



Physical activity for diabetes-related depression: A systematic review and meta-analysis



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ABSTRACT

Patients with diabetes have an increased risk of developing depression compared with non-diabetic individuals. We aimed to examine the utility of physical activity in the treatment of diabetes-related depression using a meta-analysis. Multiple databases were searched from inception to February 1, 2018. A random effects pooling model was used to examine the standardized mean difference and mean difference in the meta-analysis. A sensitivity analysis and meta-regression analyses were performed. Fourteen studies were included in a systematic review (1020 patients), while 13 were included in a meta-analysis (962 patients). Physical activity had a beneficial effect on depression as measured by Hedge's *g* (standardized mean difference = -0.59 ; 95% CI = -0.93 to -0.24). A sensitivity analysis indicated that the findings did not change in a meaningful way with the exclusion of studies with a high or unknown risk of bias in incomplete outcome data. Meta-regression analyses demonstrated that no covariate significantly influenced the main effect size. Physical activity had a significantly beneficial effect on depression as measured by the Beck Depression Inventory (mean difference = -2.90 ; 95% CI = -4.53 to -1.28). These findings suggest that physical activity may help ameliorate depression in patients with diabetes.

1. Introduction

The development of diabetes and its associated complications has been linked to a lack of exercise (Sullivan et al., 2005). Thus, some degree of physical activity is recommended for diabetic patients (American Diabetes Association, 2018). The positive effect of physical activity may result from increased glycemic control (Umpierre et al., 2011) with research showing that physical activity is associated with a reduced risk of total and cardiovascular mortality in this population (Hu et al., 2005; Lee et al., 2012).

It is possible that exercise might also be important for psychiatric symptoms given that diabetes has also been associated with poorer mental health. Specifically, two studies have reported that people with type 2 diabetes have an increased risk of developing depression compared with non-diabetic controls (Ali et al., 2006; Nouwen et al., 2010), while a systematic review and meta-analysis demonstrated a high prevalence of depressive symptoms in youth with type 1 diabetes (Buchberger et al., 2016). Furthermore, a comprehensive review has highlighted how diabetes-related depression is highly persistent and

recurrent, causing a significant negative impact on clinical outcomes and quality of life (Andreoulakis et al., 2012). Despite this, conventional pharmacological interventions for diabetes-related depression might be problematic. In particular, the use of antidepressants has been linked to an increased risk of diabetes (Salvi et al., 2017; Yoon et al., 2013), although a recent systematic review suggests their possible utility in ameliorating diabetes-related depression (Roopan and Larsen, 2017). Nonetheless, given the possible negative effects of drug-based treatments, physical activity might also have an important role in this context, especially as research has highlighted its positive effect in combating depression in other groups. One meta-analysis showed for example, that physical activity appears to be an acceptable and promising intervention for adolescents and young adults experiencing depression (Bailey et al., 2017), while another has verified its utility in the treatment of depression in elderly people (Bridle et al., 2012). Indeed, a third meta-analysis also found that resistance training was effective in treating depressive symptoms regardless of health status (Gordon et al., 2018). Moreover, a meta-analysis that adjusted for publication bias strongly suggested exercise as an evidence-based treatment for

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depression (Schuch et al., 2016).

Regarding diabetes, a recent review indicated that exercise is beneficial in combating depression in patients with type 2 diabetes (van der Heijden et al., 2013). However, as this study did not include individuals with type 1 diabetes, a systematic review of a wider range of controlled trials is warranted. In addition, to the best of our knowledge, as yet, no meta-analysis has been conducted to examine the utility of physical activity in the treatment of diabetes-related depression. The aim of the current study was to therefore examine the utility of physical activity in the treatment of diabetes-related depression using meta-analytic techniques. We hypothesized that physical activity would be beneficial for depression in diabetic individuals although its effects may differ depending on the characteristics of the study participants and protocols.

2. Material and methods

2.1. Search strategies

This meta-analysis was performed based on the PRISMA guidelines (Pikhart and Pikhartova, 2015). From inception to February 1, 2018, ZN and TI independently examined the PubMed, PsychINFO, and Web of Science databases, using the following terms, (1) “exercise” OR “physical activity” OR “fitness” OR “aerobic” OR “resistance training,” and (2) “depression” OR “melancholy,” and (3) “diabetes” OR “insulin resistance.” The specific strategies used are described in the Supplementary data. We selected and assessed full-text English language studies of randomized controlled trials. Additional articles were obtained by scanning the reference lists of included studies and previous reviews. The senior reviewer (NS) approved the final list of included studies.

2.2. Eligibility criteria

In this study physical activity was conceptualized as bodily movement produced by the contraction of skeletal muscles that increases energy expenditure above the basal level and can be categorized in various ways, including type, intensity, and purpose (US Department of Health and Human Services, 1996). Following on from this, the pre-specified inclusion criteria applied were as follows: (1) randomized controlled trials (RCTs) comparing physical activity with usual care, sham exercise or a minimal educational intervention; (2) physical activity was maintained for at least four weeks; (3) participants were adults or adolescents classified as having diabetes; and (4) RCTs including the assessment of depression. Outcomes were the change in depression from baseline to a post-intervention point. Included subjects were not necessarily diagnosed as having a major depressive disorder as defined by the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), but all of them underwent an evaluation for depressive symptoms at baseline and follow-up. We did not include trials targeting undiagnosed individuals at risk of diabetes.

2.3. Data collection and coding

ZN performed the coding of outcomes into depression by consulting with NS if and when necessary. When studies did not include mean and standard deviation values, we contacted the primary authors for additional information on these variables. If this method was not successful or feasible, we excluded these studies from the analysis.

2.4. Risk of bias in individual studies and quality appraisal

The Cochrane Collaboration's risk of bias tool (Higgins et al., 2011) was used to assess the methodological quality of the included studies. For each trial, two independent reviewers (TI and ZN) checked the following study characteristics: random sequence generation; allocation concealment; blinding of subjects and personnel; blinding of outcome assessment; incomplete outcome data, selective reporting, and other

potential sources of bias. Assessments were undertaken by two independent reviewers (TI and ZN), while the senior reviewer (NS) thereafter reconciled any disagreements.

2.5. Statistical analyses

Statistical analyses were conducted using Review Manager 5.3 for Windows and STATA 14. We calculated the effect size, indicating the difference in baseline score changes, between the physical activity condition vs. the control group. We used the standardized mean difference (SMD) expressed as Hedge's g (Lakens, 2013). If two or more outcome measures were used, the mean of these effect sizes was calculated so that each trial yielded only one overall effect. In order to assess the extent to which the true population effect size differed among studies, we employed a random effects pooling model (Riley et al., 2011). When data on the mean change from the baseline were not available, the mean change and standard deviation were calculated based on the assumption that the correlation between scores at follow-up and those at the baseline was 0.5. Heterogeneity between studies was assessed through the I^2 statistic (low, moderate, and high heterogeneity to I^2 values of 25%, 50%, and 75%, respectively) (Higgins et al., 2003).

Subgroup analyses were also conducted for age, sex, and intervention duration. A sensitivity analysis was performed to determine whether the findings changed in a meaningful way with the exclusion of studies with a high or unknown risk of bias in incomplete outcome data. Univariate meta-regression analyses were conducted, when possible, to identify which factors influenced outcomes. Funnel plots and Egger's test were used to assess potential publication bias for the meta-analyses (Egger et al., 1997; Sterne et al., 2011). In addition, the Duval and Tweedie trim and fill method was utilized to assess the magnitude of a small study effect (Duval and Tweedie, 2000).

We further sought to address the problem of synthesizing a wide variety of outcome measures for depression (Blackstone, 2002). Thus, for outcome measures evaluated in at least three studies, we respectively meta-analyzed each mean difference (MD) and standard deviation (SD) in the baseline score changes.

2.6. Quality of evidence

The quality of evidence for the outcomes was evaluated in accordance with the guidelines of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) (Guyatt et al., 2008) for risk of bias, inconsistency, indirectness, imprecision, and publication bias. The quality of evidence for each outcome was rated as very low, low, moderate, or high.

3. Results

3.1. Systematic review

The initial search yielded a total of 1712 articles. After removing duplicates, 1580 records were screened. Of these, 14 articles were eligible for inclusion in a systematic review. The PRISMA study selection flowchart is shown in Fig. 1. The 14 studies included in the systematic review encompassed 1020 subjects: 519 in the physical activity condition and 501 in the control group. The selected characteristics of the studies are shown in Table 1. There were considerable differences between the studies in terms of the participant characteristics, intervention types, and outcome measures. Three studies targeted only female patients (Schneider et al., 2016; Talakoub et al., 2012; Yucel and Uysal, 2016), one of which included adolescent subjects (Talakoub et al., 2012), while two studies included only male subjects (Saiari et al., 2011; Sardar et al., 2014). Most of the studies recruited subjects with type 2 diabetes, while two studies enrolled individuals with type 1 diabetes (Collins et al., 2011; Talakoub et al., 2012). Aerobic exercise,

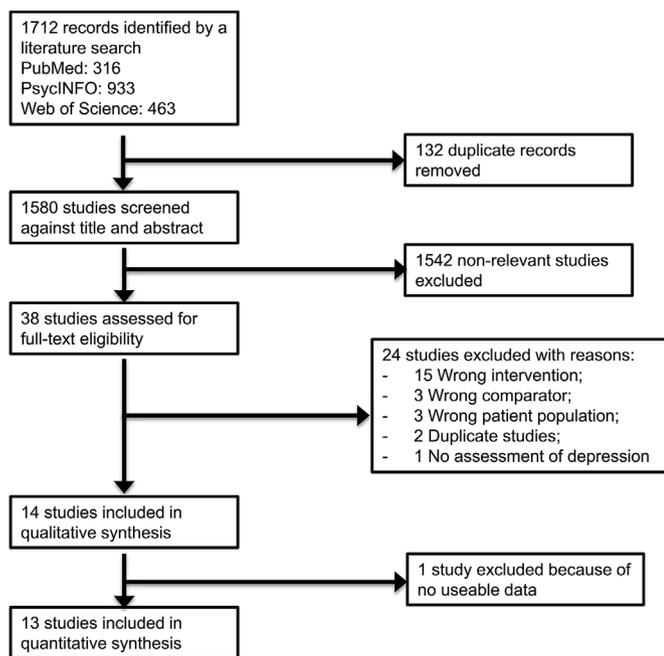


Fig. 1. PRISMA study selection flowchart.

including walking and swimming, was used in most of the trials while anaerobic exercise (resistance training) was conducted in three studies (Aylin et al., 2009; Lincoln et al., 2011; Putiri et al., 2012). The Beck Depression Inventory (BDI) (Richter et al., 1998) and the Center for Epidemiologic Studies Depression Scale (CES-D) (Roberts and Vernon, 1983) were the most frequently used measures for depression ($k = 4$). Two studies reported no subject using antidepressants during the procedure (Aylin et al., 2009; Saiari et al., 2011), while two studies demonstrated no significant between-group difference in antidepressant usage (Lincoln et al., 2011; Schneider et al., 2016). Other studies, in contrast, lacked information about the use of antidepressants. Four studies reported that there were no adverse events throughout the procedure (Aylin et al., 2009; Collins et al., 2011; Kempf and Martin, 2013; Putiri et al., 2012), while others did not provide detailed information. The risk of bias for each study is reported in Supplemental Fig. 1.

3.2. Meta-analysis with standardized mean difference

Thirteen articles were included in the meta-analysis, while one study (Ligtenberg et al. (1998)) that was lacking useable depression measured data was excluded. The meta-analysis included 962 patients with diabetes (489 in the intervention group and 473 in the control group, respectively). In most studies, the depressive symptoms were of mild or moderate severity (reported in Supplemental Table 1). A summary of the main pooled results is presented in Fig. 2. The meta-analysis showed a significant effect of physical activity on depression in diabetic individuals. (SMD = -0.59 ; 95% CI = -0.93 to -0.24). Heterogeneity was high ($p < 0.001$; $I^2 = 84\%$).

3.3. Subgroup analyses

In two subgroup analyses that were limited to trials with a duration of 12 weeks or more, or eight weeks or less, the effect sizes were statistically significant (SMD = -0.72 ; 95% CI = -1.29 to -0.15 , SMD = -0.41 ; 95% CI = -0.72 to -0.11 , respectively, described in Supplemental Figs. 2 and 3). Also, in two subgroup analyses limited to studies that included only subjects aged over 40, and studies other than trials with subjects only aged over 40 (i.e. subjects of all ages), the

effect sizes were both significant (SMD = -0.72 ; 95% CI = -1.30 to -0.14 , SMD = -0.50 ; 95% CI = -0.95 to -0.04 , respectively, described in Supplemental Figs. 4 and 5). A significant difference persisted in a subgroup analysis limited to studies that included both male and female patients (SMD = -0.77 ; 95% CI = -1.24 to -0.30 , shown in Supplemental Fig. 6). However, subgroup analyses that were limited to trials with either only male or female subjects produced non-significant results (shown in Supplemental Figs. 7 and 8).

3.4. Sensitivity analysis and meta-regression

A sensitivity analysis indicated that the findings did not change in a meaningful way with the exclusion of studies with a high or unknown risk of bias in incomplete outcome data (see Fig. 3). Meta-regression analyses demonstrated that the year of study publication, age, sex, sample size, and intervention duration did not significantly influence the main effect size (see Table 2).

3.5. Publication bias

We found little indication of publication bias. Specifically, visual inspection of the funnel plot suggested symmetry (described in Fig. 4), and Egger's test was not significant (described in Supplemental Table 2). Duval and Tweedie's trim and fill procedure demonstrated that no trimming was performed and the imputed effect size was exactly the same as the original one.

3.6. Meta-analyses with mean difference

MD and SD changes in the baseline scores were meta-analyzed for the BDI and the CES-D, which were used in three or more articles. For these outcome measures, subgroup and sensitivity analyses, and meta-regression analyses were not performed due to the small number of trials. For the BDI and the CES-D, the mean values at baseline were 12.55 and 20.07, respectively. Fig. 5 shows the pooled effect of physical activity on the BDI and the CES-D scores in patients with diabetes. Physical activity had a statistically significant effect on depression when measured by the BDI (MD = -2.90 ; 95% CI = -4.53 to -1.28). Heterogeneity was low ($p = 0.26$; $I^2 = 25\%$). In contrast, no significant group difference was found for depression when evaluated by the CES-D (MD = -2.03 ; 95% CI = -4.16 to 0.11). Heterogeneity was also low ($p = 0.44$; $I^2 = 0\%$). Funnel plots of these analyses are presented in Supplemental Figs. 9 and 10.

3.7. Grade evidence profile

Supplemental Table 3 contains detailed information about the quality of evidence assessment and the summary of findings for each of the included outcomes. Risk of bias existed in each outcome. Also, inconsistency was detected in Hedge's g , while imprecision was likely in the CES-D. Indirectness and publication bias were unlikely in all of the outcomes.

4. Discussion

To the best of our knowledge, this is the first meta-analysis to examine the effect of physical activity on depression in diabetes. The result was derived from an analysis that included 13 RCTs with 962 participants that had both type 1 and type 2 diabetes. This analysis showed that there was a significant beneficial effect of physical activity on diabetes-related depression and that the overall effect size was medium (Leppink et al., 2016). This favorable profile of physical activity was also confirmed by meta-regression analyses indicating that the intervention is independent of moderators. A sensitivity analysis further demonstrated that the overall effect size was robust.

In subgroup analyses, significant effects were also found for age

Table 1
Selected characteristics of included randomized controlled trials.

Study	No. of participants (intervention/control)	Sex	Type of diabetes	Intervention	Control	Duration	Outcome measures
Schneider et al. (2016)	15/14	Female	Type 2	Up to 150 min moderate intensity exercise per week (walking, Zumba, Pilates, step aerobics, cardio-kickboxing, and power yoga)	Usual care, encouraged to discuss treatment with physician	24 weeks	BDI, HRSD No significant between-group difference at 24-week follow-up
Yucel et al. (2016)	24/21	Female	Type 2	45–70 min Pilates training, three times per week	Usual care	12 weeks	HADS No significant between-group difference at 12-week follow-up
Pibermik-Okabivuc et al. (2015)	58/57	Mixed	Type 2	A program developed by a physiotherapist, including a personal plan	Diabetes re-education	Six weeks	CES-D No significant between-group difference at one-year follow-up
Osama and Shehab (2015)	50/50	Mixed	Type 2	40-min moderate intensity aerobic exercise, three sessions per week	Usual care	12 weeks	BDI Significant between-group effect at 12-week follow-up
Sardar et al. (2014)	27/26	Male	Type 2	45–60 min aerobic exercise, three times per week	Usual care	Eight weeks	GHQ-28 No significant between-group difference at eight-week follow-up
Kempf et al. (2013)	93/83	Mixed	Type 2	Exercise game at least 30 min per day	Usual care	12 weeks	PAID, CES-D No significant between-group difference at 12-week follow-up
Putiri et al. (2012)	5/8	Mixed	Type 2	Progressive resistance training One-hour group session per week	Usual care	12 weeks	WHO-5 Significant improvement within control group between waiting phase vs. intervention phase
Talakoub et al. (2012)	32/32	Female	Type 1	One-hour exercise, three sessions per week	No detailed information	Six weeks	BDI No information about between-group effect at 12-week follow-up
Collins et al. (2011)	73/72	Mixed	Type 1 or 2	50-min walking, four sessions per week	Video education and face-to-face encouragement by the research coordinator	24 weeks	SCL-90 No statistical information for between-group difference at six-week follow-up
Saijari et al. (2011)	30/30	Male	Type 2	30-min crawl swimming, three times per week	No detailed information	Six weeks	GDS No significant between-group difference at 24-week follow-up
Lincoln et al. (2011)	29/29	Mixed	Type 2	45-min resistance exercise training, three times per week	One-repetition maximum testing every other week	16 weeks	BDI Significant between-group difference at 8-week follow-up
Aylin et al. (2009)	18/18	Mixed	Type 2	30-min resistance training and 15–45 min walking, at least twice per week	Instruction not to undertake any formal exercise or change physical activity level	Eight weeks	CES-D No significant between-group difference at eight-week follow-up
Mckay et al. (2001)	35/33	Mixed	Type 2	Personalized physical activity program	Access to diabetes-specific articles and real-time blood glucose tracking with graphic feedback	Eight weeks	CES-D No significant between-group difference at eight-week follow-up
Ligtenberg et al. (1998)	30/28	Mixed	Type 2	One-hour intensive supervised physical training, three times per week	Diabetes education program	Six weeks	W-BQ22 No significant between-group difference at six-week follow-up

BDI; Beck Depression Inventory, HRSD; Hamilton Rating Scale for Depression, HADS; Hospital Anxiety and Depression Scale, CES-D; Center for Epidemiologic Studies Depression Scale, GHQ-28; General Health Questionnaire-28, PAID; Problem Areas in Diabetes, SCL-90; Symptom Checklist-90, GDS; Geriatric Depression Scale, W-BQ22; The 22-item Well-being Questionnaire.

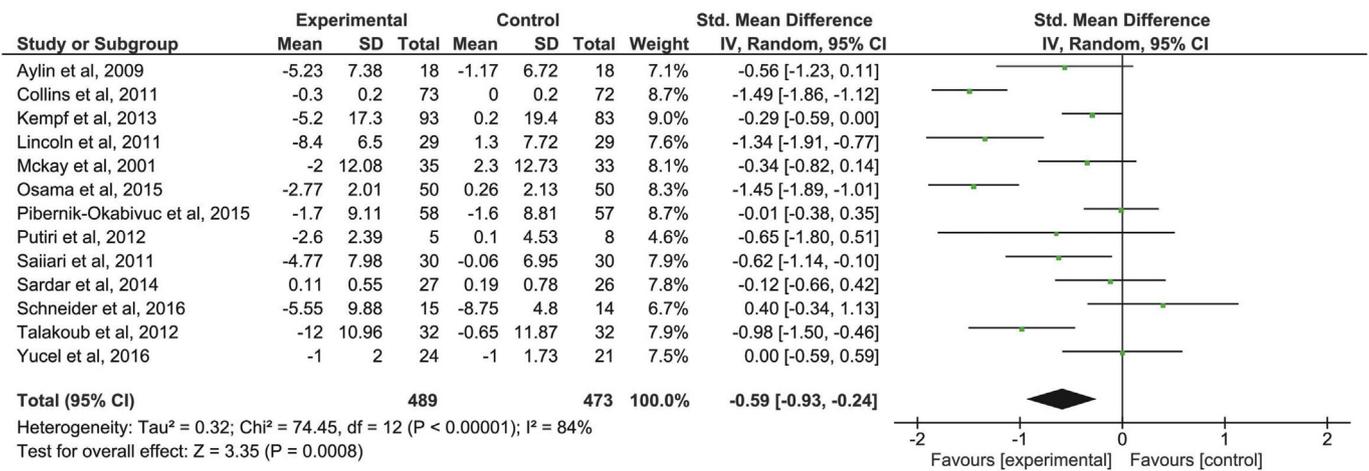


Fig. 2. Summary of pooled results: Standardized mean difference.

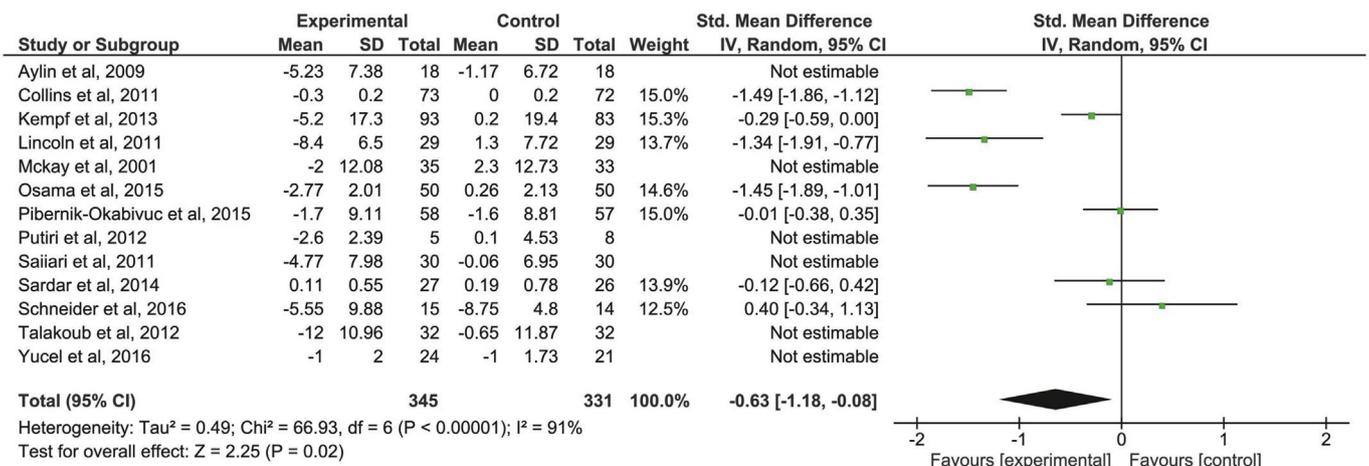


Fig. 3. Sensitivity Analysis with the exclusion of studies with a high or unknown risk of bias in incomplete outcome data.

Table 2
Summary of meta-regression analyses.

Variable	Coefficient (95% CI)	Statistics	p value
Year of study publication	-0.02 (-0.13 to 0.09)	t = -0.44	p = 0.67
Age	-0.004 (-0.04 to 0.03)	t = -0.29	p = 0.78
Sex	0.25 (-1.31 to 1.80)	t = 0.44	p = 0.68
Sample size	0.002 (-0.007 to 0.01)	t = 0.56	p = 0.58
Trial duration	0.04 (-0.02 to 0.98)	t = 1.44	p = 0.18

group (over 40/others), and for intervention duration (12 weeks or more/eight weeks or less). On the other hand, trials involving only male or female subjects produced non-significant results. However, both analyses indicated some degree of improvement with physical activity. In addition, a meta-regression analysis indicated that sex did not moderate the overall effect size. Taken together, these non-significant results might be caused by a lack of statistical power due to the small number of studies included and sample sizes (113 and 138, respectively), as well as the low depression scores at baseline, i.e., “floor effects.”

This meta-analysis included RCTs with patients with different characteristics and from diverse settings. Specifically, the severity of depression at baseline varied across studies, which might have resulted in heterogeneous results. Also, a wide spectrum of interventions may have resulted in heterogeneous effects, as has been suggested in a previous study (Gordon et al., 2018). These aspects may support the external validity of the findings of the current meta-analysis. We

examined multiple complementary electronic databases while using a broad range of search terms, which contributed to a highly sensitive search strategy. Study selection, data extraction, and risk of bias assessment were undertaken by independent reviewers. In addition, the funnel plot, Egger’s test, and the Duval and Tweedie trim and fill method suggested little indication of publication bias. Furthermore, we performed a sensitivity analysis and meta-regression analyses, which supported the robustness of the pooled SMD.

An important aspect of the current study was the meta-analysis of the pooled MD for the different measures of depression. When depression was measured by the BDI, physical activity had a significant effect. The MD for the BDI was 2.90, which was equivalent to 23.1% of the mean value at baseline. This equates to a clinically meaningful difference, as earlier research has indicated that a 17.5% reduction in scores from baseline should be regarded as a minimal clinically important difference on the BDI (Button et al., 2015). However, for the CES-D, there was no significant MD in the baseline score changes. Although it is uncertain what underlies this non-significant result, it might have been due to a lack of statistical power, as the included trials showed some evidence of a positive effect. It is also possible that low CES-D scores at baseline might have contributed to the lack of significance, i.e., a “floor effect.” These results, obtained from the MD in the specific outcome measures, lend credence to the effect measured by the SMD, and suggest high internal validity for the overall study.

The mechanisms by which diabetes-related depression might be ameliorated by physical activity should be considered. A low level of brain-derived neurotrophic factor (BDNF) in the hippocampus and

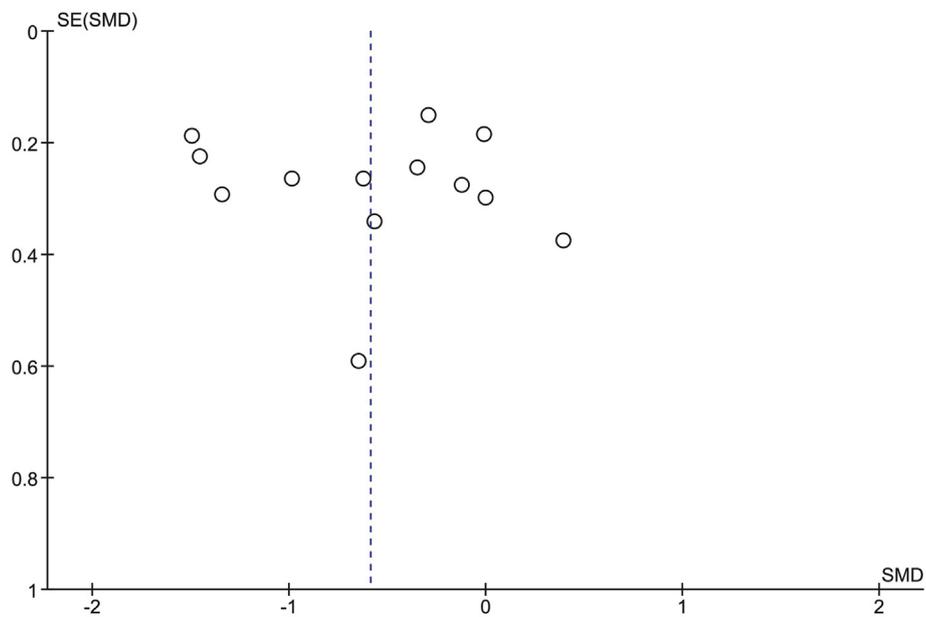


Fig. 4. Funnel plot of included studies (standard mean difference).

prefrontal cortex has been shown to play an important role in the pathophysiology of depression (Yu and Chen, 2011). In addition, a previous study verified that physical activity was correlated with increased levels of BDNF mRNA, which suggests that it might possibly have an effect on depressive symptoms (Russo-Neustadt et al., 2001). Considering that decreased levels of BDNF have also been implicated in the pathogenesis of diabetes (Krabbe et al., 2007), then physical activity may lead to an up-regulation of BDNF and have an effect on diabetes-related depression. It is also possible that variability in physical outcomes may have led to a change in depressive symptoms. For instance, hemoglobin A_{1c} has been suggested as a possible factor in the

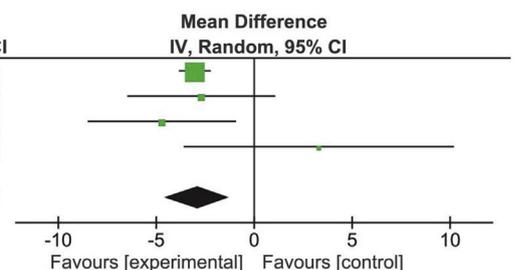
emergence of depression (Ravona-Springer et al., 2017). Thus, physical activity may have first contributed to an improvement in physical health, which in turn, may then have resulted in a favorable depression outcome.

This study has several limitations which should be considered when interpreting the results. First, in the current study, a diagnosis of major depressive disorder as defined by DSM-5 was not regarded as an eligibility criterion in each study. Therefore, we did not evaluate odds ratios for the remission of depression and number needed to treat. Also, as the depressive symptoms at baseline were mild to moderate in most of the studies, the results may not necessarily be generalizable to patients

A. Pooled results for the Beck Depression Inventory

Study or Subgroup	Experimental			Control			Weight	Mean Difference IV, Random, 95% CI
	Mean	SD	Total	Mean	SD	Total		
Osama et al, 2015	-2.77	2.01	50	0.26	2.13	50	65.1%	-3.03 [-3.84, -2.22]
Putiri et al, 2012	-2.6	2.39	5	0.1	4.53	8	14.9%	-2.70 [-6.47, 1.07]
Saiari et al, 2011	-4.77	7.98	30	-0.06	6.95	30	14.8%	-4.71 [-8.50, -0.92]
Schneider et al, 2016	-6	12.84	15	-9.3	4.43	14	5.2%	3.30 [-3.60, 10.20]
Total (95% CI)			100			102	100.0%	-2.90 [-4.53, -1.28]

Heterogeneity: Tau² = 0.88; Chi² = 4.02, df = 3 (P = 0.26); I² = 25%
 Test for overall effect: Z = 3.51 (P = 0.0004)



B. Pooled results for the Center for Epidemiologic Studies Depression Scale

Study or Subgroup	Experimental			Control			Weight	Mean Difference IV, Random, 95% CI
	Mean	SD	Total	Mean	SD	Total		
Aylin et al, 2009	-5.23	7.38	18	-1.17	6.72	18	21.4%	-4.06 [-8.67, 0.55]
Kempf et al, 2013	-1.86	14.24	93	0.54	15.61	83	23.1%	-2.40 [-6.83, 2.03]
Mckay et al, 2001	-2	12.08	35	2.3	12.73	33	13.0%	-4.30 [-10.21, 1.61]
Pibernik-Okabivuc et al, 2015	-1.7	9.11	58	-1.6	8.81	57	42.4%	-0.10 [-3.38, 3.18]
Total (95% CI)			204			191	100.0%	-2.03 [-4.16, 0.11]

Heterogeneity: Tau² = 0.00; Chi² = 2.67, df = 3 (P = 0.44); I² = 0%
 Test for overall effect: Z = 1.86 (P = 0.06)

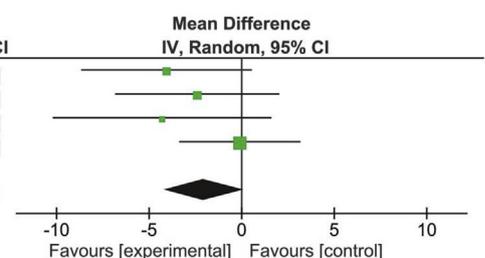


Fig. 5. A. Summary of pooled results for the Beck Depression Inventory: Mean difference. B. Summary of pooled results for the Center for Epidemiologic Studies Depression Scale: Mean difference.

with severe depressive symptoms. Second, the relatively small number of studies included in the analysis should be considered as a limitation, as this may have compromised our ability to detect differences. For example, the non-significant SMD results for the male and female subgroup analyses, and non-significant MD result for the CES-D may have been due to a lack of statistical power. Third, it is possible that confounders such as other, unknown treatments might have compromised the findings. However, these possible confounders would have been balanced within groups as the patients were randomized, and it is therefore unlikely that they would have changed the conclusion of the study. Lastly, most of the studies included had an unclear or high risk of bias. A high risk of bias was detected in the blinding of participants and personnel in all studies since it is impossible to blind subjects undergoing a physical activity intervention. Also, several trials included a high or unclear risk of bias in incomplete outcome data, where attrition bias may have been especially problematic. On the other hand, as a sensitivity analysis revealed that the main findings did not change meaningfully with the exclusion of these studies, this may have been less of an issue.

5. Conclusions

Physical activity interventions showed a medium effect size in the treatment of diabetes-related depression. This favorable profile was consolidated by a sensitivity analysis and meta-regression analyses. Thus, physical activity interventions should be considered as a possible option to improve both depressive symptoms and biological outcomes. This finding should be confirmed in future RCTs that include larger sample sizes and have a low risk of bias.

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Author contributions

All authors contributed to the study design. ZN and TI performed the article search and data extraction. All authors contributed to the interpretation of the data. ZN drafted the initial version of the manuscript. All authors drafted the manuscript and approved the final version of the manuscript.

Conflicts of interest

The authors declare no conflict of interest.

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Not applicable.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jpsychires.2019.03.014>.

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