



Deposited via The University of Leeds.

White Rose Research Online URL for this paper:

<https://eprints.whiterose.ac.uk/id/eprint/143836/>

Version: Published Version

Article:

Mishu, MP, Peckham, EJ, Wright, J et al. (2019) Interventions for preventing type 2 diabetes in adults with mental disorders in low and middle income countries. Cochrane Database of Systematic Reviews, 2019 (3). CD013281.

<https://doi.org/10.1002/14651858.CD013281>

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.
Uploaded in accordance with the publisher's self-archiving policy.

Reuse

Items deposited in White Rose Research Online are protected by copyright, with all rights reserved unless indicated otherwise. They may be downloaded and/or printed for private study, or other acts as permitted by national copyright laws. The publisher or other rights holders may allow further reproduction and re-use of the full text version. This is indicated by the licence information on the White Rose Research Online record for the item.

Takedown

If you consider content in White Rose Research Online to be in breach of UK law, please notify us by emailing eprints@whiterose.ac.uk including the URL of the record and the reason for the withdrawal request.



Cochrane
Library

Cochrane Database of Systematic Reviews

Interventions for preventing type 2 diabetes in adults with mental disorders in low and middle income countries (Protocol)

Mishu MP, Peckham EJ, Wright J, Taylor J, Tirbhowan N, Ajjan R, Al Azdi Z, Stubbs B, Churchill R, Siddiqi N

Mishu MP, Peckham EJ, Wright J, Taylor J, Tirbhowan N, Ajjan R, Al Azdi Z, Stubbs B, Churchill R, Siddiqi N.
Interventions for preventing type 2 diabetes in adults with mental disorders in low and middle income countries.
Cochrane Database of Systematic Reviews 2019, Issue 3. Art. No.: CD013281.
DOI: 10.1002/14651858.CD013281.

www.cochranelibrary.com

TABLE OF CONTENTS

HEADER	1
ABSTRACT	1
BACKGROUND	1
OBJECTIVES	4
METHODS	4
ACKNOWLEDGEMENTS	9
REFERENCES	9
APPENDICES	13
CONTRIBUTIONS OF AUTHORS	16
DECLARATIONS OF INTEREST	16
SOURCES OF SUPPORT	16

[Intervention Protocol]

Interventions for preventing type 2 diabetes in adults with mental disorders in low and middle income countries

Masuma Pervin Mishu¹, Emily J Peckham¹, Judy Wright², Johanna Taylor¹, Nilesh Tirbhowan³, Ramzi Ajjan⁴, Zunayed Al Azdi⁵, Brendon Stubbs^{6,7}, Rachel Churchill^{8,9}, Najma Siddiqi³

¹Department of Health Sciences, University of York, York, UK. ²Academic Unit of Health Economics, Leeds Institute of Health Sciences, Leeds, UK. ³Department of Health Sciences, Hull York Medical School, University of York, York, UK. ⁴Leeds Institute of Cardiovascular and Metabolic Medicine, Faculty of Medicine and Health, University of Leeds, Leeds, UK. ⁵Research and Research Uptake Division, ARK Foundation, Dhaka, Bangladesh. ⁶Institute of Psychiatry, Psychology and Neuroscience, Kings College London, London, UK. ⁷South London and Maudsley NHS Foundation Trust, London, UK. ⁸Centre for Reviews and Dissemination, University of York, York, UK. ⁹Cochrane Common Mental Disorders Group, University of York, York, UK

Contact address: Najma Siddiqi, Department of Health Sciences, Hull York Medical School, University of York, Heslington, York, - None -, Y010 5DD, UK. najma.siddiqi@york.ac.uk.

Editorial group: Cochrane Common Mental Disorders Group.

Publication status and date: New, published in Issue 3, 2019.

Citation: Mishu MP, Peckham EJ, Wright J, Taylor J, Tirbhowan N, Ajjan R, Al Azdi Z, Stubbs B, Churchill R, Siddiqi N. Interventions for preventing type 2 diabetes in adults with mental disorders in low and middle income countries. *Cochrane Database of Systematic Reviews* 2019, Issue 3. Art. No.: CD013281. DOI: 10.1002/14651858.CD013281.

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

ABSTRACT

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

To assess the effects of pharmacological, behaviour change, and organisational interventions compared to comparator intervention in preventing diabetes among people with mental illness in LMICs.

BACKGROUND

Mental disorders have been identified as substantial and increasing sources of global disease burden. They are now one of the leading causes of disability worldwide, accounting for almost a quarter of all years lived with a disability (Murray 2012; Vos 2012) and significantly increased mortality (Correll 2017; Lawrence 2010; Mitchell 2013; Scott 2009). Studies have repeatedly reported a 10 to 20 years mortality gap for people with mental illness, and, despite an overall improvement in life expectancy in recent years, the absolute mortality gap between people with mental illness and those without, is actually widening (Chesney 2014; Hayes 2017; Olfson 2015; Saha 2007). Studies from low- and middle-income

countries (LMIC) show a similar pattern of increased mortality but with an even greater reduction in life expectancy than in high-income countries (Dube 1984; Fekadu 2015; Kurihara 2011; Mogga 2006). However, only 0.5 to 2% of the health budget is allocated for the prevention and treatment of mental disorders in LMICs (Stubbs 2017), and mental illness remains a major health challenge in these countries (Rathod 2017).

A considerable proportion of the increased morbidity and mortality experienced by people with mental disorders is driven, not by the mental illness, but by comorbid physical illnesses (Hayes 2017). The vast majority of deaths (around 80%) are due to preventable physical illnesses, most commonly cardiovascular,

metabolic and respiratory diseases, and infections (Correll 2017; Crump 2013; Laursen 2011). Mental and physical disorders have a complex and bidirectional relationship. A higher prevalence of comorbid physical health conditions (e.g. diabetes and cardiovascular disease) and poorer management of these illnesses contribute to health inequalities in people with mental illness (Vancampfort 2016a; Ward 2015). People with severe mental illness (SMI) (e.g. schizophrenia and bipolar disorder) have a particularly high risk of developing conditions such as diabetes and cardiovascular disease for reasons associated with the underlying mental disorder, health risk behaviours (such as physical inactivity, smoking, poor diet) (Vancampfort 2017) and treatments that increase cardiometabolic risks and mortality (Liu 2017). Conversely, common mental disorders (e.g. depression and anxiety) are more common in people with these physical health conditions (Das-Munshi 2007).

Globally, noncommunicable chronic diseases, such as diabetes, are a major cause of morbidity and mortality (contributing to 60% of all deaths) (Miranda 2008), including in LMICs (Lopez 2006). Diabetes is strongly associated with mental illness (Vancampfort 2015a); for example, around 13% of people with SMI (Ward 2015) and 9% of people with major depressive disorder (Vancampfort 2015b) have diabetes compared to 8.5% of the general population globally (WHO 2016) and 6% in the UK (Reilly 2015). Several interventions have been found to be effective for prevention of type 2 diabetes in the general population (Merlotti 2014; White 2016). Prevention of diabetes in people with mental illness is also clearly important. However, due to a complex combination of psychological, social, and financial barriers, generic interventions to prevent diabetes may not be suitable for people with mental disorders (Chwastiak 2015). Some of the additional barriers faced by people with mental illness, not addressed by generic interventions, include social stigma, poor access to medical care (Bradford 2008), fragmentation and lack of coordination between medical and psychiatric treatment in the healthcare systems of many countries (Druss 2010), and 'diagnostic overshadowing', where physical health problems are overlooked by health professional in the presence of mental illness (Liu 2017). These difficulties compound the challenges of managing side effects of psychotropic medication and the higher prevalence of health risk behaviours.

To date, only a limited number of systematic reviews have investigated the effectiveness of interventions to prevent diabetes for people with mental illness (McGinty 2016; Taylor 2017). These reviews have reported that diabetes can be prevented or its onset delayed, but included studies were mostly from high-income countries.

A comprehensive review by McGinty and others included 33 studies of interventions for diabetes mellitus in people with SMI. It found no high-quality evidence for the effectiveness of any interventions; the best available evidence suggested a potential beneficial effect of metformin on glycated haemoglobin (HbA1c) in this

group (McGinty 2016).

Currently, little is known about the effectiveness of interventions for preventing diabetes among patients with mental illness in LMICs. The review by Taylor and colleagues, which focused on people with SMI, included 54 randomised controlled trials (RCTs) among which only a few were from LMICs (Brazil, India, China, Iran, Venezuela). However, there was no subgroup analysis for LMICs and the review excluded people with other forms of mental disorder. Although the review found some evidence for the effectiveness of pharmacological and nonpharmacological interventions for improving glycaemic measurements for patients with SMI (Taylor 2017), we cannot assume that interventions designed for high-income countries will be suitable or effective for LMICs.

Other similar reviews have investigated the effect of pharmacological (Maayan 2010; Mizuno 2014), behavioural (Bruins 2014; Caemmerer 2012; Fernández-San-Martín 2014), or both pharmacological and behavioural interventions (Faulkner 2007) on glycaemic measurements in people with SMI. They have also reported that these interventions may be effective, but again have focused only on people with SMI or those taking antipsychotic medication, and identified very few studies in LMICs. Moreover, these studies considered glycaemic effects as a secondary outcome. A review of the effectiveness of interventions designed to prevent diabetes in people with any mental disorder, focused on LMICs, is therefore needed to inform practice and future research for this population.

Description of the condition

Diabetes is a serious lifelong condition, which is a major health challenge, with increasing prevalence worldwide showing a particularly sharp rise in LMICs (Stubbs 2016).

Ninety percent of people with diabetes have type 2 diabetes (T2DM), a metabolic disorder resulting from a defect in insulin secretion, insulin action, or both, with disturbances of carbohydrates, fat, and protein metabolism. Insulin deficiency leads to hyperglycaemia (elevated levels of plasma glucose). Eventually this may lead to microvascular retinopathy (disease of the retina which results in impairment or loss of vision), nephropathy (an abnormal state of the kidney especially one associated with or secondary to some other pathological process), neuropathy (an abnormal and usually degenerative state of the nervous system or nerves) and macrovascular (cardiovascular) complications.

The 'epidemic' of diabetes over recent decades has been attributed to changes in demographics and lifestyle globally (increased life expectancy, sedentary behaviours, and consumption of high fat and carbohydrate diets) (Miranda 2008), with LMIC populations experiencing especially rapid changes, with which health policy and services have failed to keep pace (Popkin 2002). The risk of developing diabetes increases with age, obesity, lack of physical activity, dyslipidaemia (abnormal amount of lipids in the blood),

and hypertension (ADA 2017), all of which have been adversely affected by these changes.

There is evidence that mental illness and diabetes comorbidity is very common. A recent systematic review and comparative meta-analysis by Vancampfort and colleagues established that people with SMI were significantly 1.85 times (95% CI: 1.45 to 2.37) more likely to have T2DM than matched controls (Vancampfort 2016a). Other systematic reviews and meta-analyses have demonstrated that all SMI diagnosis subgroups, such as schizophrenia and bipolar disorder, have a higher risk of developing T2DM than the general population (Pillinger 2017; Stubbs 2015; Vancampfort 2013; Vancampfort 2015b). There is also good evidence of an association between diabetes and common mental disorders (Das-Munshi 2007; Moulton 2015; Vancampfort 2016b). Patients with diabetes have a two- to three-fold increased prevalence of depressive disorders (Anderson 2001; Ali 2006) and anxiety (Grigsby 2002), although this relationship is likely to be bidirectional (Golden 2008).

Description of the intervention

There are different types of interventions that target the prevention of diabetes; pharmacological, behaviour change and organisational interventions. Pharmacological interventions aimed at prevention of diabetes in people with mental disorder include diabetes medication, weight loss medication, combination of diabetes and weight loss medication, diabetes preventive medication and antipsychotic switching. Behaviour change interventions may target health risk behaviours, and include patient education programmes, psychological interventions (e.g. cognitive-behavioural therapy or counselling), behavioural approaches (e.g. motivational interviewing), self-monitoring (including telehealth, internet-based interventions, and other communication technologies) or multicomponent interventions (e.g. self-management programmes that combine education and behavioural approaches) (Taylor 2017). Organisational interventions may include interventions that aim to improve the delivery of care, such as educating health professionals, care planning, or collaborative models of care (Druss 2010). It may be that there are particular pharmacological, behavioural and lifestyle, or organisational interventions that would be more applicable to LMICs as the availability of pharmacological interventions, resources and organizational structures in LMICs are different from high-income countries. For instance, in LMICs some drugs may not be available yet, behavioural interventions might not be feasible due to lack of trained personnel or there may not be any collaborative models of care in the health system (Koyanagi 2017).

In addition, LMICs are not a homogenous group of countries; there may be variation as to what is available among LMICs. There may be an intervention that is available in some LMICs but not others. For instance, not all pharmacological interventions are available in every LMIC and there is variability in health care re-

sources and organizational structures (Mate 2013). Therefore, for this review we will include all pharmacological, behaviour change and organisational interventions, as it is difficult to define these a priori, and we do not want to risk excluding effective interventions. Moreover, trials may test interventions that are not currently available in order to justify their inclusion in subsequent national formularies.

How the intervention might work

Pharmacological interventions

There are several modes of action for medication in preventing diabetes. Diabetes medication helps regulate carbohydrate and fat metabolism, by increasing insulin sensitivity and reducing the amount of glucose produced and released by the liver. Weight loss medication or anti-obesity drugs usually act on the gastrointestinal tract by reducing absorption of dietary fat, stimulate energy expenditure and decrease fat storage, or decrease appetite. Diabetes combination medications allow patients to switch between treatments depending on clinical response. Switching to or adding an atypical antipsychotic associated with fewer metabolic side effects is hypothesised to alleviate weight gain and metabolic abnormalities caused by commonly used antipsychotics such as olanzapine and clozapine. Other medications may work by enhancing lipid profile and metabolic function and regulating or increasing insulin sensitivity (Taylor 2017).

Behaviour change interventions

These target health risk behaviours using educational, psychological, and behavioural approaches, or combinations of these. For diabetes, there has been a particular focus on self-management interventions, influenced by several theories of health behaviour change, including social cognitive theory (Bandura 1986), the theory of reasoned action and planned behaviour (Ajzen 1991), self regulation theory (Leventhal 1984) and the transtheoretical model (Prochaska 1997). All of these theories identify concepts that predict health behaviour (and that may be targeted by behaviour change interventions), with a primary focus on beliefs, attitudes, and expectations. For example, a diabetes self-management intervention based on social cognitive theory (Bandura 1986) may seek to reduce carbohydrate intake by increasing diet-related self-efficacy. These behaviour change techniques are proposed to be the 'active ingredients' that explain how a self-management intervention might work (McBain 2016).

Organisational interventions

Organisational capacity building and training programmes increase the efficacy and communication skills of mental health professionals or health workers and health services to support prevention of diabetes for people with mental illness (Liu 2017).

Why it is important to do this review

Despite the high prevalence of comorbid mental illness and diabetes, there is a lack of research on development of evidence-based interventions for prevention of diabetes in people with mental disorders in LMICs. This systematic review will summarise the evidence for pharmacological, behaviour change, and organisational interventions that are targeted at the prevention of diabetes in people with mental disorders in LMICs.

OBJECTIVES

To assess the effects of pharmacological, behaviour change, and organisational interventions compared to comparator intervention in preventing diabetes among people with mental illness in LMICs.

METHODS

Criteria for considering studies for this review

Types of studies

We will include randomised controlled trials evaluating any interventions to prevent type 2 diabetes in people with any mental disorder in LMICs. LMICs will be defined according to the Development Assistance Committee (DAC) list of all countries and territories eligible to receive official development assistance (ODA) (DAC 2017).

Types of participants

We will include studies of adults aged 18 years and over, with any mental disorder and without diabetes, conducted in LMICs. Studies that do not explicitly screen for and exclude diabetes at baseline will not be included. Mental illness diagnosis should be established using WHO International Classification of Diseases (ICD) criteria for mental and behavioural disorders (ICD-10, F20-29 and F30-31, F 32.3, F33.3) (WHO 1992) and/or the Diagnostic and Statistical Manual of Mental Disorders (DSM) (DSM-III, APA 1980; DSM-III-R, APA 1987; DSM IV, APA 2000; DSM V, APA 2013) or measures based on these. We will define SMI as

schizophrenia or other psychotic disorders, bipolar disorder, and depression with psychotic features. Common mental disorders will include depression, generalised anxiety disorder (GAD), panic disorder, phobias, social anxiety disorder, obsessive-compulsive disorder (OCD), and post-traumatic stress disorder (PTSD) (NICE 2011). Other mental disorders such as personality disorder and somatoform disorders will also be included in this review.

Where study populations are mixed (i.e. including people with and without mental disorder), studies will be included only if people with mental disorders constitute the predominant population, or if separate outcome data are provided for them.

Studies involving children or people who already have diabetes, or studies not conducted in LMICs will not be included in this review.

To be consistent with changes in the classification of, and diagnostic criteria for diabetes mellitus over the years, studies should use (and explicitly state) established standard criteria for the diagnosis of T2DM, valid at the time of the trial commencing (e.g. ADA 1999; ADA 2008; ADA 2017; WHO 1999; WHO 2006).

Types of interventions

Experimental intervention

The review will include any pharmacological, behaviour change (targeting health risk behaviours), or organisational intervention that targets the prevention of diabetes in people with any mental disorder in LMICs.

Pharmacological interventions will include any medication-related interventions, for instance: diabetes medication (e.g. metformin, pioglitazone); weight loss medication (e.g. amantadine, orlistat, sibutramine); combination of weight loss and diabetes drugs (e.g. amantadine with metformin and zonisamide; metformin with amantadine and zonisamide; metformin with sibutramine); antipsychotic switching (e.g. changing to aripiprazole, quetiapine, or ziprasidone); or use of other medications purported to prevent diabetes. These are examples of potential drugs rather than a definitive list.

Behaviour change interventions commonly target health risk behaviours (for example, improving physical activity or diet). This review will include any behaviour change intervention targeting at prevention or delaying the onset of diabetes, for example: patient education programmes, psychological interventions (e.g. cognitive behavioural therapy or counselling), behavioural approaches (e.g. motivational interviewing), self-monitoring (including telehealth, internet-based interventions and other communication technologies) and, multicomponent interventions (for example, self-management programmes that combine education and behavioural approaches).

Organisational interventions included will be those that aim to improve the delivery of care, such as educating health professionals,

care planning, or collaborative models of care. Examples, include relevant training of any health professionals working with people with mental illness, nonspecific health worker interventions, community mental health teams, mass media-delivered interventions, family interventions, physical health care monitoring, and statutory mental health services intervention.

Comparator intervention

For pharmacological interventions, comparator interventions will include no treatment (including trials employing wait-list conditions), treatment as usual, placebo drugs or an alternative type of medication for diabetes prevention.

For behaviour change and organisational interventions we will include the following comparators: usual care or treatment, attention or other psychological placebo control, or any alternative behaviour change or organisational intervention (as described above under experimental interventions).

Types of outcome measures

Primary outcomes

Our primary outcome for this review is prevention of diabetes. A clinical diagnosis of diabetes may be confirmed in the presence of symptoms by various parameters such as HbA1c, fasting blood sugar, random blood sugar or, in unclear cases, 2-hour plasma glucose following an oral glucose tolerance test (OGTT). We will accept diagnoses made using any of these parameters using cut-offs consistent with those current at the time of the study, as described in national and international guidance such as WHO (e.g. WHO 2006), National Institute of Health and Care Excellence (NICE) (e.g. NICE 2015), Diabetes UK (e.g. Diabetes UK 2018), American Diabetes Association (e.g. ADA 2017). Current cut-offs are as follows: HbA1c \geq 48 mmol/mol, a fasting blood glucose \geq 7 mmol/L or a random blood glucose \geq 11.1 mmol/L; and for OGTT 2-hour glucose \geq 11.1 mmol/L (ADA 2017). Conversion to prediabetes will not be included.

As the adverse primary outcome, we will report drop-out: the number of participants who drop out of treatment for any reason.

Secondary outcomes

- Body Mass Index (BMI)
- Waist circumference
- Blood pressure
- Cholesterol
- Depression and anxiety measured by a validated scale, e.g. Patient Health Questionnaire (PHQ 9) (Kroenke 2001), Generalised Anxiety Disorder assessment (GAD-7) (Spitzer 2006)

- Health related quality of life (evaluated with a validated generic or disease-specific instrument (Wee 2006), like: 36-Item Short Form Health Survey (SF-36) (McHorney 1993) or other validated scale). We will consider language- and culture-adapted instruments, where these are available

- All-cause mortality, defined as death from any cause

Search methods for identification of studies

Cochrane Common Mental Disorders Controlled Trials Register (CCMDCTR)

The Cochrane Common Mental Disorders Group (CCMD) maintains a specialised register of randomised controlled trials, the CCMDCTR. This register contains over 40,000 reference records (reports of RCTs) for depression, anxiety, bipolar disorder, eating disorders, self-harm, and other mental disorders within the scope of this group. The CCMDCTR is, in part, a studies-based register, with > 50% of reference records tagged to approximately 12,500 individually PICO-coded study records. Reports of trials for inclusion in the register are collated from (weekly) generic searches of MEDLINE, Embase, and PsycINFO; quarterly searches of the Cochrane Central Register of Controlled Trials (CENTRAL); and review-specific searches of additional databases. Reports of trials are also sourced from international trials registries, drug company websites, and handsearching of key journals, conference proceedings, and other (non-Cochrane) systematic reviews and meta-analyses.

Details of CCMD's core search strategies (used to identify RCTs) can be found on the Group's website (Cochrane 2014). In 2016, the Group's Specialised Register (CCMDCTR) fell out of date with the Editorial Group's move from Bristol to York.

Electronic searches

The CCMD Group's Information Specialist (JW) will cross-search the CCMDCTR (studies and references register) using the following search terms to find reports of randomised controlled trials (RCTs): (*diabet** or (*(glucose or glycaemic or glycaemic) near3 control**)) [all fields]

In addition, JW will search the following electronic databases with a comprehensive search strategy, derived from terms related to diabetes, mental disorders, LMICs, RCTs and systematic reviews. Search strategies will be informed by the review of Taylor and colleagues (Taylor 2017), the Cochrane highly-sensitive search strategies for identifying randomised controlled trials (Lefebvre 2011), and the AUHE Information Specialist LMIC geographic strategies (AUHE 2018). The searches will not be limited by date, language, or publication status. In keeping with the Cochrane MECIR conduct standards, we will run a search for retractions and errata once the included studies have been selected.

An example of the MEDLINE strategy is provided in [Appendix 1](#).

The search strategy will be translated across to the other databases listed below, using relevant subject headings and search syntax appropriate to each resource.

- CINAHL (EBSCO) (1981 to present);
- Cochrane Central Register of Controlled Trials (current issue);
- Cochrane Database of Systematic Reviews (current issue);
- Embase Classic + Embase (Ovid) (1947 to present);
- Global Health (Ovid) (1910 to present);
- Indian Medlars (indmed.nic.in/) (all available years);
- LILACs (lilacs.bvsalud.org/en/) (all available years);
- Ovid MEDLINE(R) (1946 to present), MEDLINE In-Process & Other Non-Indexed Citations, MEDLINE Epub Ahead of Print;
- PsycINFO (Ovid) (1806 to present);
- PubMed (NLM) (1946 to present);
- PakMedNet (www.pakmedinet.com/) (all available years).

Searching other resources

Some grey literature will already have been identified in searches of the electronic databases listed above (e.g. conference abstracts in EMBASE, dissertations in PsycINFO, handsearch results in Cochrane CENTRAL). However, further searching will be undertaken as listed below.

Grey literature

We will identify grey literature from:

- conference Proceedings Citation Index - Science (Clarivate Analytics Web of Science) (1990 - present);
- we will search ProQuest Dissertations & Theses Global.

Unpublished studies

We will search the following international trial registries to identify ongoing or unpublished studies (all available years):

- ISRCTN registry (Springer Nature);
- ClinicalTrials.gov (U.S. NIH);
- International Clinical Trials Registry Platform (WHO).

Reference lists

We will check the reference lists of all included studies and relevant systematic reviews to identify additional studies.

Correspondence

We will contact trial authors and subject experts to identify any additional work which is unpublished or to request additional trial data.

Data collection and analysis

Selection of studies

We will upload citations and available abstracts of the search results into Covidence ([Covidence 2017](#)) and screen for potential eligibility in two stages. Covidence is a primary screening and data extraction software, which helps to streamline the production of standard intervention reviews. The first stage will involve screening titles and abstracts to exclude studies that do not meet the inclusion criteria, carried out independently by three pairs of reviewers (MPM and EJP; NT and JT; RA and ZA). Discrepancies will be resolved through discussion, and, where an agreement cannot be reached, a third reviewer (NS) will be consulted. In the second stage, we will retrieve the full text of potentially eligible studies and independently assess them for eligibility, again by three pairs of reviewers (MPM and EJP; NT and JT; RA and ZA). We will seek any missing data that could help to assess eligibility by contacting the corresponding authors. We will present a PRISMA flow diagram to show the process of trial selection ([Liberati 2009](#)). For studies excluded during this stage, a reason for exclusion will be recorded. Discrepancies will be resolved by consulting a third reviewer (NS), who will independently assess the study under consideration. For included studies, we will link multiple reports from the same study.

Data extraction and management

For trials that fulfil our inclusion criteria, three pairs of review authors (MPM and EJP; NT and JT; RA and ZA) will extract data. For each study, one reviewer will complete a tailored and pre-piloted data collection form based on the Cochrane Consumers and Communication Group's Data Extraction Template for Cochrane Reviews (<http://cccrg.cochrane.org/author-resources>), which will then be checked independently by a second reviewer. We will resolve any discrepancies by discussion, or, if required, we will consult a third review author (NS).

To provide information for assessment of study quality and for evidence synthesis, the following data will be extracted:

1. Study population (including participant inclusion and exclusion criteria);
2. Country;
3. Setting (primary care, community, secondary care, mental health care);
4. Study design;
5. Number of intervention groups;
6. Intervention:
 - i) For pharmacological interventions: class of drug, dose, frequency, and duration;
 - ii) For behavior change and organisational interventions: description of the intervention (including process, target group, e.g. patients or healthcare professionals, and presence of other cointerventions), 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.);

iii) Behaviour change techniques. We will categorise interventions and identify behaviour change techniques using the 'template for intervention description and replication' (TIDieR) checklist (Hoffmann 2014; Hoffmann 2017).

7. Comparison intervention(s).

We will note in the 'Characteristics of included studies' table if the study authors did not report outcome data in a usable way. Where included trials reported outcome data in insufficient detail to include in a meta-analysis, for instance, reporting means without confidence intervals (CIs) or standard deviations (SDs), we will contact the study authors to request more information.

Assessment of risk of bias in included studies

We will assess the methodological quality of included randomised trials using the Cochrane 'Risk of bias' tool (Higgins 2011a). The following items will be assessed:

- Sequence generation (i.e. if allocation sequence adequately generated);
- Allocation sequence concealment (i.e. if allocation adequately concealed);
- Blinding (i.e. if knowledge of the allocated interventions adequately prevented during the study);
- Incomplete outcome data (i.e. if incomplete outcome data adequately addressed);
- Selective outcome reporting (i.e. whether reports of the study are free of suggestion of selective outcome reporting);
- Other potential sources of bias (i.e. whether the study is apparently free of other problems that could lead to a high risk of bias e.g. baseline imbalances, evidence of carry-over in cross-over trials, comparability of groups in cluster trials).

We will judge each potential source of bias as high, low or unclear and provide a supporting quotation from the study report together with a justification for our judgment in the 'Risk of bias' table. We will summarise the risk of bias judgements across different studies for each of the domains listed. Three pairs of review authors (MPM and EJP; NT and JT; RA and ZA) will independently rate the certainty of evidence for each outcome. Differences in assessment will be resolved by discussion or consultation with a third researcher (NS). Allocation concealment will be used as a marker of trial quality for the purposes of undertaking sensitivity analyses.

Measures of treatment effect

For continuous data, we will calculate the mean difference (MD) with 95% confidence interval (CI). Where trials report the same outcome using different outcome measures, we will use standardized mean difference (SMD). For binary outcomes, a standard es-

timation of the risk ratio (RR) with a 95% CI will be calculated using Review Manager (Review Manager 2014). In case an eligible study describes its findings using another effect measure, we will contact the study authors to obtain data and if we do not receive the necessary information from trial authors, we will impute these values.

Unit of analysis issues

We will take into account the level at which randomisation occurred, with respect to cross-over trials, cluster RCTs, and multiple observations for the same outcome.

We will attempt to reanalyse cluster-RCTs that have not appropriately adjusted for potential clustering of participants within clusters in their analyses by inflating the variance of the intervention effects by the design effect. We will obtain estimates of the intracluster correlation coefficient (ICC) in order to estimate the design effect through contact with authors, or impute them by using either estimates from other included trials that report ICCs or external estimates from empirical research (e.g. Bell 2013).

In the case of multiple intervention groups, we will analyse each intervention group separately against the control group and the sample size for the control group will be divided proportionately across each intervention group. Where results are reported at multiple time points in the studies, we will analyse each outcome at predefined periods of follow-up in separate meta-analyses. We will group time points as follows: less than six months, and six months or more. We have selected these time points as representing time frames in which a difference in the likelihood of responding could be expected.

If more than one comparison from the same trial is eligible for inclusion in the same meta-analysis, we will either combine groups to create a single pairwise comparison or appropriately reduce the sample size so that the same participants do not contribute data to the meta-analysis more than once (i.e. splitting the 'shared' group into two or more groups), although we acknowledge this will not account for correlation arising from the same set of participants being in multiple comparisons (Higgins 2011a).

Dealing with missing data

We will carefully evaluate important numerical data such as screened and randomly assigned participants as well as intention-to-treat, and as-treated and per-protocol populations. We will investigate attrition rates (e.g. dropouts, losses to follow-up, withdrawals), and we will critically appraise issues concerning missing data.

Data will be analysed primarily using the intention-to-treat (ITT) principle. However, if the included studies do not provide enough detail to allow for an ITT analysis, and where included trials do not report means and SDs for outcomes, data will be requested from study authors. However, if we do not receive the necessary information from trial authors, we will impute these values (Higgins

2011a; Higgins 2011b). We will investigate the impact of imputation on meta-analyses by performing sensitivity analyses.

Assessment of heterogeneity

Clinical heterogeneity will be assessed through the description of the setting, baseline measures, and intervention approach used in each study. In the case of obvious clinical heterogeneity we will not pool the data and the studies will be described.

Statistical heterogeneity will be assessed using the Chi² test and the I² statistic. The Chi² test will be considered statistically significant if $P \leq 0.10$. If heterogeneity exists between studies ($I^2 \geq 50\%$) for the primary outcome, reasons for the heterogeneity will be explored. Our exploration will follow the Cochrane Handbook guidance (Deeks 2011), which suggests the following guidance for interpretation of the I² statistic:

- 0 to 40%: might not be important
- 30% to 60%: may represent moderate heterogeneity
- 50% to 90%: may represent substantial heterogeneity
- 75% to 100%: considerable heterogeneity

We will take into account (i) magnitude and direction of effects and (ii) strength of evidence for heterogeneity (e.g. the P value from the chi²-squared test, or a confidence interval (CI) for I²) when interpreting the I² statistic.

Assessment of reporting biases

If more than 10 studies that investigate a particular outcome are identified for inclusion in this review, funnel plots will be used to assess publication biases. Quantitative analysis of publication bias such as the Egger test will also be conducted.

Data synthesis

Data from individual trials will be combined by meta-analysis if the interventions, outcomes, and patient groups are sufficiently similar (determined by expert consensus).

Data will not be pooled for meta-analysis if we detect a high degree of heterogeneity ($I^2 > 75\%$). Where data are pooled, a random-effects model will be used as a consideration of the heterogeneity of populations.

Subgroup analysis and investigation of heterogeneity

We plan to carry out the following subgroup analyses, based on characteristics of the population or intervention that might be expected to influence the primary outcome:

- Age (65 years and over) and gender, which may influence risk of diabetes;
- Type of mental disorder (SMI versus other mental disorder; people with SMI have additional risk factors for diabetes e.g. side effects of antipsychotic medication);

- Prospective identification of diabetes using a robust approach to diagnosis e.g. HbA1c or fasting blood sugar, versus studies using retrospective records, random blood glucose testing, or both;

- Intervention duration (less than three months versus three months or more; intensity of the intervention may influence outcomes);

- Duration of follow-up (less than three months versus three months or more; this is likely to influence detection of outcomes).

Sensitivity analysis

For outcomes where two or more studies are available to include in a meta-analysis, we will perform sensitivity analyses to explore the influence of the following factors (where applicable) on effect sizes:

- effect of risk of bias: studies that have not used allocation concealment will be excluded;

- effect of large trials: large trials will be excluded to establish the extent to which they dominate the results;

- effect of data imputation: trials where missing data have been imputed will be excluded.

We have restricted the planned sensitivity analyses to these as they are likely to be the most relevant in influencing findings.

'Summary of findings' table

We will prepare 'Summary of findings' tables to summarise key findings of this review. We will report the outcomes (including adverse outcomes) and present standardised effect size estimates and 95% CIs, using the GRADE approach to assess the overall quality of the evidence supporting each outcome. GRADE criteria take into account issues related not only to internal validity (risk of bias, inconsistency, imprecision, publication bias) but also to external validity, such as directness of results. We will use GRADE-proGDT to create our 'Summary of findings' tables (GRADEpro 2015), and follow standard methods as described in the *Cochrane Handbook for Systematic Reviews of Interventions* to prepare our 'Summary of findings' table (Schünemann 2017). For each of our main comparisons, the following outcomes (measured up to 12 months) will be included:

- Diabetes diagnosis determined by HbA1c or fasting blood glucose or measured via other diagnosis method current at the time the study was conducted);

- Drop-out;
- BMI;
- Health-related quality of life;
- Mortality.

The definitive list of comparisons to be included in the 'Summary of findings' tables will be agreed with clinicians once the categories

of interventions are known, guided by clinical relevance. This is because the range of interventions to be included is broad, and at this stage, we cannot know which categories of intervention will be identified by the review.

'Summary of findings' tables will be created after we have entered data into RevMan (Review Manager 2014), written up our results, and conducted the 'Risk of bias' assessment. However, the 'Summary of findings' table will be created before writing our discussion, abstract, and conclusions, to allow the opportunity to consider the impact of the risk of bias in the studies contributing to each outcome upon the mean treatment effect and our confidence in these findings.

ACKNOWLEDGEMENTS

Additional references

ADA 1999

American Diabetes Association. The expert committee on the diagnosis and classification of diabetes mellitus. *Diabetes Care* 1999;**22**:S5–19.

ADA 2008

American Diabetes Association. Standards of medical care in diabetes. *Diabetes Care* 2008;**31** (Suppl 1):S12–54.

ADA 2017

American Diabetes Association. Classification and diagnosis of diabetes. *Diabetes Care* 2017;**40**(Supplement 1):S11–S24.

Ajzen 1991

Ajzen I. The theory of planned behavior. *Organizational Behavior and Human Decision Processes* 1991;**50**:179–211.

Ali 2006

Ali S, Stone MA, Peters JL, Davies MJ, Khunti K. The prevalence of co-morbid depression in adults with Type 2 diabetes: a systematic review and meta-analysis. *Diabetic Medicine* 2006;**23**(11):1165–73.

Anderson 2001

Anderson RJ, Freedland KE, Clouse RE, Lustman PJ. The prevalence of comorbid depression in adults with diabetes: a meta-analysis. *Diabetes Care* 2001;**24**(6):1069–78.

APA 1980

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 3rd Edition. Washington, DC: American Psychiatric Association, 1980.

APA 1987

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 3rd Edition. Washington, DC: American Psychiatric Association, 1987.

The development of this protocol was supported in part by the National Institute of Health Research (NIHR) using Official Development Assistance (ODA) funding (Grant: 17/63/130: NIHR Global Health Research Group: Improving Outcomes in Mental and Physical Multimorbidity and Developing Research Capacity (IMPACT) in South Asia at the University of York).

CRG Funding Acknowledgement

The NIHR is the largest single funder of the Cochrane Common Mental Disorders Group.

Disclaimer

The views and opinions expressed therein are those of the review authors and do not necessarily reflect those of the NIHR, the NHS, or the Department of Health and Social Care.

REFERENCES

APA 2000

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 4th Edition. Washington, DC: American Psychiatric Association, 2000.

APA 2013

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 5th Edition. Washington, DC: American Psychiatric Association, 2013.

AUHE 2018

Academic Unit of Health Economics. LMICs Geographic Search Strategy; DAC List of ODA Recipients 2003–2020. medhealth.leeds.ac.uk/download/4274/lmic-geographic-search-strategy-aid-recipients-2003-2020 (accessed prior to 18 September 2018).

Bandura 1986

Bandura A, National Institute of Mental Health. *Social Foundations of Thought and Action: A Social Cognitive Theory*. Englewood Cliffs, NJ: Prentice-Hall, 1986.

Bell 2013

Bell ML, McKenzie JE. Designing psycho-oncology randomised trials and cluster randomised trials: variance components and intra-cluster correlation of commonly used psychosocial measures. *Psychooncology* 2013;**22**(8):1738–47.

Bradford 2008

Bradford DW, Kim MM, Braxton LE, Marx CE, Butterfield M, Elbogen EB. Access to medical care among persons with psychotic and major affective disorders. *Psychiatric Services* 2008;**59**:847–52.

Bruins 2014

Bruins J, Jörg F, Bruggeman R, Slooff C, Corpeleijn E, Pijnenborg M. The effects of lifestyle interventions on (long-term) weight management, cardiometabolic risk and

depressive symptoms in people with psychotic disorders: a meta-analysis. *PLOS One* 2014;**9**(12):e112276.

Caemmerer 2012

Caemmerer J, Correll CU, Maayan L. Acute and maintenance effects of non-pharmacologic interventions for antipsychotic associated weight gain and metabolic abnormalities: a meta-analytic comparison of randomized controlled trials. *Schizophrenia Research* 2012;**140**(1): 159–68.

Chesney 2014

Chesney E, Goodwin GM, Fazel S. Risks of all-cause and suicide mortality in mental disorders: a meta-review. *World Psychiatry* 2014;**13**(2):153–60.

Chwastiak 2015

Chwastiak LA, Freudenreich O, Tek C, McKibbin C, Han J, McCarron R, et al. Clinical management of comorbid diabetes and psychotic disorders. *Lancet Psychiatry* 2015;**2**(5):465–76.

Cochrane 2014

Cochrane Common Mental Disorders. Search strategies for the identification of studies. cmd.cochrane.org/ (accessed August 2018).

Correll 2017

Correll CU, Solmi M, Veronese N, Bortolato B, Rosson S, Santonastaso P, et al. Prevalence, incidence and mortality from cardiovascular disease in patients with pooled and specific severe mental illness: a large-scale meta-analysis of 3,211,768 patients and 113,383,368 controls. *World Psychiatry* 2017;**16**:163–80.

Covidence 2017 [Computer program]

Veritas Health Innovation. Covidence. Melbourne, Australia: Veritas Health Innovation, 2017.

Crump 2013

Crump C, Winkleby MA, Sundquist K, Sundquist J. Comorbidities and mortality in persons with schizophrenia: a Swedish national cohort study. *American Journal of Psychiatry* 2013;**170**(3):324–33.

DAC 2017

Development Assistance Committee (DAC). DAC List of ODA Recipients. www.oecd.org/dac/financing-sustainable-development/development-finance-standards/daclist.htm (accessed March 2018).

Das-Munshi 2007

Das-Munshi J, Stewart R, Ismail K, Bebbington PE, Jenkins R, Prince MJ. Diabetes, common mental disorders, and disability: findings from the UK National Psychiatric Morbidity Survey. *Psychosomatic Medicine* 2007;**69**(6): 543–50.

Deeks 2011

Deeks JJ, Higgins JP, Altman DG, editor(s). Chapter 9: Analysing data and undertaking meta-analyses. In: Higgins JP, Green S, editor(s). *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from handbook.cochrane.org.

Diabetes UK 2018

Diabetes UK. Diagnostic criteria for diabetes. www.diabetes.org.uk (accessed August 2018).

Druss 2010

Druss BG, Bornemann TH. Improving health and health care for persons with serious mental illness: the window for US federal policy change. *JAMA* 2010;**303**:1972–3.

Dube 1984

Dube KC, Kumar N, Dube S. Long-term course and outcome of the Agra cases in the international pilot-study of schizophrenia. *Acta Psychiatrica Scandinavica* 1984;**70**(2): 170–9.

Faulkner 2007

Faulkner G, Cohn T, Remington G. Interventions to reduce weight gain in schizophrenia. *Schizophrenia Bulletin* 2007;**33**(3):654–6.

Fekadu 2015

Fekadu A, Medhin G, Kebede D, Alem A, Cleare AJ, Prince M, et al. Excess mortality in severe mental illness: 10-year population-based cohort study in rural Ethiopia. *British Journal of Psychiatry* 2015;**206**(4):289–96.

Fernández-San-Martín 2014

Fernández-San-Martín MI, Martín-López LM, Masa-Font R, Olona-Tabueña N, Roman Y, Martín-Royo J, et al. The effectiveness of lifestyle interventions to reduce cardiovascular risk in patients with severe mental disorders: meta-analysis of intervention studies. *Community Mental Health Journal* 2014;**50**(1):81–95.

Golden 2008

Golden SH, Lazo M, Carnethon M, Bertoni AG, Schreiner Pamela J, Diez Roux AV, et al. Examining a bidirectional association between depressive symptoms and diabetes. *JAMA* 2008;**299**(28):2751–9.

GRADEpro 2015 [Computer program]

GRADE Working Group, McMaster University. GRADEpro GDT. Version accessed prior to 19 September 2018. Hamilton (ON): GRADE Working Group, McMaster University, 2015.

Grigsby 2002

Grigsby AB, Anderson RJ, Freedland KE, Clouse RE, Lustman PJ. Prevalence of anxiety in adults with diabetes. *Journal of Psychosomatic Research* 2002;**53**:1053–60.

Hayes 2017

Hayes JF, Marston L, Walters K, King MB, Osborn DPJ. Mortality gap for people with bipolar disorder and schizophrenia: UK-based cohort study 2000–2014. *British Journal of Psychiatry* 2017;**211**:175–81.

Higgins 2011a

Higgins JPT, Altman DG, Sterne JAC, editor(s). Chapter 8: Assessing risk of bias in included studies. In: Higgins JPT, Green S, editor(s). *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from handbook.cochrane.org.

Higgins 2011b

Higgins JP, Deeks JJ, Altman DG, editor(s). Chapter 16: Special topics in statistics. In: Higgins JP, Green S, editor(s). *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from handbook.cochrane.org.

Hoffmann 2014

Hoffmann TC, Glasziou PP, Boutron I, Milne R, Perera R, et al. Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. *BMJ* 2014;**348**:g1687.

Hoffmann 2017

Hoffmann TC, Oxman AD, Ioannidis JP, Moher D, Lasserson TJ, Tovey DI, et al. Enhancing the usability of systematic reviews by improving the consideration and description of interventions. *BMJ* 2017;**358**:2998.

Koyanagi 2017

Koyanagi A, Oh H, Stubbs B, Haro JM, DeVylder JE. Epidemiology of depression with psychotic experiences and its association with chronic physical conditions in 47 low- and middle-income countries. *Psychological Medicine* 2017;**47**(3):531–42.

Kroenke 2001

Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *Journal of General Internal Medicine* 2001;**16**:606–13.

Kurihara 2011

Kurihara T, Kato M, Reverger R, Tirta IG. Seventeen-year clinical outcome of schizophrenia in Bali. *European Psychiatry* 2011;**26**(5):333–8.

Laursen 2011

Laursen TM. Life expectancy among persons with schizophrenia or bipolar affective disorder. *Schizophrenia Research* 2011;**131**(1-3):101–4.

Lawrence 2010

Lawrence D, Kisely S, Pais J. The epidemiology of excess mortality in people with mental illness. *Canadian Journal of Psychiatry* 2010;**55**(12):752–60.

Lefebvre 2011

Lefebvre C, Manheimer E, Glanville J, editor(s). Chapter 6: Searching for studies. In: Higgins JP, Green S, editor(s). *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.

Leventhal 1984

Leventhal H. A perceptual-motor theory of emotion. *Advances in Experimental Social Psychology* 1984;**17**:117–82.

Liberati 2009

Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JP, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *PLOS Medicine* 2009;**6**(7):e1000100.

Liu 2017

Liu NH, Daumit GL, Dua T, Aquila R, Charlson F, Cuijpers P, et al. Excess mortality in persons with severe mental disorders: a multilevel intervention framework and priorities for clinical practice, policy and research agendas. *World Psychiatry* 2017;**16**(1):30–40.

Lopez 2006

Lopez AD, Mathers CD, Ezzati M, Jamison DT, Murray CJ. Global and regional burden of disease and risk factors, 2001: systematic analysis of population health data. *Lancet* 2006;**367**(9524):1747–57.

Maayan 2010

Maayan L, Vakhrusheva J, Correll CU. Effectiveness of medications used to attenuate antipsychotic-related weight gain and metabolic abnormalities: a systematic review and meta-analysis. *Neuropsychopharmacology* 2010;**35**:1520.

Mate 2013

Mate KS, Sifrim ZK, Chalkidou K, Cluzeau F, Cutler D, Kimball M, et al. Improving health system quality in low- and middle-income countries that are expanding health coverage: a framework for insurance. *International Journal for Quality in Health Care* 2013;**25**(5):497–504.

McBain 2016

McBain H, Mulligan K, Haddad M, Flood C, Jones J, Simpson A. Self management interventions for type 2 diabetes in adult people with severe mental illness. *Cochrane Database of Systematic Reviews* 2016, Issue 4. DOI: 10.1002/14651858.CD011361.pub2

McGinty 2016

McGinty EE, Baller J, Azrin ST, Juliano-Bult D, Daumit GL. Interventions to address medical conditions and health-risk behaviors among persons with serious mental illness: a comprehensive review. *Schizophrenia Bulletin* 2016;**42**(1): 96–124.

McHorney 1993

McHorney CA, Ware JE Jr, Raczek AE. The MOS 36-Item Short-Form Health Survey (SF-36): II. Psychometric and clinical tests of validity in measuring physical and mental health constructs. *Medical Care* 1993;**31**:247–63.

Merlotti 2014

Merlotti C, Morabito A, Pontiroli, AE. Prevention of type 2 diabetes: a systematic review and meta-analysis of different intervention strategies. *Diabetes, Obesity and Metabolism* 2014;**16**:719–27.

Miranda 2008

Miranda JJ, Kinra S, Casas JP, Davey Smith G, Ebrahim S. Non-communicable diseases in low- and middle-income countries: context, determinants and health policy. *Tropical Medicine and International Health* 2008;**13**(10):1225–34.

Mitchell 2013

Mitchell AJ, Vancampfort D, Sweers K, Van Winkel R, Yu W, De Hert M. Prevalence of metabolic syndrome and metabolic abnormalities in schizophrenia and related disorders - a systematic review and meta-analysis. *Schizophrenia Bulletin* 2013;**39**(2):306–18.

- Mizuno 2014**
Mizuno Y, Suzuki T, Nakagawa A, Yoshida K, Mimura M, Fleischhacker WW, et al. Pharmacological strategies to counteract antipsychotic-induced weight gain and metabolic adverse effects in schizophrenia: a systematic review and meta-analysis. *Schizophrenia Bulletin* 2014;**40**(6):1385–403.
- Mogga 2006**
Mogga S, Prince M, Alem A, Kebede D, Stewart R, Glozier N, et al. Outcome of major depression in Ethiopia: population-based study. *British Journal of Psychiatry* 2006;**189**:241–6.
- Moulton 2015**
Moulton CD, Pickup JC, Ismail K. The link between depression and diabetes: the search for shared mechanisms. *Lancet Diabetes & Endocrinology* 2015;**3**(6):461–71.
- Murray 2012**
Murray C, Vos T, Lozano R, Naghavi M, Flaxman A, Michaud C, et al. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012;**380**:2197–223.
- NICE 2011**
National Institute for Health and Care Excellence. Common mental health problems: identification and pathways to care, Clinical guideline 123. www.nice.org.uk/guidance/cg123 (accessed 14 August 2018).
- NICE 2015**
National Institute for Health and Care Excellence (NICE). Type 2 diabetes in adults: management. www.nice.org.uk/guidance/ng28 (accessed August 2018).
- Olfson 2015**
Olfson M, Gerhard T, Huang C, Crystal S, Stroup TS. Premature mortality among adults with schizophrenia in the United States. *JAMA Psychiatry* 2015;**72**(12):1172–81.
- Pillinger 2017**
Pillinger T, Beck K, Gobjila C, Donocik JG, Jauhar S, Howes OD. Impaired glucose homeostasis in first-episode schizophrenia: a systematic review and meta-analysis. *JAMA Psychiatry* 2017;**74**(3):261–9.
- Popkin 2002**
Popkin BM. The shift in stages of the nutrition transition in the developing world differs from past experiences. *Public Health Nutrition* 2002;**5**:205–14.
- Prochasta 1997**
Prochaska JO, Redding CA, Evers KE. The transtheoretical model of behavior change. *American Journal of Health Promotion* 1997;**12**:38–48.
- Rathod 2017**
Rathod S, Pinninti N, Irfan M, Gorczynski P, Rathod P, Gega L, et al. Mental health service provision in low- and middle-income countries. *Health Services Insights* 2017;**10**:1–7.
- Reilly 2015**
Reilly S, Olier I, Planner C, Doran T, Reeves D, Ashcroft DM, et al. Inequalities in physical comorbidity: a longitudinal comparative cohort study of people with severe mental illness in the UK. *BMJ Open* 2015;**5**(12):e009010.
- Review Manager 2014 [Computer program]**
Nordic Cochrane Centre, The Cochrane Collaboration. Review Manager 5 (RevMan 5). Version 5.3. Copenhagen: Nordic Cochrane Centre, The Cochrane Collaboration, 2014.
- Saha 2007**
Saha S, Chant D, McGrath J. A systematic review of mortality in schizophrenia: is the differential mortality gap worsening over time?. *Archives of General Psychiatry* 2007;**64**(10):1123–31.
- Schünemann 2017**
Schünemann HJ, Oxman AD, Higgins JPT, Vist GE, Glasziou P, Akl E, et al. Chapter 11: Completing ‘Summary of findings’ tables and grading the confidence in or quality of the evidence. In: Higgins JPT, Churchill R, Chandler J, Cumpston MS, editor(s). *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.2.0 (updated 2017). The Cochrane Collaboration, 2017. Available from training.cochrane.org/handbook.
- Scott 2009**
Scott KM, Von Korff M, Alonso J, Angermeyer MC, Bromet E, Fayyad J, et al. Mental-physical co-morbidity and its relationship with disability: results from the World Mental Health Surveys. *Psychological Medicine* 2009;**39**(1):33–43.
- Spitzer 2006**
Spitzer RL, Kroenke K, Williams JB, Lowe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. *Archives of Internal Medicine* 2006;**166**(10):1092–7.
- Stubbs 2015**
Stubbs B, Vancampfort D, De Hert M, Mitchell AJ. The prevalence and predictors of type two diabetes mellitus in people with schizophrenia: a systematic review and comparative meta-analysis. *Acta Psychiatrica Scandinavica* 2015;**132**(2):144–57.
- Stubbs 2016**
Stubbs B, Koyanagi A, Veronese N, Vancampfort D, Solmi M, Gaughran F, et al. Physical multimorbidity and psychosis: comprehensive cross sectional analysis including 242,952 people across 48 low- and middle-income countries. *BMC Medicine* 2016;**14**(1):189.
- Stubbs 2017**
Stubbs B, Koyanagi A, Schuch F, Firth J, Rosenbaum S, Gaughran F, et al. Physical activity levels and psychosis: a mediation analysis of factors influencing physical activity target achievement among 204,186 people across 46 low- and middle-income countries. *Schizophrenia Bulletin* 2017;**43**:536–45.
- Taylor 2017**
Taylor J, Stubbs B, Hewitt C, Ajjan RA, Alderson SL, Gilbody S, et al. The effectiveness of pharmacological and non-pharmacological interventions for improving glycaemic control in adults with severe mental illness: a

- systematic review and meta-analysis. *PLOS One* 2017;**12**(1):e0168549.
- Vancampfort 2013**
Vancampfort D, Wampers M, Mitchell AJ, Correll CU, De Hert A, Probst M, et al. A meta-analysis of cardio-metabolic abnormalities in drug naive, first-episode and multi-episode patients with schizophrenia versus general population controls. *World Psychiatry* 2013;**12**(3):240–50.
- Vancampfort 2015a**
Vancampfort D, Mitchell AJ, De Hert M, Sienaert P, Probst M, Buys R, et al. Prevalence and predictors of type 2 diabetes mellitus in people with bipolar disorder: a systematic review and meta-analysis. *The Journal of Clinical Psychiatry* 2015;**76**(11):1490–9.
- Vancampfort 2015b**
Vancampfort D, Mitchell AJ, De Hert M, Sienaert P, Probst M, Buys R, et al. Type 2 diabetes in patients with major depressive disorder: a meta-analysis of prevalence estimates and predictors. *Depression and Anxiety* 2015;**32**(10):763–73.
- Vancampfort 2016a**
Vancampfort D, Correll CU, Galling B, Probst M, De Hert M, Ward PB, et al. Diabetes mellitus in people with schizophrenia, bipolar disorder and major depressive disorder: a systematic review and large scale meta-analysis. *World Psychiatry* 2016;**15**(2):166–74.
- Vancampfort 2016b**
Vancampfort D, Rosenbaum S, Ward PB, Steel Z, Lederman O, Lamwaka AV, et al. Type 2 diabetes among people with posttraumatic stress disorder: systematic review and meta-analysis. *Psychosomatic Medicine* 2016;**78**:465–73.
- Vancampfort 2017**
Vancampfort D, Firth J, Schuch FB, Rosenbaum S, Mugisha J, Hallgren M, et al. Sedentary behavior and physical activity levels in people with schizophrenia, bipolar disorder and major depressive disorder: a global systematic review and meta-analysis. *World Psychiatry* 2017;**16**:308–15.
- Vos 2012**
Vos T, Flaxman AD, Naghavi M, Lozano R, Michaud C, Ezzati M, et al. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012;**380**(9859):2163–96.
- Ward 2015**
Ward M, Druss B. The epidemiology of diabetes in psychotic disorders. *Lancet Psychiatry* 2015;**2**(5):431–51.
- Wee 2006**
Wee HL, Tan CE, Goh SY, Li SC. Usefulness of the Audit of Diabetes-Dependent Quality-of-Life (ADDQoL) Questionnaire in patients with diabetes in a multi-ethnic Asian country. *PharmacoEconomics* 2006;**24**:673–82.
- White 2016**
White M. Population approaches to prevention of type 2 diabetes. *PLOS Medicine* 2016;**13**:e1002080.
- WHO 1992**
World Health Organization. *The ICD-10 classification of mental and behavioural disorders: clinical descriptions and diagnostic guidelines*. Geneva: WHO, 1992.
- WHO 1999**
World Health Organization. Definition, diagnosis and classification of diabetes mellitus and its complications. Report of a WHO consultation. Part 1: diagnosis and classification of diabetes 1999. <http://www.who.int/iris/handle/10665/66040> (accessed October 2018):1–59.
- WHO 2006**
WHO. Definition and diagnosis of diabetes mellitus and intermediate hyperglycaemia. www.who.int/diabetes/publications/diagnosis_diabetes2006/en/ (accessed August 2018).
- WHO 2016**
WHO. Global Report on Diabetes. apps.who.int/iris/bitstream/handle/10665/204871/9789241565257_eng.pdf?sequence=1 (accessed August 2018).
- * Indicates the major publication for the study

APPENDICES

Appendix I. Search strategy

Database: Ovid MEDLINE(R) <1946 to July Week 5 2018>

Search Strategy:

-
- 1 diabet*.tw,kf. (568532)
 - 2 exp Diabetes mellitus/ (391230)
 - 3 Glucose Tolerance Test/ (33313)
 - 4 Glycated Hemoglobin A/ (31364)
 - 5 (noninsulin*-depend* or non-insulin*-depend* or noninsulin*depend* or non-insulin*depend*).tw,kf. (12200)
 - 6 (fasting glucose or plasma glucose or glucose tolerance test* or (glyc?emic adj2 control*)).tw,kf. (87693)
 - 7 (HbA1c or A1C or A1c or Hb1c or ((glycated or glycosylated) adj h?emoglobin?)).tw,kf. (46468)
 - 8 (IDDM or NIDDM or MODY or T1DM or T2DM or T1D or T2D).tw,kf. (44357)
 - 9 or/1-8 (663621)
 - 10 exp Diabetes Insipidus/ (7654)
 - 11 diabet* insipidus.tw,kf. (8395)
 - 12 10 or 11 (10371)
 - 13 9 not 12 [DIABETES] (654765)
 - 14 exp Mental Disorders/ (1140872)
 - 15 exp Behavioral Symptoms/ (326828)
 - 16 (mental or mentally or psychiatr* or psycho* or depressi* or depressed or MDD or anxi* or phobia or phobic or agoraphobi* or dysthymi* or ADNOS).tw,kf. (1315284)
 - 17 (schizo* or hebephrenic* or oligophreni* or akathisi* or acathisi* or neuroleptic-induc*).tw,kf. (137538)
 - 18 (tardiv* adj dyskine*).tw,kf. (4218)
 - 19 (movement adj5 (disorder or disorders)).tw,kf. (16677)
 - 20 (somatoform or somatiz* or somatis* or hysteri* or briquet or multisomat* or multi somat* or MUPs or medically unexplained).tw,kf. (13094)
 - 21 ((dissociative adj3 (disorder* or reaction*)) or dissociation).tw,kf. (104569)
 - 22 (affective* adj (disorder? or disease? or illness* or symptom?)).tw,kf. (18268)
 - 23 (PTSD or psychological trauma or psychotrauma* or combat disorder? or war disorder?).tw,kf. (22286)
 - 24 ((post-trauma* or posttrauma*) adj3 (stress* or disorder?)).tw,kf. (29425)
 - 25 ((stress or cognitive or cognition or personality or impulse control or mood or paranoid or psychotic or neurologic* or nervous or nervous system or eating) adj (disorder? or illness* or disease?)).tw,kf. (140175)
 - 26 ((bipolar or behavior?al or obsessive or compulsive or panic or mood or delusional) adj (disorder? or illness* or disease?)).tw,kf. (63498)
 - 27 (trichotillomani* or OCD or obsess*-compulsi* or GAD or stress reaction? or acute stress or neuros#s or neurotic).tw,kf. (50701)
 - 28 (stress syndrome? or distress syndrome? or pain disorder? or dementia or alzheimer? or epilepsy).tw,kf. (312640)
 - 29 ((substance abuse or "substance use" or drug abuse or "drug use") adj2 disorder?).tw,kf. (14220)
 - 30 (personality adj2 disorder?).tw,kf. (18800)
 - 31 (sleep? adj2 (disorder? or syndrome?)).tw,kf. (23532)
 - 32 or/14-31 [ALL MENTAL DISORDERS] (2432067)
 - 33 Developing Countries/ (71059)
 - 34 (low* income* adj3 (countr* or nation* or economy or economies)).tw,kf. (6240)
 - 35 (middle income* adj3 (countr* or nation* or economy or economies)).tw,kf. (13271)
 - 36 (low* middle adj3 (countr* or nation* or economy or economies)).tw,kf. (1294)
 - 37 (LMIC or LMICs).tw,kf. (3055)
 - 38 ((LIC or LICs) adj3 (countr* or nation* or economy or economies)).tw,kf. (139)
 - 39 "transition* countr*".tw,kf. (283)
 - 40 ((underserved or "under served" or deprived or poor*) adj3 (country or countries or nation? or economy or economies)).tw,kf. (4809)

- 41 ((Developing or “under developed” or underdeveloped or “less* developed” or “third world”) adj3 (country or countries or nation? or economy or economies)).tw,kf. (89058)
- 42 ((Developing or “under developed” or underdeveloped or “less* developed”) adj2 world).tw,kf. (8295)
- 43 ((Africa* not “African American*”) or (Asia* not “Asian American*”).ti,ab,in,kf. (340834)
- 44 (Afghanistan* or Albania* or Algeria* or Angola* or Anguilla* or Antigua or Barbuda or Argentina* or Armenia* or Aruba* or Azerbaijan* or Bahamas or Bahrain* or Bangladesh* or Barbados or Belarus* or Belize* or Benin* or Bermuda* or Bhutan* or Bolivia* or Bosnia* or Herzegovina or Borneo or Botswana* or Brazil* or Brunei* or Bulgaria* or “Burkina Faso” or Burundi*).ti,ab,in,kf. (475308)
- 45 (Cambodia* or Cameroon* or “Cape Verde*” or “Cabo Verde*” or Caribbean* or “Cayman Is*” or Chad or Chile* or China or Chinese or (Colombia* not “British Colombia*”) or Comoros or Congo or “Cook Island*” or “Costa Rica*” or “ivory coast” or “cote d’ivoire” or Croat* or Cuba* or Cyprus or Cypriot* or Czech* or Djibouti* or Dominica*).ti,ab,in,kf. (1670756)
- 46 (Ecuador* or Egypt* or “El Salvador” or Eritrea* or Estonia* or Ethiopia* or “Falklands Is*” or Fiji* or Gabon* or Gambia* or Ghana* or Gibraltar* or Grenada* or Guatemala* or Guinea* or Guyana* or Haiti* or Honduras* or “Hong Kong*” or Hungary or Hungarian* or India or (Indian? not “American Indian?”) or Indonesia* or Iran* or Iraq* or Israel*).ti,ab,in,kf. (1304826)
- 47 (Jamaica* or Jordan* or Kazakhstan* or Kenya* or Kiribati* or Korea* or DPRK or Kosovo* or Kuwait* or Kyrgyz* or “Lao PDR” or “Lao People*” or Laos or Laotian or Latvia* or Lebanon or Lebanese or Lesotho or Liberia* or Libya* or Lithuania*).ti,ab,in,kf. (482480)
- 48 (Macao* or Macau or Macedonia* or Madagascar* or Malawi* or Malaysia* or Maldives or Mali or Malta or Maltese or “Marshall Islands” or Mauritania* or Mauritius or Mayotte* or Melanesia* or Mexico or Mexican? or Micronesia* or Moldova* or Mongolia* or Montenegro* or Morocco or Moroccan? or Mozambique* or Myanmar*).ti,ab,in,kf. (262490)
- 49 (Namibia* or Nauru* or Niue* or Nepal* or “Netherlands Antilles*” or “Dutch Antilles” or “New Caledonia*” or Nicaragua* or Niger or Nigeria* or Oman* or Pakistan* or Palau* or Palestin* or Panama or “Papua New Guinea*” or Paraguay or Peru* or Peruvian* or Philippines* or Pilipin* or Filipin* or Poland or Polish or Polynesia* or Qatar* or Romania* or Russia* or Rwanda*).ti,ab,in,kf. (498654)
- 50 (Samoa* or “Sao Toms*” or Principe* or Saudi or Senegal* or Serbia* or Seychelles or “Sierra Leone” or Singapor* or Slovak* or Sloven* or “Solomon Islands” or Somalia* or “Sri Lanka*” or “S* Kitts and Nevis” or “S* Lucia” or “S* Helena” or “S* Vincent and the Grenadines” or “South America*” or Sudan* or Suriname* or Swaziland* or Syria*).ti,ab,in,kf. (297323)
- 51 (Taiwan* or Taipei* or Tajikistan* or Tanzania* or Thai* or Timor* or Tobago or Togo or Tokelau or Tonga or Trinidad or Tunisia* or Turkey or Turkish or Turkmenistan* or “Turks and Caicos” or Tuvalu* or Uganda* or Ukrain* or “United Arab Emirates” or Uruguay* or Uzbekistan* or Vanuatu* or Venezuela* or Vietnam* or “Virgin Is*” or “Wallis and Futuna” or Futuna or “West Bank” or Gaza or Yemen* or Zambia* or Zimbabw*).ti,ab,in,kf. (639017)
- 52 exp Africa/ (239986)
- 53 west indies/ or “antigua and barbuda”/ or bahamas/ or barbados/ or “british virgin islands”/ or cuba/ or dominica/ or dominican republic/ or grenada/ or haiti/ or jamaica/ or saint lucia/ or “saint vincent and the grenadines”/ or “saint kitts and nevis”/ or “trinidad and tobago”/ (18381)
- 54 central america/ or costa rica/ or el salvador/ or guatemala/ or honduras/ or nicaragua/ or exp panama/ or mexico/ (47882)
- 55 exp south america/ (142190)
- 56 exp Atlantic Islands/ (1484)
- 57 asia/ or exp asia, central/ or exp asia, southeastern/ or exp asia, western/ or far east/ or exp china/ or exp korea/ or Taiwan/ (574049)
- 58 exp Middle East/ (119186)
- 59 pacific islands/ or exp melanesia/ or micronesia/ or palau/ or polynesia/ or exp samoa/ or tonga/ (12922)
- 60 exp Europe, Eastern/ or Cyprus/ or Malta/ or Gibraltar/ (170978)
- 61 Georgia.ti,ab. not Georgia/ (5171)
- 62 (Montserrat not (Spain or Espana)).ti,ab. (114)
- 63 or/33-62 [LMICs based on ODA DAC flows 2003 - 2020] (5556279)
- 64 randomized controlled trial.pt. (471052)
- 65 controlled clinical trial.pt. (92742)
- 66 randomized.ab. (425782)
- 67 placebo.ab. (192990)
- 68 clinical trials as topic.sh. (185222)
- 69 randomly.ab. (299878)
- 70 trial.ti. (189624)
- 71 64 or 65 or 66 or 67 or 68 or 69 or 70 (1180572)

72 exp animals/ not humans.sh. (4512703)
73 71 not 72 [RCTs - Cochrane RCT2 Precision Maximising] (1086053)
74 13 and 32 and 63 and 73 [Diabetes + Mental Illness + LMICs + RCTs] (905)
75 13 and 32 and 63 (12134)
76 limit 75 to systematic reviews (427)
77 74 or 76 [Diabetes + Mental Illness + LMICs + RCTs or Systematic Reviews] (1273)
78 (exp Child/ or Adolescent/ or exp Infant/) not exp Adult/ (1769038)
79 77 not 78 [Final Search child-only studies removed] (1232)

CONTRIBUTIONS OF AUTHORS

Drafting of protocol: MPM, EJP, JW, JT, RA, NT, ZA, BS, RC, NS

Search strategy: JW, RC, NS

DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

- MPM, EJP, RC, JT, UK.
The University of York, UK
- NS, NT, UK.
Hull York Medical School
- AZ, Bangladesh.
The ARK Foundation, Dhaka, Bangladesh
- JW and RA, UK.
The University of Leeds
- BS, UK.
Kings College, London

External sources

- MPM, UK.
National Institute of Health Research Collaboration for Applied Health Research, UK
 - National Institute of Health Research, UK.
- The development of this protocol was supported in part by the National Institute of Health Research (NIHR) using Official Development Assistance (ODA) funding (Grant: 17/63/130: NIHR Global Health Research Group: Improving Outcomes in Mental and Physical Multimorbidity and Developing Research Capacity (IMPACT) in South Asia at the University of York).