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Effectiveness of physical activity in managing co-morbid depression in adults with type 2 diabetes mellitus: A systematic review and meta-analysis

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ABSTRACT

Background: Physical activity may be effective in alleviating depressive symptoms and improving glycaemic control; however, evidence to guide practice is limited. The current review was conducted to assess the effects of physical activity on depression and glycaemic control in people with type 2 diabetes mellitus.

Methods: Randomized controlled clinical trials, from the earliest record to October 2021, which recruited adults with the diagnosis of type 2 diabetes mellitus and compared physical activity with no interventions or usual care for the management of depression were included. The outcomes were change in depression severity and glycaemic control.

Results: In 17 trials, including 1362 participants, physical activity was effective in reducing the severity of depressive symptoms (SMD = −057; 95%CI = −0.80, −0.34). However, physical activity did not have a significant effect in improving markers of glycaemic control (SMD = −0.18; 95%CI = −0.46, 0.10).

Limitations: There was substantial heterogeneity in the included studies. Furthermore, risk of bias assessment showed that most of the included studies were of low quality.

Conclusions: Physical activity can effectively reduce the severity of depressive symptoms, nonetheless, it appears that physical activity is not significantly effective in improving glycaemic control in adults who have both type 2 diabetes mellitus and depressive symptoms. The latter finding is surprising, however, given the limited evidence on which this is based, future research on the effectiveness of physical activity for depression in this population should include high quality trials with glycaemic control as an outcome.

1. Introduction

The many challenges of living with type 2 diabetes mellitus (T2DM) may negatively affect mental health and therefore individuals with T2DM are at higher risk of developing depression (Pinchevsky et al., 2020; Davies, 2019; Zhuang et al., 2017; Chireh et al., 2019; Elamoshy et al., 2018; Wang et al., 2019). In individuals with T2DM, depression worsens glycaemic control and thus increases the risk of developing secondary complications (Hermanns et al., 2013; Nouwen et al., 2019).

Treatment of depression in people with T2DM is much more challenging compared to the general population as clinicians have to consider blood glucose levels and other diabetes specific parameters, which may be adversely affected by psychotropic medication (Davies, 2019; Owens-Gary et al., 2019; Brandt et al., 2019). Moreover, the motivational deficits seen in depression may negatively impact diabetes treatment adherence and self-management activities such as diet and physical activity. Therefore, due to the complex interaction between T2DM and depression, treatment needs to consider both psychological wellbeing and glycaemic control (Davies, 2019; Perrin et al., 2019; Owens-Gary et al., 2019; Petrak and Herpertz, 2009; Petrak et al., 2015; Kulzer et al., 2013). A wide range of antidepressant medications and psychotherapeutic approaches are available to manage depression and

Abbreviations: T2DM, type 2 diabetes mellitus; HbA1c, haemoglobin A1c.

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have been shown to be effective in the general population. Although it is commonly thought that improvement in mental health may also help in achieving glycaemic control in people with depression and T2DM, studies have reported that both antidepressants and psychotherapy have limited effects on glycaemic control (Wang et al., 2017; Baumeister et al., 2014; Holt et al., 2014; Harkness et al., 2010).

In contrast to these approaches, physical activity might not only be effective in alleviating depressive symptoms but may also assist in achieving glycaemic control in people with T2DM (Kandola et al., 2019; Schuch et al., 2018; Narita et al., 2019). Antidepressant effects of physical activity have been demonstrated both in the general population and in patients with co-morbid somatic illnesses such as cardiovascular diseases and diabetes (Narita et al., 2019; Mašanović et al., 2018; Wu et al., 2017). Physical activity may have two-fold benefits for populations with comorbid mental and physical health problems: (i) it may reduce depressive symptoms through biological and psychosocial pathways and (ii) improve physical health either by improving the co-morbid condition itself or by preventing secondary complications associated with the co-morbid condition (Blumenthal et al., 2012; Knapen et al., 2015).

The available literature suggests that the positive effects of physical activity for managing depression are also applicable to people with T2DM and depression (Lysy et al., 2008; Schneider et al., 2016). Besides the general antidepressant mechanisms, physical activity in people with T2DM might stimulate additional antidepressant mechanisms to manage depression. For example, research suggests that poor glycaemic control can contribute to the emergence of depression while several lines of evidence suggest that physical activity can help in improving glycaemic control and quality of life in people with T2DM (Ravona-Springer et al., 2017; Hamer et al., 2011; Maraldi et al., 2007). Consequently, it can be hypothesized that in people with T2DM, physical activity not only exerts its antidepressant mechanisms by improving psychological status but also by improving physical health (Green et al., 2011).

Despite its numerous health benefits, there is a scarcity of high-quality evidence regarding the effectiveness of physical activity in managing depression among adults with T2DM. One systematic review assessed the effect of physical activity on managing depression in people with diabetes (Narita et al., 2019). However, it included people with both type 1 and type 2 diabetes and did not perform a subgroup analysis to report effects of physical activity in managing depression specifically in people with T2DM. Moreover, it only assessed effects of physical activity on depressive symptoms and did not evaluate the impact on glycaemic control. Moreover, it included both participants with and without a diagnosis of depression and did not differentiate between these groups. Furthermore, there were a limited number (n = 3) of databases searched and the review was limited to English language articles. Therefore, the current study aimed to comprehensively summarise the evidence, using rigorous systematic review methods, for the effects of physical activity in people with depression and T2DM.

1.1. Objectives

The objectives of the review were to assess the effects of physical activity compared with usual care or no intervention on depression and glycaemic control in people with T2DM.

2. Methods

2.1. Protocol and registration

The protocol for this systematic review and meta-analysis was registered with PROSPERO (www.crd.york.ac.uk/PROSPERO) under the registration number CRD42021273032.

2.2. Eligibility criteria

2.2.1. Study designs

Individual or cluster randomized controlled trials which compared physical activity with no intervention or usual care for the management of depression in subjects with T2DM were included. Studies that compared two forms of physical activity without another control group were excluded.

2.2.2. Participants

Clinical trials were included which recruited adults (18 years and above) with T2DM, irrespective of how the diagnosis of T2DM had been ascertained. Clinical diagnosis of depression was not mandatory for inclusion, however, individuals with T2DM who underwent an evaluation for depressive symptoms at baseline and follow-up, were included.

2.2.3. Intervention

Any form of physical activity (aerobic/anaerobic, supervised/unsupervised) alone or in combination with any other treatment modality used for managing depression was included. Physical activity was defined as "movement produced by skeletal muscle that leads to energy expenditure above resting levels" (Ainsworth et al., 2011).

There was no restriction on the duration of each session and number of total sessions.

2.2.4. Comparator

The participants in the control group received either usual care or no intervention. Usual care consisted of leaflets, brief advice or educational sessions.

2.2.5. Outcomes

The primary outcome was the change in depression severity from baseline to post intervention at the last available follow up measured on validated measures.

Secondary outcomes included improvements in glycaemic control from baseline to post intervention and last available follow up measured through Haemoglobin A1c (HbA1c).

2.3. Information sources

MEDLINE (Ovid) (1946 to October 06, 2021), EMBASE (Ovid) (1974 to 2021 October 06, 2021), AMED (1985 to October 2021), CINAHL (EBSCO) (1982 to October 2021), PsycINFO (1806 to September Week 4 2021) and Health Management Information Consortium (1979 to July 2021) were searched. Reference lists of the included articles and relevant systematic reviews were also checked to find additional articles.

2.4. Search strategy

The search strategy for the various databases is provided in supplementary file 1.

2.5. Study selection

Search results were imported into Covidence (www.covidence.org). After removal of duplicates, screening was performed at two stages; during the first stage two independent reviewers (AA and IU) screened the titles and abstracts of the studies, while during the second stage the same reviewers independently performed full text screening. Based on full text screening, studies were divided into relevant, irrelevant, and unsure categories. Studies in the "irrelevant" category were excluded and reasons for exclusion were documented, while studies in the "relevant" group were included. Studies in the "unsure" category were discussed further at a consensus meeting with the two independent reviewers. Disagreements between the two reviewers (AA and IU) were resolved by discussion and if needed, a third reviewer (MM) was

contacted to make the final decision on inclusion/exclusion.

2.6. Data collection process

The data extraction form was designed and piloted before data extraction. Two independent reviewers (AA, IU) evaluated each included study and extracted data. All discrepancies were resolved by discussion and if needed, a third reviewer (MM) resolved disagreements.

2.7. Data items

The information, extracted from the included studies was:

- Study information such as first author name, year of publication and country name.
- Participant information such as sample size and participants in each group, demographic information (mean age, gender) and clinical characteristics.
- Information about physical activity intervention; type and intensity of physical activity, modes of delivery, settings, procedures, and processes involved, duration of each session, number of total sessions and follow up duration.
- Information about control group(s)
- Information about any co-interventions used along with physical activity
- Information about outcome measures used in the study and baseline, post intervention and follow up scores (if available) of outcome measures used for assessing depressive symptoms and glycaemic control.

2.8. Risk of bias assessment

Two independent reviewers (AA, IU) evaluated the methodological quality of each included study according to the Cochrane risk of bias tool version 1. Methodological quality assessments were checked for agreement between AA and IU and any discrepancy was resolved by discussion. In cases where the discrepancy could not be resolved, a third reviewer (MM) made the final decision.

2.9. Data synthesis

Meta-analyses were conducted using random-effects models in RevMan 5.4.1 software. The I^2 statistic was used to report heterogeneity in the included studies. Funnel plots were used to assess and report publication bias.

2.10. ubgroups analysis

Subgroup analyses were conducted to assess whether findings varied according to gender, economic status of the country in which study was conducted (high income vs. low- and middle-income countries, diagnosis of depression (diagnosed vs. undiagnosed depression) and quality of the studies. The World Bank list of high income countries and low- and middle-income countries (LMICs) was used to classify countries on economic status.

3. Results

3.1. Study selection

The literature search identified 4704 records. Two records were identified through additional sources. Following removal of duplicates, 3567 articles remained. Titles and abstracts of these articles were screened, and 3442 were excluded. Full texts of the remaining 125 records were studied and 107 records were excluded, documenting reasons. Finally, 18 studies meeting eligibility criteria were included in the narrative synthesis, of which 17 studies were included in meta-analyses. (Fig. 1).

3.2. Study characteristics

Most of the included studies (n = 11) were conducted in high income countries while 7 studies were conducted in LMICs. Two were conducted between the year 2001 to 2010 and 14 between 2011 and 2020. The remaining 2 studies were conducted in 2021 (Table 1).

Most randomized controlled trials (n = 15) had two study arms. Two studies had three arms, however, we considered only two arms (physical activity and usual care) from these two studies in the analysis (Vucic Lovrencic et al., 2015; Putiri et al., 2012). One study had four arms (CBT, exercise, CBT + exercise, usual care), from which we considered three arms (exercise, CBT + exercise, usual care) in the analysis (De Groot et al., 2019b). For the latter study, we combined data of two intervention groups (exercise and CBT + exercise) for conducting meta-analysis.

3.3. Participants

The 18 studies included 1428 participants (746 in the experimental group and 682 in the control group). Most (n = 13) studies included both male and female participants, while 3 studies included only male participants (Saiiari et al., 2011; Sardar et al., 2014; Gilani and Feizabad, 2019), and 2 studies included only female participants (Schneider et al., 2016; Yucel and Uysal, 2016). Participants in 14 studies had a mean age >50 years, while participants in 4 studies had a mean age <50 years (Gilani and Feizabad, 2019; Osama and Shehab, 2015; Sardar et al., 2014; Saiiari et al., 2011).

The majority of the studies (n = 12) did not specify a clinical diagnosis or severity of depression of the included participants. Of the remaining 6 studies, two studies included participants with major depressive disorder diagnosed based on the Structured Clinical Interview for DSM-IV disorders(Schneider et al., 2016; De Groot et al., 2019b), one study included participants with Beck Depression Inventory scores (BDI) ≥14 (Piette et al., 2011), one study included participants with BDI scores >18 (Saiiari et al., 2011), one study included subjects with at least one depressive symptom on Patient Health Questionnaire-2 (PHQ-2) (Vucic Lovrencic et al., 2015), while one study included subjects with mild to moderate depression, but did not reported the method of diagnosing mild to moderate depression (Abdelbasset et al., 2020).

3.4. Intervention

Thirteen studies used a physical activity intervention alone. Of the remaining 5 studies, 2 combined physical activity with cognitive behavioural therapy (CBT) (Piette et al., 2011; De Groot et al., 2019b), one study combined it with behavioural activation (Schneider et al., 2016), one study combined it with dietary measures (Osama and Shehab, 2015), while one study combined physical activity with cognitive training (Kraiwong et al., 2021). Eleven studies used aerobic exercises as an intervention, 2 studies used resistance exercises (Lincoln et al., 2011; Putiri et al., 2012) while 5 studies used mixed types of exercises as the intervention (Martinez-Velilla et al., 2021; Kraiwong et al., 2021; Duruturk and Ozkoslu, 2019; Vucic Lovrencic et al., 2015; Aylin et al., 2009).

Four studies provided purely supervised physical activity (Lincoln et al., 2011; Duruturk and Ozkoslu, 2019; Gilani and Feizabad, 2019; Kraiwong et al., 2021), 3 studies provided purely unsupervised physical activity (Kempf and Martin, 2013; Piette et al., 2011), 3 studies provided mixed supervised and unsupervised physical activity (Aylin et al., 2009; Martinez-Velilla et al., 2021; Putiri et al., 2012), while the remaining 8 studies did not provided explicit information about supervision. A large proportion (n = 13) of studies applied low to moderate intensity exercise (McKay et al., 2001, Saiiari et al., 2011, Osama and Shehab, 2015,

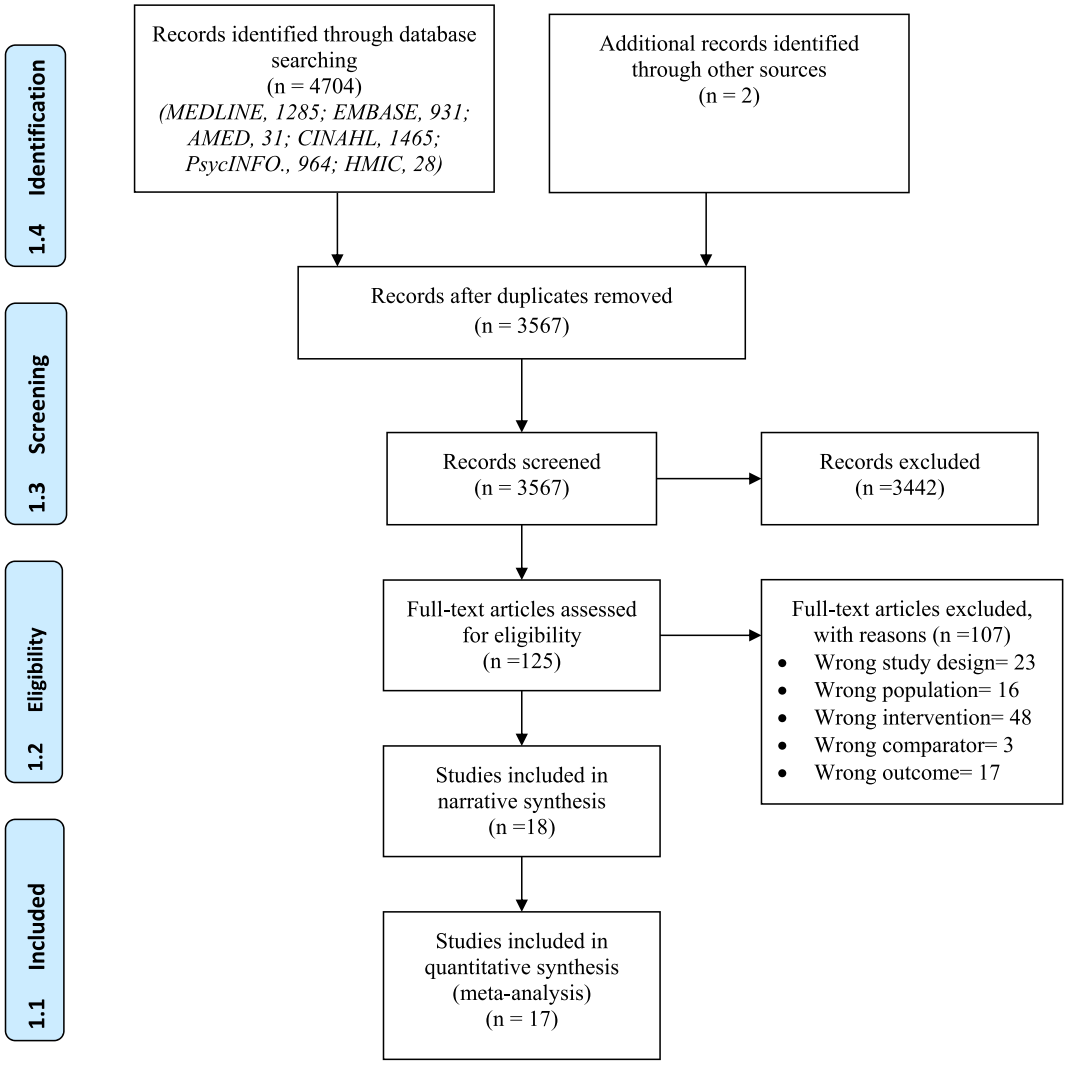

Fig. 1. PRISMA flow chart.

Sardar et al., 2014, De Groot et al., 2019b, Kraiwong et al., 2021, Schneider et al., 2016, Kempf and Martin, 2013, Vucic Lovrencic et al., 2015, Yucel and Uysal, 2016, Duruturk and Ozkoslu, 2019, Aylin et al., 2009, Gilani and Feizabad, 2019), 1 study applied high intensity exercises while the remaining 4 did not reported intensity of physical activity (Abdelbasset et al., 2020; Martinez-Velilla et al., 2021; Piette et al., 2011; Putiri et al., 2012).

3.5. Comparator

In the majority (n = 16) of the included studies the comparator was usual care. The remaining 2 studies did not describe the care received by participants in the control group (Osama and Shehab, 2015; Saiiari et al., 2011).

3.6. Outcomes

Most of the studies used the BDI (n = 8) and the Centre for Epidemiologic Studies Depression Scale (CES-D) (n = 4) for assessing depressive symptoms. Out of 18 studies, 17 reported post treatment results while only one study reported results at one-year follow up (Vucic Lovrencic et al., 2015). Of the included studies, 10 reported effects of physical activity on glycaemic control (Aylin et al., 2009, De Groot et al., 2019b, Duruturk and Ozkoslu, 2019, Kempf and Martin, 2013, Piette et al., 2011, Putiri et al., 2012, Schneider et al., 2016, Vucic Lovrencic et al., 2015, Yucel and Uysal, 2016, Kraiwong et al., 2021). All these 10 studies used HbA1c.

3.7. Risk of bias

For a large proportion (n = 11) of the included studies, four or more risk of bias domains were marked as “high risk” or “unclear risk” (Fig. 2 & Supplementary Fig. 1).

3.8. Meta-analysis

3.8.1. Depression

Seventeen studies with 1362 subjects (705 in the physical activity group, 657 in the control condition) were included in the quantitative synthesis. One study (Kraiwong et al., 2021) was excluded from the meta-analysis because it lacked useable depression data to measure post-treatment means and standard deviations (SD). Of the included 17 studies, 13 clearly reported the post-treatment means and SD for both the physical activity group and the control group. For two studies, post-treatment means, and SD were obtained from study authors through email (Kempf and Martin, 2013; Putiri et al., 2012). One study reported the 95 % confidence interval for the difference in means (Martinez-Velilla et al., 2021), from which we calculated standard error (SE) using the formula: SE = (upper limit − lower limit) / 3.92. We then calculated the SD for the SE using the formula: $SD = SE \times \sqrt{N}$.

Table 1
Summary of findings.

Author name (year)/country	Participant information		Treatment		Outcome measure (depression)	Outcome measure (glycaemic control)
	Experimental group	Control group	Experimental group	Control group		
Abdelbasset et al. (2020)/ Saudi Arabia	14 (8 M & 6 F) Mean age = 53.4 ± 5.3 years	14 (7 M & 7 F) Mean age = 52.8 ± 5.7 years	45 min proprioceptive exercises (cross-body leg swings, single-leg squat, one-leg balance, forward & backward leg swings, blind advanced one-leg balance, side lunge) 3 sessions per week for 8 weeks	Usual care	HRSD Significant (p = 0.013) between-group difference	Not reported
Aylin et al. (2009)/ Turkey	18 (15 M & 3 F) Mean age = 51.39 ± 2.02 years	18 (12 M & 6 F) Mean age = 56.06 ± 1.48 years	30–45 min resistance training under the supervision of therapist & 15–45 min home based walking, twice per week for 8 weeks	Instruction not to undertake any formal exercise during the study period	CES-D No significant (*P*-value = 0.48) between-group difference	HbA1c Significant (*P*-value = 0.01) between-group difference
De Groot et al. (2019a)/USA	Exercise group: 34 (8 M & 26 F) Mean age = 54.6 ± 10.7 years Exercise + CBT group: 34 (6 M & 28 F) Mean age = 57.1 ± 10.7 years	36 (9 M & 27 F) Mean age = 54.2 ± 10.4 years	Exercise group: 100 to 150 min of moderate intensity community-based endurance exercises per week for 12 weeks including six sessions with a personal trainer Exercise + CBT group: Exercise + 10 sessions of individual CBT for 12 weeks	Usual care	BDI-II Exercise vs usual care: Significant (P = 0.021) between-group difference Exercise + CBT vs usual care: Significant (P < 0.001) between-group difference	HbA1c Exercise vs usual care: No significant (P = 0.132) between-group difference Exercise + CBT vs usual care: Significant (P = 0.016) between-group difference
Duruturk and Ozkoslu (2019)/ Turkey	23 (12 M & 11 F) Mean age = 52.82 ± 11.86 years	21 (14 M & 7 F) Mean age = 53.04 ± 10.45 years	20–45 min callisthenic exercises (strengthening and stretching) at home, supervised through telerehabilitation approach, three times a week, for 6 weeks	Usual care	BDI Significant (P < 0.0001) between-group differences	HbA1c No significant (P = 0.42) between-group difference
Gilani and Feizabad (2019)/Iran	30 M subjects Mean age = 48.86 ± 5.76 years	30 M subjects Mean age = 49.08 ± 6.09 years	45–60 min of supervised aerobic exercise (stretching, slow running, followed by endurance training on treadmill) at 60–70 % of maximum oxygen consumption, 3 sessions per week for 12 weeks.	Usual care	GHQ-28 No significant (P = 0.078) between-group difference	Not reported
Kempf and Martin (2013)/ Germany	93 (42 M & 51 F) Mean age = 61 ± 7 years	83 (35 M & 48 F) Mean age = 60 ± 8 years	Videogame based exercises using Wii console, balance board and exercise game Wii Fit Plus, 30 min per day for 12 weeks	Usual care	CES-D No significant ($P \geq$ 0.05) between-group differences	HbA1c No significant ($P \geq$ 0.05) between-group difference
Kraiwong et al. (2021)/ Thailand	22 (7 M & 15 F) Mean age = 70.09 ± 4.45 years	15 (1 M & 14 F) Mean age = 72.87 ± 6.42 years	45 to 60 min moderate-intensity exercises (aerobics, resistance exercises, and balance training) combined with cognitive training (memory, attention, and executive functions), 3 sessions per week for 8 weeks	4 sessions of health education	PHQ-9 No significant between-group difference	HbA1c No significant between-group difference
Lincoln et al. (2011)/USA	29 (9 M & 20 F) Mean age = 66.0 ± 7.9 years	29 (12 M & 17 F) Mean age = 66.6 ± 7.4 years	45-min resistance exercise training under supervision, three times per week for 16 weeks	Phone calls every other week and one-repetition maximum testing at baseline, weeks 9 and 16	GDS Significant (P < 0.0001) between-group difference	Not reported
Martinez-Velilla et al. (2021)/ Spain	54 (29 M & 25 F) Mean age = 87 ± 4 years	49 (21 M & 28 F) Mean age = 86 ± 5 years	Two daily, 20 min progressive resistance, balance and walking exercises, 5 to 7 days per week from admission to discharge	Usual care	GDS Significant (P < 0.001) between-group difference	Not reported
McKay et al. (2001)/USA & Canada	38 subjects Overall mean age = 52.3 years (37 M & 41 F)	40 subjects	Personalized physical activity program tailored to individual needs of the participants for 8 weeks	Access to diabetes-specific articles and realtime blood glucose tracking	CES-D No significant (*P*-value = 0.101) between-group difference	Not reported
Osama and Shehab (2015)/Saudi Arabia	50 subjects Mean age = 36.35 ± 5.11 years 56 males & 44 females	50 subjects Mean age = 37.16 ± 4.32 years	40-min aerobic exercise (at 60 %–80 % maximum heart rate) on treadmill, three sessions per week for 12 weeks combined with dietary measures	No intervention	BDI Significant (P < 0.05) between-group differences	
Piette et al. (2011)/USA	145 (71 M & 74 F) Mean age = 55.1 ± 9.4 years	146 (73 M & 73 F) Mean age = 56.0 ± 10.9 years	Pedometer-based walking program plus telephone-delivered CBT for 48 weeks	Enhanced Usual Care (educational materials about depression and diabetes)	BDI Significant (P < 0.0001) between-group difference	HbA1c No significant (P-value = 0.70) between-group difference
Putiri et al. (2012)/USA	11 subjects Mean age = 58.4 ± 7.4 years	10 subjects Mean age = 59.4 ± 6.8 years	Progressive resistance training one-hour group session per week under supervision & practice same exercises at home for 30 min twice a week, for 12 weeks	Usual care	BDI Significant between-group difference	HbA1c No significant between-group difference

(*continued on next page*)

Table 1 (*continued*)

Author name (year)/country	Participant information		Treatment		Outcome measure (depression)	Outcome measure (glycaemic control)
	Experimental group	Control group	Experimental group	Control group		
Saiiari et al. (2011)/Iran	30 M subjects Age range of 28–45 years	30 M subjects	30-min crawl swimming, three to four days per week for 8 weeks	Not mentioned	BDI Significant (P = 0.001) between-group difference	Not reported
Schneider et al. (2016)/USA	15 F subjects Mean age = 53.3 ± 6.0 years	14 F subjects Mean age = 53.6 ± 8.4 years	90-min group exercise classes 2 times per week for 16 weeks, once a week for 4 weeks, and then once every other week for 4 weeks (total 24 weeks) in combination with behavioural activation therapy	Usual care/information about nutrition, exercise, and glucose monitoring	BDI, HRSD No significant (P = 0.37 on BDI; P = 0.09 on HRSD) between-group difference	HbA1c No significant (P = 0.78) between-group difference
Sardar et al. (2014)/Iran	27 M subjects Mean age = 44.93 ± 5.35 years	26 M subjects Mean age = 45.56 ± 5.41 years	45–60 min aerobic exercise (at 60 %–70 % maximum heart rate), three times per week for 8 weeks	Usual care	GHQ-28 No significant (p = 0.657) between-group difference	Not reported
Vucic Lovrencic et al. (2015)/ Croatia	66 (29 M & 37 F) Mean age = 58.5 ± 4.8 years	69 (33 M & 36 F) Mean age = 58.2 ± 5.6 years	90 min flexibility, stretching, and strengthening group exercises, weekly session for 6 weeks	Usual care & written self-help instructions to cope with mood difficulties	CES-D No significant (p = 0.656) between-group difference at 1 year follow up	HbA1c No significant (p = 0.45) between-group difference at 1 year follow up
Yucel and Uysal (2016)/ Turkey	24 F subjects Mean age = 58.50 ± 7.00 years	21 F subjects Mean age = 53.50 ± 9.00 years	45 to 70 min stretching & basic aerobic Pilates training for arms, legs, and body, three times per week for 12 weeks	Usual care	HADS-D No significant (P = 0.297) between-group difference	No significant (P = 0.367) between-group difference

BDI; Beck Depression Inventory, CES-D; Center for Epidemiologic Studies Depression Scale, CBT; Cognitive Behavioural Therapy, F; female, GHQ-28; GDS; Geriatric Depression Scale, General Health Questionnaire-28, HADS; Hospital Anxiety and Depression Scale, HRSD; Hamilton Rating Scale for Depression, M; male, min; minute, PHQ-9; Patient Health Questionnaire-9, USA; United States of America.

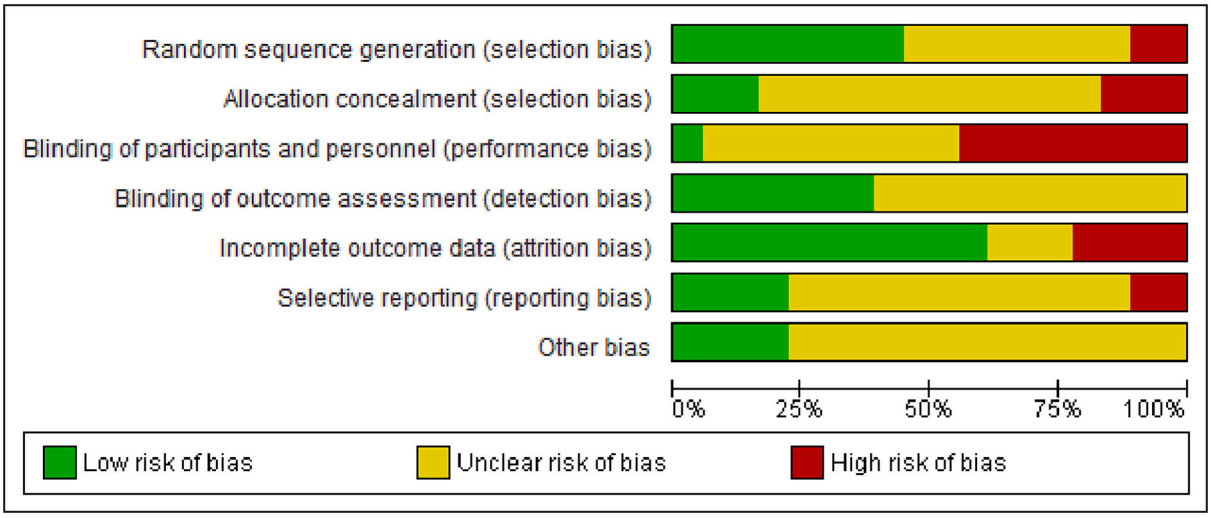

Fig. 2. Risk of bias graph.

From one study, we included 3 groups in which two were intervention groups (Exercise group and Exercise + CBT group) and one was the control group (De Groot et al., 2019b). To combine sample size, mean and SD of the two intervention groups, the following formulae were used;

The pooled results showed that physical activity was effective for improving depressive symptoms in people with T2DM (SMD = −057, 95 % CI = −0.80, −0.34). Nevertheless, chi-squared test ($P < 0.00001$) and I^2 statistic (74 %) showed that there was substantial heterogeneity in the included studies (Fig. 3).

Subgroup analysis based on economic status of the country revealed that effects of physical activity on depressive symptoms was statistically significant for both high income country studies and LMICs (SMD −0.69 for high income countries and −0.35 for LMICs). Heterogeneity was low (I^2 = 10 %) for studies conducted in LMICs while it was high (I^2 = 81 %) for studies conducted in high income countries (Fig. 4).

Physical activity showed a statistically significant effect on depression in studies which included either male participants only or both male and female, but not in studies which included female participants only (Fig. 5).

Physical activity was effective in improving depression symptoms in studies regardless of whether they included participants with or without the diagnosis of depression at baseline; however, the effect size was larger for studies which included participants without diagnosed depression (SMD −0.64 without diagnosis of depression vs. −0.43 with diagnosis of depression; Supplementary Fig. 2).

Subgroup analysis based on duration of physical activity showed that

	Group 1	Group 2	Combined groups
Sample size	N_1	N_2	$N_1 + N_2$
Mean	M_1	M_2	$\frac{N_1M_1 + N_2M_2}{N_1N_2}$
SD	SD_1	SD_2	$\sqrt{\frac{(N_1-1)SD_1^2 + (N_2-1)SD_2^2 + \frac{N_1N_2}{N_1+N_2}(M_1^2 + M_2^2 - 2M_1M_2)}{N_1+N_2-1}}$

physical activity of both long and short duration was effective, but the longer duration interventions had larger effect size (SMD −0.68 for physical activity ≥10 weeks vs. −0.43 for physical activity <10 weeks; Supplementary Fig. 4). Similarly, physical activity both alone or in combination with other interventions had positive effects in improving depressive symptoms, but studies of physical activity combined with other interventions demonstrated a larger effect size (SMD −0.71 for combined interventions vs. −0.51 for physical activity alone; Supplementary Fig. 5). In addition, effect of physical activity was statistically significant for both studies in which mean age of the participants was <50 years and in study populations ≥50 years, but effect size was larger for studies with younger participants (SMD −0.80 for mean age < 50 years vs. −0.49 for mean age ≥ 50 years; Supplementary Figs. 6). Results showed both aerobic and resistance exercises had a significant effect on improving depressive symptoms but studies of mixed types of exercises did not show a significant effect (Supplementary Fig. 7).

Visual inspection of the funnel plot showed no indication of publication bias in included studies. (Supplementary Fig. 8).

3.9. 3.8.2 Glycaemic control

Of the 10 studies included in the review which reported information about glycaemic control, nine were included in the quantitative synthesis. All nine studies reported HbA1c as a marker of glycaemic control. The results showed that physical activity did not have a significant effect in improving markers of glycaemic control (SMD = −0.18; 95 % CI = −0.46, 0.10). (Fig. 6).

Subgroup analysis showed that physical activity was effective, however, in improving glycaemic control for studies conducted in LMICs (SMD = −0.60; 95 % CI = −1.24, 0.04) but not for studies conducted in high income countries (SMD = −0.03; 95 % CI = −0.26, 0.21). (Fig. 7).

Subgroup analysis for glycaemic control based on diagnosis of depression (inclusion of subjects with or without diagnosis of depression), duration of physical activity (≥10 weeks, <10 weeks), combination of physical activity with other intervention (physical activity alone, physical activity combined with other intervention) and type of physical activity (aerobic exercises, resistance exercises, mixed types of exercises) showed that physical activity did not have a significant effect on glycaemic control for any of these subgroups. (Supplementary Figs. 9 to 12).

4. Discussion

Our review showed that physical activity improves depressive symptoms in adults with T2DM. There are consistent reports in the literature regarding the antidepressant effects of physical activity in the general population (Stubbs et al., 2018; Oberste et al., 2020; Kandola et al., 2019; Biddle et al., 2019), nevertheless, there is limited literature available regarding the effects of physical activity in managing depression among adults with co-morbid somatic illnesses, particularly T2DM. The only previous systematic review which assessed effects of physical activity in managing depressive symptoms in people with diabetes included both type 1 and type 2 diabetes, and found 13 studies (Narita et al., 2019). It also reported that physical activity reduced depression in diabetes patients. Our review focused only on studies specifically in people with T2DM but found more studies: 18 for the qualitative synthesis and 17 studies for the quantitative synthesis.

Included studies were conducted in diverse countries. The majority were from the United States of America (n = 6) followed by Iran (n = 3), Turkey (n = 3) and Saudi Arabia (n = 2). The subgroup analysis based on the economic status of the country showed that physical activity was significantly effective for managing depression in both high-income countries and LMICs, though effects were larger in high income countries. We were unable to locate any previous high-quality reviews which compared physical activity for the management of depression in high income with LMICs; however, availability of resources may be the key determinant for physical activity having a larger effect size in high-income countries. In addition, training of staff, literacy levels of the participants and socio-economic factors might affect the effectiveness of physical activity interventions in managing depression in LMICs. However, we were not able to assess these assumptions, as they were beyond the scope of our review.

We found physical activity reduced depressive symptoms in both participants with and without the diagnosis of depression verified at

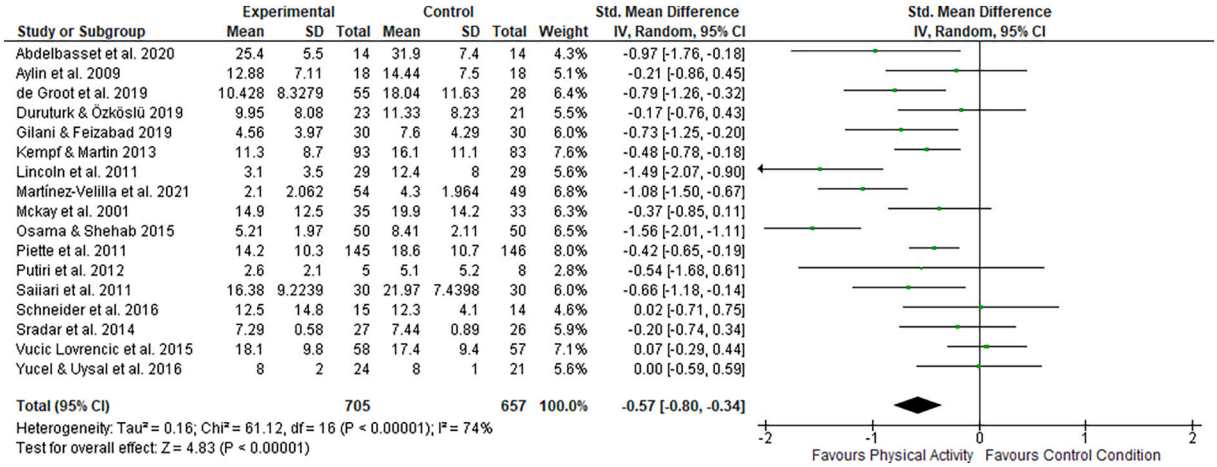

Fig. 3. Comparison of physical activity versus control condition for improving depression.

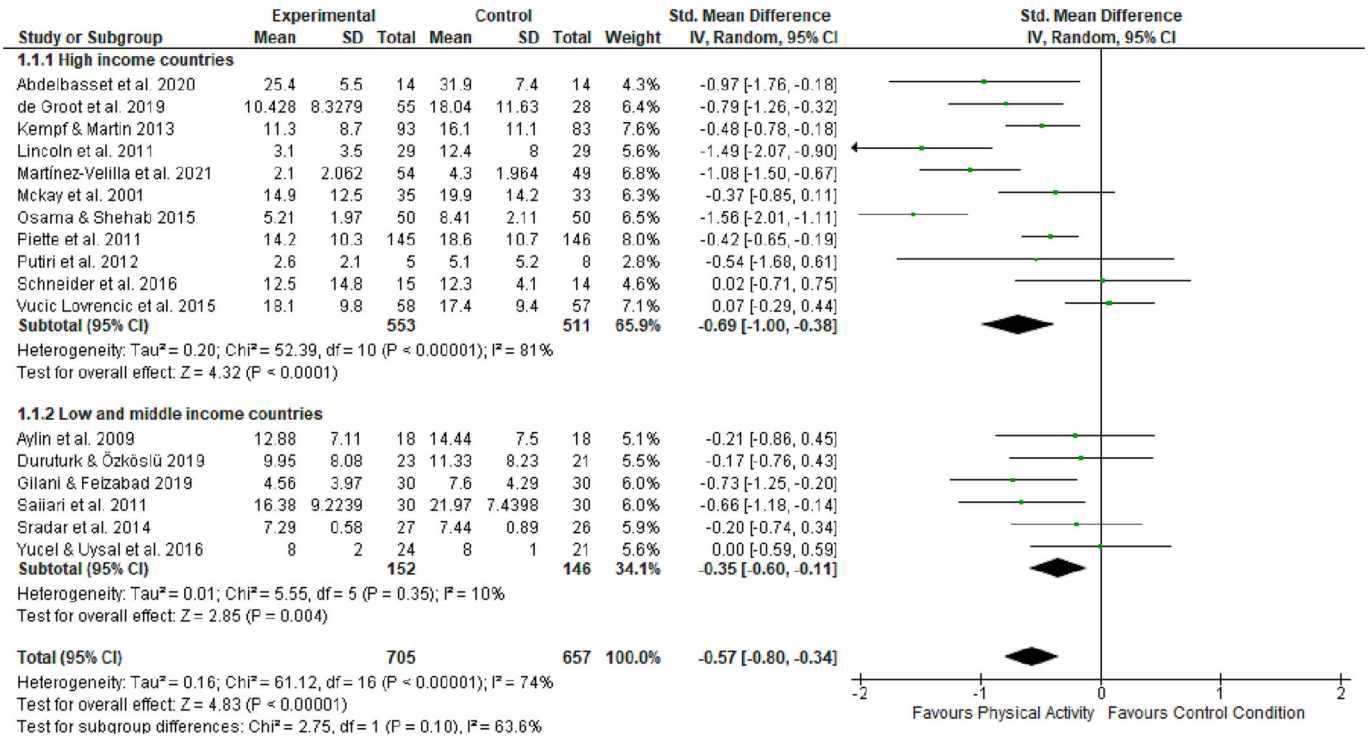

Fig. 4. Subgroup analysis for depression based on economic status of the country in which study was conducted.

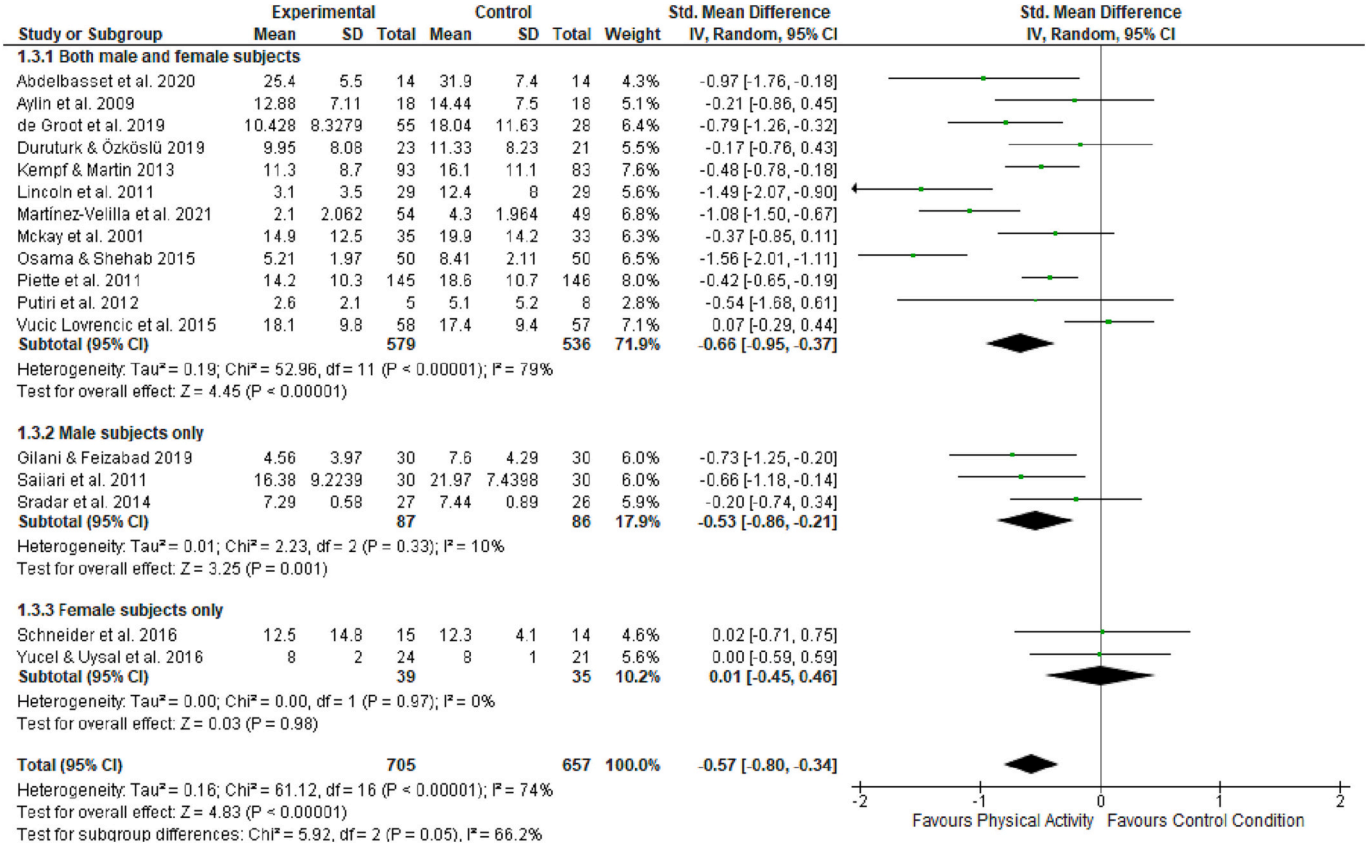

Fig. 5. Subgroup analysis for depression based on gender.

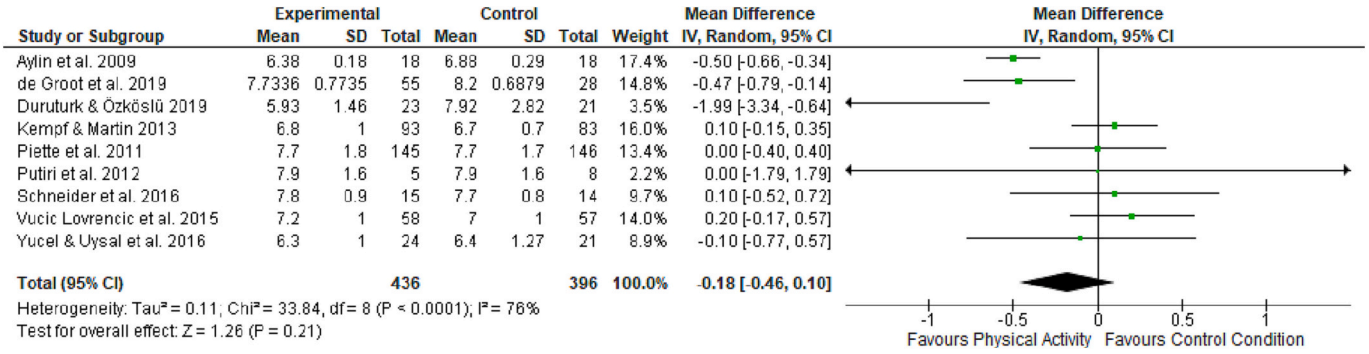

Fig. 6. Comparison of physical activity versus control condition for improving glycaemic control.

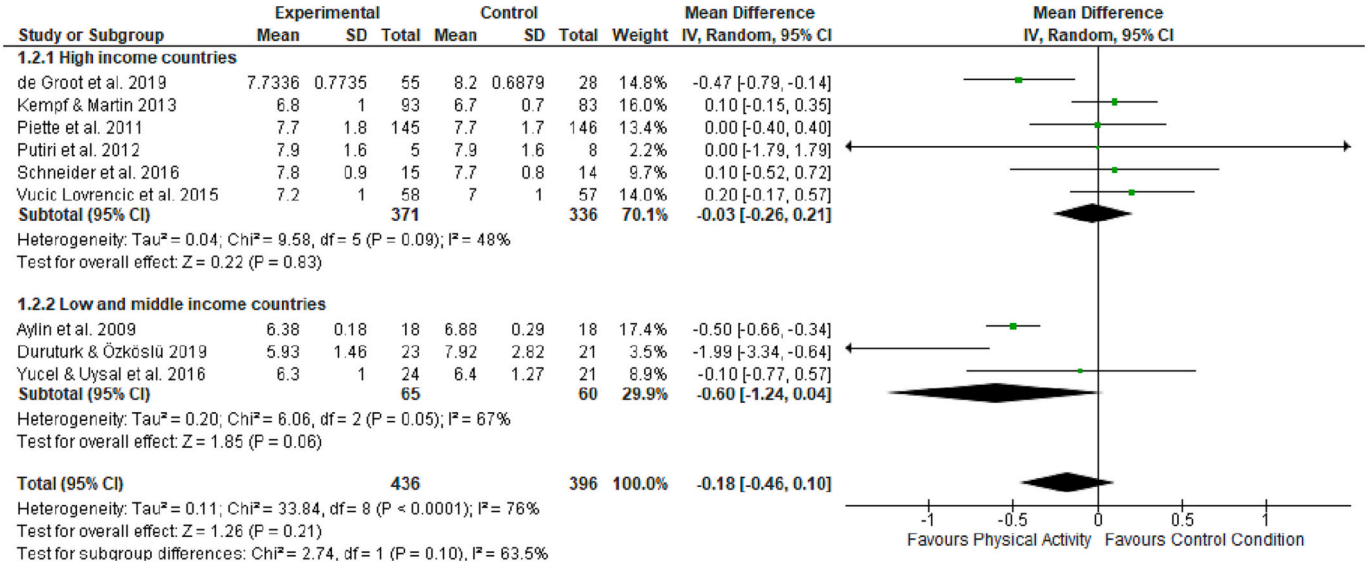

Fig. 7. Subgroup analysis for glycaemic control based on economic status of the country in which study was conducted.

baseline. However, its effects were more compelling for studies which included participants without a prior diagnosis of depression. Although there is a paucity of literature to explain why and how physical activity might be more effective in reducing depressive symptoms in subjects without a clinical diagnosis of depression, it may be that patients with a diagnosis of depression are less interested in performing physical activity and the effectiveness of physical activity may therefore be compromised (Schuch and Stubbs, 2019; Radovic et al., 2018; Helgadóttir et al., 2018). As the majority of the included studies did not specify severity of depression at baseline, it was not possible to perform subgroup analysis based on this. However, severity might also affect the effectiveness of physical activity in managing depression.

The literature suggests that physical activity can have a positive effect on depression in both men and women (Belvederi Murri et al., 2019; Wang et al., 2022; Zhang and Yen, 2015). However, in our review, in studies which included only female participants, physical activity was not effective (although it was effective in studies including both male and female participants). This discrepancy may arise due to the low number of studies (n = 2) with small sample sizes which included only female subjects. Subgroup analysis based on age revealed that physical activity was more effective for managing depression in studies with participants mean age <50 years. This suggests that physical activity might have more beneficial effects on mental health of relatively younger individuals.

Recent systematic reviews have reported that physical activity combined with other interventions, such as psychological therapies, have more beneficial effects in improving mental health (Thomas et al., 2020; De Groot et al., 2019a). Findings of the current review also showed that studies which combined physical activity with other interventions have comparatively larger effects in reducing depressive symptoms. Similarly, results showed that studies which applied physical activity intervention for longer durations are considerably more effective in managing depression among adults with T2DM. In addition, results from the current review showed that both aerobic and resistance exercises were considerably effective in improving depressive symptoms, nonetheless studies which used mixed types of exercises were not significant in managing depression. There are inconsistencies in the literature regarding the optimal duration and type of physical activity recommended for managing depression. Nonetheless, some studies suggested that rather than focusing on duration and type of physical activity, attention must be focused on motivating patients with depressive symptoms to perform something physical. They assume that it is not the determinants of physical activity (i.e. type and duration) that determine the effectiveness of physical activity in treating depression, rather there are other mechanisms such as breaking the pattern of sustained behaviours via exercise and other psychological and contextual factors through which physical activity exerts its positive effects in reducing depressive symptoms (Helgadóttir et al., 2016; Nyström et al., 2015; Robertson et al., 2012; Schuch et al., 2016; Danielsson et al., 2013).

We found only a limited number of studies reporting effects of physical activity on glycaemic control. The findings showed that physical activity did not have a significant effect in improving HbA1c levels, though it modestly assists (SMD −0.18) in achieving glycaemic control

in people with T2DM. It is interesting to note that when we applied a fixed effect model on HbA1c data, it showed significant results (SMD = −0.27; 95 % CI = −0.37, 0.16) for improving glycaemic control (Supplementary Fig. 13). However, as per our review protocol, we reported findings of random effects model in results. Contrary to findings of the current review, previous studies have reported that physical activity considerably improves HbA1c in individuals with T2DM (Shah et al., 2021; Liu et al., 2019; Wake, 2020; Amanat et al., 2020). Our findings are based on only the handful of studies which have reported effects of physical activity on both depressive symptoms and glycaemic control and may therefore not be robust for glycaemic control related outcomes. Furthermore, in the current review we conducted meta-analysis based on mean and SD, as the majority of the studies reported mean and SD as a measure of central tendency and dispersion; baseline differences may therefore have biased the post-intervention results. For instance, in Kemp & Martin study, HbA1c baseline scores in the physical activity group and control group were 7.1 ± 1.3 % and 6.8 ± 0.9 % respectively while post treatment scores were 6.8 ± 1.0 and 6.7 ± 0.7 respectively. There was a reduction in HbA1c in the physical activity group only (−0.3 ± 1.1 %), but not in the control group (−0.1 ± 0.5 %); nevertheless, the forest plot for our meta-analysis showed results in favour of the control group due to baseline differences. The subgroup analysis for glycaemic control based on economic status of the country showed that physical activity did have significant effects on achieving glycaemic control in LMICs, (which is more consistent with the wider literature). Nonetheless, due to the wide confidence interval and small sample size, these findings should be interpreted with caution.

To the best of our knowledge, the current review is the first to report on the effects of physical activity in managing depression specifically in individuals with T2DM. We published a review protocol and followed established methods for a high-quality systematic review of effectiveness studies (Moher et al., 2009; Higgins et al., 2019). We performed a comprehensive search to locate all relevant RCTs and conducted subgroup analyses, agreed a priori, to investigate important differences relevant to guiding practice and policy.

4.1. Limitations

There are some limitations to acknowledge in interpreting the findings of this review, relating to both the studies included in the review and review methods. First, there was substantial heterogeneity in the methods and results of included studies. Risk of bias assessments showed that most studies were of low quality. Second, only a very limited number of studies reported effects of physical activity on glycaemic control, making it difficult to draw firm conclusions for this part of our review. Finally, although we searched a number of different databases and used broad search terms, it is possible that we missed some studies.

The review has important implications for policy, practice, and future research. We found physical activity alone or in combination with other interventions is effective for improving depression symptoms in individuals with T2DM. Despite this evidence, physical activity is still underutilized, especially in LMICs. Unlike antidepressants, which are widely prescribed, clinicians do not regularly assess or prescribe physical activity in routine care. Thus, the challenge remains to translate evidence on the health benefits of physical activity to use in practice in the health care system. There is an urgent need for policies and guidance to promote the prescription of physical activity for the management of depression in clinical settings. Future research should focus on implementation and scale up strategies to promote exercise prescription in the management of depression in routine clinical care.

5. Conclusion

We found that physical activity can effectively reduce depressive symptoms in adults with T2DM. Furthermore, physical activity might be a suitable adjunct to other interventions in managing depression in T2DM in both high-income countries and LMICs. Nonetheless, it appears that physical activity may not be significantly effective in improving glycaemic control in adults who have both type 2 diabetes mellitus and depressive symptoms. Our finding that physical activity may not be effective in achieving glycaemic control in T2DM is surprising. Given the limited evidence on which this is based, future research on the effectiveness of physical activity for depression in this population should include high quality trials with glycaemic control as an outcome.

CRediT authorship contribution statement

A Arsh, N Siddiqi, C Carswell and S Afaq designed the study. A Arsh and I Ullah reviewed the studies, extracted data, completed the risk of bias assessment and analysed the findings. M Bhatti resolved discrepancies in the reviewing process. A Arsh wrote the manuscript. N Siddiqi, C Carswell and S Afaq and M Bhatti critically revised the manuscript. All authors contributed to and have approved the final manuscript.

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Conflict of interest

None.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jad.2023.02.122.

References

Abdelbasset, W.K., Alrawaili, S.M., Nambi, G., Yassen, E., Moawd, S.A., Ahmed, A.S., 2020. Therapeutic effects of proprioceptive exercise on functional capacity, anxiety, and depression in patients with diabetic neuropathy: a 2-month prospective study. Clin. Rheumatol. 39, 3091–3097.

Ainsworth, B.E., Haskell, W.L., Herrmann, S.D., Meckes, N., Bassett, D.R., Tudor-Locke, C., Greer, J.L., Vezina, J., Whitt-Glover, M.C., Leon, A.S., 2011. 2011 compendium of physical activities: a second update of codes and MET values. Med. Sci. Sports Exerc. 43, 1575–1581.

Amanat, S., Ghahri, S., Dianatinasab, A., Fararouei, M., Dianatinasab, M., 2020. Exercise and type 2 diabetes. In: Physical Exercise for Human Health, pp. 91–105.

Aylin, K., Arzu, D., Sabri, S., Handan, T.E., Ridvan, A., 2009. The effect of combined resistance and home-based walking exercise in type 2 diabetes patients. Int. J. Diabetes Dev. Countries 29, 159–165.

Baumeister, H., Hutter, N., Bengel, J., 2014. Psychological and pharmacological interventions for depression in patients with diabetes mellitus: an abridged Cochrane review. Diabet. Med. 31, 773–786.

Belvederi Murri, M., Ekkekakis, P., Magagnoli, M., Zampogna, D., Cattedra, S., Capobianco, L., Serafini, G., Calcagno, P., Zanetidou, S., Amore, M., 2019. Physical exercise in major depression: reducing the mortality gap while improving clinical outcomes. Front Psychiatry 762.

Biddle, S.J., Ciaccioni, S., Thomas, G., Vergeer, I., 2019. Physical activity and mental health in children and adolescents: an updated review of reviews and an analysis of causality. Psychol. Sport Exerc. 42, 146–155.

Blumenthal, J.A., Babyak, M.A., O'Connor, C., Keteyian, S., Landzberg, J., Howlett, J., Kraus, W., Gottlieb, S., Blackburn, G., Swank, A., 2012. Effects of exercise training on

depressive symptoms in patients with chronic heart failure: the HF-ACTION randomized trial. JAMA 308, 465–474.
Brandt, L.R., Hidalgo, L., Diez-Canseco, F., Araya, R., Mohr, D.C., Menezes, P.R., Miranda, J.J., 2019. Addressing depression comorbid with diabetes or hypertension in resource-poor settings: a qualitative study about user perception of a nurse-supported smartphone app in Peru. JMIR Ment. Health 6, e11701.
Chireh, B., Li, M., D'Arcy, C., 2019. Diabetes increases the risk of depression: a systematic review, meta-analysis and estimates of population attributable fractions based on prospective studies. Prev. Med. Rep. 14, 100822.
Danielsson, L., Noras, A.M., Waern, M., Carlsson, J., 2013. Exercise in the treatment of major depression: a systematic review grading the quality of evidence. Physiother. Theory Pract. 29, 573–585.
Davies, M., 2019. Psychological aspects of diabetes management. Medicine 47, 131–134.
De Groot, M., Shubrook, J.H., Hornsby Jr., W.G., Pillay Jr., Y., Mather Jr., K.J., Fitzpatrick Jr., K., Yang Jr., Z., Saha Jr., C., 2019. Program ACTIVE II: outcomes from a randomized, multistate community-based depression treatment for rural and urban adults with type 2 diabetes. Diabetes Care 42, 1185–1193.
De Groot, M., Shubrook, J.H., Hornsby Jr., W.G., Pillay, Y., Mather, K.J., Fitzpatrick, K., Yang, Z., Saha, C., 2019. Program ACTIVE II: outcomes from a randomized, multistate community-based depression treatment for rural and urban adults with type 2 diabetes. Diabetes Care 42, 1185–1193.
Duruturk, N., Ozkoslu, M.A., 2019. Effect of tele-rehabilitation on glucose control, exercise capacity, physical fitness, muscle strength and psychosocial status in patients with type 2 diabetes: a double blind randomized controlled trial. Prim. Care Diabetes 13, 542–548.
Elamoshy, R., Bird, Y., Thorpe, L., Moraros, J., 2018. Risk of depression and suicidality among diabetic patients: a systematic review and meta-analysis. J. Clin. Med. 7, 445.
Gilani, S.R.M., Feizabad, A.K., 2019. The effects of aerobic exercise training on mental health and self-esteem of type 2 diabetes mellitus patients. Health Psychol. Res. 7, 6576.
Green, A.J., Fox, K.M., Grandy, S., 2011. Impact of regular exercise and attempted weight loss on quality of life among adults with and without type 2 diabetes mellitus. J. Obes. 2011.
Hamer, M., Batty, G., Kivimaki, M., 2011. Haemoglobin A1C, fasting glucose and future risk of elevated depressive symptoms over 2-years follow up in the english longitudinal study of ageing. Psychol. Med. 41, 1889.
Harkness, E., Macdonald, W., Valderas, J., Coventry, P., Gask, L., Bower, P., 2010. Identifying psychosocial interventions that improve both physical and mental health in patients with diabetes: a systematic review and meta-analysis. Diabetes Care 33, 926–930.
Helgadóttir, B., Hallgren, M., Ekblom, Ö., Forsell, Y., 2016. Training fast or slow? Exercise for depression: a randomized controlled trial. Prev. Med. 91, 123–131.
Helgadóttir, B., Hallgren, M., Kullberg, C.L., Forsell, Y., 2018. Sticking with it? Factors associated with exercise adherence in people with mild to moderate depression. Psychol. Sport Exerc. 35, 104–110.
Hermanns, N., Caputo, S., Dzida, G., Khunti, K., Meneghini, L.F., Snoek, F., 2013. Screening, evaluation and management of depression in people with diabetes in primary care. Prim. Care Diabetes 7, 1–10.
Higgins, J.P., Thomas, J., Chandler, J., Cumpston, M., Li, T., Page, M.J., Welch, V.A., 2019. Cochrane Handbook for Systematic Reviews of Interventions. John Wiley & Sons.
Holt, R.I., de Groot, M., Golden, S.H., 2014. Diabetes and depression. Curr. Diab. Rep. 14, 1–9.
Kandola, A., Ashdown-Franks, G., Hendrikse, J., Sabiston, C.M., Stubbs, B., 2019. Physical activity and depression: towards understanding the antidepressant mechanisms of physical activity. Neurosci. Biobehav. Rev. 107, 525–539.
Kempf, K., Martin, S., 2013. Autonomous exercise game use improves metabolic control and quality of life in type 2 diabetes patients - a randomized controlled trial. BMC Endocr. Disord. 13, 57.
Knapen, J., Vancampfort, D., Moriën, Y., Marchal, Y., 2015. Exercise therapy improves both mental and physical health in patients with major depression. Disabil. Rehabil. 37, 1490–1495.
Kraiwong, R., Vongsirinavarat, M., Rueankam, M., Sumalrot, T., 2021. Effects of physical-cognitive training on physical and psychological functions among older adults with type 2 diabetes and balance impairment: a randomized controlled trial. J. Exerc. Rehabil. 17, 120–130.
Kulzer, B., Albus, C., Herpertz, S., Kruse, J., Lange, K., Lederbogen, F., Petrak, F., 2013. Psychosocial aspects of diabetes mellitus (Part 1). Diabetol. Stoffwechsel 8, 198–242.
Lincoln, A.K., Shepherd, A., Johnson, P.L., Castaneda-Sceppa, C., 2011. The impact of resistance exercise training on the mental health of older Puerto Rican adults with type 2 diabetes. J. Gerontol. B Psychol. Sci. Soc. Sci. 66, 567–570.
Liu, J.-X., Zhu, L., Li, P.-J., Li, N., Xu, Y.-B., 2019. Effectiveness of high-intensity interval training on glycemic control and cardiorespiratory fitness in patients with type 2 diabetes: a systematic review and meta-analysis. Aging Clin. Exp. Res. 31, 575–593.
Lysy, Z., da Costa, D., Dasgupta, K., 2008. The association of physical activity and depression in type 2 diabetes. Diabet. Med. 25, 1133–1141.
Maraldi, C., Volpato, S., Penninx, B.W., Yaffe, K., Simonsick, E.M., Strotmeyer, E.S., Cesari, M., Kritchevsky, S.B., Perry, S., Ayonayon, H.N., 2007. Diabetes mellitus, glycemic control, and incident depressive symptoms among 70-to 79-year-old persons: the health, aging, and body composition study. Arch. Intern. Med. 167, 1137–1144.
Martinez-Velilla, N., Valenzuela, P.L., Saez De Asteasu, M.L., ZAMBOM-Ferraresi, F., Ramirez-Velez, R., Garcia-Hermoso, A., Librero-Lopez, J., Gorricho, J., Perez, F.E., Lucia, A., Izquierdo, M., 2021. Effects of a tailored exercise intervention in acutely hospitalized oldest old diabetic adults: an ancillary analysis. J. Clin. Endocrinol. Metab. 106, e899–e906.
Mašanović, B., Popović, S., Bjelica, D., Vukotic, M., Zoric, G., 2018. The effects of physical activity on depressive symptoms among elderly people: a systematic review. In: Proceedings World Congress of Performance Analysis of Sport XII.
McKay, H.G., King, D., Eakin, E.G., Seeley, J.R., Glasgow, R.E., 2001. The diabetes network internet-based physical activity intervention: a randomized pilot study. Diabetes Care 24, 1328–1334.
Moher, D., Liberati, A., Tetzlaff, J., Altman, D.G., Group*, P., 2009. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Ann. Intern. Med. 151, 264–269.
Narita, Z., Inagawa, T., Stickley, A., Sugawara, N., 2019. Physical activity for diabetes-related depression: a systematic review and meta-analysis. J. Psychiatr. Res. 113, 100–107.
Nouwen, A., Adriaanse, M., van Dam, K., Iversen, M.M., Viechtbauer, W., Peyrot, M., Caramlau, I., Kokoszka, A., Kanc, K., de Groot, M., 2019. Longitudinal associations between depression and diabetes complications: a systematic review and meta-analysis. Diabet. Med. 36, 1562–1572.
Nyström, M.B., Neely, G., Hassmen, P., Carlbring, P., 2015. Treating major depression with physical activity: a systematic overview with recommendations. Cogn. Behav. Ther. 44, 341–352.
Oberste, M., Medele, M., Javelle, F., Lioba Wunram, H., Walter, D., Bloch, W., Bender, S., Fricke, O., Joisten, N., Walzik, D., 2020. Physical activity for the treatment of adolescent depression: a systematic review and meta-analysis. Front. Physiol. 11, 185.
Osama, A.-J., Shehab, A.E.-K., 2015. Psychological wellbeing and biochemical modulation in response to weight loss in obese type 2 diabetes patients. Afr. Health Sci. 15, 503–512.
Owens-Gary, M.D., Zhang, X., Jawanda, S., Bullard, K.M., Allweiss, P., Smith, B.D., 2019. The importance of addressing depression and diabetes distress in adults with type 2 diabetes. J. Gen. Intern. Med. 34, 320–324.
Perrin, N., Bodicoat, D., Davies, M., Robertson, N., Snoek, F., Khunti, K., 2019. Effectiveness of psychoeducational interventions for the treatment of diabetes-specific emotional distress and glycaemic control in people with type 2 diabetes: a systematic review and meta-analysis. Prim. Care Diabetes 13, 556–567.
Petrak, F., Baumeister, H., Skinner, T.C., Brown, A., Holt, R.I., 2015. Depression and diabetes: treatment and health-care delivery. Lancet Diabetes Endocrinol. 3, 472–485.
Petrak, F., Herpertz, S., 2009. Treatment of depression in diabetes: an update. Curr. Opin. Psychiatry 22, 211–217.
Piette, J.D., Richardson, C., Himle, J., Duffy, S., Torres, T., Vogel, M., Barber, K., Valenstein, M., 2011. A randomized trial of telephonic counseling plus walking for depressed diabetes patients. Med. Care 49, 641–648.
Pinchevsky, Y., Butkow, N., Raal, F.J., Chirwa, T., Rothberg, A., 2020. Demographic and clinical factors associated with development of type 2 diabetes: a review of the literature. Int. J. Gen. Med. 13, 121–129.
Putiri, A.L., Lovejoy, J.C., Gillham, S., Sasagawa, M., Bradley, R., Sun, G.-C., 2012. Psychological effects of yi ren medical qigong and progressive resistance training in adults with type 2 diabetes mellitus: a randomized controlled pilot study. Altern. Ther. Health Med. 18, 30–34.
Radovic, S., Melvin, G.A., Gordon, M.S., 2018. Clinician perspectives and practices regarding the use of exercise in the treatment of adolescent depression. J. Sports Sci. 36, 1371–1377.
Ravona-Springer, R., Heymann, A., Schmeidler, J., Moshier, E., Guerrero-Berroa, E., Soleimani, L., Sano, M., Leroith, D., Preiss, R., Tzukran, R., 2017. Hemoglobin A1c variability predicts symptoms of depression in elderly individuals with type 2 diabetes. Diabetes Care 40, 1187–1193.
Robertson, R., Robertson, A., Jepson, R., Maxwell, M., 2012. Walking for depression or depressive symptoms: a systematic review and meta-analysis. Ment. Health Phys. Act. 5, 66–75.
Saiiari, A., Moslehi, M., Sajadiyan, M., 2011. Effects of crawl swimming on depression in type 2 diabetic patients. Procedia Soc. Behav. Sci. 30, 2156–2160.
Sardar, M.A., Boghrabadi, V., Sohrabi, M., Aminzadeh, R., Jalalian, M., 2014. The effects of aerobic exercise training on psychosocial aspects of men with type 2 diabetes mellitus. Global J. Health Sci. 6, 196.
Schneider, K.L., Panza, E., Handschin, B., Ma, Y., Busch, A.M., Waring, M.E., Appelhans, B.M., Whited, M.C., Keeney, J., Kern, D., 2016. Feasibility of pairing behavioral activation with exercise for women with type 2 diabetes and depression: the get it study pilot randomized controlled trial. Behav. Ther. 47, 198–212.
Schuch, F.B., Stubbs, B., 2019. The role of exercise in preventing and treating depression. Curr. Sports Med. Rep. 18, 299–304.
Schuch, F.B., Vancampfort, D., Firth, J., Rosenbaum, S., Ward, P.B., Silva, E.S., Hallgren, M., Ponce De Leon, A., Dunn, A.L., Deslandes, A.C., 2018. Physical activity and incident depression: a meta-analysis of prospective cohort studies. Am. J. Psychiatr. 175, 631–648.
Schuch, F.B., Vancampfort, D., Richards, J., Rosenbaum, S., Ward, P.B., Stubbs, B., 2016. Exercise as a treatment for depression: a meta-analysis adjusting for publication bias. J. Psychiatr. Res. 77, 42–51.
Shah, S.Z., Karam, J.A., Zeb, A., Ullah, R., Shah, A., Haq, I.U., Ali, I., Darain, H., Chen, H., 2021. Movement is improvement: the therapeutic effects of exercise and general physical activity on glycemic control in patients with type 2 diabetes mellitus: a systematic review and meta-analysis of randomized controlled trials. Diabetes Ther. 12, 707–732.
Stubbs, B., Vancampfort, D., Smith, L., Rosenbaum, S., Schuch, F., Firth, J., 2018. Physical activity and mental health. Lancet Psychiatry 5, 873.
Thomas, J., Thirlaway, K., Bowes, N., Meyers, R., 2020. Effects of combining physical activity with psychotherapy on mental health and well-being: a systematic review. J. Affect. Disord. 265, 475–485.

Vucic Lovrencic, M., Pibernik-Okanovic, M., Sekerija, M., Prasek, M., Ajdukovic, D., Kos, J., Hermanns, N., 2015. Improvement in depressive symptoms is associated with reduced oxidative damage and inflammatory response in type 2 diabetic patients with subsyndromal depression: the results of a randomized controlled trial comparing psychoeducation, physical exercise, and enhanced treatment as usual. Int. J. Endocrinol. 2015, 210406.

Wake, A.D., 2020. Antidiabetic effects of physical activity: how it helps to control type 2 diabetes. In: Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy, 13, p. 2909.

Wang, F., Wang, S., Zong, Q.Q., Zhang, Q., Ng, C., Ungvari, G., Xiang, Y.T., 2019. Prevalence of comorbid major depressive disorder in type 2 diabetes: a meta-analysis of comparative and epidemiological studies. Diabet. Med. 36, 961–969.

Wang, X., Cai, Z.-D., Jiang, W.-T., Fang, Y.-Y., Sun, W.-X., Wang, X., 2022. Systematic review and meta-analysis of the effects of exercise on depression in adolescents. Child Adolesc. Psychiatry Ment. Health 16, 1–19.

Wang, Z.-D., Xia, Y.-F., Zhao, Y., Chen, L.-M., 2017. Cognitive behavioural therapy on improving the depression symptoms in patients with diabetes: a meta-analysis of randomized control trials. Biosci. Rep. 37.

Wu, P.-L., Lee, M., Huang, T.-T., 2017. Effectiveness of physical activity on patients with depression and Parkinson's disease: a systematic review. PLoS One 12, e0181515.

Yucel, H., Uysal, O., 2016. Pilates-based mat exercises and parameters of quality of life in women with type 2 diabetes. Iran Red Crescent Med J 18, 1.

Zhang, J., Yen, S.T., 2015. Physical activity, gender difference, and depressive symptoms. Health Serv. Res. 50, 1550–1573.

Zhuang, Q.-S., Shen, L., Ji, H.-F., 2017. Quantitative assessment of the bidirectional relationships between diabetes and depression. Oncotarget 8, 23389.