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Recruitment, attrition and intervention completion in clinical trials of psychosocial interventions involving people with early and emerging psychosis: a systematic review protocol

Bróna Nic Giolla Easpaig ,[1] Jianxia Zhai,[2] Richard Gray ,[3] Ellie Brown,[4,5] Daniel Bressington[2]

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For numbered affiliations see end of article.

Correspondence to
Dr Bróna Nic Giolla Easpaig; b.nicgiollaeaspaig@cdu.edu.au

ABSTRACT

Introduction Psychosocial interventions for people experiencing early and emerging psychosis have demonstrated efficacy in reducing symptom severity and supporting recovery; however, much remains unknown about optimising treatment and future research trials are required. Gaining a better understanding of feasibility in trials of psychosocial interventions involving this population would inform the design and planning of future research and support the development of high-quality evidence. The aim of this systematic review is to evaluate the recruitment rate, study attrition rates and intervention completion of psychosocial intervention randomised controlled trial studies involving people with early and emerging psychosis.

Methods and analysis The systematic review will be reported in adherence with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols 2015 guideline. The Cochrane Library, PubMed, Medline, PsycINFO, Web of Science and CINAHL databases will be searched from inception to September 2021 to identify potentially relevant studies. The title and abstracts of returned records will be assessed for eligibility against the inclusion/exclusion criteria by two reviewers, independently, and records which appear eligible will be included. The full texts of included records will then be assessed using the same procedure. Qualitative and quantitative synthesis will be undertaken. Proportion meta-analyses will be used to calculate the recruitment rate, study attrition rate and intervention completion rate, while subgroup analyses will explore differences among subgroups of study and intervention characteristics.

Ethics and dissemination This study will collate and analyse anonymised data from published research and therefore, ethical approval is not necessary. Study results will be disseminated via publication in academic journals.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This protocol offers a method of identifying, collating and examining feasibility data, which can be tailored for relevance to the study of other populations and intervention types.
⇒ The meta-analytic strategy will yield calculations of participant recruitment, study attrition and intervention completion rates, which can help to inform the design and planning of future psychosocial intervention trials involving people with early and emerging psychosis.
⇒ Searches will be limited to studies published in the English language and as such may not capture the full range of relevant trials.

INTRODUCTION

Timely access to acceptable, evidence-based care for people experiencing early and emerging psychosis is critical for fostering better long-term outcomes.[1 2] For the purposes of this study, this early phase of psychosis is understood to refer to a period of up to 5 years following initial engagement for the treatment of psychosis, as well as the prodrome—the period preceding the onset of psychosis.[3] This includes the period, sometimes termed 'ultra-high risk' or 'clinical high risk', which is characterised by the presence of some psychotic such as symptoms and poor or deteriorating function, but which does not meet the threshold for diagnosis.[1 4] The emergence and onset of psychosis nearly always occurs during adolescence or in young adulthood, and is often highly distressing for the individual and their family and friends.[5] Providing timely treatment for clinical symptoms and functional impairments through early intervention services has been repeatedly shown to decrease the likelihood of enduring psychosocial disability, and impact long-term recovery.[6] There is an extensive suite of pharmacological and non-pharmacological treatment options for people experiencing early and emerging psychosis.[1 3 5 7] Among the non-pharmacological treatment options,

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psychosocial interventions hold promise.[8] Psychosocial interventions for early and emerging psychosis have demonstrated efficacy in reducing symptom severity, in addition to promoting longer-term recovery and functioning.[8–12] However, many trials of psychosocial interventions for people with early or emerging psychosis are underpowered, with small sample sizes and there is a lack of existing evidence, particularly in relation to attrition, to inform the estimate of sample sizes required to generate high-quality evidence.

Growing a high-quality evidence base concerning psychosocial interventions for early and emerging psychosis is paramount for informing the selection of efficacious and acceptable interventions. These efforts are hindered by a paucity of knowledge concerning feasibility for non-pharmacological interventions across a range of conditions.[13 14] This is a gap to address, particularly given age of onset in early and emerging psychosis, as previous studies conducted in young people and adults with depression indicate that certain types of interventions (ie, cognitive–behavioural approaches) may have lower study attrition rates.[15] Whereas, longer treatment duration was associated with higher attrition rates in trials of interventions for depression in adults,[16] but no relationships were identified between dropout rates and types of interventions in children with depression.[14] These findings suggest that features of the intervention (eg, duration), as well as the study population (eg, age group), may be important when considering feasibility and acceptability in trials. A previous meta-analyses of 43 studies concerning non-pharmacological interventions reported an attrition rate ranging from 0–63% in trials involving people with schizophrenia,[13] while a composite dropout rate of 13% was reported in trials of people with a schizophrenia spectrum disorder in a meta-analysis of 74 studies.[17] We note that none of these studies reported subgroup analyses that would allow insight into the attrition rates in trials with those in the early and emerging psychosis period. Following searches of MEDLINE, PROSPERO and OSF, we have not identified any systematic review and meta-analysis of the feasibility of psychosocial intervention trials involving people with early and emerging psychosis. Hence, it will inform the design and planning of future studies to calculate the average study attrition rate for trials of psychosocial interventions with this population, as this is currently unavailable.

Review aim and objectives

The aim of this systematic review is to evaluate the recruitment rate, study attrition and intervention completion rates of psychosocial intervention randomised controlled trials (RCTs) involving people with early and emerging psychosis. The specific objectives of the review are to:

1. Determine the number of participants needed to be invited to get one to consent.
2. Determine the proportion of participants who completed baseline measures.
3. Determine the number of participants randomised.
4. Determine the proportion of participants completing treatment.
5. Determine the proportion of participants completing the final outcome measure (ie, at the study end point).
6. Calculate an estimate of study attrition prevalence rates (for both the intervention and control groups).
7. Determine any participant, study characteristic or intervention factors related to attrition.
8. Determine the most common stated reasons for declining the invitation to participate and for attrition.

METHODS AND ANALYSIS

The Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols 2015 guidelines is used to report on this systematic review protocol (please see online supplemental file 1).[18] This protocol is registered on the Open Science Framework (see: https://archive.org/details/osf-registrations-58rfn-v1) with the following registration number: doi:10.17605/OSF.IO/58RFN.

Eligibility criteria

The following criteria will be used to determine study inclusion.

Population

Studies will be eligible for inclusion if they include participants: aged 15 years and over with a diagnosis of early psychosis (using any diagnostic criteria that includes but is not limited to international classification of disease and diagnostic and statistical manual), diagnosed within previous 5 years; or participants without a confirmed diagnosis that are described as ‘ultra-high risk (or similar); or who are described as being treated by early psychosis/ultra-high risk clinical services; or are described as being eligible to receive early psychosis/ultra-high risk clinical services.

Intervention

Studies will be eligible if they report RCTs of any type of discrete psychosocial intervention (defined as: interpersonal or informational activities, techniques, or strategies that target biological, behavioural, cognitive, emotional, interpersonal, social, or environmental factors with the aim of improving health functioning and well-being).[19] Examples of psychosocial interventions are cognitive–behavioural therapy, mindfulness, family intervention, art therapy and behavioural activation. All modality and delivery methods will be considered.

Comparator

Trials consisting of an experimental treatment group along with any comparator intervention including treatment as usual control groups, wait list control groups, attention control groups or any type of active control groups will be eligible. Trials that test/evaluate a psychosocial intervention as an adjunct treatment to usual pharmacological treatment are included; however, trials that are solely evaluating pharmacotherapy as a discreet

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intervention will be excluded. In the event a trial evaluates an experimental pharmacological intervention in a third arm (in addition to psychosocial intervention and comparator arms), the study would be included but feasibility data would not be extracted for the pharmacological arm.

Outcome

We will include trials reporting any outcome relating to clinical symptoms or psychosocial functioning, such as quality of life, depression or social cognition.

Study design

Any type of RCT (pilot, feasibility, cluster or full-scale study) will be considered eligible if it includes at least two treatment arms and reports any relevant feasibility data concerning recruitment, attrition and retention.

Information sources

Searches will be undertaken in six electronic databases: the Cochrane Library, PubMed, Medline, PsycINFO, Web of Science and CINAHL. In addition, reference lists of relevant articles and reviews will be reviewed to identify other potentially eligible articles. Grey literature will not be searched as it may be challenging to ascertain whether the literature has been subjected to comprehensive peer review on par with studies published in commercial academic journals.[20 21]

Search strategy

The search strategy for the databases listed was developed by the research team in consultation with a research librarian. Searches employed a combination of Medical Subject Headings and keywords pertinent to psychosis, first onset/ high risk, interventions and study design (please see online supplemental file 2 for search strategies for each of the databases). As an example, the terms used to search the PubMed database are shown in figure 1.

Searches were conducted from inception until September 2021 and limited to articles in the English language.

Selection process

Records retrieved from the searches will be imported into EndNote V.X9 (citation management software), and duplicates subsequently removed. The remaining records will then be uploaded to the Covidence (literature review management tool). The Covidence systematic review management system will be used for the selection and extraction stages. Covidence is an auditable system that allows reviewers to independently screen titles/abstract and main texts of potentially relevant studies. Screening of the title and abstract records will be conducted by five independent reviewers (JZ, BNGE, EB, RJG and DTB). Each record will be examined for eligibility by two members of the five-member team of reviewers, blinded to one another's decision about the record. Where records appeared to meet the inclusion/exclusion criteria, the corresponding full texts will then be uploaded into Covidence and assessed via the same procedure. The reasons for the exclusion of full texts will be documented. Instances in which reviewers give conflicting decisions concerning the title/abstract records or full-text records

Psychotic Disorder[MeSH Terms] OR Schizophrenia[MeSH Terms] OR Schizoaffective Disorder[MeSH Terms] OR psychosis[Title/Abstract] OR schizoaffective disorder[Title/Abstract] OR schizophre*[Title/Abstract] OR psychotic disorder*[Title/Abstract]

AND

first-episode[Title/Abstract] OR newly diagnosed[Title/Abstract] OR onset[Title/Abstract] OR early stage[Title/Abstract] OR emerging[Title/Abstract] OR prodrom* [Title/Abstract] OR prediction[Title/Abstract] OR attenuat*[Title/Abstract] OR APS[Title/Abstract] OR BLIPS[Title/Abstract] OR brief limited[Title/Abstract] OR brief intermittent[Title/Abstract] OR risk[Title/Abstract] OR ultra-high risk[Title/Abstract] OR genetic high risk[Title/Abstract] OR clinical high risk[Title/Abstract] OR GRD [Title/Abstract] OR at risk mental state[Title/Abstract] OR risk of progression[Title/Abstract] OR progression to first-episode [Title/Abstract] OR basic symptoms[Title/Abstract]

AND

intervention*[Title/Abstract] OR therap*[Title/Abstract]

AND

Clinical Trial[MeSH Terms] OR randomized controlled trial[Title/Abstract] OR RCT[Title/Abstract] OR clinical trial[Title/Abstract]

Figure 1 Peer-reviewed literature search for PubMed database.

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will be resolved by a third reviewer via the Covidence system or by team discussion. Inter-rater reliability will be assessed using the Cohen's kappa to determine the degree of agreement between reviewers.

Data collection process

A draft data extraction template will be developed by the research team in alignment with the aim and objectives of the study. Two research team members will independently trial the data extraction template from a shared subset of included papers. Comparison of completed templates and feedback from team members will enable refining of the template as needed. Using the finalised template, each team member will be allocated a portion of the included papers for data extraction. Data extracted from a cross section of 20% of papers will be examined for accuracy by an independent team member.

Data items

The extracted data will include: (1) characteristics of included RCTs (ie, author, country, clinical setting, programme recruitment processes, study participant characteristics, type of psychosocial intervention, comparator intervention); (2) characteristics of psychosocial interventions (types, delivery mode, duration, number of sessions, frequency); (3) reporting details (ie, whether Consolidated Standards of Reporting Trials (CONSORT) diagram is presented and treatment fidelity details); (4) feasibility data within included studies, as follows:

- Recruitment rate—defined as the proportion of eligible participants (following screening) who agreed to take part in the study (calculated as number of participants recruited (numerator)/number of eligible participants (denominator)).
- Baseline completion rate—defined as the number of participants who completed baseline measures (overall and each separate treatment group).
- Intervention completion rate (overall and each separate treatment group)—defined as the proportion of participants who completed the allocated intervention (completion as defined by each study, eg, a minimum of 80% attendance). Calculated as number of participants allocated to the intervention that completed the minimum attendance (numerator)/number of participants allocated to treatment (denominator).
- Final outcome measure completion rate—defined as the proportion of participants who complete the follow-up assessment (ie, the study defined primary outcome measure or where not stated the outcome measure reported first in the article). This will be calculated as number of randomised participants who completed the measure (numerator)/number of participants randomised (denominator).
- Attrition rate (overall and each separate treatment group)—defined as the proportion of participants at defined study points who discontinued the intervention or were lost to follow-up (calculated as number of participants that withdraw (numerator)/number of participants randomised (denominator)). Attrition rates will be calculated as three points: after randomisation, during the intervention and at final follow-up.

The included literature will be reviewed to identify any cases in which multiple manuscripts report on the same study via cross-referencing study details to avoid double counting. Where this is the case, the most recent manuscript will be considered to be the main data source and the earlier manuscripts will be checked to establish the accuracy of reporting and extract relevant data as appropriate. These data will be managed and analysed in accordance with the available guidance appropriate to those data and each record will represent a single trial, although the data may originate from different manuscripts.[22] Authors of the corresponding manuscripts will be contacted should clarification be needed.

Data synthesis

- If sufficiently detailed data can be extracted from included studies, qualitative and quantitative synthesis will be conducted.
- Qualitative synthesis.
- Characteristics of included studies and the psychosocial interventions will be summarised and synthesised. The most common reasons given for declining the invitation to participate and study withdrawal will be summarised. As the synthesis will be primarily focused on categorising these data, a qualitative content analysis[23] will be conducted in Microsoft Excel.[24]

Quantitative synthesis

Proportion meta-analyses will be used to calculate the recruitment rate, study attrition rate and intervention completion rate using the metafor package in R.[25 26] A random effects model will be used as substantial heterogeneity is expected between studies. Where there are at least four studies, subgroup analyses will be conducted to explore the recruitment rates, study attrition rates and intervention completion rates for different subgroups of study/intervention factors/characteristics.[27] These will include: geographical locations of study, sample size (median<30 or ≥30), type of therapeutic modalities, type of control interventions, treatment duration (<12 or ≥12 weeks), number of sessions, follow-up duration (<26 or ≥26 weeks), reported reasons for dropout (no, yes), treatment fidelity checked (no, yes) and reported a CONSORT flowchart (no, yes).

Ethics and dissemination

This study will collate and analyse anonymised data from published research and therefore, ethical approval is not necessary. Data collection has not yet commenced, and it is anticipated that the study will be completed by October 2022. Study results will be disseminated via publication in academic journals.

Patient and public involvement

There was no involvement of patients and the public in the development of this systematic review protocol. We

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will seek the input of an expert by experience consultant with lived experiences of psychosis in the process of interpreting study findings.

DISCUSSION

As far as we are aware, this will be the first systematic review and meta-analysis to provide calculations of core components of feasibility in trials of psychosocial interventions involving people with early and emerging psychosis. Results concerning participation recruitment, study attrition rates and intervention completion will be helpful in guiding the design and planning of future trials, especially where any intervention and/or population-specific considerations may be merited. By doing so, the chances of future trials being underpowered will be mitigated by realistic sample sizes and engagement of adequate recruitment sites from the beginning. The findings of the study will be informative to efforts to further grow a high-quality evidence base concerning the efficacy and acceptability of psychosocial interventions as a treatment option for people with early and emerging psychosis. Searches will be limited to studies published in the English language and therefore, some relevant trials may be omitted.

Author affiliations
[1]College of Nursing and Midwifery, Charles Darwin University, Casuarina, Darwin, Australia
[2]College of Nursing & Midwifery, Charles Darwin University, Casuarina, Northern Territory, Australia
[3]School of Nursing, La Trobe University, Bundoora, Victoria, Australia
[4]Centre for Youth Mental Health, Medicine, Dentistry and Health Sciences, University of Melbourne, Melbourne, Victoria, Australia
[5]Orygen Youth Health, Parkville, Victoria, Australia

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ORCID iDs
Bróna Nic Giolla Easpaig http://orcid.org/0000-0001-6787-056X
Richard Gray http://orcid.org/0000-0001-9694-4206

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