offline (e.g., in-person) recruitment as an approach to improving diversity amongst clinical trial participants.

Methods: This study employed a mixed-methods approach involving three work packages: (1) Evidence review of recently published randomised trials in mental health to assess the impact of online recruitment versus off-line recruitment in clinical trials. (2) A qualitative study to investigate the experiences, opinions and ideas of key partners on use of online recruitment as an approach. (3) 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.

Results:

WP1: 97 studies were included for review and analysis. The review findings did not show any relationship between type of recruitment strategy and recruitment to target, X^2 (2,N=94) =1.27, p>0.53, or any increase in inclusivity for age, sex and ethnicity.

WP2: Three focus groups and three interviews were conducted with a total of 23 participants. Four overarching themes were identified: (1) recruitment reach; (2) demographic factors that affect selection of recruitment method; (3) safety of technology, and; (4) practical challenges.

WP3: The findings from WP1 and WP2 resulted in development of a list of recommendations for researchers on participant recruitment for consideration during the design of future mental health clinical trials.

Conclusions: The key finding of RE-MIND is that greater consideration should be given to using a strategy that adopts multiple recruitment methods (both online and offline) tailored to the study population, offering flexibility and choice to enable wider participation. To do this, earlier planning and PPI engagement at the design stage of a trial is essential alongside adequate resourcing and staff training to ensure the credibility of online methods for both staff and patients.

SECTION 3: INTRODUCTION

Lack of diversity in trial samples is a moral, ethical and scientific issue (1, 2). Homogenous participant groups can skew findings and impact wider generalisability (3). Greater inclusivity would result in more robust data to inform decisions in healthcare and treatment innovations, potentially reducing disparity in health outcomes (4). Health inequalities came to the forefront during the COVID-19 pandemic, where older adults, people with existing health conditions, people from minoritised ethnic backgrounds and those experiencing socioeconomic disadvantage in the UK continue to be disproportionately affected (5).

Despite being the gold standard of research to determine effectiveness/efficacy, randomised controlled trials (RCTs) often struggle with participant recruitment, engagement and retention, particularly for trials of mental health interventions (6). There are a number of reasons why recruitment to mental health trials is particularly challenging. Clinicians may have concerns about the perceived vulnerability of their patients resulting in issues with decision making because of lack of equipoise, or burden of research or concerns regarding consent and the lack of capacity to provide informed consent (7, 8). Potential participants may also have concerns about cultural stigma and stigma surrounding mental health (9), or concerns regarding the intervention itself (6).

In recognition of the need to reduce disparities in participation in research, the National Institute for Health Research (NIHR) Clinical Research Network commissioned the INCLUDE project to provide a framework for researchers and funders when developing research protocols and includes examples of how to broaden inclusivity (10). The NIHR also developed their Equality, Diversity and Inclusion (EDI) Strategy 2022-2027 to ensure the implementation of inclusive practice in research, culture and systems (11).

Whilst clinical trials of mental health conditions have been traditionally conducted in a clinical face-to-face setting, since the late 1990s, there has been a trend towards online or 'digital' trials (12). We've defined online recruitment strategies as the use of Internet technologies to recruit research participants (e.g., social media). This

approach offers researchers the opportunity to modify their recruitment strategies based on feedback and engagement to allow a targeted strategy to reach specific audiences (13, 14). In comparison to more conventional (offline) recruitment models (e.g., in clinic recruitment), online recruitment may reach communities who are not currently engaged with specialist mental health services. This is likely to be particularly important for conditions where specialist care is only offered at centres typically in large cities (15), or when recruiting hard-to-reach populations (16).

Despite these apparent 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 is considered to reflect differences in usage, resources and internet skills (17). It is not known if online delivery of trial procedures (e.g., recruitment or intervention delivery) has the potential to exacerbate health inequalities and create barriers to trial participation for under-served populations.

The RE-MIND study aimed to identify and provide considerations for use of online methods in the recruitment of participants into mental health trials, with a focus on the impact on inclusivity.

SECTION 4: METHODS

This study used a convergent mixed methods approach (18) which involved three work packages (WPs):

WP1: The NIHR Journals Library and two leading mental health journals, Lancet Psychiatry and JAMA Psychiatry were searched for RCTs and feasibility/pilot studies that met our inclusion criteria. This cohort was chosen as representing high quality research in the field of mental health producing a significant number of articles for inclusion. Data were extracted using a bespoke tool developed by the research team and reviewed by several of the study co-investigators focusing on:

- Trial design, year, type of intervention, diagnosis, setting and location by country.
- Whether the trial reached the planned sample size target.
- Participant baseline characteristics (e.g., age, gender, ethnicity).

- Type of recruitment strategies used.

Textual data on efficiency of recruitment strategies used was also extracted where reported by the trial authors. The quantitative data extrapolated was guided by the INCLUDE list of under-served groups (10). Descriptive data on the published trials that met the eligibility criteria was presented broken down by the type of recruitment strategy used. Continuous data were summarised in terms of frequency counts and percentages and categorical data were compared using the Pearson's Chi squared statistical test to evaluate group differences.

WP2: A qualitative study investigated the experiences, opinions and ideas of key partners (research staff and patients and public involvement members with experience working in mental health research) on the use of online recruitment as an approach in mental health clinical trials. Focus groups and semi-structured interviews with research staff working on mental health research and Patient and Public Involvement (PPI) partners were conducted. Research staff were identified via the NIHR Clinical Research Network (CRN), and the UK Trial Managers Network (UKTMN). We approached potential PPI participants via existing groups including the "Sprouting Minds" Young Persons Advisory Group (YPAG), the Deep End group, and the NIHR Research Design Service (RDS). Qualitative data were analysed using thematic analysis to identify the barriers and facilitators to the use of the different recruitment strategies as well as any efficiency of these strategies.

WP3: Data from WP1 and WP2 were triangulated for convergent, discrepant or complementary information. Findings were used to identify factors that impact online recruitment to mental health trials and to inform the development of recommendations for future research.

SECTION 5: RESULTS AND CONCLUSION

After screening 191 article abstracts, 94 were excluded, leaving a total of 97 for review. Appendix 1 summarises the baseline characteristics of included trials and appendix 2 shows the number of trials that recruited to target by recruitment strategy. Most studies were RCTs (n=90), recruited through hospital settings (n=54) and conducted geographically in Europe or North America (n=81). The most represented conditions

were emotional (n=35) and psychotic disorders (n=19). Only two articles were found solely to use online recruitment strategies. Our findings did not show any relationship between type of recruitment strategy (offline, online or mixed) and whether the trial recruited to target X^2 (2,N=94) =1.27, p>0.53 (three trials did not report a sample size). Where trials/studies used a mixed recruitment strategy, although the range of methods used were reported e.g., website, twitter, mail-out etc, they did not report a breakdown of how many participants were recruited via each method therefore this could not be further explored. The study also found that recruitment strategy had little effect on whether a trial recruited to target for any of the included disorders.

In terms of overall numbers of people recruited there was little difference between the three recruitment strategies on inclusivity. Only a small number of articles (n=7) reported identification of 'other gender' other than male or female, which predominantly recruited using offline strategies (n=6), four of which recruited to target. When looking at inclusion of ethnicity, offline and mixed strategies appear preferable. Where only online strategies were used, (n=2) recruitment remained predominantly white. Online only strategies of recruitment were reported for trials recruiting adult populations only. Although, it's not possible to make conclusions on such a small sample.

A total of three FGs and three interviews were conducted with a total of 23 participants (15 PPI partners and eight research staff). Our sample included people who identified as male, female and non-binary as well as representation from white, Asian and Black ethnic groups and were aged between 20 and 70+ years of age. Four broad themes were identified: (1) recruitment reach; (2) demographic factors that affect selection of recruitment method; (3) safety of technology, and; (4) practical challenges to online recruitment. Our findings highlighted the importance of using a multi methods approach to recruitment to support diversity and inclusive engagement regardless of participant characteristics, for example age, gender, ethnicity, access to technology or type of mental illness. Integration of online methods is becoming more acceptable to researchers and participants and was thought to widen participation in mental health research due to its flexibility and sensitivity to individual needs in relation to the complexities of mental illness. However, for online recruitment to be successful adequate resources and training was required to understand the growing range of

digital media and platforms available including which platforms would be most appropriate for different trial populations. In addition, clarity on data protection and data safety for the variety of digital platforms was needed for both researchers and patients to feel confident using these tools.

The triangulation between WP1 and 2 findings resulted in a list of recommendations for researchers on participant recruitment for consideration during the design of future mental health clinical trials. The recommendations were reviewed by the research team. Six main factors were highlighted in the list including inclusivity, age, complexity of mental health illnesses, data management, and staff training and support.

In conclusion, no evidence was found to show an association between the use of any of the recruitment strategies (online, offline or mixed) and whether the trial recruited to target, or in relation to increased inclusivity and diversity in mental health clinical trials. However, our findings are hindered by the small number of online-only studies.

The evidence from RE-MIND suggests that for mental health trials, offline recruitment remains the preferred option which may be driven by convenience, efficiency and access to eligible patients through existing clinics. However, we recommend investigating this further. RE-MIND also demonstrated that greater consideration should be given to online or mixed methods recruitment strategies that adopt a tailored approach offering flexibility and choice to enable wider participation. To our knowledge this is the first study to develop a list of recommendations for researchers to consider for participant recruitment strategies during the design of mental health clinical trials.

SECTION 6: DISSEMINATION

The principal output from this study is the list of recommendations for researchers to consider when designing mental health clinical trials.

The project resulted in three journal publications submitted to BMC Medical Research Methodology. These publications cover the methods, findings and recommendations of the three stages of the study, which will have relevance to the wider mental health research community as well as those working in clinical trials in general.

The research team will also disseminate the project through various seminars and conferences including the School of Medicine Summer Seminar Series and the International Clinical Trials Methodology Conference (ICTMC) 2024. A summary of findings will also be made available to our PPI partners including an infographic.

Finally, the list of recommendations will be freely available as a tool on the NCTU website alongside the open access journal publications once published.

SECTION 7: ACKNOWLEDGEMENTS

Funding acknowledgement and Disclaimer:

Nottingham Clinical Trials Unit, University of Nottingham
Mrs Kirsty Sprange (Assistant Professor of Clinical Trials)
Dr Mais Iflaifel (Research Fellow and a clinical pharmacist)
Prof Edmund Juszczak (Professor of Clinical Trials and Statistics in Medicine)

NIHR MindTech MedTech Co-operative, Institute of Mental Health, School of Medicine, University of Nottingham
Dr Charlotte Hall (Principal Research Fellow)
Dr Jennifer Martin (Senior Programme Manager for Mental Health and Technology Research)

School of Health Sciences, Institute of Mental Health, University of Nottingham
Dr Stefan Rennick-Egglestone (Senior Research Fellow)

Previously: Health Services Research Unit, University of Aberdeen
Now: COUCH Health, Manchester
Dr Heidi Green

Centre for Ethnic Health Research, Leicester/ Diabetes Research Centre, University of Leicester

Dr Andrew Willis

NIHR Evaluation, Trials and Studies Coordinating Centre (NETSCC), Southampton

Dr Mark Townsend

SECTION 8: REFERENCES

1.   Caplan A, Friesen P. Health disparities and clinical trial recruitment: Is there a duty to tweet? PLoS Biol. 2017;15(3):e2002040.
2.   Corneli A, Hanlen-Rosado E, McKenna K, Araojo R, Corbett D, Vasisht K, et al. Enhancing Diversity and Inclusion in Clinical Trials. Clinical Pharmacology & Therapeutics. 2023;113(3):489-99.
3.   Clark LT, Watkins L, Piña IL, Elmer M, Akinboboye O, Gorham M, et al. Increasing Diversity in Clinical Trials: Overcoming Critical Barriers. Curr Probl Cardiol. 2019;44(5):148-72.
4.   Kotera Y, Rennick-Egglestone S, Ng F, Llewellyn-Beardsley J, Ali Y, Newby C, et al. Assessing Diversity and Inclusivity is the Next Frontier in Mental Health Recovery Narrative Research and Practice. JMIR Ment Health 2023;10:e44601.
5.   El-Khatib Z, Jacobs GB, Ikomey GM, Neogi U. The disproportionate effect of COVID-19 mortality on ethnic minorities: Genetics or health inequalities? EClinicalMedicine. 2020;23:100430.
6.   Liu Y, Pencheon E, Hunter RM, Moncrieff J, Freemantle N. Recruitment and retention strategies in mental health trials - A systematic review. PLoS One. 2018;13(8):e0203127.
7.   Mason V, Shaw A, Wiles N, Mulligan J, Peters T, Sharp D, et al. GPs' experiences of primary care mental health research: a qualitative study of the barriers to recruitment. Fam Pract. 2007;24(5):518-25.

8.   Howard L, de Salis I, Tomlin Z, Thornicroft G, Donovan J. Why is recruitment to trials difficult? An investigation into recruitment difficulties in an RCT of supported employment in patients with severe mental illness. Contemporary Clinical Trials. 2009;30(1):40-6.

9.   Corbie-Smith G, Thomas SB, St George DM. Distrust, race, and research. Arch Intern Med. 2002;162(21):2458-63.

10.   National Institute for Health Research. Improving inclusion of under-served groups in clinical research: Guidance from the NIHR INCLUDE project 2020 [Available from: www.nihr.ac.uk/documents/improving-inclusion-of-under-served-groups-in-clinical-research-guidance-from-include-project/25435

11.   The National Institute for Health and Care Research. Equality, Diversity and Inclusion   Strategy   2022-2027   2022   [Available   from: https://www.nihr.ac.uk/documents/equality-diversity-and-inclusion-strategy-2022-2027/31295.

12.   Barak A. Psychological applications on the internet: A discipline on the threshold of a new millennium. Applied and Preventive Psychology. 1999;8(4):231-45.

13.   AkerS L, Gordon JS. Using Facebook for Large-Scale Online Randomized Clinical Trial Recruitment: Effective Advertising Strategies. J Med Internet Res. 2018;20(11):e290.

14.   Shere M, Koren G. The role of social media in recruiting for clinical trials in pregnancy. The FASEB Journal. 2013;27(S1):675.1-.1.

15.   Hall CL, Sanderson C, Brown BJ, Andrén P, Bennett S, Chamberlain LR, et al. Opportunities and challenges of delivering digital clinical trials: lessons learned from a randomised controlled trial of an online behavioural intervention for children and young people. Trials. 2020;21(1):1011.

16.   House of Commons Library. Mental health statistics: prevalence, services and funding   in   England   2020   [Available   from: https://commonslibrary.parliament.uk/research-briefings/sn06988/.

17.   Scheerder A, van Deursen A, van Dijk J. Determinants of Internet skills, uses and outcomes. A systematic review of the second- and third-level digital divide. Telematics and Informatics. 2017;34(8):1607-24.

18.   Fetters MD, Curry LA, Creswell JW. Achieving integration in mixed methods designs-principles and practices. Health Serv Res. 2013;48(6 Pt 2):2134-56.

SECTION 9: APPENDICES

Supporting documents will be available on the RE-MIND webpage on the NCTU website https://www.nctu.ac.uk/

Appendix 1: Baseline characteristics of included trials

Article characteristics	Recruitment strategy Total articles (n-=97)		
	Offline	Mixed	Online
Data source			
JAMA Psychiatry	19	28	2

Lancet Psychiatry	30	9	-
NIHR Journals Library	8	1	-
Trial design			
Randomised controlled trial	61	27	2
Randomised feasibility/pilot study	5	2	-
Type of intervention			
Psychological/behavioural	38	21	2
Drug	22	5	-
Mixed	3	2	-
Surgical/device	3	1	-
Setting			
Hospital (Government or private)	38	16	-
Primary and community care (including care homes)	17	6	-
Academic institution e.g., University	6	6	2
Mixed	5	1	-
Country/region			
Europe	35	9	2
North America	18	17	-
Australia	3	1	-
Africa	3	-	-
Asia	3	-	-
North America and Europe	2	1	-
Australia and Europe	1	-	-
North America, Europe and Asia	1	-	-
South America	-	1	-
Type of disorder			
Emotional disorder (depression, anxiety)	25	10	-
Psychotic disorders (schizophrenia, persecutory delusions)	18	1	-
Personality/Behavioural disorders	8	1	-
Trauma-related disorders (PTSD)	5	4	-
Neurodevelopmental disorders (Autism, Tics, ADHD)	2	4	-
Other[a]	3	1	-
Bipolar disorders	2	2	-
Phobias	-	2	1
Sleep disorders	1	1	1
Dementias	1	1	-
Obsessive Compulsive Disorder (OCD) and related disorders	-	2	-
Eating disorders	1	-	-

[a] – articles that included patients with a range of disorder types
[b] – where data was available on the target sample size compared to the randomised total

Table 2: Recruited to target by recruitment strategy

	Recruited to target[a]		
Recruitment strategy	**N (%)**	**Y (%)**	**Total**
Offline	22 (33)	44 (67)	66
Mixed	10 (38)	16 (61)	26
Online	-	2 (100)	2
Total	**32**	**62**	**94**

[a] – Reported where data was available, 3 articles did not report whether target recruitment was achieved

SECTION 10: CONFLICT OF INTEREST DECLARATION

The authors all declared no conflicts of interest with relevance to this project.