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Occupational therapy delivered by specialists versus non-specialists for people with schizophrenia (Protocol)

Morris K, Syed A, Reid G, Spencer S

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[Intervention Protocol]

Occupational therapy delivered by specialists versus non-specialists for people with schizophrenia

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ABSTRACT

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

To examine the effects of occupational therapy delivered by occupational therapists compared to occupational therapy delivered by any other person for people with schizophrenia. Our secondary objectives are to determine whether the response differs by specific type (e.g. hospital versus non-hosptial setting), intensity (e.g. more therapist contact time or more frequent task repetition), or duration of occupational therapy.

BACKGROUND

Description of the condition

Schizophrenia is a severe mental illness that is characterised by positive symptoms, such as hallucinations and delusions; negative symptoms, such as catatonia, flattened affect, thought disorder (disrupted speech), and lack of motivation; and cognitive symptoms, such as problems with memory and attention (Carpenter 1994; Fioravanti 2005; NIMH 2014). Schizophrenia can occur as an isolated episode. However, for most people with schizophrenia it is a chronic illness characterised by a cycle of remission and relapse, which often leads to long-term disability (Bustillo 2000). It is among the top 15 medical conditions associated with impaired functioning (Murray 2013; NICE 2014). The first episode of schizophrenia most frequently occurs in males in their early 20s and females in their late 20s. It is associated with impairment of both psychosocial and occupational functioning (APA 2013).

The World Health Organization (WHO) estimates that more than 21 million people worldwide are living with schizophrenia (WHO 2015). The median incidence of schizophrenia is estimated at 15.2 cases per 100,000 of the general population with lifetime prevalence estimated at 7.2 per 1000 of the general population (McGrath 2008). Prevalence is higher in males compared to females (rate ratio 1.4:1) and the mortality risk for people with schizophrenia is two to three times that of the general population, with an all-cause standardised mortality ratio of 2.6:1 (McGrath 2008).

A number of factors, including migrant status, urban living, and residence in developed countries, are also associated with an in-

creased risk of schizophrenia (McGrath 2008; McGrath 2009). The global burden of disease is substantial. Schizophrenia is defined as the most disabling condition in this disease classification group, and accounts for 7.4% of total disability-adjusted life years (DALYs) attributable to mental and substance use disorders. The peak burden occurs between 25 to 50 years of age (Whiteford 2013). It is estimated that only 21% of people of working age with schizophrenia are in paid employment (Marwaha 2007), with combined direct costs of treatment and indirect costs to society (e.g. unemployment, absenteeism, and premature mortality) in England during 2004/2005 of around GBP 6.7 billion (Mangalore 2007). The cost of schizophrenia is estimated at GBP 11.8 billion per year in England, with a public sector cost of GBP 7.2 billion (Andrews 2012). The costs arise from a range of factors, including inpatient time, loss of employment, disrupted education, homelessness, associated physical health problems, substance misuse, contact with the criminal justice system, and unpaid care provided by family members.

Description of the intervention

Occupational therapy is a complex intervention that incorporates the dynamic interchange of a range of personal and environmental factors (Creek 2005). While antipsychotic drugs are the mainstay of treatment for people with schizophrenia, these are often only part of a larger package of care that involves multiple healthcare professionals and therapies. Occupational therapists are a core member of multi-professional teams that care for people with schizophrenia, and have unique skills in activity and occupational analysis that complement the skills of other members of the multi-professional team (Creek 2005; WFOT 2010).

Occupational therapy is designed to support and enable continued participation in daily life through engagement in activities and occupations meaningful to the individual (WFOT 2010). Occupational therapists are uniquely trained to work across a broad range of physical, mental health, and social settings where the emphasis of therapy is on improving function rather than treating the symptoms of schizophrenia. Through modification of daily activities or the environment, or both, occupational therapists facilitate meaningful engagement in life activities (Creek 2003; WFOT 2010). Occupational therapy is not prescriptive and a wide range of interventions are used when working with people, depending on their individual needs, preferences, and interests (Creek 2005; WFOT 2010). Common occupational therapy interventions include helping children with disabilities to participate fully in school and social situations, helping people recovering from injury to regain skills, and providing support for older adults who are experiencing physical and cognitive changes.

Schizophrenia impacts on a person's ability to participate in activities and engage with social roles (NICE 2014). Occupational therapists work in both hospital and community settings using a combination of individual and group interventions (Cook 2007; Smith 2014). The occupational therapist aims to use the activities that are important to the individual to help them increase skills that can help them live a fulfilling life (Urlic 2010).

How the intervention might work

People with schizophrenia can experience difficulty engaging in everyday life (Nagle 2002). This has been attributed to negative symptoms (Mairs 2004), and to symptom severity (Bejerholm 2004).

Occupational therapy interventions for people with long-term mental health issues, such as schizophrenia, aim to improve quality of life and social participation (Bryant 2014). This is achieved through adaptation of activities and environments important to the individual to enable skill development and building of their confidence in the execution of everyday tasks (Bryant 2014; Cook 2007; Smith 2014). This may include:

- practical self care;
- domestic skills, such as cooking and budgeting;
- work skills;
- leisure activities;
- development of social skills;
- carer support.

Occupational therapy focuses on occupations and personal strengths, rather than problems, and thereby promotes the development of self-determination, confidence, and understanding of health and well-being needs (COT 2006). Occupational therapists are trained to analyse, grade, and adapt occupations to suit personal circumstances and individual needs, and they actively involve people with the therapy within the framework of their own treatment and recovery journey. Occupational therapist-led interventions improve the quality of life and well-being for people with long-term mental health conditions, such as schizophrenia (Aubin 1999). The development and maintenance of these skills has been shown to reduce readmission to hospital (Smith 2014).

Why it is important to do this review

Currently there are no published formal evaluations of the evidence on the effectiveness of specialist-administered occupational therapy compared to occupational therapy delivered by other healthcare providers for people with schizophrenia. We aim to evaluate the effectiveness of training specialised occupational therapists for enhancing the outcomes of occupational therapy. This will provide clinically useful information to enhance the quality of care among people with schizophrenia, to help clinicians in developing integrated care pathways and to assist health policymakers in planning resource allocation.

OBJECTIVES

To examine the effects of occupational therapy delivered by occupational therapists compared to occupational therapy delivered by any other person for people with schizophrenia. Our secondary objectives are to determine whether the response differs by specific type (e.g. hospital versus non-hosptial setting), intensity (e.g. more therapist contact time or more frequent task repetition), or duration of occupational therapy.

METHODS

Criteria for considering studies for this review

Types of studies

We will include all relevant randomised controlled trials (RCTs). If a trial is described as 'double blind' but implies randomisation, we will include such trials in a sensitivity analysis (see the 'Sensitivity analysis' section). We will exclude quasi-randomised studies, such as those that allocate participants by alternate days of the week. Where people are given additional treatments alongside occupational therapy, we will only include data if the adjunct treatment is evenly distributed between groups and only the occupational therapy is randomised.

Types of participants

We will include people diagnosed with schizophrenia or related disorders, including schizophreniform disorder, schizoaffective disorder, and delusional disorder, by any means of diagnosis and irrespective of age, sex or severity of illness. If trials include participants with a range of mental illness, we will only include data reported separately for people with schizophrenia.
We will aim to ensure that all information is as relevant to the current care of people with schizophrenia as possible. Therefore, we propose to clearly highlight the current clinical state (acute, early post-acute, partial remission, remission), the stage (prodromal, first episode, early illness, persistent) and whether the included studies primarily focused on people with particular problems (e.g. negative symptoms, treatment-resistant illnesses).

Types of interventions

1. Occupational therapy delivered by occupational therapists

The study publication is unlikely to report the credentials of occupational therapists. We will therefore define an occupational therapist as anyone the study authors describe as such.

2. Occupational therapy delivered by anyone other than occupational therapists

For example, doctors, nurses, allied health professionals, or support staff.
Where the included studies do not state who delivered the occupational therapy interventions, we will contact the study authors for clarification. We will exclude studies where we were are unable to ascertain which professionals delivered the occupational therapy.

Types of outcome measures

We aim to divide outcomes into short-term (less than six months), medium-term (seven to 12 months), and long-term (more than one year) outcomes.

Primary outcomes

1. Activities of daily living (ADL)

For example, standard occupational therapy assessments, such as those based on the Model of Human Occupation (Kielhofner 2008) (such as the Model of Human Occupation Screeing Tool (Parkinson 2006)), or Assessment of Motor and Process Skills (AMPS 2010), or the Canadian Occupational Performance Measure (Law 2005).
1.1 Clinically important change ADL (as defined by individual study)

2. Global state

2.1 Clinically important change global state (as defined by individual study)

3. Adverse effect

3.1 Any clinically important adverse effect (as defined by individual study)

Secondary outcomes

1. Activities of daily living (ADL)

1.1 Any change in ADL (as defined by individual study)
1.2 Average endpoint/change score ADL scale

2. Global state

2.2 Any change in global state (as defined by individual study)
2.3 Average endpoint/change score global state scale e.g. the Brief Psychiatric Rating Scale (BPRS) (Overall 1988)

3. Adverse effect/event

3.1 Any specific effects (as defined by individual study)
3.2 Average endpoint/change score adverse effect scale
3.2 Death (suicide or natural cause)

4. Quality of life

4.1 Clinically important change quality of life (as defined by individual study)
4.2 Any change in quality of life (as defined by individual study)
4.3 Average endpoint/change score quality of life scale e.g. the EuroQoL EQ-5D score (EuroQol Group 1990)

5. Social functioning

5.1 Clinically important change social functioning (as defined by individual study)
5.2 Any change in social functioning (as defined by individual study)
5.3 Average endpoint/change score social functioning scale e.g. the Social Functioning Scale (Birchwood 1990), or the Social Occupational Functioning Scale (Saraswat 2006)

6. Employment status

Employment may be paid or unpaid, as defined by the original included studies.
6.1 Number of participants in employment

7. Mental state

7.1 Clinically important change mental state (as defined by individual study)
7.2 Any change in mental state
7.3 Average endpoint/change score mental state scale e.g. Scale for the Assessment of Negative Symptoms (Andreasen 1989)

8. Service use

8.1 Hospital admission
8.2 Length of stay

9. Economic

9.1 Direct cost of care
9.2 Indirect cost of care

'Summary of findings' table

We will use the GRADE approach to interpret findings (Schünemann 2008). We will use GRADE to import data from Review Manager (RevMan) 5.3 to create 'Summary of findings' tables. These tables provide outcome-specific information concerning the overall quality of evidence from each included study in the comparison, the magnitude of the effect of the interventions examined, and the sum of available data on all outcomes we rate as important to patient care and decision making. We aim to include the following main outcomes in the 'Summary of findings' table:

- Activities of daily living: clinically important change (as defined by individual study)
- Global state: clinically important change global state (as defined by individual study)
- Social functioning: clinically important change social functioning (as defined by individual study)
- Adverse effect: any significant adverse effect
- Quality of life: clinically important change quality of life (as defined by individual study
- Employment status: number of participants in employment
- Service use: hospital admission

Search methods for identification of studies

Electronic searches

Cochrane Schizophrenia Group's Trials Register

The Information Specalist of the Cochrane Schizophrenia Group will search the Cochrane Schizophrenia Group's Study-Based Register of Trials using the following search strategy which has been developed based on a literature review and in consultation with the review authors:
(*(CMOP)* OR *(COPM)* OR *(MOHO)* OR * CMOP * OR * COPM * OR *Domestic Skill* OR *Ergotherap* OR *KAWA Model* OR *Meaningful Activit* OR * MOHO * OR *MOHOST* OR *Occupation* OR *Purposeful Activit* OR *Vocation* OR *Volition* Questionnaire* OR *VQ* OR *Work Skill*) in Title OR Abstract Fields of REFERENCE OR (*Ergotherapy* OR *Occupation* OR *Vocation* OR (*Work* AND *Skill*)) in Interventions Field of STUDY
In such a study-based register, searching the major concept retrieves all the synonym keywords and relevant studies because all the studies are already organised based on their interventions and linked to the relevant topics.
The Cochrane Schizophrenia Group's Register of Trials is compiled by systematic searches of major resources (including AMED, BIOSIS, CINAHL, Embase, MEDLINE, PsycINFO, PubMed, and registries of clinical trials) and their monthly updates, handsearches, grey literature, and conference proceedings (see Group's Module). There are no language, date, document type, or publication status limitations for inclusion of records into the register.

Searching other resources

1. Reference searching

We will inspect references of all included studies for further relevant studies.

2. Personal contact

We will contact the first author of each included study for information regarding unpublished trials. We will note the outcome of this contact in the included or awaiting assessment studies tables.

Data collection and analysis

Selection of studies

Two review authors, KM and AS, will independently screen citations from the searches by title/abstract to identify articles that potentially meet the inclusion criteria of the review. One review author, SS, will independently re-inspect a random 20% sample to ensure reliability of the review authors' assessments. Where disputes arise, we will retrieve the full-text article(s) for further assessment. Two review authors, KM and AS, will obtain and inspect the full-text articles of potentially relevant abstracts. Again, SS will re-inspect a random 20% of the reports in order to ensure reliable selection. Where it is not possible to resolve disagreement by discussion, we will attempt to contact the study authors for clarification. We will list all excluded studies and their reasons for exclusion in a 'Characteristics of excluded studies' table. Also, we were construct a PRISMA diagram to illustrate the study selection process.

Data extraction and management

1. Extraction

Two review authors, KM and AS, will extract data from all included studies. In addition, to ensure reliability, SS will independently extract data from a random sample of these studies, which will comprise 10% of the total. Again, we will discuss any disagreement, document decisions, and, if necessary, contact study authors for clarification. Review author SS will help to resolve any remaining issues and we will document these final decisions in the review text. We will attempt to extract data only presented in graphs and figures whenever possible, but will include data only if two review authors independently have the same result. We will attempt to contact study authors through an open-ended request in order to obtain missing information or for clarification whenever necessary. For multi-centre studies, where possible, we will extract data relevant to each component centre separately.

2. Management

2.1 Forms

We will extract data onto standardised data extraction forms.

2.2 Scale-derived data

We will include continuous data from rating scales only if:

- the psychometric properties of the measuring instrument have been described in a peer-reviewed journal (Marshall 2000); and
- the measuring instrument has not been written or modified by one of the trial authors for that particular trial.

Ideally the measuring instrument should either be:

- a self-report; or
- completed by an independent rater or relative (not the therapist).

We realise that this is not often reported clearly, therefore we will note the instrument mode of completion in the 'Description of studies' section of the review.

2.3 Endpoint versus change data

There are advantages of using both endpoint and change data. Change data can remove a component of between-person variability from the analysis. On the other hand, calculation of change needs two assessments (baseline and endpoint), which can be difficult in unstable and difficult to measure conditions, such as schizophrenia. We have decided to primarily use endpoint data, and only use change data if the former are unavailable. We will combine endpoint and change data in the analysis as we aim to use mean difference (MD) values rather than standardised mean difference (SMD) values throughout (Higgins 2011).

2.4 Skewed data

Continuous data on clinical and social outcomes are often not normally distributed. To avoid the pitfall of applying parametric tests to non-parametric data, we will apply the following standards to all data before inclusion.

For endpoint data N > 200

We will enter data from trials with at least 200 participants because skewed data pose less of a problem in large studies.

Change data

We will enter all change data because where continuous data scales include potential negative values (such as change data), it is difficult to identify whether the data are skewed.

For endpoint data N < 200

- When a scale starts from the nite number zero, we will subtract the lowest possible value from the mean, and divide this by the standard deviation (SD). If this value is lower than one, it strongly suggests a skew and we will exclude such data. If this ratio is higher than one but below two, there is suggestion of skew. We will enter these data and test whether their inclusion or exclusion would change the results substantially. Finally, if the ratio is larger than two we will include such data, because skew is less likely (Altman 1996; Higgins 2011);
- if a scale starts from a positive value (such as the Positive and Negative Syndrome Scale (PANSS) (Kay 1986), which can have values from 30 to 210), we will modify the calculation described above to take the scale starting point into account. In these cases skew is present if 2 SD > (S-S min), where S is the mean score and 'S min' is the minimum score.

2.5 Common measure

To facilitate comparison between trials, we aim to convert variables that can be reported in different metrics, such as days in hospital (mean days per year, per week or per month) to a common metric (e.g. mean days per month).

2.6 Conversion of continuous to binary

Where possible, we will attempt to convert outcome measures to dichotomous data. This can be done by identifying cut-off points on rating scales and dividing participants accordingly into 'clinically improved' or 'not clinically improved'. It is generally assumed that if there is a 50% reduction in a scale-derived score, such as the BPRS (Overall 1962) or the PANSS (Kay 1986), this could be considered as a clinically significant response (Leucht 2005a; Leucht 2005b). If data based on these thresholds are unavailable, we will use the primary cut-off presented by the original study authors.

2.7 Direction of graphs

Where possible, we will enter data in such a way that the area to the left of the line of no effect indicates a favourable outcome for occupational therapists. Where keeping to this makes it impossible to avoid outcome titles with clumsy double-negatives (e.g. 'not unimproved'), we will report data where the left of the line indicates an unfavourable outcome and note this in the relevant graphs.

Assessment of risk of bias in included studies

Two review authors, SS and KM, will independently assess the risk of bias in the included trials using the criteria described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). This set of criteria is based on the evidence of associations between the overestimate of effect and high risk of bias of the article, such as sequence generation, allocation concealment, blinding, incomplete outcome data, and selective reporting.
If the review authors disagree, we will decide the final rating by consensus with the involvement of a third review author (AS). Where included trials provide inadequate details of randomisation and other characteristics of trials, we will contact the trial authors in order to obtain further information. We will report non-concurrence in quality assessment, and we will resolve by discussion any disputes regarding to which category we will allocate a trial.
We will report the results of the 'Risk of bias' assessments in the included trials within the review text and in the 'Summary of findings' table.

Measures of treatment effect

1. Binary data

For binary outcomes we will calculate a standard estimation of the risk ratio (RR) and its 95% confidence interval (CI). It has been shown that RRs are more intuitive than odds ratios (ORs) (Boissel 1999), and clinicians tend to interpret ORs as RRs (Deeks 2000). The number needed to treat for an additional beneficial outcome (NNTH)/number needed to treat for an additional harmful outcome (NNTH) statistic with its CIs is intuitively attractive to clinicians, but is problematic both in its accurate calculation in meta-analyses and interpretation (Hutton 2009). For binary data presented in the 'Summary of findings' table(s), we will calculate illustrative comparative risks where possible.

2. Continuous data

For continuous outcomes we will estimate the MD between groups. We prefer not to calculate effect size measures (SMD). However, if the included trials use scales of very considerable similarity, we will assume there is a small difference in measurement, and we will calculate effect size and transform the effect back to the units of one or more of the specific instruments.

Unit of analysis issues

1. Cluster-randomised trials

Studies increasingly employ cluster randomisation (such as randomisation by clinician or practice), but analysis and pooling of

clustered data poses problems. Firstly, study authors often fail to account for intra-class correlation in cluster-randomised studies, which leads to a 'unit of analysis' error whereby P values are spuriously low, CIs unduly narrow, and statistical significance overestimated (Divine 1992). This causes type I errors (Bland 1997; Gulliford 1999).

Where trial authors do not account for clustering in primary studies, we will present data in a table with an asterisk (*) to indicate the presence of a probable unit of analysis error. In subsequent versions of this review we will seek to contact first authors of the included studies to obtain intra-class correlation coefficients (ICCs) for their clustered data and to adjust for this by using accepted methods (Gulliford 1999). Where clustering has been incorporated into the analysis of primary studies, we will present these data as if from a non-cluster randomised study but we will adjust for the clustering effect.

We have sought statistical advice and have been advised that the binary data as presented in a report should be divided by a 'design effect'. This is calculated using the mean number of participants per cluster (m) and theICC [Design effect = 1+(m-1)*ICC] (Donner 2002). If the ICC is not reported we will assume it to be 0.1 (Ukoumunne 1999).

If cluster-randomised studies have been appropriately analysed taking into account ICCs and relevant data documented in the report, synthesis with other studies will be possible using the generic inverse variance technique.

2. Cross-over trials

A major concern of cross-over trials is the carry-over effect. It occurs if an effect (e.g. pharmacological, physiological, or psychological) of the treatment in the first phase is carried over to the second phase. As a consequence, on entry to the second phase the participants can differ systematically from their initial state despite a wash-out phase. For the same reason, cross-over trials are inappropriate if the condition of interest is unstable (Elbourne 2002). Cross-over study designs would be inappropriate for this intervention (occupational therapists) as it would not be possible to conceal the interventions or to avoid carry-over effects. However, if we identify cross-over studies that meet the inclusion criteria of this review, we will only use data from the first phase of these studies in our analyses.

3. Studies with multiple treatment groups

Where a study involves more than two treatment arms, we will present the additional treatment arms in comparisons if relevant. If data are binary, we will simply add and combine these data within the two-by-two table. If data are continuous, we will combine data following the formula in Section 7.7.3.8 (Combining groups) of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). If the additional treatment arms are irrelevant, we will not use these data.

Dealing with missing data

1. Overall loss of credibility

Data must lose credibility at some degree of loss of follow-up (Xia 2009). Should more than 50% of data be unaccounted for regarding any particular outcome, we will not reproduce these data or use them within analyses. If, however, more than 50% of those in one study arm are lost, but the total loss is less than 50%, we will address this within the 'Summary of findings' table(s) by downgrading the quality of the evidence. Finally, we will also downgrade the quality of the evidence should the loss be between 25% to 50% in total.

2. Binary

In the case where attrition for a binary outcome is between 0% and 50% and where the trial authors do not clearly describe these data, we will present data on an intention-to-treat (ITT) basis. We will assume that those participants that leave the study early have the same rates of negative outcome as those who complete the study, with the exception of the outcomes of death and adverse effects. For these outcomes, we will use the rate of those who stay in the study - in that particular trial arm - for those who did not. We will undertake a sensitivity analysis to test how prone the primary outcomes are to change when we compare data only from people who complete the study to that point to the ITT analysis using the above assumptions.

3. Continuous

3.1 Attrition

In the case where attrition for a continuous outcome is between 0% and 50%, and the trial(s) only report data from people who complete the study to that point, we will use these data.

3.2 SDs

If the included trials do not report SD values, we will first try to obtain the missing values from the trial authors. If these data are unavailable, where there are missing measures of variance for continuous data, but an exact standard error (SE) and CIs are available for group means, and either the P value or 't' value are available for the MDs, we will calculate them according to the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). When the trial authors only report the SE values, we will calculate SD values using the formula SD = SE * square root (n). Chapters 7.7.3 and 16.1.3 of the *Cochrane Handbook for Systematic Reviews of Interventions* present detailed formula for estimating SDs from P values, t or F values, CIs, ranges, or other statistics

(Higgins 2011). If these formula do not apply, we will calculate the SDs according to a validated imputation method which is based on the SDs of the other included studies (Furukawa 2006). Although some of these imputation strategies can introduce error, the alternative would be to exclude a given study's outcome and thus to lose information. Nevertheless we will examine the validity of the imputations in a sensitivity analysis by excluding imputed values.

3.3 Assumptions about participants who left the trials early or were lost to follow-up

Various methods are available to account for participants who leave the trials early or are lost to follow-up. Some trials just present the results of study completers, while other studies use the method of last observation carried forward (LOCF). More recently, methods such as multiple imputation or mixed-effects models for repeated measurements (MMRM) have become more of a standard. While the latter methods seem to be somewhat better than LOCF (Leon 2006), we feel that the high percentage of participants leaving the studies early and the differences in the reasons for leaving the studies early between groups is often the core problem in randomised trials of people with schizophrenia. Therefore, we will not exclude studies based on the statistical approach the trial authors use. However, we will preferably use the more sophisticated approaches, e.g. we will prefer MMRM or multiple-imputation to LOCF and we will only present completer analyses if some kind of ITT data are unavailable at all. Moreover, we will address this issue in the 'incomplete outcome data' item of the 'Risk of bias' tool.

Assessment of heterogeneity

1. Clinical heterogeneity

We will consider all included studies initially, without seeing comparison data, to judge clinical heterogeneity. We will simply inspect all studies for clearly outlying participants or situations that we had not predicted would arise. When such situations or participant groups arise, we will fully discuss.

2. Methodological heterogeneity

We will consider all included studies initially, without seeing comparison data, to judge methodological heterogeneity. We will simply inspect all studies for clearly outlying methods that we had not predicted would arise. When such methodological outliers arise, we will fully discuss.

3. Statistical heterogeneity

3.1 Visual inspection

We will visually inspect graphs to investigate the possibility of statistical heterogeneity.

3.2 Employing the I^2 statistic

We will investigate heterogeneity between studies by considering the I^2 statistic method alongside the Chi^2 test P value. The I^2 statistic provides an estimate of the percentage of inconsistency thought to be due to chance (Higgins 2003). The importance of the observed value of I^2 statistic depends on:

- the magnitude and the direction of effects; and
- the strength of the evidence for heterogeneity (e.g. P value from Chi^2 test, or a CI for the I^2 statistic value).

We will interpret an I^2 statistic estimate greater than or equal to around 50% accompanied by a statistically significant Chi^2 test value as evidence of substantial levels of heterogeneity (Section 9.5.2 of the *Cochrane Handbook for Systematic Reviews of Interventions (*Higgins 2011)). When we observe substantial levels of heterogeneity in the primary outcome, we will explore the reasons for heterogeneity (see the 'Subgroup analysis and investigation of heterogeneity' section).

Assessment of reporting biases

1. Protocol versus full study

Reporting biases arise when the dissemination of research findings is influenced by the nature and direction of results. These are described in Section 10.1 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We will try to locate protocols of included randomised trials. If the protocol is available, we will compare outcomes in the protocol and in the published report. If the protocol is not available, we will compare outcomes listed in the methods section of the trial report with actually reported results.

2. Funnel plot

Reporting biases arise when the dissemination of research findings is influenced by the nature and direction of results (Egger 1997). These are again described in Section 10 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We are aware that funnel plots may be useful in investigating reporting biases but are of limited power to detect small-study effects. We will not use funnel plots for outcomes where there are 10 or fewer included studies, or where all studies are of similar size. In other cases, where

funnel plots are possible, we will seek statistical advice in their interpretation.

Data synthesis

We understand that there is no closed argument for preference for use of fixed- or random-effects models. The random-effects method incorporates an assumption that the different studies are estimating different, yet related, intervention effects. This often seems to be true to us and the random-effects model takes into account differences between studies even if there is no statistically significant heterogeneity. There is, however, a disadvantage to the random-effects model. It places added weight on small studies, which are often the most biased ones. Depending on the direction of effect, these studies can either inflate or deflate the effect size. Occupational therapists deliver therapy that is diverse in nature and we may therefore make an a priori assumption that included studies will estimate different but related effects. We will therefore use a random-effects model for all analyses.

Subgroup analysis and investigation of heterogeneity

1. Subgroup analyses

1.1 Primary outcomes

For the primary outcomes we will, if possible, determine whether the response to therapy varies according to the following subgroups:

- duration of therapy: short- (up to eight weeks) versus long-term;
- specific type: hospital versus non-hosptial setting;
- intensity: more therapist contact time or more frequent task repetition (intensive programme).

1.2 Clinical state, stage, or problem

We propose to undertake this review and provide an overview of the effects of occupational therapy delivered by occupational therapists for people with schizophrenia in general. However, if the included trials report data for subgroups of people in the same clinical state, stage, and with similar problems, we will report these for the primary outcomes.

2. Investigation of heterogeneity

We will report whether inconsistency is high. First, we will investigate whether data are entered correctly. Second, if data are correct we will visually inspect the graph and successively remove studies outside of the company of the rest to see if homogenity is restored. For this Cochrane Review we have decided that should this occur with data contributing to the summary finding of no more than around 10% of the total weighting, we will present such data. If not, we will not pool data and will discuss any relevant issues. We know of no supporting research for this 10% cut-off but we are investigating use of prediction intervals as an alternative to this unsatisfactory state.

When unanticipated clinical or methodological heterogeneity are obvious, we will simply state hypotheses regarding these for future reviews or future versions of this review. We do not anticipate undertaking analyses relating to these.

Sensitivity analysis

1. Implication of randomisation

We aim to include trials in a sensitivity analysis if the trial authors describe them in some way as to imply randomisation. For the primary outcomes we will include these studies. If their inclusion does not result in a substantive difference, they will remain in the analyses. If their inclusion does result in important clinically significant but not necessarily statistically significant differences, we will not add the data from these lower quality studies to the results of the better quality trials, but will present such data within a subcategory.

2. Assumptions for lost binary data

Where we have to make assumptions regarding participants lost to follow-up (see the 'Dealing with missing data' section), we will compare the findings of the primary outcomes when we use our assumption(s) and when we use data only from participants who complete the study to that point. If there is a substantial difference, we will report the results and discuss them but will continue to employ our assumption.

Where we must make assumptions regarding missing SD data (see the 'Dealing with missing data' section), we will compare the findings of the primary outcomes when we use our assumption(s) and when we use data only from participants who complete the study to that point. We will undertake a sensitivity analysis to test how prone the results are to change when we compare completer-only data only to the imputed data using the above assumption. If there is a substantial difference, we will report the results and discuss them but will continue to employ our assumption.

3. Risk of bias

For the primary outcomes, we will analyse the effects of excluding trials that we judge to be at high risk of bias across one or more of the domains of randomisation (implied as randomised with no further details available, allocation concealment, blinding, and outcome reporting). If the exclusion of trials at high risk of bias does not substantially alter the direction of effect or the precision

of the effect estimates, then we will include the data from these trials in the analysis.

4. Imputed values

For the primary outcomes, we will undertake a sensitivity analysis to assess the effects of including data from trials where we use imputed values for the ICC in calculating the design effect in cluster-randomised trials.
If we note substantial differences in the direction or precision of effect estimates in any of the sensitivity analyses we have listed above, we will not pool data from the excluded trials with the other trials that contribute to the outcome, but we will present them separately.

5. Fixed- and random-effects models

We will synthesise all data using a random-effects model. However, we will also synthesise data for the primary outcome using a fixed-effect model to evaluate whether this alters the significance of the results.

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Sally Spencer wrote the protocol.

Karen Morris, Aleena Syed, and Graeme Reid reviewed and drafted parts of the protocol.

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Sally Spencer: none known.

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