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# BMJ Open

## Effect of music intervention on mental health in patients with diabetes mellitus: a protocol for a systematic review and meta-analysis of randomized controlled trials

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# Effect of music intervention on mental health in patients with diabetes mellitus: a protocol for a systematic review and meta-analysis of randomized controlled trials

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## ABSTRACT

**Introduction** About 463 million adults aged 20 to 79 have diabetes globally and mental disorders often exist in diabetic patients as comorbidities. The comorbidities can lead to deterioration of diseases, increased difficulty in treatment, even as well as the terrible mortality. Music intervention has been applied in the treatment of the comorbidities for 12 years, but there are no any recommendations due to lacking of evidence. Thus, a meta-analysis is necessary to be conducted to evaluate the effect of music intervention.

**Methods and analysis** We will retrieve the following nine online electronic databases: PubMed, Web of Science, Embase, EBSCO, Cochrane Library, Chinese National Knowledge Infrastructure (CNKI), Wanfang Database, Chinese Scientific Journal Database (VIP) and Chinese Biomedical and Medical Database (CBM), from their inception until August 2019. Only randomized controlled trials (RCTs) of music intervention for depression or anxiety with diabetes will be involved. The primary outcomes include depression score and anxiety score measured by scales, and the secondary outcome is safety. Data extraction will be implemented by 2 researchers independently. Risk of bias will be evaluated through Cochrane Collaboration's Risk of Bias tool. Eventually, all the data will be analyzed via the software Review Manager V.5.3.

**Ethics and dissemination** This meta-analysis will provide information about music intervention applied to treat depression or anxiety in diabetic patients. There is no required ethical approval because this is a protocol for meta-analysis. The results of this study will be published to a peer reviewed journal.

**Trial registration number** CRD42019146439

### Strengths and limitations of this study

· This meta-analysis will provide evidence of the effectiveness and safety of music intervention applied to treat depression or anxiety in diabetic patients for the first time.

· This systematic review will furnish evidence reference for guideline of relevant areas.

· This meta-analysis will be implemented on the basis of rigorous international gold-standard methodology and integrated search strategy.

· A language bias may exist in this meta-analysis because it will include studies only in English and Chinese on account of the language barrier.

## INTRODUCTION

### Description of the conditions

According to the newest “IDF Diabetes Atlas (9<sup>th</sup> edition)” published by International Diabetes Federation (IDF), about 463 million adults aged 20 to 79 have diabetes globally (1 in 11).[1] It is well known that diabetes has a significant influence on life quality because it can cause a lot of complications such as retinopathy, renal disease, cardiovascular disease, neurological disease and foot ulcers which may result in lower extremity amputation.[2]

In addition to physical complications, some mental disorders often exist in diabetic patients as comorbidities. A few studies suggested that depression was more prevalent in diabetic patients compared to those without.[3,4] At the same time, depression could also increase the risk of incident of diabetes,[5-7] which suggested that depression had a bidirectional association with diabetes. And the relation between anxiety and diabetes was confirmed to be the same. People with diabetes were more susceptible to concurrent anxiety[8,9] while reversely anxiety was a risk factor of diabetic incidents.[10] Individuals with chronic diseases and also comorbid depression or anxiety have obviously higher health-care utilization, functional disability, work absence and mortality risk than those without.[11,12]

### Description of the intervention

When it comes to the treatment of diabetes with depression or anxiety, conventional glucose-lowering treatment combined with drug therapy or psychological intervention are the routine treatments.[13,14] Music intervention is also a successful therapy using music for treatment by professionals, which can be divided into two major categories, namely music therapy and music medicine, although the distinction between them are often neglected.[15] A lot of studies suggested that music, no matter what type of it is, demonstrated a remarkable effect in alleviating depression and anxiety among patients with various diseases.[16-18] As for diabetes, recent studies showed that music intervention could improve fasting blood-glucose and systolic blood pressure in diabetic patients.[19,20] Good control of blood glucose, blood lipids and blood pressure can effectively

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4 reduce the incidence of serious complications of diabetes.[21]  
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### 7 8 **How the intervention might work**

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10 Music psychology researches have shown the special potential of music that music listening can  
11 give rise to complex emotional experiences[22, 23] and strengthen ability to deal with complex  
12 negative emotions in everyday life.[24] The proposed mechanisms of music intervention on  
13 depression and anxiety span several domains. Firstly, music intervention can exert  
14 neurophysiological and neurochemical effects, such as triggering endorphin release[25] and  
15 stimulating cognitive functioning.[26] Secondly, music intervention can promote positive self-  
16 emotions including enhancing the sense of happiness[27] and activating self-efficacy and self-  
17 confidence through experiences of success.[28] Lastly, music intervention can build up sociability,  
18 such as interaction skills[29] and interpersonal relationship.[30] Furthermore, there are published  
19 studies indicated that music intervention combined with diabetic routine treatments could improve  
20 depression score, anxiety score, fasting glucose and glycosylated hemoglobin (HbA1c).[31,32]  
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### 33 **Why it is important to this review**

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35 From the above, many studies indicated the bidirectional relationship between diabetes and mental  
36 disorders. Music intervention, as a therapeutic method, was applied to alleviate depression and  
37 anxiety and improve related indicators of diabetes. By searching literatures, it can be found that  
38 some reviews evaluated the effect of music intervention on patients with mental disorders,[33-35]  
39 while no related systematic review and meta-analysis can be searched about the effect of music  
40 intervention on mental health of patients with diabetes. Therefore, if music intervention can be  
41 proved to be both valid and with few side effects through this study, it is worth being promoted and  
42 applied in clinic all over the world to benefit more people since this method is easy to be operated.  
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### 52 **Objectives**

53  
54 The purpose of this review is to systematically assess the effect of music intervention on depression  
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4 and anxiety of diabetic patients. We also look forward to furnish evidence reference for related  
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6 guideline.

## 9 10 **METHODS**

### 11 **Study registration**

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13 The protocol of the meta-analysis has been registered in International Prospective Register of  
14 Systematic Reviews (PROSPERO), and CRD42019146439 is the registration number. This  
15 systematic review protocol will be conducted and reported severely on the basis of Preferred  
16 Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[36] statement guidelines,  
17 and the crucial protocol amendments will be documented in the full review.  
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### 25 **Eligibility criteria**

26 We will severely screen studies that have compliance with following inclusion criteria.

#### 30 31 Type of studies

32 We will only cover randomized controlled trials (RCTs) in English or Chinese, excepting Quasi-  
33 RCTs and cluster RCTs. Experiments on animals and nonrandomized clinical trials will be out of  
34 our consideration. Articles with significant overlap with other articles through print or e-publishing  
35 will fail to be included. Duplicate publications, that is results originated from a single experiment  
36 but measured by other standards and then published as disparate papers, will also be excluded.  
37 Publications with originality is our first choice. The publication status will not be restricted.  
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#### 46 47 Type of Participants

48 Diabetic Patients with depression or anxiety symptoms, regardless of the type of diabetes and no  
49 restriction on gender, age, race, economic ability and education level. Patients of other disease or  
50 healthy persons will be excluded.  
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### Type of interventions and controls

Interventions include music alone or music in combination with other interventions. No restriction on the type of music. Other interventions refer to: (1) routine treatment for diabetes which mainly includes pharmacologic approaches to glycemic treatment, lifestyle management, etc. according to the newest guideline of American Diabetes Association (ADA);[37,38] (2) Other therapies such as acupuncture therapy,[39] metabolic surgery[40] etc. When intervention is music alone, controls can be no treatment, placebo or other active therapies. Notably, when intervention is music combined with active therapies, the control must be the same active therapies.

### Type of outcome measures

This review aims at systematically assessing the effect of music intervention on depression or anxiety of diabetic patients, so we choose depression score and anxiety score as the primary outcomes which can give an index to the degree of depression and anxiety by scales such as SDS, HAMD, SAS or HAMA.

Primary outcomes: Depression score and anxiety score. Depression score is measured using self-rating depression scale (SDS) or Hamilton depression scale (HAMD). Anxiety score is measured using self-rating anxiety scale (SAS) or Hamilton anxiety scale (HAMA).

Secondary outcomes: Safety. Measurement via incidence of adverse effects.

## Search methods

### Search resources

We will retrieve the following nine online electronic databases: PubMed, Web of Science, Embase, EBSCO, Cochrane Library, Chinese National Knowledge Infrastructure (CNKI), Wanfang Database, Chinese Scientific Journal Database (VIP) and Chinese Biomedical and Medical Database (CBM), from their inception until August 2019. We also scrutinized the reference list of relevant publications for additional studies.

### Search strategies

The search strategy will include the MeSH terms for diabetes mellitus, depression, anxiety and music therapy, combined with their respective free-text terms. The search details of the PubMed was simply shown in table 1.

**Table 1 Example of PubMed search strategy.**

Number	Search terms
#1	"Diabetes Mellitus"[Mesh]
#2	"Depression"[Mesh]) OR Depressions[Title/Abstract]) OR Depressive Symptoms[Title/Abstract] OR Depressive Symptom[Title/Abstract] OR Symptom, Depressive[Title/Abstract] OR Symptoms, Depressive[Title/Abstract] OR Emotional Depression[Title/Abstract] OR Depression, Emotional[Title/Abstract] OR Depressions, Emotional[Title/Abstract] OR Emotional Depressions[Title/Abstract]
#3	"Anxiety"[Mesh] OR Hypervigilance [Title/Abstract] OR Nervousness [Title/Abstract]
#4	#2 OR #3
#5	"Music Therapy"[Mesh] OR Therapy, Music [Title/Abstract]
#6	randomized controlled trial [Publication Type] OR randomized [Title/Abstract] OR placebo [Title/Abstract]
#7	#1 AND #4 AND #5 AND #6

### Data collection and analysis

#### Studies selection

Firstly, two researchers (L-yZ and YT) will respectively screen the keywords, titles and abstracts of all obtained studies using endnote x9 software and determine whether trials have compliance with inclusion criteria. Secondly, we will also get access to the full text of all studies of possible relevance for further assessment. Each of excluded study will be noted with reasons. Any

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4 disagreements will be settled through consensus or referral to the third researcher (YZ). The  
5  
6 specific selection steps were presented in the figure 1.  
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#### 9 10 Data extraction

11 Two researchers (L-yZ and YT) will independently extract and tabulate the following data items  
12  
13 via Microsoft Excel:

- 14 1. General information (including publication year and name of the first author).
- 15 2. Study design (including random method, allocation concealment and blinding).
- 16 3. Participants (including sample size, gender, age, depression score, anxiety score and course of  
17 disease).
- 18 4. Treatment (including interventions, controls, music type and the course of treatment).
- 19 5. Outcomes (SDS, HAMD, SAS or HAMA and safety).

20  
21 If there is any different opinion, the final decision will go to the third researcher (X-xF) to be  
22 made. If the required data are unavailable from literatures, one researcher (YZ) will send an e-mail  
23 to the corresponding author and ask for further information  
24  
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#### 26 27 Assessment of risk of bias

28 The Cochrane Collaboration's Risk of Bias tool[41] will be applied to evaluate the risk of bias of  
29 all included RCT studies by two authors (L-zW and YZ). The following domains will be assessed:  
30 sequence generation, allocation concealment, blinding of participants and personnel, blinding of  
31 outcome assessors, incomplete outcome data, selective reporting and other sources of bias. The  
32 assessments will be classified into "low", "unclear" or "high" of risk.  
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#### 35 36 Data analysis

37 RevMan 5.3. software provided by the Cochrane collaboration will be used to analyze the data.  
38 Considering that all outcomes (depression score, anxiety score and safety) are continuous variables,  
39 the weighted mean difference (WMD) and 95% confidence interval (CI) will be calculated when  
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the quantitative data are from the same measurement method or small data scale. On the contrary, the standardized mean difference (SMD) and 95% CI will be calculated.

A meta-analysis will be implemented if the included studies are adequately homogenous. *P*-value and *I*<sup>2</sup> will be used to assess the heterogeneity of statistic. When *P*-value >0.05 and *I*<sup>2</sup> ≤50%, the fixed-effects model will be used for statistical combination. When *P*-value <0.05 or *I*<sup>2</sup> >50%, subgroup analyses or sensitivity analyses will be performed. If a meta-analysis is unavailable, descriptive summaries will be provided.

#### Assessment of reporting bias

Publication bias will be implemented, if there are more than 10 studies included, through a funnel plot.

#### Patient and public involvement

Patients and public involvement will fail to be included in this study.

#### Evidence assessed

GRADE guideline will be used to evaluate the quality of evidence.[42] To fulfil transparency and simplification, the quality of evidence can be assessed by 4 levels: “high”, “medium”, “low” and “very low”. GRADE profiler 3.2 will be applied for analysis.

## DISCUSSION

Depression and anxiety often occur independently or simultaneously during the development of many chronic diseases. In recent years, the number of studies about comorbid depression or anxiety in diabetics are continually increasing, not only because the two-way relationship between depression/anxiety and diabetes can lead to deterioration of diseases, increased difficulty in treatment, even as well as the terrible mortality,[43-46] but also because therapeutic methods for treating the comorbidities is limited and unsatisfactory. On the one hand, some antidepressant drugs,

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4 such as nortriptyline and sertraline, may complicate glycemic control.[47] On the other hand,  
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6 psychotherapy requires a professional psychiatrist and it is expensive.

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8 Music intervention has been proved by many literatures to have a beneficial effect on depression  
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10 and anxiety, such as strengthening awareness and sensitiveness for positive emotions.[48]  
11 Noticeably, a few studies also show that music intervention can reduce blood glucose and HbA1c  
12 simultaneously.[20,49] Therefore, music intervention is an applicable method for treating  
13 depression and anxiety with diabetes. Additionally, music intervention, almost no side effects, is  
14 safer than pharmacotherapy, easier to be operated and costs less than psychotherapy, so it is  
15 conducive to clinical promotion and application.

16  
17 Since 2007,[50] music intervention has been applied in the treatment of depression and anxiety  
18 with diabetes for 12 years. Nonetheless, no any systematic review or meta-analysis were conducted  
19 to evaluate the potential benefits and harms of this therapy method. Thus, this study intends to  
20 provide strong evidence for music intervention applied to treat mental disorders in diabetic patients  
21 and synchronously furnish evidence reference for related guideline.

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23 However, a language bias may exist in this meta-analysis because it will include studies only in  
24 English and Chinese because of the language barrier. Therefore, some related studies from medical  
25 databases in other languages might be missed.

26  
27 In conclusion, this meta-analysis will be conducive to assess underlying benefits and harms of  
28 music intervention on comorbid depression or anxiety with diabetes. Moreover, the results of this  
29 study might not merely furnish reference basis for related guideline, but also may attract more  
30 attention on music intervention, which can be a chance to facilitate its clinical application and  
31 ultimately benefit more patients.

## 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 **ETHICS AND DISSEMINATION**

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50 There is no required ethical approval because this is a protocol for meta-analysis. The results of  
51 this study will be published to a peer reviewed journal.  
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**Contributions** L-yZ and C-gX contributed to the conception of the study. The manuscript of the protocol was drafted by L-yZ, and was revised by XxF and C-gX. L-yZ and YT will also independently screen the potential studies and extract data from included studies. L-zW and YZ will assess the risk of bias and accomplish data synthesis. XxF will arbitrate any disagreements. C-gX will ensure that no errors occur during the review. All authors have approved the publication of the protocol.

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**Competing interests** None.

**Patient consent for publication** Not required.

**Provenance and peer review** Not commissioned; externally peer reviewed.

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## References

1. International Diabetes Federation. IDF Diabetes Atlas (9<sup>th</sup> edition), 2019. Available: <http://www.diabetesatlas.org/>. Accessed November 9, 2019
2. World Health Organization. Global report on diabetes, 2014. Available: <https://www.who.int/news-room/fact-sheets/detail/diabetes>. Accessed November 9, 2019
3. Ali S, Stone MA, Peters JL, et al. The prevalence of co-morbid depression in adults with Type 2 diabetes: a systematic review and meta-analysis. *Diabet Med* 2006;23(11):1165–1173. doi:10.1111/j.1464-5491.2006.01943.x

4. Anderson RJ, Freedland KE, Clouse RE, et al. The prevalence of comorbid depression in adults with diabetes: a meta-analysis. *Diabetes Care* 2001;24(6):1069–1078.  
doi:10.2337/diacare.24.6.1069
5. Knol MJ, Twisk JW, Beekman AT, et al. Depression as a risk factor for the onset of type 2 diabetes mellitus. A meta-analysis. *Diabetologia* 2006;49(5):837–845.doi:10.1007/s00125-006-0159-x
6. Cosgrove MP, Sargeant LA, Griffin SJ. Does depression increase the risk of developing type 2 diabetes?. *Occup Med (Lond)* 2008;58(1):7–14.doi:10.1093/occmed/kqm105
7. Mezuk B, Eaton WW, Albrecht S, et al. Depression and type 2 diabetes over the lifespan: a meta-analysis. *Diabetes Care* 2008;31(12):2383–2390.doi:10.2337/dc08-0985
8. Grigsby AB, Anderson RJ, Freedland KE, et al. Prevalence of anxiety in adults with diabetes: a systematic review. *J Psychosom Res* 2002; 53: 1053–1060.doi:10.1016/s0022-3999(02)00417-8
9. Smith KJ, Beland M, Clyde M, et al. Association of diabetes with anxiety: a systematic review and metaanalysis. *J Psychosom Res* 2013; 74: 89–99.  
doi:10.1016/j.jpsychores.2012.11.013
10. Smith KJ, Deschênes SS, Schmitz N. Investigating the longitudinal association between diabetes and anxiety: a systematic review and meta-analysis. *Diabet Med* 2018;35(6):677–693.doi:10.1111/dme.13606
11. Egede LE. Major depression in individuals with chronic medical disorders: prevalence, correlates and association with health resource utilization, lost productivity and functional disability. *Gen Hosp Psychiatry* 2007;29:409–416.doi:10.1016/j.genhosppsy.2007.06.002
12. Naicker K, Johnson JA, Skogen JC, et al. Type 2 Diabetes and Comorbid Symptoms of Depression and Anxiety: Longitudinal Associations With Mortality Risk. *Diabetes Care* 2017;40(3):352–358.doi:10.2337/dc16-2018
13. van der Feltz-Cornelis CM, Nuyen J, Stoop C, et al. Effect of interventions for major depressive disorder and significant depressive symptoms in patients with diabetes



- mellitus: a systematic review and meta-analysis. *Gen Hosp Psychiatry* 2010;32(4):380–395.  
doi:10.1016/j.genhosppsy.2010.03.011
14. Komsuoglu Celikyurt I, Mutlu O, Ulak G, et al. Exenatide treatment exerts anxiolytic- and antidepressant-like effects and reverses neuropathy in a mouse model of type-2 diabetes. *Med Sci Monit Basic Res* 2014;20:112–117.doi:10.12659/MSMBR.891168
15. Leubner D, Hinterberger T. Reviewing the Effectiveness of Music Interventions in Treating Depression. *Front Psychol* 2017;8:1109.doi:10.3389/fpsyg.2017.01109
16. Thaut MH, Gardiner JC, Holmberg D, et al. Neurologic music therapy improves executive function and emotional adjustment in traumatic brain injury rehabilitation. *Ann N Y Acad Sci* 2009;1169:406–416.doi:10.1111/j.1749-6632.2009.04585.x
17. Kim DS, Park YG, Choi JH, et al. Effects of music therapy on mood in stroke patients. *Yonsei Med J* 2011;52(6):977–981.doi:10.3349/ymj.2011.52.6.977
18. Nwebube C, Glover V, Stewart L. Prenatal listening to songs composed for pregnancy and symptoms of anxiety and depression: a pilot study. *BMC Complement Altern Med* 2017;17(1):256.doi:10.1186/s12906-017-1759-3
19. Lin XX, Ji JM, Zhou GY. Influence of listening to Jiao tune music on sleep quality and blood glucose in the elderly patients with type 2 diabetes accompanied by insomnia. *Journal of rehabilitation* 2017;27(01):44-48.
20. Mandel SE, Davis BA, Secic M. Effects of music therapy and music-assisted relaxation and imagery on health-related outcomes in diabetes education: a feasibility study. *Diabetes Educ* 2013;39(4):568–581.doi:10.1177/0145721713492216
21. Centers for Disease Control and Prevention. National Diabetes Statistics Report, 2014.  
Available: <https://www.cdc.gov/diabetes/pdfs/data/2014-report-estimates-of-diabetes-and-its-burden-in-the-united-states.pdf>. Accessed November 9, 2019
22. Gabrielsson A, Wik SL. Strong experiences related to music: a descriptive system. *Music Sci* 2003;7(2):157–217.
23. Zentner M, Grandjean D, Scherer KR. Emotions evoked by the sound of music:

- 1  
2  
3  
4 characterization, classification, and measurement. *Emotion* 2008;8(4):494–521.  
5  
6 doi:10.1037/1528-3542.8.4.494  
7  
8 24. Saarikallio S. Music as emotional self-regulation throughout adulthood. *Psychol Music*  
9  
10 2011;39(3):307–327.  
11  
12 25. Gök Ugur H, Yaman Aktaş Y, Orak OS, et al. The effect of music therapy on depression and  
13  
14 physiological parameters in elderly people living in a Turkish nursing home: a randomized-  
15  
16 controlled trial. *Aging Ment Health* 2017;21(12):1280–1286.  
17  
18 doi:10.1080/13607863.2016.1222348  
19  
20 26. Guétin S, Portet F, Picot MC, et al. Effect of music therapy on anxiety and depression in  
21  
22 patients with Alzheimer's type dementia: randomised, controlled study. *Dement Geriatr Cogn*  
23  
24 *Disord* 2009;28(1):36–46. doi:10.1159/000229024  
25  
26 27. Cheung DSK, Lai CKY, Wong FKY, et al. The effects of the music-with-movement  
27  
28 intervention on the cognitive functions of people with moderate dementia: a randomized  
29  
30 controlled trial. *Aging Ment Health* 2018;22(3):306–315.  
31  
32 doi:10.1080/13607863.2016.1251571  
33  
34 28. Wang SC, Yu CL, Chang SH. Effect of music care on depression and behavioral problems in  
35  
36 elderly people with dementia in Taiwan: a quasi-experimental, longitudinal study. *Aging*  
37  
38 *Ment Health* 2017;21(2):156–162. doi:10.1080/13607863.2015.1093602  
39  
40 29. Ashida S. The effect of reminiscence music therapy sessions on changes in depressive  
41  
42 symptoms in elderly persons with dementia. *J Music Ther* 2000;37(3):170–182.  
43  
44 doi:10.1093/jmt/37.3.170  
45  
46 30. Giovagnoli AR, Manfredi V, Parente A, et al. Cognitive training in Alzheimer's disease: a  
47  
48 controlled randomized study. *Neurol Sci* 2017;38(8):1485–1493. doi:10.1007/s10072-017-  
49  
50 3003-9  
51  
52 31. Deng HX, Gao GS, Li ZM, et al. Application of receiving music therapy in elderly patients  
53  
54 with diabetes. *Chinese journal of health and nutrition (1st Ten-days of month)*  
55  
56 2013;23(3):1186-1186.

- 1  
2  
3  
4 32. Zhang ZW. Application of music therapy and psychotherapy adjuvant therapy in type 2  
5 diabetes. *Chinese medical science* 2011,01(18):150-151.  
6  
7  
8 33. Solanki MS, Zafar M, Rastogi R. Music as a therapy: role in psychiatry. *Asian J Psychiatr*  
9 2013;6(3):193–199.doi:10.1016/j.ajp.2012.12.001  
10  
11 34. Petrovsky D, Cacchione PZ, George M. Review of the effect of music interventions on  
12 symptoms of anxiety and depression in older adults with mild dementia. *Int Psychogeriatr*  
13 2015;27(10):1661–1670.doi:10.1017/S1041610215000393  
14  
15 35. Aalbers S, Fusar-Poli L, Freeman RE, et al. Music therapy for depression. *Cochrane*  
16 *Database Syst Rev* 2017;11(11):CD004517. Published 2017 Nov 16.  
17 doi:10.1002/14651858.CD004517.pub3  
18  
19 36. Shamseer L, Moher D, Clarke M, et al. Preferred reporting items for systematic review and  
20 meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. *BMJ*  
21 2015;350:g7647.doi:10.1136/bmj.g7647  
22  
23 37. American Diabetes Association. 9. Pharmacologic Approaches to Glycemic Treatment:  
24 Standards of Medical Care in Diabetes-2019. *Diabetes Care* 2019;42(Suppl 1):S90–S102.  
25 doi:10.2337/dc19-S009  
26  
27 38. American Diabetes Association. 5. Lifestyle Management: Standards of Medical Care in  
28 Diabetes-2019. *Diabetes Care* 2019;42(Suppl 1):S46–S60.doi:10.2337/dc19-S005  
29  
30 39. Feng Y, Fang Y, Wang Y, et al. Acupoint Therapy on Diabetes Mellitus and Its Common  
31 Chronic Complications: A Review of Its Mechanisms. *Biomed Res Int* 2018;2018:3128378.  
32 doi:10.1155/2018/3128378  
33  
34 40. Pérez-Pevida B, Escalada J, Miras AD, et al. Mechanisms Underlying Type 2 Diabetes  
35 Remission After Metabolic Surgery. *Front Endocrinol (Lausanne)* 2019;10:641.  
36 doi:10.3389/fendo.2019.00641  
37  
38 41. Higgins JPT, Green S. Cochrane Handbook for systematic reviews of interventions version  
39 5.1.0 (updated March 2011). The Cochrane collaboration, 2011. Available:  
40 <http://www.handbook.cochrane.org/>  
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4 42. Balshem H, Helfand M, Schunemann HJ, et al. GRADE guidelines: 3. Rating the quality of  
5 evidence. *J Clin Epidemiol* 2011;64:401–406.doi:10.1016/j.jclinepi.2010.07.015  
6  
7  
8 43. Gonzalez JS, Peyrot M, McCarl LA, et al. Depression and diabetes treatment nonadherence: a  
9 meta-analysis. *Diabetes Care* 2008;31(12):2398–2403.doi:10.2337/dc08-1341  
10  
11  
12 44. Trief PM, Foster NC, Chaytor N, et al. Longitudinal Changes in Depression Symptoms and  
13 Glycemia in Adults With Type 1 Diabetes. *Diabetes Care* 2019;42(7):1194–1201.  
14  
15 doi:10.2337/dc18-2441  
16  
17 45. Novak M, Mucsi I, Rhee CM, et al. Increased Risk of Incident Chronic Kidney Disease,  
18 Cardiovascular Disease, and Mortality in Patients With Diabetes With Comorbid Depression.  
19  
20  
21  
22  
23  
24 46. Lustman PJ, Anderson RJ, Freedland KE, et al. Depression and poor glycemic control: a  
25 meta-analytic review of the literature. *Diabetes Care* 2000;23(7):934–942.  
26  
27  
28  
29  
30  
31  
32  
33  
34 47. Roopan S, Larsen ER. Use of antidepressants in patients with depression and comorbid  
35 diabetes mellitus: a systematic review. *Acta Neuropsychiatr* 2017;29(3):127–139.  
36  
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44 48. Croom AM. Music, neuroscience, and the psychology of well-being: a précis. *Front Psychol*  
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49. Abd-Elshafy SK, Khalaf GS, Abo-Kerisha MZ, et al. Not All Sounds Have Negative Effects  
on Children Undergoing Cardiac Surgery. *J Cardiothorac Vasc Anesth* 2015;29(5):1277–  
1284.doi:10.1053/j.jvca.2015.01.005
50. Yu SJ, Sun ZY, Zhou J, et al. Exploration of music behavioral intervention in the treatment of  
diabetes mellitus. *Hebei med* 2007;13(8):903-906.

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**Identification**

**Screening**

**Eligibility**

**Included**

Records identified through Searching (n=?)  
 Wanfang (n=?)      CNKI (n=?)  
 CBM (n=?)          VIP (n=?)  
 EMBASE (n=?)      ChiCTR (n=?)  
 PubMed (n=?)      Cochrane Library (n=?)  
 ClinicalTrials.gov (n=?)

Records identified through other sources (n=?)

Duplicate records excluded (n=?)

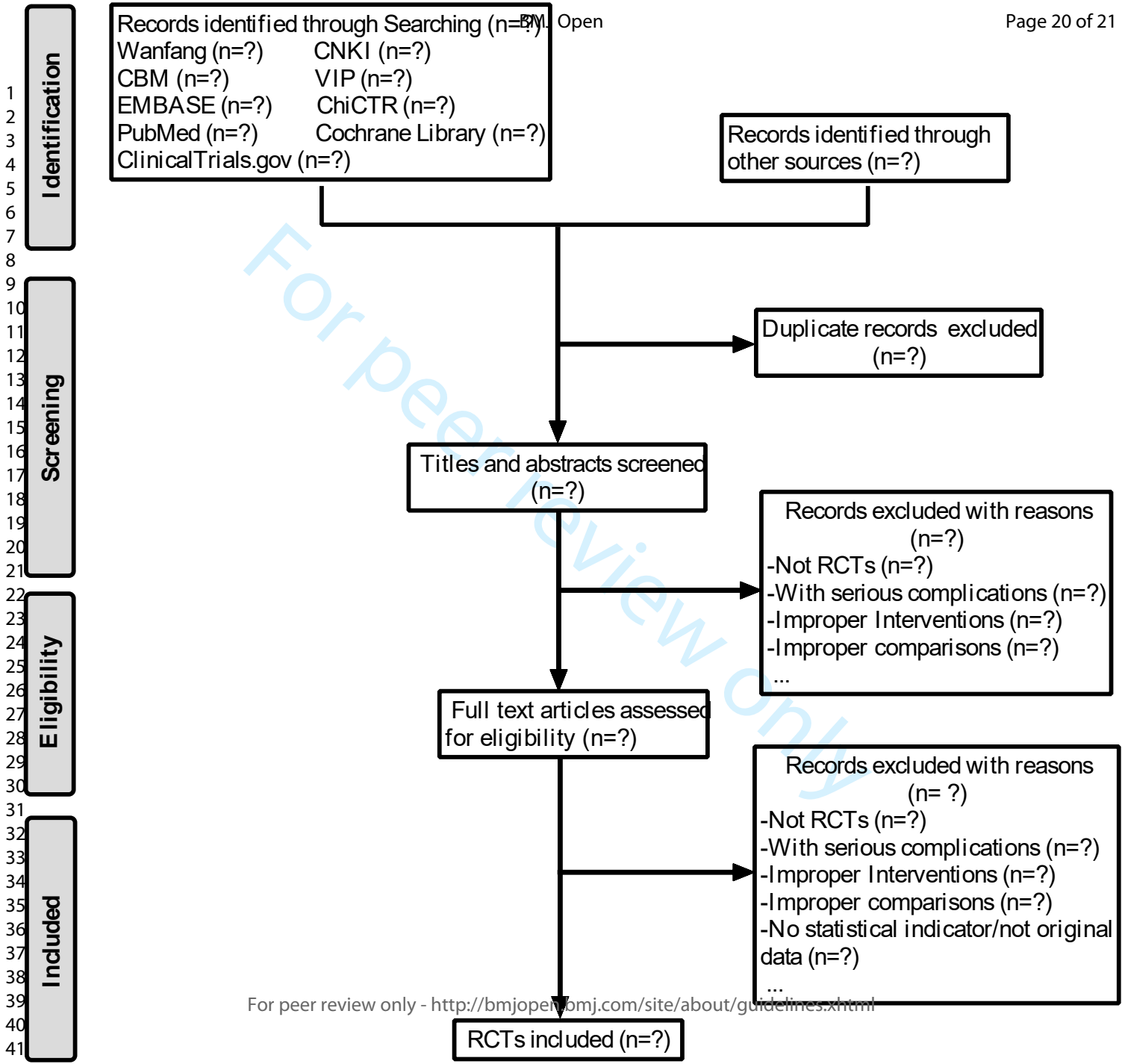
Titles and abstracts screened (n=?)

Records excluded with reasons (n=?)  
 -Not RCTs (n=?)  
 -With serious complications (n=?)  
 -Improper Interventions (n=?)  
 -Improper comparisons (n=?)  
 ...

Full text articles assessed for eligibility (n=?)

Records excluded with reasons (n=?)  
 -Not RCTs (n=?)  
 -With serious complications (n=?)  
 -Improper Interventions (n=?)  
 -Improper comparisons (n=?)  
 -No statistical indicator/not original data (n=?)  
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RCTs included (n=?)



## PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol\*

Section and topic	Item No	Checklist item
<b>ADMINISTRATIVE INFORMATION</b>		
Title:		
Identification <b>P<sub>1</sub></b>	1a	Identify the report as a protocol of a systematic review
Update <b>None</b>	1b	If the protocol is for an update of a previous systematic review, identify as such
Registration <b>P<sub>2</sub></b>	2	If registered, provide the name of the registry (such as PROSPERO) and registration number
Authors:		
Contact <b>P<sub>1</sub></b>	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author
Contributions <b>P<sub>11</sub></b>	3b	Describe contributions of protocol authors and identify the guarantor of the review
Amendments <b>None</b>	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments
Support:		
Sources <b>P<sub>12</sub></b>	5a	Indicate sources of financial or other support for the review
Sponsor <b>None</b>	5b	Provide name for the review funder and/or sponsor
Role of sponsor or funder <b>None</b>	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol
<b>INTRODUCTION</b>		
Rationale <b>P<sub>4-5</sub></b>	6	Describe the rationale for the review in the context of what is already known
Objectives <b>P<sub>6-7</sub></b>	7	Provide an explicit statement of the question(s) the review will address with reference to participants <b>P<sub>6</sub></b> , interventions <b>P<sub>7</sub></b> , comparators <b>P<sub>7</sub></b> , and outcomes <b>P<sub>7</sub></b> (PICO)
<b>METHODS</b>		
Eligibility criteria <b>P<sub>5</sub></b>	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review
Information sources <b>P<sub>6</sub>, P<sub>7</sub>, P<sub>9</sub></b>	9	Describe all intended information sources (such as electronic databases <b>P<sub>7</sub></b> , contact with study authors <b>P<sub>9</sub></b> , trial registers <b>P<sub>6</sub></b> or other grey literature sources <b>P<sub>7</sub></b> ) with planned dates of coverage <b>P<sub>7</sub></b>
Search strategy <b>P<sub>8</sub></b>	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated
Study records:		

Data management <b>P<sub>9</sub></b>	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review
Selection process <b>P<sub>8-9</sub></b>	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)
Data collection process <b>P<sub>9</sub></b>	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators
Data items <b>P<sub>9</sub></b>	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications
Outcomes and prioritization <b>P<sub>7</sub></b>	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale
Risk of bias in individual studies <b>P<sub>9</sub></b>	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis
Data synthesis <b>P<sub>9-10</sub></b>	15a	Describe criteria under which study data will be quantitatively synthesised <b>P<sub>9-10</sub></b>
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as $I^2$ , Kendall's $\tau$ ) <b>P<sub>9-10</sub></b>
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression) <b>P<sub>10</sub></b>
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned <b>P<sub>10</sub></b>
Meta-bias(es) <b>P<sub>10</sub></b>	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)
Confidence in cumulative evidence <b>P<sub>10</sub></b>	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)

**\* It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

*From: Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart L, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015 Jan 2;349(jan02 1):g7647.*



# BMJ Open

## Effect of music intervention on mental health in patients with diabetes mellitus: a protocol for a systematic review and meta-analysis of randomized controlled trials

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<b>Primary Subject Heading</b>:	Diabetes and endocrinology
Secondary Subject Heading:	Mental health, Complementary medicine
Keywords:	DIABETES & ENDOCRINOLOGY, MENTAL HEALTH, COMPLEMENTARY MEDICINE

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# Effect of music intervention on mental health in patients with diabetes mellitus: a protocol for a systematic review and meta-analysis of randomized controlled trials

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**Word count:**2745 words (excluding title page, abstract, references, figures and tables)

## ABSTRACT

**Introduction** About 463 million adults aged 20 to 79 have diabetes globally and mental disorders often exist in diabetic patients as comorbidities. The comorbidities can lead to deterioration of diseases, increased difficulty in treatment, even as well as the great mortality. Music intervention has been applied in the treatment of the comorbidities for 12 years, but there are not recommendations due to lacking of evidence. Thus, a meta-analysis is necessary to be conducted to evaluate the effect of music intervention.

**Methods and analysis** We will search the following nine online electronic databases: PubMed, Web of Science, Embase, EBSCO, Cochrane Library, Chinese National Knowledge Infrastructure (CNKI), Wanfang Database, Chinese Scientific Journal Database (VIP) and Chinese Biomedical and Medical Database (CBM), from their inception until the present. We also plan to search other relevant resources, including grey literatures and the reference lists of relevant publications. Only randomized controlled trials (RCTs) of music intervention for depression or anxiety with diabetes will be involved. The primary outcomes include depression score and anxiety score measured by scales, and the secondary outcome is safety. Data extraction will be implemented by two researchers independently. Risk of bias will be evaluated through Cochrane Collaboration's Risk of Bias tool. Eventually, all the data will be analyzed via the software Review Manager V.5.3.

**Ethics and dissemination** This meta-analysis will provide information about music intervention applied to treat depression or anxiety in diabetic patients. There is no required ethical approval because this is a protocol for meta-analysis. The results of this study will be published to a peer reviewed journal.

**Trial registration number** CRD42019146439

### Strengths and limitations of this study

· This meta-analysis will provide evidence of the effectiveness and safety of music intervention applied to treat depression or anxiety in diabetic patients for the first time.

· This systematic review will furnish evidence reference for guideline of relevant areas.

· This meta-analysis will be implemented on the basis of rigorous international gold-standard methodology and integrated search strategy.

· A language bias may exist in this meta-analysis because it will include studies only in English and Chinese on account of the language barrier.

## INTRODUCTION

### Description of the condition

According to the newest “IDF Diabetes Atlas (9<sup>th</sup> edition)” published by International Diabetes Federation (IDF), about 463 million adults aged 20 to 79 have diabetes globally (1 in 11).[1] It is well known that diabetes has a significant influence on life quality because it can cause a lot of complications such as retinopathy, renal disease, cardiovascular disease, neurological disease and foot ulcers which may result in lower extremity amputation.[2]

In addition to physical complications, some mental disorders often exist in diabetic patients as comorbidities. Some studies have indicated that depression is more prevalent in diabetic patients compared to those without this disease.[3,4] At the same time, depression could also increase the risk of incidence of diabetes,[5-7] which suggests that depression has a bidirectional association with diabetes. And the relation between anxiety and diabetes has been confirmed to be the same. People with diabetes are more susceptible to concurrent anxiety[8,9] while reversely anxiety is a risk factor of diabetic incidents.[10] Individuals with chronic diseases and also comorbid depression or anxiety have obviously higher health-care utilization, functional disability, work absence and mortality risk than those without them.[11,12]

### Description of the intervention

When it comes to the treatment of diabetes with depression or anxiety, conventional glucose-lowering treatment combined with drug therapy or psychological intervention are the routine treatments.[13,14] Music intervention is also a successful therapy using music for treatment by professionals, which can be divided into two major categories, namely music therapy and music medicine.[15] The official definition of music therapy is the “...clinical and evidence-based use of music interventions to accomplish individualized goals within a therapeutic relationship by a credentialed professional who has completed an approved music therapy program”.[16] A trained music therapist leads the treatment process, choosing the type of music, the form of music presentation (pre-recorded or live), and the treatment setting (singing, playing instruments,

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4 composing, etc.) based on the patient's condition, ultimately resulting in a therapeutic scheme that  
5 is best for the patient. By comparison, music medicine is defined as the passive listening to pre-  
6 recorded music, which can be implemented independently by medical or healthcare professionals  
7 instead of music therapists.[17] In brief, music therapy focuses on active music therapy and  
8 personalized treatments while music medicine belongs to passive music listening and non-  
9 personalized therapy. It is significant to emphasize the distinction between music therapy and music  
10 medicine because some literatures suggest that the effect of the former is better than the latter in a  
11 great many outcomes.[18-19]

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A lot of studies have suggested that music, no matter what type of it is, demonstrates a remarkable  
effect in alleviating depression and anxiety among patients with various diseases.[20-22] As for  
diabetes, recent studies have showed that music intervention could improve fasting blood-glucose  
and systolic blood pressure in diabetic patients.[23,24] Good control of blood glucose, blood lipids  
and blood pressure can effectively reduce the incidence of serious complications of diabetes.[25]

### **How the intervention might work**

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Researches about music psychology have shown the special potential of music. Music, as a stimulus,  
can not only trigger a variety of emotional experiences,[26, 27] but also strengthen ability to deal  
with negative emotions in everyday life.[28] The proposed mechanisms of music intervention on  
depression and anxiety span several domains. Firstly, music intervention can exert  
neurophysiological and neurochemical effects, such as triggering endorphin release[29] and  
stimulating cognitive functioning.[30] Secondly, music intervention can promote positive self-  
emotions including enhancing the sense of happiness[31] and activating self-efficacy and self-  
confidence through experiences of success.[32] Lastly, music intervention can build up sociability,  
such as interaction skills[33] and interpersonal relationship.[34] Furthermore, there are published  
studies indicating that music intervention combined with diabetic routine treatments could improve  
depression score, anxiety score, fasting glucose and glycosylated hemoglobin (HbA1c).[35,36]

### **Why it is important to do this review**

From the above, many studies have indicated the bidirectional relationship between diabetes and mental disorders. Music intervention, as a therapeutic method, has been applied to alleviate depression and anxiety and improve related indicators of diabetes. By searching literatures, it can be found that some reviews evaluated the effect of music intervention on patients with mental disorders,[37-39] while no related systematic review and meta-analysis can be searched about the effect of music intervention on mental health of patients with diabetes. Therefore, if music intervention can be proved to be both valid and with few side effects through this study, it is worth being promoted and applicated in clinic all over the world to benefit more people since this method is easy to be operated.

### **Objectives**

The purpose of this review is to systematically assess the effect of music intervention and compare the effects between music therapy and music medicine on depression and anxiety of diabetic patients. Additionally, it is also our expectation to furnish evidence reference for related guideline.

## **METHODS**

### **Study registration**

The protocol of the meta-analysis has been registered in International Prospective Register of Systematic Reviews (PROSPERO), and CRD42019146439 is the registration ID. This protocol has been planned severely on the basis of Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols (PRISMA-P)[40] statement guidelines. The results will be reported in conformity to the PRISMA Statement for Reporting Systematic Reviews and Meta-Analyses of Studies That Evaluate Healthcare Interventions.[41]

### **Eligibility criteria**

We will severely screen studies that have compliance with following inclusion criteria.



### Type of studies

We will only cover randomized controlled trials (RCTs) in English or Chinese, excepting Quasi-RCTs and cluster RCTs. Experiments on animals and nonrandomized clinical trials will be out of our consideration. Articles with significant overlap with other articles through print or e-publishing will fail to be included. Duplicate publications, that is results originated from a single experiment but measured by other standards and then published as disparate papers, will also be excluded. Publications with originality is our first choice. The publication status will not be restricted.

### Type of Participants

Diabetic Patients with depression or anxiety symptoms, regardless of the type of diabetes and no restriction on gender, age, race, economic ability and education level. Patients of other disease or healthy persons will be excluded.

### Type of interventions and controls

Interventions include music intervention (music therapy or music medicine) alone or music intervention in combination with other interventions. No restriction on the type of music. Other interventions refer to: (1) routine treatments for diabetes which mainly include pharmacologic approaches to glycemetic treatment, diabetes self-management education and support (DSMES),, etc. according to the newest guideline of American Diabetes Association (ADA);[42,43] (2) other therapies such as acupoint therapy,[44] metabolic surgery,[45] etc. When intervention is music intervention alone, controls can be no treatment, placebo or other active therapies. Notably, when intervention is music intervention combined with active therapies, the control must be the same active therapies.

### Type of outcome measures

This review aims at systematically assessing the effect of music intervention on depression or

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4 anxiety of diabetic patients, so we choose depression score and anxiety score as the primary  
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6 outcomes, which can give an index to the degree of depression and anxiety by scales.

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8 Primary outcomes: Depression score and anxiety score. Depression score is measured using self-  
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10 rating depression scale (SDS), Hamilton depression scale (HAMD) or other validated scales for  
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12 depression. Anxiety score is measured using self-rating anxiety scale (SAS), Hamilton anxiety  
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14 scale (HAMA) or other validated scales for anxiety.

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16 Secondary outcomes: Safety. Measurement via incidence of adverse effects.  
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## 19 20 **Search methods**

### 21 22 Search resources

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24 We will search the following nine online electronic databases: PubMed, Web of Science, Embase,  
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26 EBSCO, Cochrane Library, Chinese National Knowledge Infrastructure (CNKI), Wanfang  
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28 Database, Chinese Scientific Journal Database (VIP) and Chinese Biomedical and Medical  
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30 Database (CBM), from their inception to the present. We also plan to search other relevant  
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32 resources as far as possible, including: (1) grey literatures (like conference literatures and  
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34 dissertations) from the following four sources: OpenGrey ([www.opengrey.eu/](http://www.opengrey.eu/)), CNKI  
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36 ([www.cnki.net](http://www.cnki.net)), Open Access Theses and Dissertations ([oatd.org](http://oatd.org)) and British Library EThOS  
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38 ([ethos.bl.uk/](http://ethos.bl.uk/)); (2) the reference lists of relevant publications for additional studies.  
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### 41 42 Search strategies

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44 The search strategy will include the MeSH terms for diabetes mellitus, depression, anxiety, music  
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46 therapy, music and singing, combined with their respective free-text terms. The search details of  
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48 the PubMed are simply shown in table 1.  
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**Table 1 Example of PubMed search strategy.**

Number	Search terms
#1	"Diabetes Mellitus"[Mesh]
#2	"Depression"[Mesh] OR Depressions[Title/Abstract] OR Depressive Symptoms[Title/Abstract] OR Depressive Symptom[Title/Abstract] OR Symptom, Depressive[Title/Abstract] OR Symptoms, Depressive[Title/Abstract] OR Emotional Depression[Title/Abstract] OR Depression, Emotional[Title/Abstract] OR Depressions, Emotional[Title/Abstract] OR Emotional Depressions[Title/Abstract]
#3	"Anxiety"[Mesh] OR Hypervigilance [Title/Abstract] OR Nervousness [Title/Abstract]
#4	#2 OR #3
#5	"Music Therapy"[Mesh] OR Therapy, Music [Title/Abstract]
#6	"Music"[Mesh] OR music intervention[Title/Abstract] OR music medicine[Title/Abstract] OR music listening[Title/Abstract] OR audio recording[Title/Abstract] OR mp3 hearing[Title/Abstract]
#7	"Singing"[Mesh] OR sing[Title/Abstract] OR sings[Title/Abstract] OR song[Title/Abstract] OR compose[Title/Abstract] OR composing[Title/Abstract]
#8	#5 OR #6 OR #7
#9	randomized controlled trial [Publication Type] OR randomized [Title/Abstract] OR placebo [Title/Abstract]
#10	#1 AND #4 AND #8AND #9

### Data collection and analysis

#### Studies selection

Firstly, two researchers (L-yZ and YT) will respectively screen the keywords, titles and abstracts of all obtained studies using endnote x9 software and determine whether trials have compliance with inclusion criteria. Secondly, we will also get access to the full text of all studies of possible relevance for further assessment. Each of excluded study will be noted with reasons. Any disagreements will be settled through consensus or referral to the third researcher (YZ). The

specific selection steps are presented in the figure 1.

#### Data extraction

Two researchers (L-yZ and YT) will independently extract and tabulate the following data items via Microsoft Excel:

1. General information (including publication year and name of the first author).
2. Study design (including random method, allocation concealment and blinding).
3. Participants (including sample size, gender, age, area, depression score, anxiety score and course of disease).
4. Treatment (including interventions, controls, music type and the course of treatment).
5. Outcomes (including depression score, anxiety score and safety).

If there is any different opinion, the final decision will go to the third researcher (X-xF) to be made.

#### Assessment of risk of bias

The Cochrane Collaboration's Risk of Bias tool[46] will be applied to evaluate the risk of bias of all included RCT studies by two authors (L-zW and YZ). The following domains will be assessed: sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessors, incomplete outcome data, selective reporting and other sources of bias. The assessments will be classified into "low", "unclear" or "high" of risk.

#### Measures of treatment effect

Considering that all outcomes (depression score, anxiety score and safety) are continuous variables, the mean difference (MD) and 95% confidence interval (CI) will be calculated when the quantitative data are from the same measurement method or small data scale. On the contrary, the standardized mean difference (SMD) and 95% CI will be calculated.

### Unit of analysis issues

For the standard research which has one experimental group with one control group, the unit of analysis is based on the individual. For the multi-arm study which has more than two intervention groups, the recommended method is to create a single pair-wise comparison through combining groups.

### Dealing with missing data

If the required data are unavailable from literatures, one researcher (YZ) will send an e-mail to the corresponding author and ask for further information.

### Assessment of heterogeneity

A meta-analysis will be implemented if the included studies are adequately homogenous. *P*-value and *I*<sup>2</sup> will be used to assess the heterogeneity of statistic. When *P*-value >0.05 and *I*<sup>2</sup> ≤50%, the heterogeneity is regarded as acceptable. When *P*-value <0.05 or *I*<sup>2</sup> >50%, the heterogeneity is considered as significant.

### Assessment of reporting bias

Publication bias will be implemented, if there are more than 10 studies included, through a funnel plot.

### Data synthesis

RevMan 5.3. software provided by the Cochrane collaboration will be used to analyze the data. If the included studies are adequately homogenous, fixed-effects model will be used for statistical combination. Since all outcomes are continuous variables, the mean difference (MD) and 95% confidence interval (CI) will be calculated when the outcomes are from the same measurement method or small data scale. On the contrary, the standardized mean difference (SMD) and 95% CI will be calculated. If there is significant heterogeneity among the included studies, subgroup

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4 analyses or sensitivity analyses will be performed. If a meta-analysis is unavailable, descriptive  
5 summaries will be provided.  
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#### 8 9 Subgroup analysis

10 The subgroup analyses are planned as follows:

- 11 1. Type of music intervention (music therapy or music medicine).
  - 12 2. Type of scales (SDS, HAMD, SAS, HAMA or other validated scales for depression or anxiety).
  - 13 3. Different age groups.
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#### 21 Sensitivity analysis

22 Sensitivity analyses will be performed through including or excluding a specific study, such as a  
23 study without a clear allocation concealment or randomization method, to observe whether the  
24 results changed.  
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#### 31 Patient and public involvement

32 Patients and public involvement will fail to be included in this study.  
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#### 37 Evidence assessed

38 GRADE guideline will be used to evaluate the quality of evidence.[47] To fulfil transparency and  
39 simplification, the quality of evidence can be assessed by 4 levels: “high”, “medium”, “low” and  
40 “very low”. GRADE profiler 3.2 will be applied for analysis.  
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## 46 **DISCUSSION**

47 Depression and anxiety often occur independently or simultaneously during the development of  
48 many chronic diseases. In recent years, the number of studies about comorbid depression or anxiety  
49 in diabetics are continually increasing, not only because the two-way relationship between  
50 depression/anxiety and diabetes can lead to deterioration of diseases, increased difficulty in  
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4 treatment, even as well as the great mortality,[48-51] but also because therapeutic methods for  
5 treating the comorbidities are limited and unsatisfactory. On the one hand, some antidepressant  
6 drugs, such as nortriptyline and sertraline, may complicate glycemic control.[52] On the other hand,  
7 psychotherapy based on verbal communication requires a professional psychiatrist and it is  
8 expensive.  
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13 Music intervention has been proved by many literatures to have a beneficial effect on depression  
14 and anxiety, such as strengthening awareness and sensitiveness for positive emotions.[53]  
15 Noticeably, a few studies also show that music intervention can reduce blood glucose and HbA1c  
16 simultaneously.[24,54] Therefore, music intervention is an applicable method for treating  
17 depression and anxiety with diabetes. Additionally, music intervention, almost no side effects, is  
18 safer than pharmacotherapy, easier to be operated and costs less than psychotherapy based on verbal  
19 communication, so it is conducive to clinical promotion and application.  
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27 Since 2007,[55] music intervention has been applied in the treatment of depression and anxiety  
28 with diabetes for 12 years. Nonetheless, there are not systematic review or meta-analysis conducted  
29 to evaluate the potential benefits and harms of this therapy method. Thus, this study intends to  
30 provide strong evidence for music intervention applied to treat mental disorders in diabetic patients  
31 and synchronously furnish evidence reference for related guideline.  
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37 However, a language bias may exist in this meta-analysis because it will include studies only in  
38 English and Chinese because of the language barrier. Therefore, some related studies from  
39 medical databases in other languages might be missed.  
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43 In conclusion, this meta-analysis will be conducive to assess underlying benefits and harms of  
44 music intervention on comorbid depression or anxiety with diabetes. Moreover, the results of this  
45 study might not merely furnish reference basis for related guideline, but also may attract more  
46 attention on music intervention, which can be a chance to facilitate its clinical application and  
47 ultimately benefit more patients.  
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## 54 **ETHICS AND DISSEMINATION**

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There is no required ethical approval because this is a protocol for meta-analysis. The results of this study will be published to a peer reviewed journal.

## Figure legend

**Figure 1** Flowchart to present the search process.

**Contributions** L-yZ and C-gX contributed to the conception of the study. The manuscript of the protocol was drafted by L-yZ, and was revised by XxF and C-gX. L-yZ and YT will also independently screen the potential studies and extract data from included studies. L-zW and YZ will assess the risk of bias and accomplish data synthesis. XxF will arbitrate any disagreements. C-gX will ensure that no errors occur during the review. All authors have approved the publication of the protocol.

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**Competing interests** None.

**Patient consent for publication** Not required.

**Provenance and peer review** Not commissioned; externally peer reviewed.

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## References

1. International Diabetes Federation. IDF Diabetes Atlas (9<sup>th</sup> edition), 2019. Available:



- 1  
2  
3  
4 <http://www.diabetesatlas.org/>. Accessed November 9, 2019
- 5  
6 2. World Health Organization. Global report on diabetes, 2014. Available:  
7 <https://www.who.int/news-room/fact-sheets/detail/diabetes>. Accessed November 9, 2019
- 8  
9  
10 3. Ali S, Stone MA, Peters JL, et al. The prevalence of co-morbid depression in adults with  
11 Type 2 diabetes: a systematic review and meta-analysis. *Diabet Med* 2006;23(11):1165–  
12 1173. doi:10.1111/j.1464-5491.2006.01943.x
- 13  
14  
15 4. Anderson RJ, Freedland KE, Clouse RE, et al. The prevalence of comorbid depression in  
16 adults with diabetes: a meta-analysis. *Diabetes Care* 2001;24(6):1069–1078.  
17 doi:10.2337/diacare.24.6.1069
- 18  
19  
20  
21 5. Knol MJ, Twisk JW, Beekman AT, et al. Depression as a risk factor for the onset of type 2  
22 diabetes mellitus. A meta-analysis. *Diabetologia* 2006;49(5):837–845. doi:10.1007/s00125-  
23 006-0159-x
- 24  
25  
26  
27 6. Cosgrove MP, Sargeant LA, Griffin SJ. Does depression increase the risk of developing type  
28 2 diabetes?. *Occup Med (Lond)* 2008;58(1):7–14. doi:10.1093/occmed/kqm105
- 29  
30  
31 7. Mezuk B, Eaton WW, Albrecht S, et al. Depression and type 2 diabetes over the lifespan: a  
32 meta-analysis. *Diabetes Care* 2008;31(12):2383–2390. doi:10.2337/dc08-0985
- 33  
34  
35 8. Grigsby AB, Anderson RJ, Freedland KE, et al. Prevalence of anxiety in adults with diabetes:  
36 a systematic review. *J Psychosom Res* 2002; 53: 1053–1060. doi:10.1016/s0022-  
37 3999(02)00417-8
- 38  
39  
40 9. Smith KJ, Beland M, Clyde M, et al. Association of diabetes with anxiety: a systematic  
41 review and metaanalysis. *J Psychosom Res* 2013; 74: 89–99.  
42 doi:10.1016/j.jpsychores.2012.11.013
- 43  
44  
45 10. Smith KJ, Deschênes SS, Schmitz N. Investigating the longitudinal association between  
46 diabetes and anxiety: a systematic review and meta-analysis. *Diabet Med* 2018;35(6):677–  
47 693. doi:10.1111/dme.13606
- 48  
49  
50  
51 11. Egede LE. Major depression in individuals with chronic medical disorders: prevalence,  
52 correlates and association with health resource utilization, lost productivity and functional  
53  
54  
55  
56

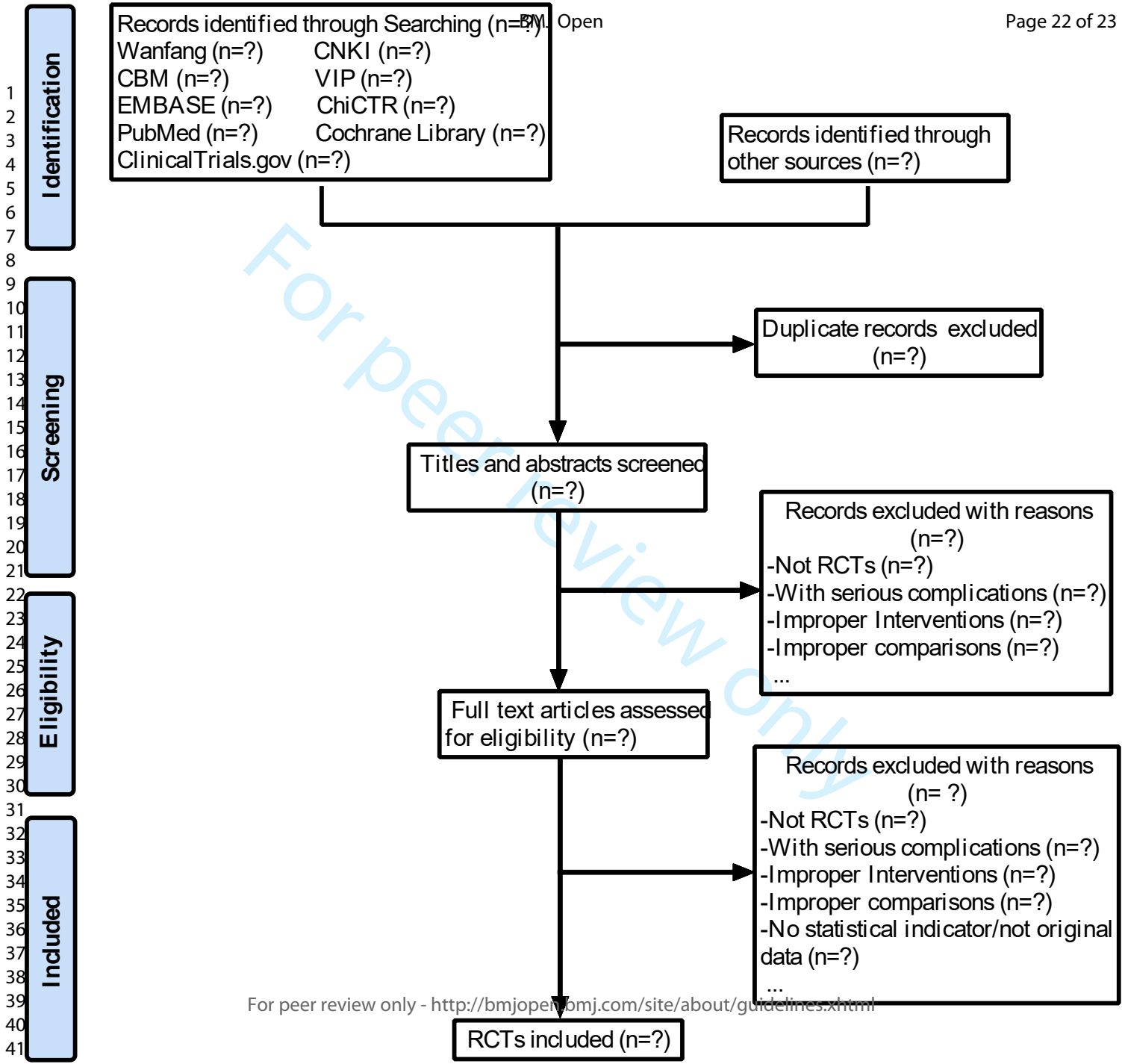
- 1  
2  
3  
4 disability. *Gen Hosp Psychiatry* 2007;29:409–416.doi:10.1016/j.genhosppsy.2007.06.002
- 5  
6 12. Naicker K, Johnson JA, Skogen JC, et al. Type 2 Diabetes and Comorbid Symptoms of  
7  
8 Depression and Anxiety: Longitudinal Associations With Mortality Risk. *Diabetes Care*  
9  
10 2017;40(3):352–358.doi:10.2337/dc16-2018
- 11  
12 13. van der Feltz-Cornelis CM, Nuyen J, Stoop C, et al. Effect of interventions for major  
13  
14 depressive disorder and significant depressive symptoms in patients with diabetes mellitus:  
15  
16 a systematic review and meta-analysis. *Gen Hosp Psychiatry* 2010;32(4):380–395.  
17  
18 doi:10.1016/j.genhosppsy.2010.03.011
- 19  
20 14. Komsuoglu Celikyurt I, Mutlu O, Ulak G, et al. Exenatide treatment exerts anxiolytic- and  
21  
22 antidepressant-like effects and reverses neuropathy in a mouse model of type-2 diabetes. *Med*  
23  
24 *Sci Monit Basic Res* 2014;20:112–117.doi:10.12659/MSMBR.891168
- 25  
26 15. Leubner D, Hinterberger T. Reviewing the Effectiveness of Music Interventions in Treating  
27  
28 Depression. *Front Psychol* 2017;8:1109.doi:10.3389/fpsyg.2017.01109
- 29  
30 16. American Music Therapy Association. What is music therapy?, 2013.Available:  
31  
32 <https://www.musictherapy.org/about/musictherapy/>. Accessed January 9, 2020.
- 33  
34 17. Dileo C. A classification model for music and medicine. National Association of Music  
35  
36 Therapy, Washington, DC, 1999: 1-6.
- 37  
38 18. Raglio A, Bellelli G, Mazzola P, et al. Music, music therapy and dementia: a review of  
39  
40 literature and the recommendations of the Italian Psychogeriatric Association. *Maturitas*  
41  
42 2012;72(4):305–310.doi:10.1016/j.maturitas.2012.05.016
- 43  
44 19. Dileo C. Effects of music and music therapy on medical patients: a meta-analysis of the  
45  
46 research and implications for the future. *J Soc Integr Oncol* 2006;4(2):67–70.  
47  
48 doi:10.2310/7200.2006.002
- 49  
50 20. Thaut MH, Gardiner JC, Holmberg D, et al. Neurologic music therapy improves executive  
51  
52 function and emotional adjustment in traumatic brain injury rehabilitation. *Ann N Y Acad Sci*  
53  
54 2009;1169:406–416.doi:10.1111/j.1749-6632.2009.04585.x
- 55  
56 21. Kim DS, Park YG, Choi JH, et al. Effects of music therapy on mood in stroke patients.

- 1  
2  
3  
4 *Yonsei Med J* 2011;52(6):977–981.doi:10.3349/ymj.2011.52.6.977
- 5  
6 22. Nwebube C, Glover V, Stewart L. Prenatal listening to songs composed for pregnancy and  
7 symptoms of anxiety and depression: a pilot study. *BMC Complement Altern Med*  
8 2017;17(1):256.doi:10.1186/s12906-017-1759-3
- 9  
10  
11 23. Lin XX, Ji JM, Zhou GY. Influence of listening to Jiao tune music on sleep quality and blood  
12 glucose in the elderly patients with type 2 diabetes accompanied by insomnia. *Journal of*  
13 *rehabilitation* 2017;27(01):44-48.
- 14  
15  
16 24. Mandel SE, Davis BA, Secic M. Effects of music therapy and music-assisted relaxation and  
17 imagery on health-related outcomes in diabetes education: a feasibility study. *Diabetes Educ*  
18 2013;39(4):568–581.doi:10.1177/0145721713492216
- 19  
20  
21 25. Centers for Disease Control and Prevention. National Diabetes Statistics Report, 2014.  
22 Available: [https://www.cdc.gov/diabetes/pdfs/data/2014-report-estimates-of-diabetes-and-its-](https://www.cdc.gov/diabetes/pdfs/data/2014-report-estimates-of-diabetes-and-its-burden-in-the-united-states.pdf)  
23 [burden-in-the-united-states.pdf](https://www.cdc.gov/diabetes/pdfs/data/2014-report-estimates-of-diabetes-and-its-burden-in-the-united-states.pdf). Accessed November 9, 2019
- 24  
25  
26 26. Gabrielsson A, Wik SL. Strong experiences related to music: a descriptive system. *Music Sci*  
27 2003;7(2):157–217.
- 28  
29  
30 27. Zentner M, Grandjean D, Scherer KR. Emotions evoked by the sound of music:  
31 characterization, classification, and measurement. *Emotion* 2008;8(4):494–521.  
32 doi:10.1037/1528-3542.8.4.494
- 33  
34  
35 28. Saarikallio S. Music as emotional self-regulation throughout adulthood. *Psychol Music*  
36 2011;39(3):307–327.
- 37  
38  
39 29. Gök Ugur H, Yaman Aktaş Y, Orak OS, et al. The effect of music therapy on depression and  
40 physiological parameters in elderly people living in a Turkish nursing home: a randomized-  
41 controlled trial. *Aging Ment Health* 2017;21(12):1280–1286.  
42 doi:10.1080/13607863.2016.1222348
- 43  
44  
45 30. Gómez Gallego M, Gómez García J. Music therapy and Alzheimer's disease: Cognitive,  
46 psychological, and behavioural effects. *Neurologia* 2017;32(5):300–308.  
47 doi:10.1016/j.nrl.2015.12.003
- 48  
49  
50  
51  
52  
53  
54  
55  
56

- 1  
2  
3  
4 31. Cheung DSK, Lai CKY, Wong FKY, et al. The effects of the music-with-movement  
5 intervention on the cognitive functions of people with moderate dementia: a randomized  
6 controlled trial. *Aging Ment Health* 2018;22(3):306–315.  
7  
8 doi:10.1080/13607863.2016.1251571  
9  
10  
11 32. Wang SC, Yu CL, Chang SH. Effect of music care on depression and behavioral problems in  
12 elderly people with dementia in Taiwan: a quasi-experimental, longitudinal study. *Aging*  
13 *Ment Health* 2017;21(2):156–162.doi:10.1080/13607863.2015.1093602  
14  
15  
16 33. Bieleninik L, Geretsegger M, Mössler K, et al. Effects of Improvisational Music Therapy vs  
17 Enhanced Standard Care on Symptom Severity Among Children With Autism Spectrum  
18 Disorder: The TIME-A Randomized Clinical Trial. *JAMA* 2017;318(6):525–535.  
19  
20  
21  
22  
23  
24  
25  
26 34. Giovagnoli AR, Manfredi V, Parente A, et al. Cognitive training in Alzheimer's disease: a  
27 controlled randomized study. *Neurol Sci* 2017;38(8):1485–1493.doi:10.1007/s10072-017-  
28 3003-9  
29  
30  
31 35. Deng HX, Gao GS, Li ZM, et al. Application of receiving music therapy in elderly patients  
32 with diabetes. *Chinese journal of health and nutrition (1st Ten-days of month)*  
33  
34  
35  
36 2013,23(3):1186-1186.  
37  
38 36. Zhang ZW. Application of music therapy and psychotherapy adjuvant therapy in type 2  
39 diabetes. *Chinese medical science* 2011,01(18):150-151.  
40  
41 37. Solanki MS, Zafar M, Rastogi R. Music as a therapy: role in psychiatry. *Asian J Psychiatr*  
42  
43  
44 2013;6(3):193–199.doi:10.1016/j.ajp.2012.12.001  
45  
46 38. Petrovsky D, Cacchione PZ, George M. Review of the effect of music interventions on  
47 symptoms of anxiety and depression in older adults with mild dementia. *Int Psychogeriatr*  
48  
49 2015;27(10):1661–1670.doi:10.1017/S1041610215000393  
50  
51 39. Aalbers S, Fusar-Poli L, Freeman RE, et al. Music therapy for depression. *Cochrane*  
52  
53  
54  
55  
56  
57  
58  
59  
60

- 1  
2  
3  
4 40. Shamseer L, Moher D, Clarke M, et al. Preferred reporting items for systematic review and  
5 meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. *BMJ*  
6 2015;350:g7647.doi:10.1136/bmj.g7647  
7  
8  
9  
10 41. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic  
11 reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and  
12 elaboration. *BMJ* 2009;339:b2700.doi:10.1136/bmj.b2700  
13  
14  
15 42. American Diabetes Association. 9. Pharmacologic Approaches to Glycemic Treatment:  
16 Standards of Medical Care in Diabetes-2020. *Diabetes Care* 2020;43(Suppl 1):S98–S110.  
17 doi:10.2337/dc20-S009  
18  
19  
20  
21 43. American Diabetes Association. 5. Facilitating Behavior Change and Well-being to Improve  
22 Health Outcomes: Standards of Medical Care in Diabetes-2020. *Diabetes Care*  
23 2020;43(Suppl 1):S48–S65. doi:10.2337/dc20-S005  
24  
25  
26  
27 44. Feng Y, Fang Y, Wang Y, et al. Acupoint Therapy on Diabetes Mellitus and Its Common  
28 Chronic Complications: A Review of Its Mechanisms. *Biomed Res Int* 2018;2018:3128378.  
29 doi:10.1155/2018/3128378  
30  
31  
32  
33 45. Pérez-Pevida B, Escalada J, Miras AD, et al. Mechanisms Underlying Type 2 Diabetes  
34 Remission After Metabolic Surgery. *Front Endocrinol (Lausanne)* 2019;10:641.  
35 doi:10.3389/fendo.2019.00641  
36  
37  
38  
39 46. Higgins JPT, Thomas J, Chandler J, et al. Cochrane Handbook for Systematic Reviews of  
40 Interventions version 6.0 (updated July 2019). Cochrane, 2019. Available:  
41 www.training.cochrane.org/handbook.  
42  
43  
44  
45 47. Balshem H, Helfand M, Schunemann HJ, et al. GRADE guidelines: 3. Rating the quality of  
46 evidence. *J Clin Epidemiol* 2011;64:401–406.doi:10.1016/j.jclinepi.2010.07.015  
47  
48  
49 48. Gonzalez JS, Peyrot M, McCarl LA, et al. Depression and diabetes treatment nonadherence: a  
50 meta-analysis. *Diabetes Care* 2008;31(12):2398–2403.doi:10.2337/dc08-1341  
51  
52  
53 49. Trief PM, Foster NC, Chaytor N, et al. Longitudinal Changes in Depression Symptoms and  
54 Glycemia in Adults With Type 1 Diabetes. *Diabetes Care* 2019;42(7):1194–1201.  
55  
56

- 1  
2  
3  
4 doi:10.2337/dc18-2441
- 5  
6 50. Novak M, Mucsi I, Rhee CM, et al. Increased Risk of Incident Chronic Kidney Disease,  
7  
8 Cardiovascular Disease, and Mortality in Patients With Diabetes With Comorbid Depression.  
9  
10 *Diabetes Care* 2016;39(11):1940–1947. doi:10.2337/dc16-0048
- 11  
12 51. Lustman PJ, Anderson RJ, Freedland KE, et al. Depression and poor glycemic control: a  
13  
14 meta-analytic review of the literature. *Diabetes Care* 2000;23(7):934–942.  
15  
16 doi:10.2337/diacare.23.7.934
- 17  
18 52. Roopan S, Larsen ER. Use of antidepressants in patients with depression and comorbid  
19  
20 diabetes mellitus: a systematic review. *Acta Neuropsychiatr* 2017;29(3):127–139.  
21  
22 doi:10.1017/neu.2016.54
- 23  
24 53. Croom AM. Music, neuroscience, and the psychology of well-being: a précis. *Front Psychol*  
25  
26 2012;2:393. doi:10.3389/fpsyg.2011.00393
- 27  
28 54. Abd-Elshafy SK, Khalaf GS, Abo-Kerisha MZ, et al. Not All Sounds Have Negative Effects  
29  
30 on Children Undergoing Cardiac Surgery. *J Cardiothorac Vasc Anesth* 2015;29(5):1277–  
31  
32 1284. doi:10.1053/j.jvca.2015.01.005
- 33  
34 55. Yu SJ, Sun ZY, Zhou J, et al. Exploration of music behavioral intervention in the treatment of  
35  
36 diabetes mellitus. *Hebei med* 2007;13(8):903-906.  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
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## PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol\*

Section and topic	Item No	Checklist item
<b>ADMINISTRATIVE INFORMATION</b>		
Title:		
Identification <b>P<sub>1</sub></b>	1a	Identify the report as a protocol of a systematic review
Update <b>None</b>	1b	If the protocol is for an update of a previous systematic review, identify as such
Registration <b>P<sub>2</sub></b>	2	If registered, provide the name of the registry (such as PROSPERO) and registration number
Authors:		
Contact <b>P<sub>1</sub></b>	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author
Contributions <b>P<sub>14</sub></b>	3b	Describe contributions of protocol authors and identify the guarantor of the review
Amendments <b>None</b>	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments
Support:		
Sources <b>P<sub>14</sub></b>	5a	Indicate sources of financial or other support for the review
Sponsor <b>None</b>	5b	Provide name for the review funder and/or sponsor
Role of sponsor or funder <b>None</b>	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol
<b>INTRODUCTION</b>		
Rationale <b>P<sub>4-6</sub></b>	6	Describe the rationale for the review in the context of what is already known
Objectives <b>P<sub>7-8</sub></b>	7	Provide an explicit statement of the question(s) the review will address with reference to participants <b>P<sub>7</sub></b> , interventions <b>P<sub>7</sub></b> , comparators <b>P<sub>7</sub></b> , and outcomes <b>P<sub>7-8</sub></b> (PICO)
<b>METHODS</b>		
Eligibility criteria <b>P<sub>6-7</sub></b>	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review
Information sources <b>P<sub>6</sub>, P<sub>8</sub>, P<sub>11</sub></b>	9	Describe all intended information sources (such as electronic databases <b>P<sub>8</sub></b> , contact with study authors <b>P<sub>11</sub></b> , trial registers <b>P<sub>6</sub></b> or other grey literature sources <b>P<sub>8</sub></b> ) with planned dates of coverage <b>P<sub>8</sub></b>
Search strategy <b>P<sub>9</sub></b>	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated
Study records:		



Data management P <sub>10</sub>	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review
Selection process P <sub>9-10</sub>	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)
Data collection process P <sub>10</sub>	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators
Data items P <sub>10</sub>	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications
Outcomes and prioritization P <sub>7-8</sub>	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale
Risk of bias in individual studies P <sub>10</sub>	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis
Data synthesis P <sub>10-12</sub>	15a	Describe criteria under which study data will be quantitatively synthesised P <sub>11</sub>
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I <sup>2</sup> , Kendall's $\tau$ ) P <sub>10-11</sub>
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression) P <sub>12</sub>
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned P <sub>12</sub>
Meta-bias(es) P <sub>11</sub>	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)
Confidence in cumulative evidence P <sub>12</sub>	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)

**\* It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

*From: Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart L, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015 Jan 2;349(jan02 1):g7647.*

# BMJ Open

## Effect of music intervention on mental health in patients with diabetes mellitus: a protocol for a systematic review and meta-analysis of randomized controlled trials

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# Effect of music intervention on mental health in patients with diabetes mellitus: a protocol for a systematic review and meta-analysis of randomized controlled trials

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## ABSTRACT

**Introduction** About 463 million adults aged 20 to 79 have diabetes globally and mental disorders often exist in diabetic patients as comorbidities. The comorbidities can lead to deterioration of diseases, increased difficulty in treatment, even as well as the great mortality. Music intervention has been applied in the treatment of the comorbidities for 12 years, but there are not recommendations due to lacking of evidence. Thus, a meta-analysis is necessary to be conducted to evaluate the effect of music intervention.

**Methods and analysis** We will search the following nine online electronic databases: PubMed, Web of Science, Embase, EBSCO, Cochrane Library, Chinese National Knowledge Infrastructure (CNKI), Wanfang Database, Chinese Scientific Journal Database (VIP) and Chinese Biomedical and Medical Database (CBM), from their inception until March 2020. We also plan to search other relevant resources, including grey literatures and the reference lists of relevant publications. Only randomized controlled trials (RCTs) of music intervention for depression or anxiety with diabetes will be involved. The primary outcomes include depression score and anxiety score measured by scales, and the secondary outcome is safety. Data extraction will be implemented by two researchers independently. Risk of bias will be evaluated through Cochrane Collaboration's Risk of Bias tool. Eventually, all the data will be analyzed via the software Review Manager V.5.3.

**Ethics and dissemination** This meta-analysis will provide information about music intervention applied to treat depression or anxiety in diabetic patients. There is no required ethical approval because this meta-analysis is on the basis of published data. The results of this systematic review will be published to a peer reviewed journal.

**Trial registration number** CRD42019146439

### Strengths and limitations of this study

· This meta-analysis will furnish evidence of the effectiveness and safety of music intervention applied to treat depression or anxiety in diabetic patients without precedent.

· On the basis of our comprehensive search strategy, the relevant original studies will fail to be omitted.

· Two authors will implement data extraction and estimation of the risk of bias separately.

· We will only cover randomized controlled trials (RCTs) in this study.

· A language bias may exist in this meta-analysis because it will include studies only in English and Chinese on account of the language barrier.

## INTRODUCTION

### Description of the condition

According to the newest “IDF Diabetes Atlas (9<sup>th</sup> edition)” published by International Diabetes Federation (IDF), about 463 million adults aged 20 to 79 have diabetes globally (1 in 11).[1] It is well known that diabetes has a significant influence on life quality because it can cause a lot of complications such as retinopathy, renal disease, cardiovascular disease, neurological disease and foot ulcers which may result in lower extremity amputation.[2]

In addition to physical complications, some mental disorders often exist in diabetic patients as comorbidities. Some studies have indicated that depression is more prevalent in diabetic patients compared to those without this disease.[3,4] At the same time, depression could also increase the risk of incidence of diabetes,[5-7] which suggests that depression has a bidirectional association with diabetes. And the relation between anxiety and diabetes has been confirmed to be the same. People with diabetes are more susceptible to concurrent anxiety[8,9] while reversely anxiety is a risk factor of diabetic incidents.[10] Individuals with chronic diseases and also comorbid depression or anxiety have obviously higher health-care utilization, functional disability, work absence and mortality risk than those without them.[11,12]

### Description of the intervention

When it comes to the treatment of diabetes with depression or anxiety, conventional glucose-lowering treatment combined with drug therapy or psychological intervention are the routine treatments.[13,14] Music intervention is also a successful therapy using music for treatment by professionals, which can be divided into two major categories, namely music therapy and music medicine.[15] The official definition of music therapy is the “...clinical and evidence-based use of music interventions to accomplish individualized goals within a therapeutic relationship by a credentialed professional who has completed an approved music therapy program”.[16] A trained music therapist leads the treatment process, choosing the type of music, the form of music presentation (pre-recorded or live), and the treatment setting (singing, playing instruments,

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4 composing, etc.) based on the patient's condition, ultimately resulting in a therapeutic scheme that  
5 is best for the patient. By comparison, music medicine is defined as the passive listening to pre-  
6 recorded music, which can be implemented independently by medical or healthcare professionals  
7 instead of music therapists.[17] In brief, music therapy focuses on active music therapy and  
8 personalized treatments while music medicine belongs to passive music listening and non-  
9 personalized therapy. It is significant to emphasize the distinction between music therapy and music  
10 medicine because some literatures suggest that the effect of the former is better than the latter in a  
11 great many outcomes.[18-19]

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19 A lot of studies have suggested that music, no matter what type of it is, demonstrates a  
20 remarkable effect in alleviating depression and anxiety among patients with various diseases.[20-  
21 22] As for diabetes, recent studies have showed that music intervention could improve fasting  
22 blood-glucose and systolic blood pressure in diabetic patients.[23,24] Good control of blood  
23 glucose, blood lipids and blood pressure can effectively reduce the incidence of serious  
24 complications of diabetes.[25]

### 31 32 33 **How the intervention might work**

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Researches about music psychology have shown the special potential of music. Music, as a stimulus,  
can not only trigger a variety of emotional experiences,[26, 27] but also strengthen ability to deal  
with negative emotions in everyday life.[28] The proposed mechanisms of music intervention on  
depression and anxiety span several domains. Firstly, music intervention can exert  
neurophysiological and neurochemical effects, such as triggering endorphin release[29] and  
stimulating cognitive functioning.[30] Secondly, music intervention can promote positive self-  
emotions including enhancing the sense of happiness[31] and activating self-efficacy and self-  
confidence through experiences of success.[32] Lastly, music intervention can build up sociability,  
such as interaction skills[33] and interpersonal relationship.[34] Furthermore, there are published  
studies indicating that music intervention combined with diabetic routine treatments could improve  
depression score, anxiety score, fasting glucose and glycosylated hemoglobin (HbA1c).[35,36]



### **Why it is important to do this review**

From the above, many studies have indicated the bidirectional relationship between diabetes and mental disorders. Music intervention, as a therapeutic method, has been applied to alleviate depression and anxiety and improve related indicators of diabetes. By searching literatures, it can be found that some reviews evaluated the effect of music intervention on patients with mental disorders,[37-39] while no related systematic review and meta-analysis can be searched about the effect of music intervention on mental health of patients with diabetes. Therefore, if music intervention can be proved to be both valid and with few side effects through this study, it is worth being promoted and applicated in clinic all over the world to benefit more people since this method is easy to be operated.

### **Objectives**

The purpose of this review is to systematically assess the effect of music intervention and compare the effects between music therapy and music medicine on depression and anxiety of diabetic patients. Additionally, it is also our expectation to furnish evidence reference for related guideline.

## **METHODS**

### **Study registration**

Our protocol for the meta-analysis has been registered on the International Prospective Register of Systematic Reviews (PROSPERO), and CRD42019146439 is the registration ID. This protocol has been planned severely on the basis of Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols (PRISMA-P)[40] statement guidelines. The results will be reported in conformity to the PRISMA Statement for Reporting Systematic Reviews and Meta-Analyses of Studies That Evaluate Healthcare Interventions.[41]

### **Eligibility criteria**

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4 Studies that have compliance with the following inclusion criteria will be rigorously screened.

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6 Type of studies

7 We will merely cover randomized controlled trials (RCTs) in English or Chinese, excepting Quasi-  
8 RCTs and cluster RCTs. Experiments on animals and nonrandomized clinical trials will be out of  
9 our consideration. Articles with significant overlap with other articles through print or e-publishing  
10 will fail to be included. Duplicate publications, that is results originated from a single experiment  
11 but measured by other standards and then published as disparate papers, will also be excluded.  
12 Publications with originality is our first choice. The publication status will not be restricted.  
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21 Type of Participants

22 Diabetic Patients with depression or anxiety symptoms, regardless of the type of diabetes and no  
23 restriction on gender, age, race, economic ability and education level. Patients of other disease or  
24 healthy persons will be excluded.  
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31 Type of interventions and controls

32 Interventions include music intervention (music therapy or music medicine) alone or music  
33 intervention in combination with other interventions. No restriction on the type of music. Other  
34 interventions refer to: (1) routine treatments for diabetes which mainly include pharmacologic  
35 approaches to glycemic treatment, diabetes self-management education and support (DSMES), etc.  
36 according to the newest guideline of American Diabetes Association (ADA);[42,43] (2) other  
37 therapies such as acupoint therapy,[44] metabolic surgery,[45] etc. When intervention is music  
38 intervention alone, controls can be no treatment, placebo or other active therapies. Notably, when  
39 intervention is music intervention combined with active therapies, the control must be the same  
40 active therapies.  
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51 Type of outcome measures

52 This review aims at systematically assessing the effect of music intervention on depression or  
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4 anxiety of diabetic patients, so we choose depression score and anxiety score as the primary  
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6 outcomes, which can give an index to the degree of depression and anxiety by scales.

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8 Primary outcomes: Depression score and anxiety score. Depression score is measured using self-  
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10 rating depression scale (SDS), Hamilton depression scale (HAMD) or other validated scales for  
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12 depression. Anxiety score is measured using self-rating anxiety scale (SAS), Hamilton anxiety  
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14 scale (HAMA) or other validated scales for anxiety.

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16 Secondary outcomes: Safety. Measurement via incidence of adverse effects.  
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## 19 **Search methods**

### 20 Search resources

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22 We will search the following nine online electronic databases: PubMed, Web of Science, Embase,  
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24 EBSCO, Cochrane Library, Chinese National Knowledge Infrastructure (CNKI), Wanfang  
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26 Database, Chinese Scientific Journal Database (VIP) and Chinese Biomedical and Medical  
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28 Database (CBM), from their inception to March 2020. We also plan to search other relevant  
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30 resources as far as possible, including: (1) grey literatures (like conference literatures and  
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32 dissertations) from the following four sources: OpenGrey ([www.opengrey.eu/](http://www.opengrey.eu/)), CNKI  
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34 ([www.cnki.net](http://www.cnki.net)), Open Access Theses and Dissertations ([oatd.org](http://oatd.org)) and British Library EThOS  
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36 ([ethos.bl.uk/](http://ethos.bl.uk/)); (2) the reference lists of relevant publications for additional studies.  
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### 39 Search strategies

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41 The search strategy will include the MeSH terms for diabetes mellitus, depression, anxiety, music  
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43 therapy, music and singing, combined with their respective free-text terms. The search details of  
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45 the PubMed are simply shown in table 1.  
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**Table 1 Example of PubMed search strategy.**

Number	Search terms
#1	"Diabetes Mellitus"[Mesh]
#2	"Depression"[Mesh] OR Depressions[Title/Abstract] OR Depressive Symptoms[Title/Abstract] OR Depressive Symptom[Title/Abstract] OR Symptom, Depressive[Title/Abstract] OR Symptoms, Depressive[Title/Abstract] OR Emotional Depression[Title/Abstract] OR Depression, Emotional[Title/Abstract] OR Depressions, Emotional[Title/Abstract] OR Emotional Depressions[Title/Abstract]
#3	"Anxiety"[Mesh] OR Hypervigilance [Title/Abstract] OR Nervousness [Title/Abstract]
#4	#2 OR #3
#5	"Music Therapy"[Mesh] OR Therapy, Music [Title/Abstract]
#6	"Music"[Mesh] OR music intervention[Title/Abstract] OR music medicine[Title/Abstract] OR music listening[Title/Abstract] OR audio recording[Title/Abstract] OR mp3 hearing[Title/Abstract]
#7	"Singing"[Mesh] OR sing[Title/Abstract] OR sings[Title/Abstract] OR song[Title/Abstract] OR compose[Title/Abstract] OR composing[Title/Abstract]
#8	#5 OR #6 OR #7
#9	randomized controlled trial [Publication Type] OR randomized [Title/Abstract] OR placebo [Title/Abstract]
#10	#1 AND #4 AND #8AND #9

### Data collection and analysis

#### Studies selection

Firstly, two researchers (L-yZ and YT) will respectively screen the keywords, titles and abstracts of all obtained studies using endnote x9 software and determine whether trials have compliance with inclusion criteria. Secondly, we will also get access to the full text of all studies of possible relevance for further assessment. Each of excluded study will be noted with reasons. Any disagreements will be settled through consensus or referral to the third researcher (XxF). The

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4 specific selection steps are presented in the figure 1.  
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#### 7 Data extraction

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9 Two researchers (L-yZ and YT) will independently extract and tabulate the following data items  
10 via Microsoft Excel:  
11

- 12 1. General information (including publication year and name of the first author).
- 13 2. Study design (including random method, allocation concealment and blinding).
- 14 3. Participants (including sample size, gender, age, area, depression score, anxiety score and course  
15 of disease).
- 16 4. Treatment (including interventions, controls, music type and the course of treatment).
- 17 5. Outcomes (including depression score, anxiety score and safety).

18  
19 If there is any different opinion, the final decision will go to the third researcher (XxF) to be  
20 made.  
21  
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#### 23 Assessment of risk of bias

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25 The Cochrane Collaboration's Risk of Bias tool[46] will be applied to evaluate the risk of bias of  
26 all included RCT studies by two authors (L-zW and YZ). The following domains will be assessed:  
27 sequence generation, allocation concealment, blinding of participants and personnel, blinding of  
28 outcome assessors, incomplete outcome data, selective reporting and other sources of bias. The  
29 assessments will be classified into "low", "unclear" or "high" of risk.  
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#### 32 Measures of treatment effect

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34 Considering that all outcomes (depression score, anxiety score and safety) are continuous variables,  
35 the mean difference (MD) and 95% confidence interval (CI) will be calculated when the  
36 quantitative data are from the same measurement method or small data scale. On the contrary, the  
37 standardized mean difference (SMD) and 95% CI will be calculated.  
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### Unit of analysis issues

For the standard research which has one experimental group with one control group, the unit of analysis is based on the individual. For the multi-arm study which has more than two intervention groups, the recommended method is to create a single pair-wise comparison through combining groups.

### Dealing with missing data

If the required data are unavailable from literatures, one researcher (YZ) will send an e-mail to the corresponding author and ask for further information.

### Assessment of heterogeneity

A meta-analysis will be implemented if the included studies are adequately homogenous.  $P$ -value and  $I^2$  will be used to assess the heterogeneity of statistic. When  $P$ -value  $>0.05$  and  $I^2 \leq 50\%$ , the heterogeneity is regarded as acceptable. When  $P$ -value  $<0.05$  or  $I^2 >50\%$ , the heterogeneity is considered as significant.

### Assessment of reporting bias

Publication bias will be implemented, if there are more than 10 studies included, through a funnel plot.

### Data synthesis

RevMan 5.3. software provided by the Cochrane collaboration will be used to analyze the data. If the included studies are adequately homogenous, fixed-effects model will be used for statistical combination. Since all outcomes are continuous variables, the mean difference (MD) and 95% confidence interval (CI) will be calculated when the outcomes are from the same measurement method or small data scale. On the contrary, the standardized mean difference (SMD) and 95% CI will be calculated. If there is significant heterogeneity among the included studies, subgroup

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4 analyses or sensitivity analyses will be performed. If a meta-analysis is unavailable, descriptive  
5 summaries will be provided.  
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#### 8 9 Subgroup analysis

10 The subgroup analyses are planned as follows:

- 11 1. Type of music intervention (music therapy or music medicine).
  - 12 2. Type of scales (SDS, HAMD, SAS, HAMA or other validated scales for depression or anxiety).
  - 13 3. Different age groups.
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#### 21 Sensitivity analysis

22 Sensitivity analyses will be performed through including or excluding a specific study, such as a  
23 study without a clear allocation concealment or randomization method, to observe whether the  
24 results changed.  
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#### 31 Evidence assessed

32 GRADE guideline will be used to evaluate the quality of evidence.[47] In the light of the GRADE  
33 method, the quality of evidence can be assessed by 4 levels: “high”, “medium”, “low” and “very  
34 low”. GRADE profiler 3.2 will be applied for analysis.  
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#### 41 Patient and public involvement

42 Since this study is a systematic review, patients or the public will fail to participate.  
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## 46 **DISCUSSION**

47 Depression and anxiety often occur independently or simultaneously during the development of  
48 many chronic diseases. In recent years, the number of studies about comorbid depression or anxiety  
49 in diabetics are continually increasing, not only because the two-way relationship between  
50 depression/anxiety and diabetes can lead to deterioration of diseases, increased difficulty in  
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4 treatment, even as well as the great mortality,[48-51] but also because therapeutic methods for  
5 treating the comorbidities are limited and unsatisfactory. On the one hand, some antidepressant  
6 drugs, such as nortriptyline and sertraline, may complicate glycemic control.[52] On the other hand,  
7 psychotherapy based on verbal communication requires a professional psychiatrist and it is  
8 expensive.  
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13 Music intervention has been proved by many literatures to have a beneficial effect on depression  
14 and anxiety, such as strengthening awareness and sensitiveness for positive emotions.[53]  
15 Noticeably, a few studies also show that music intervention can reduce blood glucose and HbA1c  
16 simultaneously.[24,54] Therefore, music intervention is an applicable method for treating  
17 depression and anxiety with diabetes. Additionally, music intervention, almost no side effects, is  
18 safer than pharmacotherapy, easier to be operated and costs less than psychotherapy based on verbal  
19 communication, so it is conducive to clinical promotion and application.  
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27 Since 2007,[55] music intervention has been applied in the treatment of depression and anxiety  
28 with diabetes for 12 years. Nonetheless, there are not systematic review or meta-analysis conducted  
29 to evaluate the potential pros and cons of this therapy method. Thus, this study intends to provide  
30 strong evidence for music intervention applied to treat mental disorders in diabetic patients and  
31 synchronously furnish evidence reference for related guideline.  
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37 However, a language bias may exist in this meta-analysis because it will include studies only in  
38 English and Chinese because of the language barrier. Therefore, some related studies from  
39 medical databases in other languages might be missed.  
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43 In conclusion, this meta-analysis will be conducive to assess underlying benefits and harms of  
44 music intervention on comorbid depression or anxiety with diabetes. Moreover, the results of this  
45 study might not merely furnish evidence reference for guideline of relevant areas, but also may  
46 attract more attention on music intervention, which can be a chance to facilitate its clinical  
47 application and ultimately benefit more patients.  
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## 54 **ETHICS AND DISSEMINATION**

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There is no required ethical approval because this meta-analysis is on the basis of published data. The results of this systematic review will be published to a peer reviewed journal.

## Figure legend

**Figure 1** Flowchart to present the search process.

**Contributions** L-yZ and C-gX contributed to the conception of the study. The manuscript of the protocol was drafted by L-yZ, and was revised by XxF and C-gX. L-yZ and YT will also independently screen the potential studies and extract data from included studies. L-zW and YZ will assess the risk of bias and accomplish data synthesis. XxF will arbitrate any disagreements. C-gX will ensure that no errors occur during the review. All authors have approved the publication of the protocol.

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**Competing interests** None declared.

**Patient consent for publication** Not required.

**Provenance and peer review** Not commissioned; externally peer reviewed.

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## REFERENCES

1. International Diabetes Federation. IDF Diabetes Atlas (9<sup>th</sup> edition), 2019. Available:

- 1  
2  
3  
4 <http://www.diabetesatlas.org/>. Accessed November 9, 2019
- 5  
6 2. World Health Organization. Global report on diabetes, 2014. Available:  
7 <https://www.who.int/news-room/fact-sheets/detail/diabetes>. Accessed November 9, 2019
- 8  
9  
10 3. Ali S, Stone MA, Peters JL, et al. The prevalence of co-morbid depression in adults with  
11 Type 2 diabetes: a systematic review and meta-analysis. *Diabet Med* 2006;23(11):1165–  
12 1173. doi:10.1111/j.1464-5491.2006.01943.x
- 13  
14  
15 4. Anderson RJ, Freedland KE, Clouse RE, et al. The prevalence of comorbid depression in  
16 adults with diabetes: a meta-analysis. *Diabetes Care* 2001;24(6):1069–1078.  
17 doi:10.2337/diacare.24.6.1069
- 18  
19  
20  
21 5. Knol MJ, Twisk JW, Beekman AT, et al. Depression as a risk factor for the onset of type 2  
22 diabetes mellitus. A meta-analysis. *Diabetologia* 2006;49(5):837–845. doi:10.1007/s00125-  
23 006-0159-x
- 24  
25  
26  
27 6. Cosgrove MP, Sargeant LA, Griffin SJ. Does depression increase the risk of developing type  
28 2 diabetes?. *Occup Med (Lond)* 2008;58(1):7–14. doi:10.1093/occmed/kqm105
- 29  
30  
31 7. Mezuk B, Eaton WW, Albrecht S, et al. Depression and type 2 diabetes over the lifespan: a  
32 meta-analysis. *Diabetes Care* 2008;31(12):2383–2390. doi:10.2337/dc08-0985
- 33  
34  
35 8. Grigsby AB, Anderson RJ, Freedland KE, et al. Prevalence of anxiety in adults with diabetes:  
36 a systematic review. *J Psychosom Res* 2002; 53: 1053–1060. doi:10.1016/s0022-  
37 3999(02)00417-8
- 38  
39  
40 9. Smith KJ, Beland M, Clyde M, et al. Association of diabetes with anxiety: a systematic  
41 review and metaanalysis. *J Psychosom Res* 2013; 74: 89–99.  
42 doi:10.1016/j.jpsychores.2012.11.013
- 43  
44  
45 10. Smith KJ, Deschênes SS, Schmitz N. Investigating the longitudinal association between  
46 diabetes and anxiety: a systematic review and meta-analysis. *Diabet Med* 2018;35(6):677–  
47 693. doi:10.1111/dme.13606
- 48  
49  
50  
51 11. Egede LE. Major depression in individuals with chronic medical disorders: prevalence,  
52 correlates and association with health resource utilization, lost productivity and functional  
53  
54  
55  
56

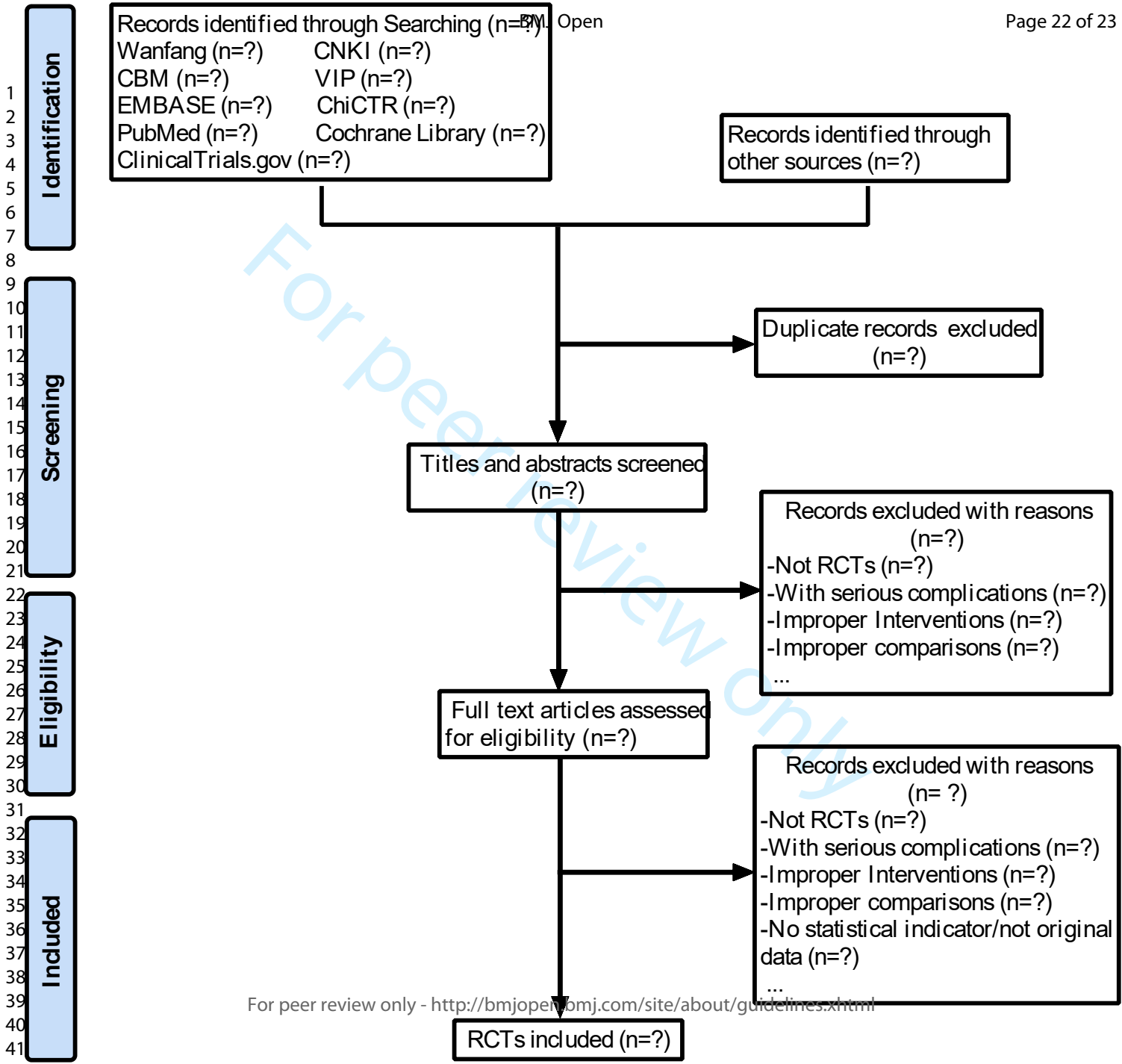
- 1  
2  
3  
4 disability. *Gen Hosp Psychiatry* 2007;29:409–416.doi:10.1016/j.genhosppsy.2007.06.002
- 5  
6 12. Naicker K, Johnson JA, Skogen JC, et al. Type 2 Diabetes and Comorbid Symptoms of  
7  
8 Depression and Anxiety: Longitudinal Associations With Mortality Risk. *Diabetes Care*  
9  
10 2017;40(3):352–358.doi:10.2337/dc16-2018
- 11  
12 13. van der Feltz-Cornelis CM, Nuyen J, Stoop C, et al. Effect of interventions for major  
13  
14 depressive disorder and significant depressive symptoms in patients with diabetes mellitus:  
15  
16 a systematic review and meta-analysis. *Gen Hosp Psychiatry* 2010;32(4):380–395.  
17  
18 doi:10.1016/j.genhosppsy.2010.03.011
- 19  
20 14. Komsuoglu Celikyurt I, Mutlu O, Ulak G, et al. Exenatide treatment exerts anxiolytic- and  
21  
22 antidepressant-like effects and reverses neuropathy in a mouse model of type-2 diabetes. *Med*  
23  
24 *Sci Monit Basic Res* 2014;20:112–117.doi:10.12659/MSMBR.891168
- 25  
26 15. Leubner D, Hinterberger T. Reviewing the Effectiveness of Music Interventions in Treating  
27  
28 Depression. *Front Psychol* 2017;8:1109.doi:10.3389/fpsyg.2017.01109
- 29  
30 16. American Music Therapy Association. What is music therapy?, 2013.Available:  
31  
32 <https://www.musictherapy.org/about/musictherapy/>. Accessed January 9, 2020.
- 33  
34 17. Dileo C. A classification model for music and medicine. National Association of Music  
35  
36 Therapy, Washington, DC, 1999: 1-6.
- 37  
38 18. Raglio A, Bellelli G, Mazzola P, et al. Music, music therapy and dementia: a review of  
39  
40 literature and the recommendations of the Italian Psychogeriatric Association. *Maturitas*  
41  
42 2012;72(4):305–310.doi:10.1016/j.maturitas.2012.05.016
- 43  
44 19. Dileo C. Effects of music and music therapy on medical patients: a meta-analysis of the  
45  
46 research and implications for the future. *J Soc Integr Oncol* 2006;4(2):67–70.  
47  
48 doi:10.2310/7200.2006.002
- 49  
50 20. Thaut MH, Gardiner JC, Holmberg D, et al. Neurologic music therapy improves executive  
51  
52 function and emotional adjustment in traumatic brain injury rehabilitation. *Ann N Y Acad Sci*  
53  
54 2009;1169:406–416.doi:10.1111/j.1749-6632.2009.04585.x
- 55  
56 21. Kim DS, Park YG, Choi JH, et al. Effects of music therapy on mood in stroke patients.

- 1  
2  
3  
4 *Yonsei Med J* 2011;52(6):977–981.doi:10.3349/ymj.2011.52.6.977
- 5  
6 22. Nwebube C, Glover V, Stewart L. Prenatal listening to songs composed for pregnancy and  
7 symptoms of anxiety and depression: a pilot study. *BMC Complement Altern Med*  
8 2017;17(1):256.doi:10.1186/s12906-017-1759-3
- 9  
10  
11 23. Lin XX, Ji JM, Zhou GY. Influence of listening to Jiao tune music on sleep quality and blood  
12 glucose in the elderly patients with type 2 diabetes accompanied by insomnia. *Journal of*  
13 *rehabilitation* 2017;27(01):44-48.
- 14  
15  
16 24. Mandel SE, Davis BA, Secic M. Effects of music therapy and music-assisted relaxation and  
17 imagery on health-related outcomes in diabetes education: a feasibility study. *Diabetes Educ*  
18 2013;39(4):568–581.doi:10.1177/0145721713492216
- 19  
20  
21 25. Centers for Disease Control and Prevention. National Diabetes Statistics Report, 2014.  
22 Available: [https://www.cdc.gov/diabetes/pdfs/data/2014-report-estimates-of-diabetes-and-its-](https://www.cdc.gov/diabetes/pdfs/data/2014-report-estimates-of-diabetes-and-its-burden-in-the-united-states.pdf)  
23 [burden-in-the-united-states.pdf](https://www.cdc.gov/diabetes/pdfs/data/2014-report-estimates-of-diabetes-and-its-burden-in-the-united-states.pdf). Accessed November 9, 2019
- 24  
25  
26 26. Gabrielsson A, Wik SL. Strong experiences related to music: a descriptive system. *Music Sci*  
27 2003;7(2):157–217.
- 28  
29  
30 27. Zentner M, Grandjean D, Scherer KR. Emotions evoked by the sound of music:  
31 characterization, classification, and measurement. *Emotion* 2008;8(4):494–521.  
32 doi:10.1037/1528-3542.8.4.494
- 33  
34  
35 28. Saarikallio S. Music as emotional self-regulation throughout adulthood. *Psychol Music*  
36 2011;39(3):307–327.
- 37  
38  
39 29. Gök Ugur H, Yaman Aktaş Y, Orak OS, et al. The effect of music therapy on depression and  
40 physiological parameters in elderly people living in a Turkish nursing home: a randomized-  
41 controlled trial. *Aging Ment Health* 2017;21(12):1280–1286.  
42 doi:10.1080/13607863.2016.1222348
- 43  
44  
45 30. Gómez Gallego M, Gómez García J. Music therapy and Alzheimer's disease: Cognitive,  
46 psychological, and behavioural effects. *Neurologia* 2017;32(5):300–308.  
47 doi:10.1016/j.nrl.2015.12.003
- 48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

- 1  
2  
3  
4 31. Cheung DSK, Lai CKY, Wong FKY, et al. The effects of the music-with-movement  
5 intervention on the cognitive functions of people with moderate dementia: a randomized  
6 controlled trial. *Aging Ment Health* 2018;22(3):306–315.  
7  
8 doi:10.1080/13607863.2016.1251571  
9  
10  
11 32. Wang SC, Yu CL, Chang SH. Effect of music care on depression and behavioral problems in  
12 elderly people with dementia in Taiwan: a quasi-experimental, longitudinal study. *Aging*  
13 *Ment Health* 2017;21(2):156–162.doi:10.1080/13607863.2015.1093602  
14  
15  
16 33. Bieleninik L, Geretsegger M, Mössler K, et al. Effects of Improvisational Music Therapy vs  
17 Enhanced Standard Care on Symptom Severity Among Children With Autism Spectrum  
18 Disorder: The TIME-A Randomized Clinical Trial. *JAMA* 2017;318(6):525–535.  
19  
20  
21  
22  
23  
24  
25  
26 34. Giovagnoli AR, Manfredi V, Parente A, et al. Cognitive training in Alzheimer's disease: a  
27 controlled randomized study. *Neurol Sci* 2017;38(8):1485–1493.doi:10.1007/s10072-017-  
28 3003-9  
29  
30  
31 35. Deng HX, Gao GS, Li ZM, et al. Application of receiving music therapy in elderly patients  
32 with diabetes. *Chinese journal of health and nutrition (1st Ten-days of month)*  
33  
34  
35  
36  
37 36. Zhang ZW. Application of music therapy and psychotherapy adjuvant therapy in type 2  
38 diabetes. *Chinese medical science* 2011,01(18):150-151.  
39  
40  
41 37. Solanki MS, Zafar M, Rastogi R. Music as a therapy: role in psychiatry. *Asian J Psychiatr*  
42  
43  
44  
45 38. Petrovsky D, Cacchione PZ, George M. Review of the effect of music interventions on  
46 symptoms of anxiety and depression in older adults with mild dementia. *Int Psychogeriatr*  
47  
48  
49  
50 39. Aalbers S, Fusar-Poli L, Freeman RE, et al. Music therapy for depression. *Cochrane*  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

- 1  
2  
3  
4 40. Shamseer L, Moher D, Clarke M, et al. Preferred reporting items for systematic review and  
5 meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. *BMJ*  
6 2015;350:g7647.doi:10.1136/bmj.g7647  
7  
8  
9  
10 41. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic  
11 reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and  
12 elaboration. *BMJ* 2009;339:b2700.doi:10.1136/bmj.b2700  
13  
14  
15 42. American Diabetes Association. 9. Pharmacologic Approaches to Glycemic Treatment:  
16 Standards of Medical Care in Diabetes-2020. *Diabetes Care* 2020;43(Suppl 1):S98–S110.  
17 doi:10.2337/dc20-S009  
18  
19  
20  
21 43. American Diabetes Association. 5. Facilitating Behavior Change and Well-being to Improve  
22 Health Outcomes: Standards of Medical Care in Diabetes-2020. *Diabetes Care*  
23 2020;43(Suppl 1):S48–S65. doi:10.2337/dc20-S005  
24  
25  
26  
27 44. Feng Y, Fang Y, Wang Y, et al. Acupoint Therapy on Diabetes Mellitus and Its Common  
28 Chronic Complications: A Review of Its Mechanisms. *Biomed Res Int* 2018;2018:3128378.  
29 doi:10.1155/2018/3128378  
30  
31  
32  
33 45. Pérez-Pevida B, Escalada J, Miras AD, et al. Mechanisms Underlying Type 2 Diabetes  
34 Remission After Metabolic Surgery. *Front Endocrinol (Lausanne)* 2019;10:641.  
35 doi:10.3389/fendo.2019.00641  
36  
37  
38  
39 46. Higgins JPT, Thomas J, Chandler J, et al. Cochrane Handbook for Systematic Reviews of  
40 Interventions version 6.0 (updated July 2019). Cochrane, 2019. Available:  
41 www.training.cochrane.org/handbook.  
42  
43  
44  
45 47. Balshem H, Helfand M, Schunemann HJ, et al. GRADE guidelines: 3. Rating the quality of  
46 evidence. *J Clin Epidemiol* 2011;64:401–406.doi:10.1016/j.jclinepi.2010.07.015  
47  
48  
49 48. Gonzalez JS, Peyrot M, McCarl LA, et al. Depression and diabetes treatment nonadherence: a  
50 meta-analysis. *Diabetes Care* 2008;31(12):2398–2403.doi:10.2337/dc08-1341  
51  
52  
53 49. Trief PM, Foster NC, Chaytor N, et al. Longitudinal Changes in Depression Symptoms and  
54 Glycemia in Adults With Type 1 Diabetes. *Diabetes Care* 2019;42(7):1194–1201.  
55  
56

- 1  
2  
3  
4 doi:10.2337/dc18-2441
- 5  
6 50. Novak M, Mucsi I, Rhee CM, et al. Increased Risk of Incident Chronic Kidney Disease,  
7  
8 Cardiovascular Disease, and Mortality in Patients With Diabetes With Comorbid Depression.  
9  
10 *Diabetes Care* 2016;39(11):1940–1947. doi:10.2337/dc16-0048
- 11  
12 51. Lustman PJ, Anderson RJ, Freedland KE, et al. Depression and poor glycemic control: a  
13  
14 meta-analytic review of the literature. *Diabetes Care* 2000;23(7):934–942.  
15  
16 doi:10.2337/diacare.23.7.934
- 17  
18 52. Roopan S, Larsen ER. Use of antidepressants in patients with depression and comorbid  
19  
20 diabetes mellitus: a systematic review. *Acta Neuropsychiatr* 2017;29(3):127–139.  
21  
22 doi:10.1017/neu.2016.54
- 23  
24 53. Croom AM. Music, neuroscience, and the psychology of well-being: a précis. *Front Psychol*  
25  
26 2012;2:393. doi:10.3389/fpsyg.2011.00393
- 27  
28 54. Abd-Elshafy SK, Khalaf GS, Abo-Kerisha MZ, et al. Not All Sounds Have Negative Effects  
29  
30 on Children Undergoing Cardiac Surgery. *J Cardiothorac Vasc Anesth* 2015;29(5):1277–  
31  
32 1284. doi:10.1053/j.jvca.2015.01.005
- 33  
34 55. Yu SJ, Sun ZY, Zhou J, et al. Exploration of music behavioral intervention in the treatment of  
35  
36 diabetes mellitus. *Hebei med* 2007;13(8):903-906.  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
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## PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol\*

Section and topic	Item No	Checklist item
<b>ADMINISTRATIVE INFORMATION</b>		
Title:		
Identification <b>P<sub>1</sub></b>	1a	Identify the report as a protocol of a systematic review
Update <b>None</b>	1b	If the protocol is for an update of a previous systematic review, identify as such
Registration <b>P<sub>2</sub></b>	2	If registered, provide the name of the registry (such as PROSPERO) and registration number
Authors:		
Contact <b>P<sub>1</sub></b>	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author
Contributions <b>P<sub>14</sub></b>	3b	Describe contributions of protocol authors and identify the guarantor of the review
Amendments <b>None</b>	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments
Support:		
Sources <b>P<sub>14</sub></b>	5a	Indicate sources of financial or other support for the review
Sponsor <b>None</b>	5b	Provide name for the review funder and/or sponsor
Role of sponsor or funder <b>None</b>	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol
<b>INTRODUCTION</b>		
Rationale <b>P<sub>4-6</sub></b>	6	Describe the rationale for the review in the context of what is already known
Objectives <b>P<sub>7-8</sub></b>	7	Provide an explicit statement of the question(s) the review will address with reference to participants <b>P<sub>7</sub></b> , interventions <b>P<sub>7</sub></b> , comparators <b>P<sub>7</sub></b> , and outcomes <b>P<sub>7-8</sub></b> (PICO)
<b>METHODS</b>		
Eligibility criteria <b>P<sub>6-7</sub></b>	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review
Information sources <b>P<sub>6</sub>, P<sub>8</sub>, P<sub>11</sub></b>	9	Describe all intended information sources (such as electronic databases <b>P<sub>8</sub></b> , contact with study authors <b>P<sub>11</sub></b> , trial registers <b>P<sub>6</sub></b> or other grey literature sources <b>P<sub>8</sub></b> ) with planned dates of coverage <b>P<sub>8</sub></b>
Search strategy <b>P<sub>9</sub></b>	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated
Study records:		

Data management P <sub>10</sub>	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review
Selection process P <sub>9-10</sub>	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)
Data collection process P <sub>10</sub>	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators
Data items P <sub>10</sub>	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications
Outcomes and prioritization P <sub>7-8</sub>	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale
Risk of bias in individual studies P <sub>10</sub>	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis
Data synthesis P <sub>10-12</sub>	15a	Describe criteria under which study data will be quantitatively synthesised P <sub>11</sub>
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I <sup>2</sup> , Kendall's $\tau$ ) P <sub>10-11</sub>
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression) P <sub>12</sub>
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned P <sub>12</sub>
Meta-bias(es) P <sub>11</sub>	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)
Confidence in cumulative evidence P <sub>12</sub>	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)

**\* It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

*From: Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart L, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015 Jan 2;349(jan02 1):g7647.*

# BMJ Open

## Effect of music intervention on mental health in patients with diabetes mellitus: protocol for a systematic review and meta-analysis of randomized controlled trials

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# Effect of music intervention on mental health in patients with diabetes mellitus: protocol for a systematic review and meta-analysis of randomized controlled trials

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## ABSTRACT

**Introduction** About 463 million adults aged 20 to 79 have diabetes globally. Mental disorders often exist in diabetic patients as comorbidities, which can lead to aggravation of the diseases, increased difficulties in treatment, as well as elevated mortality rates. Music intervention has been applied in the treatment of comorbidities for 12 years now, but there are still no recommendations due to the lack of evidence. Thus, a meta-analysis is necessary to evaluate the effect of music intervention in treating mental disorders of diabetic patients.

**Methods and analysis** We will search the following nine online electronic databases from their inception until March 2020: PubMed, Web of Science, Embase, EBSCO, Cochrane Library, Chinese National Knowledge Infrastructure (CNKI), Wanfang Database, Chinese Scientific Journal Database (VIP) and Chinese Biomedical and Medical Database (CBM). We also plan to search other relevant resources, including grey literature and the reference lists of relevant publications. Only randomized controlled trials (RCTs) of music intervention to treat depression or anxiety in diabetic patients will be involved. The primary outcomes include the depression score and anxiety score measured on certain scales, and the secondary outcome is safety. Data extraction will be independently implemented by two researchers. The risk of bias will be evaluated through the Cochrane Collaboration's Risk of Bias tool. Eventually, all the data will be analyzed via the Review Manager 5.3 software.

**Ethics and dissemination** This meta-analysis will provide information about applying music intervention to treat depression or anxiety in diabetic patients. No ethical approval is required because this meta-analysis is based on published data. The results of this systematic review will be published in a peer-reviewed journal.

**PROSPERO registration number** CRD42019146439

### Strengths and limitations of this study

- This meta-analysis will be the first to provide evidence on the effectiveness and safety of applying music intervention to treat depression or anxiety in diabetic patients.
- Based on our comprehensive search strategy, the relevant original studies will be included.
- Two authors will separately implement data extraction and estimation of the risk of bias.
- We will only cover randomized controlled trials (RCTs) in this study.
- A language bias may exist in this meta-analysis because it will include only the studies in English and Chinese due to the language barrier.

## INTRODUCTION

According to the newest “IDF Diabetes Atlas (9<sup>th</sup> edition)” published by the International Diabetes Federation (IDF), about 463 million adults aged 20 to 79 have diabetes mellitus globally (1 in 11).[1] Diabetes has a well-known significant influence on the patient’s quality of life (QoL) due to its complications, such as retinopathy, cardiovascular, neurological or renal diseases, as well as foot ulcers, which may result in the amputation of lower extremity.[2]

In addition to the physical complications, diabetic patients may also develop mental disorders as comorbidities. Some studies have indicated that depression is more prevalent in diabetic patients compared with non-diabetics.[3,4] Meanwhile, depression could also increase the risk of diabetes,[5-7] which suggests a bidirectional diabetes-depression relation; a similar relation has been confirmed between anxiety and diabetes: people with diabetes are more susceptible to concurrent anxiety[8,9] while anxiety is a risk factor of diabetes.[10] Individuals with chronic diseases who have comorbid depression or anxiety have obviously higher healthcare utilization, functional disability, work absence, and mortality risk than healthy ones.[11,12]

When it comes to the treatment of diabetes with comorbid depression or anxiety, conventional glucose-lowering treatments combined with antidepressants, anti-anxiety medications, or psychological intervention are the routine treatments.[13,14] Music intervention is also a successful therapy, which can be divided into two major categories: music therapy and music medicine.[15] The official definition of music therapy is the “clinical and evidence-based use of music interventions to accomplish individualized goals within a therapeutic relationship by a credentialed professional who has completed an approved music therapy program”.[16] Based on the patient’s condition, a trained music therapist conducts the treatment by choosing the type of music, the form of music presentation (pre-recorded or live), and the treatment setting (singing, playing instruments, composing, etc.), ultimately resulting in a therapeutic scheme that is best suited for the patient. On the other hand, music medicine is defined as passive listening to pre-recorded music, which can be independently implemented by medical or healthcare professionals instead of music therapists.[17] In brief, music therapy focuses on active music therapy and



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4 personalized treatments, while music medicine belongs to passive music listening and non-  
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6 personalized therapy. It is important to emphasize the distinction between music therapy and  
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8 music medicine because some studies suggest that the effect of the former is better than the latter  
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10 with regard to many outcomes.[18-19]

11 A lot of studies suggested that music, with all its types, demonstrates a remarkable effect in  
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13 alleviating depression and anxiety among patients with various diseases.[20-22] As for diabetes,  
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15 recent studies have shown that music intervention could improve fasting blood glucose and  
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17 systolic blood pressure in diabetic patients.[23,24] Good control of blood glucose and blood  
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19 pressure can effectively reduce the incidence of serious complications of diabetes.[25]

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21 Previous research on music psychology showed the special potential of music. As a stimulus,  
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23 music can not only trigger a variety of emotional experiences,[26, 27] but it can also strengthen  
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25 the ability to deal with negative emotions in everyday life.[28] The proposed mechanisms behind  
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27 the effects of music intervention on depression and anxiety span across several domains. Firstly,  
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29 music intervention can exert neurophysiological and neurochemical effects, such as triggering the  
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31 release of endorphin[29] and stimulating cognitive functioning.[30] Secondly, music intervention  
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33 can promote positive self-conscious emotions including enhancing the sense of happiness[31] and  
34  
35 activating self-efficacy and self-confidence through experiencing success.[32] Lastly, music  
36  
37 intervention can enhance the sociable aspects, such as interaction skills[33] and interpersonal  
38  
39 relationships.[34] Furthermore, many published studies indicated that music intervention  
40  
41 combined with the diabetic routine treatments could improve the depression score, anxiety score,  
42  
43 and the values of fasting glucose and glycosylated hemoglobin (HbA1c).[35,36]

44  
45 By searching the literature, it can be found that some reviews evaluated the effect of music  
46  
47 intervention on the patients with mental disorders,[37-39] while no related systematic reviews or  
48  
49 meta-analyses can be found about the effect of music intervention on the mental health of diabetic  
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51 patients. Therefore, a review that can show music intervention to be both valid and with few side  
52  
53 effects would be useful to indicate that this intervention is worth being promoted and clinically  
54  
55 applied to benefit more people with this easy-operated method.

## OBJECTIVE

In this review, we present a meta-analysis to systematically assess the effect of music intervention and compare the effects of music therapy and those of music medicine on depression and anxiety of diabetic patients. Additionally, it serves to establish an evidence reference for related guidelines.

## METHODS AND ANALYSIS

### Study registration

Our protocol for the meta-analysis has been registered in the International Prospective Register of Systematic Reviews (PROSPERO) with the registration ID of CRD42019146439. This protocol has been strictly planned based on the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols (PRISMA-P)[40] statement guidelines. The results will be reported in accordance with the PRISMA Statement for Reporting Systematic Reviews and Meta-Analyses of Studies That Evaluate Healthcare Interventions.[41]

### Eligibility criteria

#### Type of studies

This analysis will merely cover the randomized controlled trials (RCTs) in English or Chinese, except for Quasi-RCTs and cluster RCTs. The experiments on animals and nonrandomized clinical trials will not be considered. The articles with a significant overlap with other articles through printing or e-publishing will not be included. Duplicate publications, in which the results originated from a single experiment but were measured by other standards and then published as disparate papers, will also be excluded. The main choice is original publications, regardless of the publication status.

#### Type of participants

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4 Diabetic patients with depression or anxiety symptoms, regardless of the type of diabetes, gender,  
5 age, race, economic ability, and education level. Patients with other diseases or healthy persons  
6 will be excluded.  
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#### 10 11 Type of interventions and controls 12

13 The interventions include music intervention (music therapy or music medicine, no restriction on  
14 the type of music) alone or combined with other interventions that refer to the following therapies:  
15 (1) routine treatments for diabetes, which mainly include pharmacologic approaches to glycemic  
16 treatment, diabetes self-management education and support (DSMES), and others, according to  
17 the newest guideline of the American Diabetes Association (ADA);[42,43] (2) other therapies  
18 such as acupoint therapy,[44] metabolic surgery,[45] etc. When the used intervention is the music  
19 intervention alone, the controls can be people with no treatment, placebo, or other active therapies,  
20 while the same therapies should be used with the controls when the music intervention is used  
21 combined with active therapies.  
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#### 33 Type of outcome measures 34

35 Since this review aims at the systematic assessment of the effect of music intervention on  
36 depression or anxiety in diabetic patients, we will choose the depression and anxiety scores as the  
37 primary outcomes, which can indicate the degree of depression and anxiety on certain scales.  
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40 The depression score is measured using the self-rating depression scale (SDS), Hamilton  
41 depression scale (HAMD), or other validated scales for depression. The anxiety score is measured  
42 using the self-rating anxiety scale (SAS), Hamilton anxiety scale (HAMA), or other validated  
43 scales for anxiety.  
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48 The secondary outcome is the safety, measured via the incidence of adverse effects.  
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## 52 **Search methods** 53

### 54 Search resources 55 56 57 58 59 60

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4 The following nine online electronic databases will be searched from their inception to March  
5 2020: PubMed, Web of Science, Embase, EBSCO, Cochrane Library, Chinese National  
6 Knowledge Infrastructure (CNKI), Wanfang Database, Chinese Scientific Journal Database (VIP)  
7 and Chinese Biomedical and Medical Database (CBM). We also plan to search other relevant  
8 resources as far as possible, including: (1) grey literature (like conference literature and  
9 dissertations) from the following four sources: OpenGrey ([www.opengrey.eu/](http://www.opengrey.eu/)), CNKI  
10 ([www.cnki.net](http://www.cnki.net)), Open Access Theses and Dissertations ([oatd.org](http://oatd.org)), and the British Library  
11 EThOS ([ethos.bl.uk/](http://ethos.bl.uk/)); (2) the reference lists of relevant publications for additional studies.  
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### 21 Search strategies

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23 The search strategy will include the MeSH terms of diabetes mellitus, depression, anxiety, music  
24 therapy, music and singing, combined with their respective free-text terms. The search details of  
25 PubMed are simplified in table 1.  
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**Table 1** Example of PubMed search strategy

Number	Search terms
#1	"Diabetes Mellitus"[Mesh]
#2	"Depression"[Mesh] OR Depressions[Title/Abstract] OR Depressive Symptoms[Title/Abstract] OR Depressive Symptom[Title/Abstract] OR Symptom, Depressive[Title/Abstract] OR Symptoms, Depressive[Title/Abstract] OR Emotional Depression[Title/Abstract] OR Depression, Emotional[Title/Abstract] OR Depressions, Emotional[Title/Abstract] OR Emotional Depressions[Title/Abstract]
#3	"Anxiety"[Mesh] OR Hypervigilance [Title/Abstract] OR Nervousness [Title/Abstract]
#4	#2 OR #3
#5	"Music Therapy"[Mesh] OR Therapy, Music [Title/Abstract]
#6	"Music"[Mesh] OR music intervention[Title/Abstract] OR music medicine[Title/Abstract] OR music listening[Title/Abstract] OR audio recording[Title/Abstract] OR mp3 hearing[Title/Abstract]
#7	"Singing"[Mesh] OR sing[Title/Abstract] OR sings[Title/Abstract] OR song[Title/Abstract] OR compose[Title/Abstract] OR composing[Title/Abstract]
#8	#5 OR #6 OR #7
#9	randomized controlled trial [Publication Type] OR randomized [Title/Abstract] OR placebo [Title/Abstract]
#10	#1 AND #4 AND #8AND #9

### Data collection and analysis

#### Studies selection

First, two researchers (L-yZ and YT) will respectively screen the keywords, titles, and abstracts of all the obtained studies using the EndNote X9 software and determine whether the trials comply with the inclusion criteria. Then, we will also get access to the full text of all the studies with possible relevance for further assessment. Each of the excluded studies will be noted with the exclusion reasons. Any disagreements will be settled through consensus or referral to a third researcher (XxF). The specific selection steps are presented in figure 1.

## Data extraction

Two researchers (L-yZ and YT) will independently extract and tabulate the following data items using the Microsoft Excel software:

1. General information (including the publication year and name of the first author).
2. Study design (including the random method, allocation concealment, and blinding).
3. Participants (including the sample size, gender, age, area, depression score, anxiety score, and course of disease).
4. Treatment (including the interventions, controls, music type, and the course of treatment).
5. Outcomes (including the depression score, anxiety score, and safety).

In the case of different opinions, the final decision will be made by the third researcher (XxF).

## Assessment of risk of bias

In order to evaluate the risk of bias of all the included RCT studies, the Cochrane Collaboration's Risk of Bias tool[46] will be applied by two authors (L-zW and YZ). The assessed domains will be the following: sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessors, incomplete outcome data, selective reporting, and other sources of bias. The assessments will be classified into "low", "unclear" or "high" risk.

## Measures of treatment effect

Considering that all the outcomes (depression score, anxiety score, and safety) are continuous variables, when the quantitative data are from the same measurement method or a small data scale, the mean difference (MD) and 95% confidence interval (CI) will be calculated. Otherwise, the standardized mean difference (SMD) and 95% CI will be calculated.

## Unit of analysis issues

For the standard research that has one experimental group with one control group, the unit of

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4 analysis is the individual. For the multi-arm study with more than two intervention groups, the  
5 recommended method is to create a single pair-wise comparison by combining the groups.  
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#### 8 9 Dealing with missing data

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11 If the required data are unavailable from the literature, one researcher (YZ) will contact the  
12 corresponding author via email and ask for further information.  
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#### 15 16 17 Assessment of heterogeneity

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19 A meta-analysis will be implemented if the included studies are adequately homogenous. The p  
20 value and  $I^2$  are used to assess the heterogeneity of the statistics. The heterogeneity is considered  
21 to be acceptable when p value  $> 0.05$  and  $I^2 \leq 50\%$  and significant when p value  $< 0.05$  or  $I^2 >$   
22 50%.  
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#### 28 29 Assessment of reporting bias

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31 The publication bias will be implemented if more than 10 studies are included through a funnel  
32 plot.  
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#### 35 36 37 Data synthesis

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39 The Review Manager 5.3 software, provided by the Cochrane collaboration, will be used to  
40 analyze the data. If the included studies are adequately homogenous, then a fixed-effects model  
41 will be used for the statistical combination. Since all the outcomes are continuous variables in this  
42 meta-analysis, we will calculate the mean difference (MD) and 95% confidence interval (CI)  
43 when the outcomes are from the same measurement method or a small data scale. Otherwise, we  
44 will calculate the standardized mean difference (SMD) and 95% CI. If there is significant  
45 heterogeneity among the included studies, subgroup or sensitivity analyses will be performed. If a  
46 meta-analysis is unavailable, descriptive summaries will be provided.  
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### Subgroup analysis

The subgroup analyses are planned as follows:

1. The type of music intervention (music therapy or music medicine).
2. The type of scales (SDS, HAMD, SAS, HAMA, or other validated depression or anxiety scales).
3. The different age groups.

### Sensitivity analysis

The sensitivity analyses will be performed by including or excluding a specific study, such as a study without clear allocation concealment or a randomization method, to observe whether the results change.

### Evaluating the evidence

The GRADE guideline will be used to evaluate the quality of evidence.[47] Based on the GRADE method, the quality of evidence can be assessed by 4 levels: “high”, “medium”, “low” and “very low”. The GRADE profiler 3.2 software will be applied for the analysis.

### Patient and public involvement

No patients or volunteers from the public will be involved in this study.

## **DISCUSSION**

Depression and anxiety often occur independently or simultaneously during the development of many chronic diseases. In recent years, an increasing number of studies have been investigating the comorbid depression or anxiety in diabetics. This increased interest is not only because the bidirectional relationship between depression/anxiety and diabetes can lead to deterioration of the diseases, increased difficulties in treatment, as well as elevated mortality rates,[48-51] but also because the therapeutic methods for treating the comorbidities are limited and unsatisfactory. On



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4 the one hand, some antidepressant drugs, such as nortriptyline and sertraline, may complicate the  
5 glycaemic control.[52] On the other hand, psychotherapy that is based on verbal communication  
6 requires a professional psychiatrist and is expensive.  
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10 Music intervention has been proved by many studies to have a beneficial effect on depression  
11 and anxiety, as it strengthens the awareness and sensitiveness for positive emotions.[53]  
12 Noticeably, a few studies also showed that music intervention can simultaneously reduce blood  
13 glucose and HbA1c levels.[24,54] Therefore, music intervention is an applicable method to treat  
14 depression and anxiety in diabetic patients. Additionally, this almost side-effect-free intervention  
15 is safer than pharmacotherapy, easier to be operated and costs less than psychotherapy based on  
16 verbal communication; thus, it is conducive to clinical promotion and application.  
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23 Although music intervention has been applied in the treatment of depression and anxiety with  
24 diabetes for 12 years now,[55] there is still no systematic review or meta-analysis to evaluate the  
25 potential pros and cons of this therapeutic method. Thus, this study intends to provide strong  
26 evidence on the benefits of applying music intervention to treat mental disorders in diabetic  
27 patients and synchronously provide evidence to which related guidelines can refer.  
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33 However, a language bias may exist in this meta-analysis because it includes only the studies in  
34 English and Chinese due to the language barrier. Therefore, some related studies from the  
35 medical databases in other languages might be missed.  
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39 In conclusion, this meta-analysis will help to assess the underlying benefits and harms of music  
40 intervention on comorbid depression or anxiety in diabetic patients. Moreover, the results of this  
41 study will represent a reference for the guidelines of relevant areas, attracting more attention to  
42 the music intervention, and facilitating its clinical application to benefit more patients.  
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## 48 **ETHICS AND DISSEMINATION**

49 Since this meta-analysis used published data, no ethical approval was required. The results of this  
50 systematic review will be published in a peer-reviewed journal.  
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## Figure legend

**Figure 1** Flowchart to present the search process.

**Contributions** L-yZ and C-gX contributed to the conception of the study. The manuscript of the protocol was drafted by L-yZ and revised by XxF and C-gX. L-yZ and YT will independently screen the potential studies and extract the data from the included studies. L-zW and YZ will assess the risk of bias and accomplish data synthesis. XxF will arbitrate any disagreements. C-gX will ensure that no errors occur during the review. All the authors approved the publication of the protocol.

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**Competing interests** None declared.

**Patient consent for publication** Not required.

**Provenance and peer review** Not commissioned; externally peer reviewed.

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## REFERENCES

1. International Diabetes Federation. IDF Diabetes Atlas (9<sup>th</sup> edition), 2019. Available: <http://www.diabetesatlas.org/> [Accessed 9 Nov 2019].
2. World Health Organization. Global report on diabetes, 2014. Available: <https://www.who.int/news-room/fact-sheets/detail/diabetes> [Accessed 9 Nov 2019].

3. Ali S, Stone MA, Peters JL, et al. The prevalence of co-morbid depression in adults with type 2 diabetes: a systematic review and meta-analysis. *Diabet Med* 2006;23:1165–73. doi:10.1111/j.1464-5491.2006.01943.x
4. Anderson RJ, Freedland KE, Clouse RE, et al. The prevalence of comorbid depression in adults with diabetes: a meta-analysis. *Diabetes Care* 2001;24:1069–78. doi:10.2337/diacare.24.6.1069
5. Knol MJ, Twisk JW, Beekman AT, et al. Depression as a risk factor for the onset of type 2 diabetes mellitus. A meta-analysis. *Diabetologia* 2006;49:837–45. doi:10.1007/s00125-006-0159-x
6. Cosgrove MP, Sargeant LA, Griffin SJ. Does depression increase the risk of developing type 2 diabetes?. *Occup Med (Lond)* 2008;58:7–14. doi:10.1093/occmed/kqm105
7. Mezuk B, Eaton WW, Albrecht S, et al. Depression and type 2 diabetes over the lifespan: a meta-analysis. *Diabetes Care* 2008;31:2383–90. doi:10.2337/dc08-0985
8. Grigsby AB, Anderson RJ, Freedland KE, et al. Prevalence of anxiety in adults with diabetes: a systematic review. *J Psychosom Res* 2002;53:1053–60. doi:10.1016/s0022-3999(02)00417-8
9. Smith KJ, Beland M, Clyde M, et al. Association of diabetes with anxiety: a systematic review and meta-analysis. *J Psychosom Res* 2013;74:89–99. doi:10.1016/j.jpsychores.2012.11.013
10. Smith KJ, Deschênes SS, Schmitz N. Investigating the longitudinal association between diabetes and anxiety: a systematic review and meta-analysis. *Diabet Med* 2018;35:677–93. doi:10.1111/dme.13606
11. Egede LE. Major depression in individuals with chronic medical disorders: prevalence, correlates and association with health resource utilization, lost productivity and functional disability. *Gen Hosp Psychiatry* 2007;29:409–16. doi:10.1016/j.genhosppsy.2007.06.002
12. Naicker K, Johnson JA, Skogen JC, et al. Type 2 diabetes and comorbid symptoms of depression and anxiety: longitudinal associations with mortality risk. *Diabetes Care* 2017;40:352–8. doi:10.2337/dc16-2018

- 1  
2  
3  
4 13. van der Feltz-Cornelis CM, Nuyen J, Stoop C, et al. Effect of interventions for major  
5 depressive disorder and significant depressive symptoms in patients with diabetes mellitus: a  
6 systematic review and meta-analysis. *Gen Hosp Psychiatry* 2010;32:380–  
7  
8 95.doi:10.1016/j.genhosppsy.2010.03.011  
9  
10  
11 14. Komsuoglu Celikyurt I, Mutlu O, Ulak G, et al. Exenatide treatment exerts anxiolytic- and  
12 antidepressant-like effects and reverses neuropathy in a mouse model of type-2 diabetes. *Med*  
13  
14 *Sci Monit Basic Res* 2014;20:112–7.doi:10.12659/MSMBR.891168  
15  
16  
17 15. Leubner D, Hinterberger T. Reviewing the effectiveness of music interventions in treating  
18 depression. *Front Psychol* 2017;8:1109.doi:10.3389/fpsyg.2017.01109  
19  
20  
21 16. American Music Therapy Association. What is music therapy?, 2013.Available:  
22  
23 <https://www.musictherapy.org/about/musictherapy/> [Accessed 9 Jan 2020].  
24  
25  
26 17. Dileo C. A classification model for music and medicine. National Association of Music  
27  
28  
29  
30 18. Raglio A, Bellelli G, Mazzola P, et al. Music, music therapy and dementia: a review of  
31 literature and the recommendations of the Italian Psychogeriatric Association. *Maturitas*  
32  
33 2012;72:305–10.doi:10.1016/j.maturitas.2012.05.016  
34  
35  
36 19. Dileo C. Effects of music and music therapy on medical patients: a meta-analysis of the  
37 research and implications for the future. *J Soc Integr Oncol* 2006;4:67–  
38  
39 70.doi:10.2310/7200.2006.002  
40  
41 20. Thaut MH, Gardiner JC, Holmberg D, et al. Neurologic music therapy improves executive  
42 function and emotional adjustment in traumatic brain injury rehabilitation. *Ann N Y Acad Sci*  
43  
44 2009;1169:406–16.doi:10.1111/j.1749-6632.2009.04585.x  
45  
46  
47 21. Kim DS, Park YG, Choi JH, et al. Effects of music therapy on mood in stroke patients.  
48  
49 *Yonsei Med J* 2011;52:977–81.doi:10.3349/ymj.2011.52.6.977  
50  
51 22. Nwebube C, Glover V, Stewart L. Prenatal listening to songs composed for pregnancy and  
52 symptoms of anxiety and depression: a pilot study. *BMC Complement Altern Med*  
53  
54 2017;17:256.doi:10.1186/s12906-017-1759-3  
55  
56

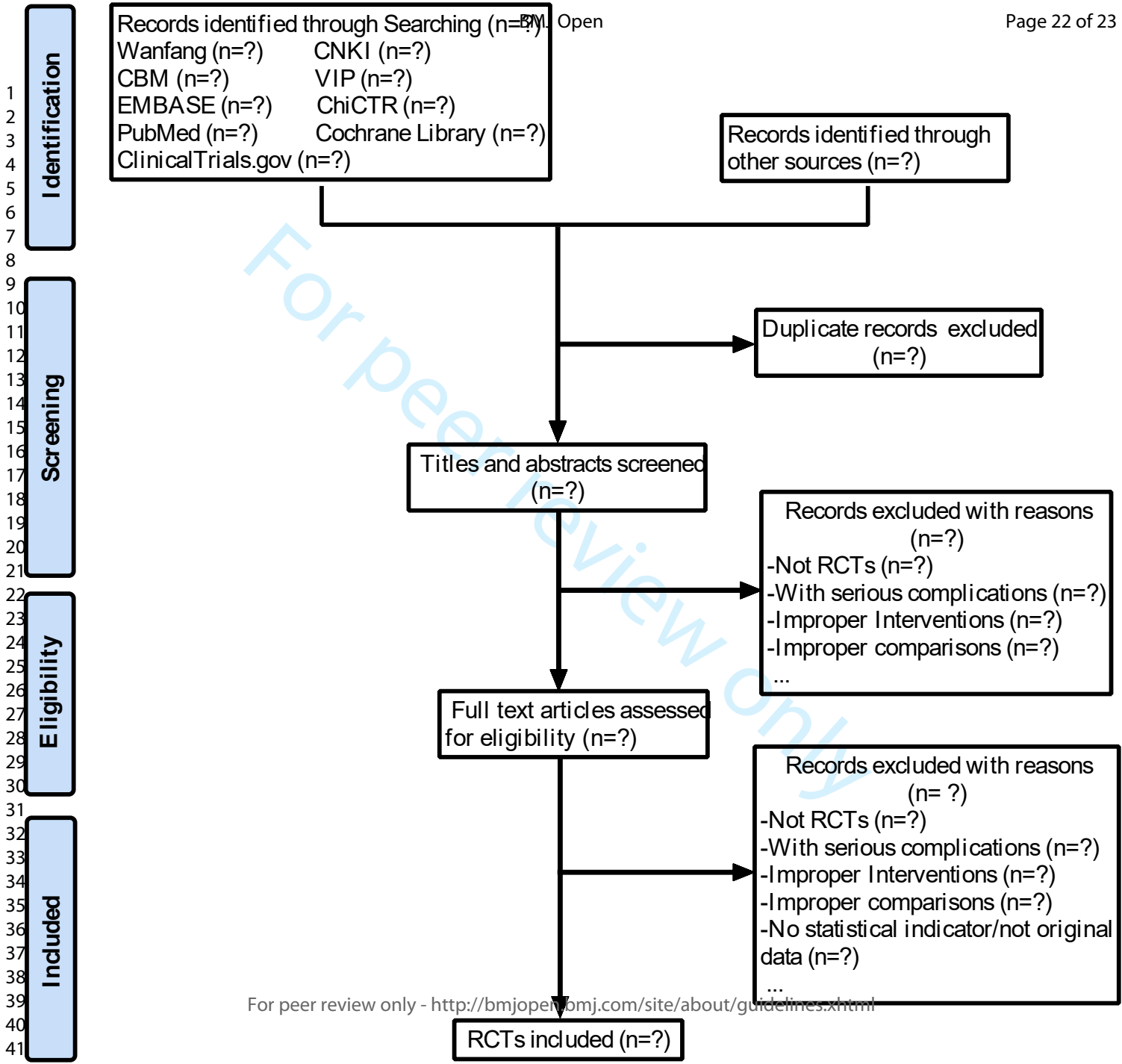
- 1  
2  
3  
4 23. Lin XX, Ji JM, Zhou GY. Influence of listening to Jiao tune music on sleep quality and blood  
5 glucose in elderly patients with type 2 diabetes accompanied by insomnia. *Journal of Fujian*  
6 *University of Traditional Chinese Medicine* 2017;27:44-8.doi:CNKI:SUN:FYXB.0.2017-01-  
7 011  
8  
9  
10  
11 24. Mandel SE, Davis BA, Secic M. Effects of music therapy and music-assisted relaxation and  
12 imagery on health-related outcomes in diabetes education: a feasibility study. *Diabetes Educ*  
13 2013;39:568–81.doi:10.1177/0145721713492216  
14  
15  
16  
17 25. Centers for Disease Control and Prevention. National diabetes statistics report, 2020.  
18 Available: <https://www.cdc.gov/diabetes/data/statistics/statistics-report.html> [Accessed 3 Jul  
19 2020].  
20  
21  
22  
23 26. Gabrielsson A, Wik SL. Strong experiences related to music: a descriptive system. *Music Sci*  
24 2003;7:157–217.doi:0.1177/102986490300700201  
25  
26  
27 27. Zentner M, Grandjean D, Scherer KR. Emotions evoked by the sound of music:  
28 characterization, classification, and measurement. *Emotion* 2008;8:494–  
29 521.doi:10.1037/1528-3542.8.4.494  
30  
31  
32  
33 28. Saarikallio S. Music as emotional self-regulation throughout adulthood. *Psychol Music*  
34 2011;39:307–27.doi:10.1177/0305735610374894  
35  
36  
37 29. Gök Ugur H, Yaman Aktaş Y, Orak OS, et al. The effect of music therapy on depression and  
38 physiological parameters in elderly people living in a Turkish nursing home: a randomized-  
39 controlled trial. *Aging Ment Health* 2017;21:1280–6.doi:10.1080/13607863.2016.1222348  
40  
41  
42  
43 30. Gómez Gallego M, Gómez García J. Music therapy and Alzheimer's disease: Cognitive,  
44 psychological, and behavioural effects. *Neurologia* 2017;32:300–  
45 8.doi:10.1016/j.nrl.2015.12.003  
46  
47  
48 31. Cheung DSK, Lai CKY, Wong FKY, et al. The effects of the music-with-movement  
49 intervention on the cognitive functions of people with moderate dementia: a randomized  
50 controlled trial. *Aging Ment Health* 2018;22:306–15.doi:10.1080/13607863.2016.1251571  
51  
52  
53  
54 32. Wang SC, Yu CL, Chang SH. Effect of music care on depression and behavioral problems in  
55  
56  
57  
58  
59  
60

- 1  
2  
3  
4 elderly people with dementia in Taiwan: a quasi-experimental, longitudinal study. *Aging*  
5 *Ment Health* 2017;21:156–62.doi:10.1080/13607863.2015.1093602
- 6  
7  
8 33. Bieleninik L, Geretsegger M, Mössler K, et al. Effects of improvisational music therapy vs  
9 enhanced standard care on symptom severity among children with autism spectrum disorder:  
10 the TIME-A randomized clinical trial. *JAMA* 2017;318(6):525–  
11 535.doi:10.1001/jama.2017.9478
- 12  
13  
14 34. Giovagnoli AR, Manfredi V, Parente A, et al. Cognitive training in Alzheimer's disease: a  
15 controlled randomized study. *Neurol Sci* 2017;38:1485–93.doi:10.1007/s10072-017-3003-9
- 16  
17  
18 35. Deng HX, Gao GS, Li ZM, et al. Study of the effect of music therapy in the treatment of  
19 elderly patients with diabetes. *China Health Care and Nutrition*  
20 2013;23:1186.doi:10.3969/j.issn.1004-7484(s).2013.03.206
- 21  
22  
23 36. Zhang ZW. Study of the effect of music therapy and psychotherapy adjuvant therapy in the  
24 treatment of type 2 diabetes. *China Medicine and Pharmacy* 2011,01:150-  
25 1.doi:CNKI:SUN:GYKX.0.2011-18-103
- 26  
27  
28 37. Solanki MS, Zafar M, Rastogi R. Music as a therapy: role in psychiatry. *Asian J Psychiatr*  
29 2013;6:193–9.doi:10.1016/j.ajp.2012.12.001
- 30  
31  
32 38. Petrovsky D, Cacchione PZ, George M. Review of the effect of music interventions on  
33 symptoms of anxiety and depression in older adults with mild dementia. *Int Psychogeriatr*  
34 2015;27:1661–70.doi:10.1017/S1041610215000393
- 35  
36  
37 39. Aalbers S, Fusar-Poli L, Freeman RE, et al. Music therapy for depression. *Cochrane*  
38 *Database Syst Rev* 2017;11:CD004517.doi:10.1002/14651858.CD004517.pub3
- 39  
40  
41 40. Shamseer L, Moher D, Clarke M, et al. Preferred reporting items for systematic review and  
42 meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. *BMJ*  
43 2015;350:g7647.doi:10.1136/bmj.g7647
- 44  
45  
46 41. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic  
47 reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and  
48 elaboration. *BMJ* 2009;339:b2700.doi:10.1136/bmj.b2700
- 49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

- 1  
2  
3  
4 42. American Diabetes Association. 9. Pharmacologic approaches to glycemic treatment:  
5 standards of medical care in diabetes-2020. *Diabetes Care* 2020;43(Suppl 1):S98–  
6 110.doi:10.2337/dc20-S009  
7  
8  
9  
10 43. American Diabetes Association. 5. Facilitating behavior change and well-being to improve  
11 health outcomes: standards of medical care in diabetes-2020. *Diabetes Care* 2020;43(Suppl  
12 1):S48–65.doi:10.2337/dc20-S005  
13  
14  
15 44. Feng Y, Fang Y, Wang Y, et al. Acupoint therapy on diabetes mellitus and its common  
16 chronic complications: a review of its mechanisms. *Biomed Res Int*  
17 2018;2018:3128378.doi:10.1155/2018/3128378  
18  
19  
20 45. Pérez-Pevida B, Escalada J, Miras AD, et al. Mechanisms underlying type 2 diabetes  
21 remission after metabolic surgery. *Front Endocrinol (Lausanne)*  
22 2019;10:641.doi:10.3389/fendo.2019.00641  
23  
24  
25 46. Higgins JPT, Thomas J, Chandler J, et al. Cochrane Handbook for Systematic Reviews of  
26 Interventions version 6.0 (updated July 2019). Cochrane, 2019. Available:  
27 www.training.cochrane.org/handbook [Accessed 3 Jul 2020].  
28  
29  
30  
31 47. Balshem H, Helfand M, Schunemann HJ, et al. GRADE guidelines: 3. Rating the quality of  
32 evidence. *J Clin Epidemiol* 2011;64:401–6.doi:10.1016/j.jclinepi.2010.07.015  
33  
34  
35 48. Gonzalez JS, Peyrot M, McCarl LA, et al. Depression and diabetes treatment nonadherence: a  
36 meta-analysis. *Diabetes Care* 2008;31:2398–403.doi:10.2337/dc08-1341  
37  
38  
39 49. Trief PM, Foster NC, Chaytor N, et al. Longitudinal changes in depression symptoms and  
40 glycemia in adults with type 1 diabetes. *Diabetes Care* 2019;42:1194–201.doi:10.2337/dc18-  
41 2441  
42  
43  
44  
45 50. Novak M, Mucsi I, Rhee CM, et al. Increased risk of incident chronic kidney disease,  
46 cardiovascular disease, and mortality in patients with diabetes with comorbid depression.  
47 *Diabetes Care* 2016;39:1940–7.doi:10.2337/dc16-0048  
48  
49  
50  
51 51. Lustman PJ, Anderson RJ, Freedland KE, et al. Depression and poor glycemic control: a  
52 meta-analytic review of the literature. *Diabetes Care* 2000;23:934–  
53  
54  
55  
56  
57  
58  
59  
60

- 1  
2  
3  
4 42.doi:10.2337/diacare.23.7.934  
5  
6 52. Roopan S, Larsen ER. Use of antidepressants in patients with depression and comorbid  
7  
8 diabetes mellitus: a systematic review. *Acta Neuropsychiatr* 2017;29:127–  
9  
10 39.doi:10.1017/neu.2016.54  
11  
12 53. Croom AM. Music, neuroscience, and the psychology of well-being: a précis. *Front Psychol*  
13  
14 2012;2:393.doi:10.3389/fpsyg.2011.00393  
15  
16 54. Abd-Elshafy SK, Khalaf GS, Abo-Kerisha MZ, et al. Not all sounds have negative effects on  
17  
18 children undergoing cardiac surgery. *J Cardiothorac Vasc Anesth* 2015;29:1277–  
19  
20 84.doi:10.1053/j.jvca.2015.01.005  
21  
22 55. Yu SJ, Sun ZY, Zhou J, et al. Study of the effect of music therapy and psychological  
23  
24 intervention in the treatment of diabetic patients. *Hebei med* 2007;13:903-  
25  
26 6.doi:10.3969/j.issn.1006-6233.2007.08.010  
27  
28  
29  
30  
31  
32  
33  
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## PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol\*

Section and topic	Item No	Checklist item
<b>ADMINISTRATIVE INFORMATION</b>		
Title:		
Identification <b>P<sub>1</sub></b>	1a	Identify the report as a protocol of a systematic review
Update <b>None</b>	1b	If the protocol is for an update of a previous systematic review, identify as such
Registration <b>P<sub>2</sub></b>	2	If registered, provide the name of the registry (such as PROSPERO) and registration number
Authors:		
Contact <b>P<sub>1</sub></b>	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author
Contributions <b>P<sub>14</sub></b>	3b	Describe contributions of protocol authors and identify the guarantor of the review
Amendments <b>None</b>	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments
Support:		
Sources <b>P<sub>14</sub></b>	5a	Indicate sources of financial or other support for the review
Sponsor <b>None</b>	5b	Provide name for the review funder and/or sponsor
Role of sponsor or funder <b>None</b>	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol
<b>INTRODUCTION</b>		
Rationale <b>P<sub>4-5</sub></b>	6	Describe the rationale for the review in the context of what is already known
Objectives <b>P<sub>6-7</sub></b>	7	Provide an explicit statement of the question(s) the review will address with reference to participants <b>P<sub>6-7</sub></b> , interventions <b>P<sub>7</sub></b> , comparators <b>P<sub>7</sub></b> , and outcomes <b>P<sub>7</sub></b> (PICO)
<b>METHODS</b>		
Eligibility criteria <b>P<sub>6-7</sub></b>	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review
Information sources <b>P<sub>6-8</sub>, P<sub>11</sub></b>	9	Describe all intended information sources (such as electronic databases <b>P<sub>7-8</sub></b> , contact with study authors <b>P<sub>11</sub></b> , trial registers <b>P<sub>6</sub></b> or other grey literature sources <b>P<sub>8</sub></b> ) with planned dates of coverage <b>P<sub>8</sub></b>
Search strategy <b>P<sub>9</sub></b>	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated

Study records:		
Data management P <sub>10</sub>	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review
Selection process P <sub>9</sub>	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)
Data collection process P <sub>10</sub>	11c	Describe planned method of extracting data from reports (such as piloting forms done independently, in duplicate), any processes for obtaining and confirming data from investigators
Data items P <sub>10</sub>	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications
Outcomes and prioritization P <sub>7</sub>	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale
Risk of bias in individual studies P <sub>10</sub>	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis
Data synthesis P <sub>10-12</sub>	15a	Describe criteria under which study data will be quantitatively synthesised P <sub>10-11</sub>
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I <sup>2</sup> , Kendall's $\tau$ ) P <sub>11</sub>
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression) P <sub>12</sub>
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned P <sub>11</sub>
Meta-bias(es) P <sub>11</sub>	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)
Confidence in cumulative evidence P <sub>12</sub>	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)

**\* It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

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