PROSPERO International prospective register of systematic reviews

A systematic review of pharmacological and non-pharmacological interventions for improving diabetes outcomes in people with severe mental illness

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Citation

Review question(s)

1. What is the clinical effectiveness of pharmacological and non-pharmacological interventions for improving diabetes outcomes in people with severe mental illness?

For studies included in the literature review:2. What are the methods used for case identification?3. What are the strategies used to recruit participants?4. What are the outcomes examined?5. What are the intervention theories, strategies and components?

Searches

The following databases will be searched to identify randomised controlled trials (RCTs) of interventions for improving diabetes outcomes in people with severe mental illness:

Cochrane Database of Systematic Reviews (Wiley)

Database of Abstracts of Reviews of Effect (Wiley)

Cochrane Central Register of Controlled Trials (CENTRAL) (Wiley)

EMBASE Classic+EMBASE (Ovid) (1947 – present)

Ovid MEDLINE(R) (1946 – present)

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

PsycINFO (Ovid) (1806 – present)

ClinicalTrials.gov (U.S. NIH)

ISRCTN registry (Springer)

International Clinical Trials Registry Platform (WHO)

Conference Proceedings Citation Index – Science (Thomson Reuters Web of Science) (1990 – present)

PubMed (NLM) (1946 – present)

CINAHL (Ebsco) (1981 – present)

There are no restrictions for publication period.

Only articles published in English language and peer reviewed journals will be included in this review.

Types of study to be included
Randomised controlled trials only

Condition or domain being studied
Compared to the general population, people with severe mental illness (SMI) are more likely to experience poor physical health, with increased prevalence of cardiovascular disease, diabetes, stroke, asthma and some cancers. Mortality rates are also significantly higher in the SMI population, with life expectancy estimated to be around 15 years less than for the general population. Although cardiovascular disease accounts for the largest proportion of deaths caused by physical illness, increased mortality can in part be explained by higher prevalence of type 2 diabetes in people with SMI, a co-morbid relationship that carries a three- to four-fold increased risk of death than for the general population.

Diabetes is more than twice as prevalent among people with SMI, and compared to the general diabetic population, is associated with poorer outcomes. The reasons for this are not well understood, but are related to a combination of features of the mental illness, metabolic side effects of psychotropic medication, lifestyle factors, and the organisation of health services. Wider socio-economic inequalities facing people with SMI may also increase the risk of developing diabetes, and the multi-factorial nature of risk can make it difficult to prevent and manage diabetes in this population. Despite the increased risk and poor outcomes associated with diabetes, the physical health needs of people with SMI have long been overlooked, in part due to poor assessment, monitoring and recording practices, but also because of diagnostic overshadowing, poor co-ordination between primary and secondary care, a lack of evidence and clarity about who should manage physical health needs, and barriers to accessing and receiving appropriate care and interventions.

The UK government is committed to tackling physical health inequalities, and to improving care provision for people with SMI. Focusing on diabetes is particularly attractive as effective management could also improve outcomes of other co-morbid conditions that are prevalent in SMI, e.g. through reducing modifiable cardiovascular risk factors. However, little is currently known about what interventions may work for the SMI population. Although there is evidence to support the use of pharmacological and non-pharmacological interventions for preventing and managing diabetes more generally, including patient education and self-management programmes, we cannot assume that interventions designed for this broader population will be acceptable to or effective for people with SMI. This systematic review will therefore summarise the evidence base for pharmacological and non-pharmacological interventions that are targeted to improve diabetes outcomes in people with SMI.

Participants/ population
Inclusion criteria:

Adults aged 18 years and over with a diagnosis of schizophrenia, bipolar disorder, psychosis or other non-organic psychotic disorders including schizoaffective disorder and severe depression (established using any recognised diagnostic criteria).

Where populations are mixed, studies will be included if this is the predominant population or if separate outcome data are provided for those with SMI.

Exclusion criteria:

Studies involving children only

Studies involving diabetes type 1 only

Intervention(s), exposure(s)
The review will include any pharmacological or non-pharmacological* intervention that is targeted to improve diabetes outcomes in people with SMI.

* Non-pharmacological interventions may include patient education programmes; psychological interventions (for

example, cognitive-behavioural therapy or counselling); behavioural approaches such as motivational interviewing or lifestyle interventions (for example improving physical activity or diet); self-monitoring (including telehealth, internet-based interventions, and other communication technologies and monitoring interventions); multi-component interventions (for example self-management programmes that combine education and behavioural approaches); and interventions that aim to improve the delivery of care, such as educating health professionals, care planning, or collaborative models of care.

Comparator(s)/ control
Any comparator, including usual care, no (or minimal) intervention, or an alternative intervention.

Context
Intervention studies delivered in primary care, secondary or community care settings.

Outcome(s)
Primary outcomes
In people without diabetes, the study must measure one of the following outcomes:

Incidence of diabetes (diagnosis should have been established using the standard criteria valid at the time of the trial, for example ADA 1999; ADA 2008; WHO 1998)

Glycaemic control measured via HbA1c or fasting blood glucose

In people with diabetes, the study must measure at least one of the following outcomes:

Glycaemic control measured via HbA1c or fasting blood glucose

Weight

Body Mass Index

Diabetic complications (which include: cardiovascular disease (myocardial infarction and angina), renal failure, micro albuminuria, amputations, diabetic eye disease, diabetic neuropathy, and stroke)

Secondary outcomes
All secondary outcomes will be extracted.

Particular outcomes of interest include:- blood pressure; lipid profile; hypoglycaemia; medication adherence; physical activity; diet; smoking; A&E attendance; hospital admissions (non-mental health); mental health admissions; healthcare costs; mortality; self-management; self-efficacy; quality of life; psychological symptoms (for example depression and anxiety; positive and negative symptoms); adverse events of the intervention.

Data extraction, (selection and coding)
Study selection:

Citations and available abstracts of the search results will be uploaded into EndNote (version X7) and screened for potential eligibility in two stages. The first stage will involve screening titles and abstracts to exclude studies that do not meet the inclusion criteria, and will be carried out by two reviewers (JT and NM). To reduce the potential for bias, all studies will be screened independently by the two reviewers. Discrepancies will be resolved through consensus, and where an agreement cannot be reached a third reviewer will be consulted.

In the second stage, the full text of potentially eligible studies will be retrieved and independently assessed for eligibility by two reviewers (JT and NM). Any missing data that could help to assess eligibility will be sought by contacting the corresponding authors. For studies that are excluded during this stage, a reason for exclusion will be recorded for later reporting. Discrepancies at this stage will be resolved by consulting a third reviewer, who will independently assess the study under consideration. If consensus cannot be reached the decision will be taken by majority view. For included studies, multiple reports from the same study will be linked.

Data extraction:

Data for assessment of study quality and evidence synthesis will be extracted into RevMan (version 5) using a tailored and pre-piloted data collection template based on the Cochrane Consumers and Communication Group's Data Extraction Template for Cochrane Reviews (http://cccrg.cochrane.org/author-resources). Data will be extracted by one reviewer (NM), and then checked independently by a second reviewer (JT). Discrepancies will be resolved through consulting a third reviewer. Missing data will be requested from study authors.

Information will be extracted on the following:

1. Study reference

2. Study population (including participant inclusion and exclusion criteria)

3. Country

4. Setting (primary care, community, secondary care, mental health care)

5. Study design

6. Intervention aim

7. Number of intervention groups

8. Intervention:

a) For pharmacological interventions: class of drug, dose, frequency, and duration

b) For non-pharmacological interventions: description of the intervention (including process, target group, e.g. patients or healthcare professionals, and presence of other co-interventions), theory (informing intervention design), target (including strategies, applications and components), context of intervention (i.e. primary health facility), provider and mode of delivery (phone, face to face, group, online), intensity (length, frequency and number of contacts), duration (period of time over which contacts delivered), details about group leader (demographics, training, professional status etc.).

9. Behaviour change techniques

10. Comparison intervention(s)

11. Number of participants

12. Participant demographics (age, gender, ethnicity, index of deprivation/ social class where specified)

13. Participant diagnoses (including diagnostic criteria) and baseline characteristics

14. Recruitment method

15. Indicators of acceptability of intervention

16. Primary outcome measure

17. Secondary outcome measures

18. Mediators (factors explaining the relationship between two variables)

19. Moderators (factors explaining the strength of the relationship between two variables)

20. Adverse events

21. Type of analysis (e.g. Intention to treat, available case, sensitivity analysis)

22. Primary outcomes intervention arm

23. Primary outcomes control arm

24. Secondary outcomes intervention arm

25. Secondary outcomes control arm

26. Overall effect size/relative effect of intervention

27. Funding source

28. Random sequence generation

29. Treatment allocation concealment

30. Blinding of participants

31. Blinding of outcomes to assessors

32. Incomplete outcome data (attrition bias)

33. Selective reporting of outcomes (reporting bias)

34. Other sources of bias

Risk of bias (quality) assessment
The quality of evidence will be assessed using the Cochrane Collaboration's tool for assessing risk of bias (Higgins et al., 2011) to assess six domains of bias (selection, performance, detection, attrition, reporting, 'other') as having either a 'low', 'high' or 'unclear' risk of bias. One researcher will review all studies with a subset reviewed by a second researcher and disagreements will be resolved through discussion or consulting a third reviewer. The criteria are:

1. Randomisation sequence generation (checking for possible selection bias): was the allocation sequence adequately generated? We will describe for each included study the methods used to generate the allocation sequence. The methods will be assessed as:

Low risk of bias (any truly random process, e.g. random number table; computer random number generator).

High risk of bias (any non-random process, e.g. odd or even date of birth; hospital or clinic record number).

Unclear risk of bias.

2.Treatment allocation concealment (checking for possible selection bias): was the allocated intervention adequately concealed from study participants and clinicians and other healthcare or research staff at the enrolment stage? We will assess whether intervention allocation could have been foreseen in advance of, or during, recruitment or changed after recruitment:

Low risk of bias (e.g. telephone or central randomisation; consecutively numbered sealed opaque envelopes).

High risk of bias (open random allocation; unsealed or non-opaque envelopes, alternation; date of birth).

Unclear risk of bias.

3. Blinding (checking for possible performance bias): were the personnel assessing outcomes and analysing data sufficiently blinded to the intervention allocation throughout the trial? Given the nature of the interventions being evaluated, blinding of either the care providers or the patients receiving care will not have been feasible. We will assess methods used to blind outcome assessment as:

Low, high or unclear risk of bias for participants.

Low, high or unclear risk of bias for personnel.

4. Completeness of outcome data (checking for possible attrition bias through withdrawals, dropouts, protocol deviations): were participant exclusions, attrition and incomplete outcome data adequately addressed in the published report? We will indicate for each included study the completeness of outcome data for each main outcome, including attrition and exclusions from the analysis. We will state the number lost to follow up (compared with the total randomised participants), reasons for attrition/exclusion where reported, and any re-inclusions in analyses which we undertake. We will assess methods as:

Low risk of bias (e.g. no missing outcome data; missing outcome data balanced across groups).

High risk of bias (e.g. numbers or reasons for missing data imbalanced across groups; 'as treated' analysis done with substantial departure of intervention received from that assigned at randomization).

Unclear risk of bias.

5. Selective outcome reporting: is there evidence of selective outcome reporting and might this have affected the study results? We will describe for each included study how we investigated the possibility of selective outcome reporting bias and what we found. We will assess the methods as:

Low risk of bias (where it is clear that all of the study's pre-specified outcomes and all expected outcomes of interest to the review have been reported).

High risk of bias (where not all the study's pre-specified outcomes have been reported; one or more reported primary outcomes were not pre-specified; outcomes of interest are reported incompletely and so cannot be used; study fails to include results of a key outcome that would have been expected to have been reported).

Unclear risk of bias.

6. Other sources of bias: was the trial apparently free of any other problems that could produce a high risk of bias? We will describe for each included study any important concerns we have about other possible sources of bias. We will assess whether each study is free of other problems that could put it at risk of bias:

Low risk of other bias.

High risk of other bias.

Unclear whether there is risk of other bias.

We will make explicit judgements about risk of bias for important outcomes both within and across studies. With reference to (1) to (6) above we will assess the likely magnitude and direction of the bias and whether we consider it is likely to impact on the findings. We plan to explore the impact of the level of bias through undertaking sensitivity analyses, temporarily removing those studies at high risk of bias from the meta-analysis to see what impact this will have on the treatment effect.

The results of the assessment will be included in the review through systematic narrative description and analysis of each of these domains, leading to an overall assessment of the risk of bias of included studies and a judgement about the internal validity of the review's results.

References

Higgins J, Altman D, Gøtzsche P, Jüni P, Moher D, Oxman A et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ 2011; 343: d5928.

Strategy for data synthesis

We anticipate that there will be limited scope for meta-analysis because of the range of different outcomes measured across the small number of existing trials. However, where studies have used the same type of intervention and comparator, with the same outcome measure, we will pool the results for meta-analysis using a random-effects model, with standardised mean differences for continuous outcomes. If there is evidence in the trials of abnormally distributed data, we will report this. For dichotomous data, we will present results as summary risk ratio (RR), with 95% confidence intervals.

In studies where the effects of clustering have not been taken into account, we will adjust the standard deviations for the design effect. Heterogeneity is expected to be significant between studies due to differences in interventions, participants, study design, outcomes and methodological quality. Heterogeneity will be assessed using the I-squared statistic. We will consider an I-squared value greater than 50% indicative of substantial heterogeneity. We will conduct sensitivity analyses based on study quality. We will look for evidence of publication bias by constructing funnel plots.

We will also conduct a narrative synthesis of the findings from the included studies, structured around the type of intervention, target population characteristics, type of outcome, and intervention theories and mechanisms of action. The synthesis will follow the framework developed by Popay et al. (2006), which sets out four key elements for a narrative synthesis 1) developing a theory of how the intervention works, why and for whom; 2) developing a preliminary synthesis; 3) exploring relationships within and between studies, and; 4) assessing the robustness of the synthesis product. Appropriate tools and techniques will be selected for each element, which will be carried out iteratively, and are likely to include textual descriptions; tabulation; groupings and clusters; translating data to integrate themes and concepts reported across the studies; visual representations of relationship between study characteristics and results; and conceptual mapping. The synthesis product will be assessed through critical reflection and discussion with the review team, drawing on the quality assessment performed as part of the review.

Synthesis tables of included studies will be designed. Within each of these sets of tables, interventions will be further grouped according to type of study, intervention and participant characteristics, and study outcomes. Descriptive information will be displayed in tabular form and summarised to address secondary research questions.

Due to the heterogeneity of existing diabetes interventions and the combination of strategies often employed to deliver a complex intervention, the review will initially categorise interventions as pharmacological, non-pharmacological or multi-component (where interventions combine medication and a non-pharmacological approach). Where possible, pharmacological interventions will be grouped by type of drug, and non-pharmacological interventions as either behavioural (defined as those targeting a change in behaviour, e.g. increasing physical activity levels or improving coping mechanisms) or structural (defined as those targeting a change in the environment, e.g. collaborative care model or specialist diabetes nurse). To determine if these categories are appropriate for comparing effects, the narrative synthesis will examine the intervention theories and mechanisms of action using the grouping and clustering tool and conceptual mapping, and revise categories accordingly through discussion with the review team.

References

Popay J, Roberts H, Sowden A, Petticrew M, Arai L, Rodgers M, Britten N, Roen K, Duffy S. Guidance on the conduct of narrative synthesis in systematic reviews: a product from the ESRC methods programme. 2006, Lancaster: Institute for Health Research.

Analysis of subgroups or subsets

None planned

Dissemination plans

The results of the review will be disseminated locally, nationally and internationally through the following channels:

1. A paper will be submitted to a leading peer-reviewed journal in this field, and conference presentations will be given.

2. Summary findings will be published on the project website and on the mental health and co-morbidities theme section of the NIHR CLAHRC Yorkshire and Humber website. Key messages will be disseminated using the project Twitter feed, with links to other organisations including user groups and charities.

3. Findings will be disseminated to healthcare professionals and commissioners involved in diabetes/mental health care through professional journals and magazines, conferences and meetings, input into professional diabetes/mental health care education and training, and via the CLAHRC and project stakeholder group.

4. Key messages will be disseminated to people with diabetes and their carers through the project and collaborating organisation websites, printed materials, and electronic forums. The project's PPI panel will help to disseminate key messages to ensure wider reach to users, carers, and other relevant stakeholders.

Contact details for further information
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DIAMONDS Research Programme Website: www.diamonds.nihr.ac.uk

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Conflicts of interest
None known

Language
English

Country
England

Subject index terms status
Subject indexing assigned by CRD

Subject index terms
Humans; Diabetes Mellitus; Mental Disorders

Any other information
This review is being undertaken as part of the DIAMONDS (Diabetes and Mental Illness – Improving Outcomes and Services) programme of research. This research will examine inequalities faced by people with severe mental illness (SMI) and diabetes, and develop and evaluate inventions in an aim to improve outcomes and service provision.

Stage of review
Completed but not published

Date of registration in PROSPERO
13 February 2015

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20 July 2016

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Stage of review at time of this submission	Started	Completed
Preliminary searches	Yes	Yes
Piloting of the study selection process	Yes	Yes
Formal screening of search results against eligibility criteria	Yes	Yes
Data extraction	Yes	Yes
Risk of bias (quality) assessment	Yes	Yes
Data analysis	Yes	Yes