Nutrition, Metabolism & Cardiovascular Diseases (2016) xx, 1–14

Available online at www.sciencedirect.com

Nutrition, Metabolism & Cardiovascular Diseases

journal homepage: www.elsevier.com/locate/nmcd

SYSTEMATIC REVIEWS AND META-ANALYSES

Impact of lifestyle interventions on depressive symptoms in individuals at-risk of, or with, type 2 diabetes mellitus: A systematic review and meta-analysis of randomized controlled trials

A. Cezaretto [a], S.R.G. Ferreira [a], S. Sharma [b], B. Sadeghirad [c,d], F. Kolahdooz [b,*]

[a] *School of Public Health, Department of Epidemiology, University of São Paulo, Av. Dr. Arnaldo 715, São Paulo, SP 01246-904, Brazil*
[b] *Indigenous and Global Health Research Group, Department of Medicine, Faculty of Medicine & Dentistry, University of Alberta, 5-10 University Terrace, 8303 112 Street, Edmonton, Alberta T6G 2T4, Canada*
[c] *Health Research Methodology, Department of Clinical Epidemiology & Biostatistics, McMaster University, ON, Canada*
[d] *Regional Knowledge Hub and WHO Collaborating Centre for HIV Surveillance, Institute for Futures Studies in Health, Kerman University of Medical Sciences, Kerman, Iran*

Received 26 August 2015; received in revised form 17 March 2016; accepted 12 April 2016
Available online ■ ■ ■

KEYWORDS
Lifestyle intervention;
Depression;
Diabetes

Abstract *Background and Aim:* Depression affects one in four individuals with type 2 diabetes mellitus (T2DM). The impact of T2DM lifestyle interventions on depression is unclear. The aim of this analysis was to examine the influence of lifestyle interventions on depressive symptoms scores in individuals at-risk of or with T2DM.
Method and Results: Major bibliographic databases were searched for studies published in English from 1990 to 2015. Meta-analysis was conducted by random-effects model. Nineteen studies were included in the meta-analyses. A significant reduction in depression scores was shown for lifestyle interventions in the pooled analysis (Standardized Mean Difference (SMD): −0.165; 95%CI: −0.265, −0.064; I^2:67.9%) and when limited to individuals with T2DM (SMD: −0.202; 95%CI: −0.288, −0.079; I^2:72.5%). In subgroup analyses the most effective intervention methods were *face-to-face* individual consultations (SMD: −0.241; 95%CI: −0.403, −0.078, I^2: 50.8%) with a duration of *≤6 months* (SMD: −0.203; 95%CI: −0.381, −0.026, I^2:59.9%). Interventions were most effective when delivered four times a month (SMD: −0.247; 95%CI: −0.441, −0.053, I^2:76.3%).
Conclusions: Lifestyle interventions were effective in improving depression among people with T2DM.

Introduction

Depression is a global health concern which affects approximately 350 million people and by 2030 will be the leading cause of disease burden worldwide [1]. According to the World Mental Health Survey, one in 20 people reported having an episode of depression in their lifetime [2,3]. Depression is a major contributor to Disability

* Corresponding author. Indigenous and Global Health Research Group, Department of Medicine, Faculty of Medicine and Dentistry, University of Alberta, Unit 5-10 University Terrace, 8303 112 Street, Edmonton, Alberta T6G 2T4, Canada. Tel.: +1 780 492 3214; fax: +1 780 492 3018.
E-mail address: fariba.kolahdooz@ualberta.ca (F. Kolahdooz).

http://dx.doi.org/10.1016/j.numecd.2016.04.009
0939-4753/

Adjusted Life Years (DALYs) in developed countries [4,5]. Depressive individuals experience reduced quality of life and productivity, highlighting the importance of depression management [6,7]. Although depression is the most prevalent mental disorder in primary health care [5], it has not been appropriately recognized and treated [3,8,9], which leads to high costs for the public health care system and individuals [10]. Unhealthy lifestyles, including inadequate diet and/or physical inactivity, are common among individuals with depression and favor the development of chronic diseases, such as type 2 diabetes mellitus (T2DM) [11–13]. A meta-analysis reported a 1.8-fold higher mortality rate among people with depression [14].

Globally, 347 million people suffer from diabetes, of whom 90% have T2DM [15]. By 2025, the T2DM prevalence in adults is expected to increase by 122%, and in developing countries, it is projected to increase by 170% [15]. Its influence on health care systems includes lost days of work, premature mortality [16], physical disability [17], and excessive hospital admissions mainly due to cardiovascular complications [18]. To decrease the adverse impact on health care systems, there has been substantial investment in T2DM prevention [11–13,19]. However, implementing interventions to improve lifestyle [12,13], and to promote long-term maintenance of healthy behaviors, remains a challenge for health professionals.

There is a bidirectional association between depression and T2DM [20]. Depressed individuals may have up to a 60% higher risk of developing T2DM [21,22]. Concurrently, 25% of individuals with T2DM have depression during their lifetime [23]. Both conditions negatively influence quality of life [24], treatment adherence [25], and survival rates [26]. This association may also affect self-care and health care costs [27]. Previous studies suggest that management of depression may help to improve outcomes of diabetes treatment [28,29]. Moreover, integrating screening and management of depression with diabetes treatment has been recommended in international diabetes guidelines [30]. This approach allows patients with these chronic diseases to receive person-centered care and information on both conditions [31].

There is a consensus on the deleterious impact of depression associated with T2DM. A meta-analysis evaluating the impact of exercise on depression showed an increase in physical activity improved response to treatment for depression [32]. A recent systematic review assessing the effect of exercise on psychological aspects, particularly in people with diabetes, found only one in four studies that showed improved depression symptoms after the intervention when compared with the control group [33]. However, the importance of lifestyle interventions, considering also dietary changes, used to improve depression in adults at-risk of or with T2DM is unclear. This review comprehensively examines the effect of lifestyle interventions on depression management in individuals at-risk of or with T2DM by investigating: 1) the effect of lifestyle interventions on depression outcomes; 2) the effect of lifestyle interventions on dietary habits; 3) the degree of heterogeneity among the studies; 4) the potential sources of heterogeneity using subgroup analyses by methods, duration, and frequency of interventions.

Method

This systematic review followed the methods proposed by the Cochrane Collaboration [34] and was in accordance with the PRISMA Statement for Reporting Meta-analyses of Studies that Evaluate Health Care Interventions [35]. Risk of bias was assessed by the Cochrane Risk of Bias Tool (Appendix 1) [34]. We included intervention studies that: (i) examined adults (≥18 years old) at-risk of, or with T2DM; (ii) used biochemical tests to diagnose glucose tolerance disturbance; (iii) utilized standardized and validated assessment tools for depression with pre-established cut-off scores; and (iv) were published in English. Literature was excluded if it: (i) did not report depression based on standard and validated instruments with pre-established cut-offs from the literature to identify depression; (ii) focused only on treating depression; or (iii) contained duplicated data from another study. The duplicates were determined by thoroughly examining the study information about the study location and year, and the number, age, and sex of the participants. In general, studies focused on lifestyle (diet and/or physical activity) interventions directed at adults (≥18 years) at-risk of or with T2DM. All study participants received a minimum of four weeks intervention, a depression assessment at baseline, and a post-intervention. Participants "at-risk" were defined by the presence of impaired glucose tolerance or impaired fasting glucose [11]. T2DM was diagnosed by biochemical tests (75-g oral glucose tolerance test, fasting plasma glucose or glycated hemoglobin) according to the American Diabetes Association criteria [36].

Search strategy

We searched bibliographic databases PubMed/Medline, EMBASE, CINAHL, COCHRANE, PsycINFO, and Scopus, and identified studies on dietary/lifestyle interventions for individuals at-risk of or with T2DM published in the English language from January 1990 to March 2015. We used the following medical subject heading (MeSH) terms and/or pertinent text words for the search: "depression", "major depression", "depressive symptoms", "depressive disorder", "diabetes," "lifestyle intervention," "diet," and "dietary intervention." Two reviewers (AC, FK) independently assessed study titles and abstracts. In addition, the reference lists of all relevant reviews and selected papers were screened for additional studies. When deemed necessary, the first authors of selected publications were contacted for additional information [37–39]. We conducted a secondary search for relevant non-English publications to avoid excluding them. We identified 12 potentially relevant non-English studies; based on our review of the abstracts they were deemed irrelevant.

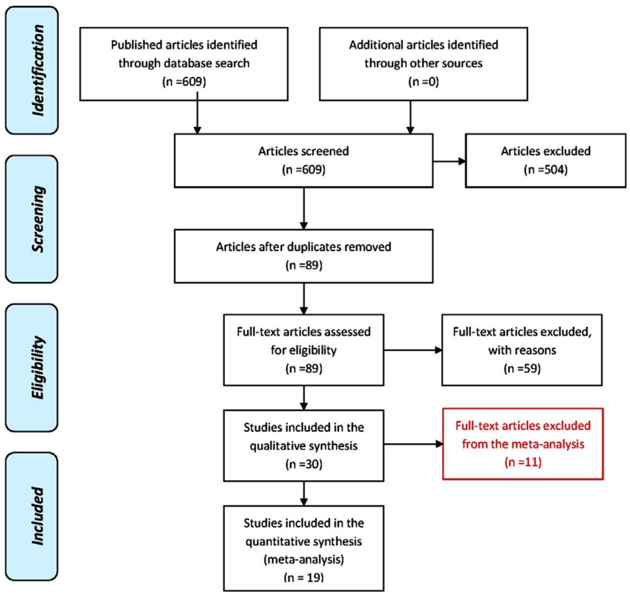


Figure 1 Summary of published study selection process.

Data extraction

The following information was extracted from the selected studies: i) study information (author's name, year of data collection, and study location), ii) participants (sample size, baseline age, diagnosis of T2DM or pre-T2DM, impaired fasting glycemia and/or impaired glucose tolerance, methods of depression assessment, and use of antidepressants), and iii) intervention details (type, frequency and duration of intervention, method of supervision, and duration of follow-up). The number of participants with measures of depression was recorded. Extracted data were inspected for concordance by two authors (AC, FK). If a study used more than one intervention in addition to a control group, the most complete intervention with the greatest combination of the strategies was used for meta-analysis.

Statistical analysis

For each study, the standardized effect size was calculated by dividing the mean difference in depression scores between the control and intervention groups by its standard deviation (SD) [40]. When the SD of changes in scores was not reported, we applied the imputation method based on reported mean and SD at follow-up. A correlation was assumed for a correlation coefficient of r = 0.5. The Standardized Mean

Table 1 General characteristics of the studies excluded[a] from the meta-analyses on the effectiveness of lifestyle intervention for diabetes prevention among people with depressive symptoms.

Author, Country	Age (yrs)	Sample size	Population with or at-risk of diabetes mellitus (DM)	Depression assessment	Duration of the intervention (months)	Reason for exclusion
[84] U.S.A.	25–79	M = 80 F = 232	At-risk of DM confirmed by predictive algorithm[d]	CES-D	12	Mean difference not reported
[85] Germany[b]	46.1[c]	M = 70 F = 125	At-risk of DM confirmed by OGTT	SCL-90-R	9	No control group
[86] U.S.A.	≥25	M = 1029 F = 2158	At-risk of DM confirmed by OGTT	BDI and/or antidepressant use	12	Results reported in percentage
[83] Italy	65–74	M = 30 F = 22	DM confirmed by FBS	BDI and GDS-15	2	Intervention used low protein diet
[37] U.S.A.	≥18	M = 124 F = 171	DM confirmed by physician	PHQ-9	12	Mean difference not reported
[87] United Kingdom	59.5[c]	M = 453 F = 371	DM confirmed by physician	HADS	12	Mean difference not reported
[88] U.S.A.[b]	43–66	M = 6 F = 6	DM confirmed by physician	CES-D	6	No control group
[39] Germany[b]	58.8[c]	M = 136 F = 191	DM confirmed by physician	CES-D	3	No control group
[12] Australia[b]	40–75	M = 65 F = 172	At-risk of DM confirmed by Diabetes Risk Score too	HADS	8	No control group
[89] U.S.A.	63[c]	M = 665 F = 221	DM confirmed by Welborn criteria	PHQ-9	6	Results reported in percentage
[90] U.S.A	58.5[c]	M = 115 F = 214	DM confirmed by physician	SCL-20	12	Results reported in percentage

OGTT, Oral Glucose Tolerance Test; FBS, Fasting Blood Sugar; BDI, Beck Depression Inventory; CES-D, Centre for Epidemiological Studies-Depression Scale; SCL-90-R, Self-reported Symptom Checklist; PHQ-9, Patient Health Questionnaire-9; GDS-15, 15-item Geriatric Depression Scale; SCL-20, Hopkins Symptom Checklist-20; WBQ22, patient Well-Being Questionnaire; HADS, Hospital Anxiety and Depression Scale; DASS-21, Depression, Anxiety and Stress Scale.

[a] Studies excluded due to missing data or not reporting in means and standard deviation or error or confidence interval.

[b] Non-Randomized trial.

[c] Mean age in years.

[d] Validated predictive algorithm based on age, gender, ethnicity, fasting blood glucose, systolic blood pressure, HDL cholesterol, BMI and family history of diabetes.

Please cite this article in press as: Cezaretto A, et al., Impact of lifestyle interventions on depressive symptoms in individuals at-risk of, or with, type 2 diabetes mellitus: A systematic review and meta-analysis of randomized controlled trials, Nutrition, Metabolism & Cardiovascular Diseases (2016), http://dx.doi.org/10.1016/j.numecd.2016.04.009

Please cite this article in press as: Cezaretto A, et al., Impact of lifestyle interventions on depressive symptoms in individuals at-risk of, or with, type 2 diabetes mellitus: A systematic review and meta-analysis of randomized controlled trials, Nutrition, Metabolism & Cardiovascular Diseases (2016), http://dx.doi.org/10.1016/j.numecd.2016.04.009

Table 2 General characteristics of the studies included in the meta-analyses on the effectiveness of lifestyle intervention for diabetes prevention among people with depressive symptoms.

Reference number, Country	Age[a] (yrs)	Sample size n (%male)	Population with or at-risk of diabetes mellitus (DM)	Depression assessment	Intervention			
					Duration (months)	Type and strategies	Frequency and consultant	Goals
[43] Finland	57.6	522 (33%)	At-risk of DM confirmed by OGTT	BDI	36	In-person nutrition counseling and individualized exercise sessions. .	- 7 in-person sessions with nutritionist in the 1st year - 1 session every 3 months until end of the study - Nutritionist + Personal Trainer	Weight reduction of ≥5%; <30% daily energy intake from fat; <10% of energy intake from saturated fat; fiber intake to ≥15 g/1000 kcal; moderate exercise for ≥30 min/day
[44] U.S.A.	45.7	58 (10.3%)	At-risk of DM confirmed by OGTT	CES-D	6	Culturally relevant education from a nutritionist and nurse practitioner, on healthy lifestyles and strategies for overcoming barriers to change.	-620 min in-person sessions - 5 telephone sessions - Nurse practitioners (NP)	Limit calories, fat and processed foods and increase exercise to at least 30 min, 5 days/week to lose 5–7% of initial weight
[47] U.S.A.	61.5	335 (49.9%)	DM confirmed by physician	PHQ-9	2	Use of a tailored self-management intervention (TSM) through a CD_ROM program that focuses on healthy eating, physical activity and identifies benefits and barriers to change while providing customized goal-setting and action-planning.	- 1 session prior to next diabetes-related doctor appointment - 2 follow-up phone calls (1 week and 1 month after first visit) - Health newsletter 6 weeks after first visit - Computer program + Health educators	Decrease dietary fat and increase fruit and vegetable intake.
[48] U.S.A.	60.9	279 female	DM confirmed by Welborn criteria	CES-D	24	Mediterranean Lifestyle Program (emphasis on vegetables, legumes and fish while discouraging consumption of red meat, butter and cream), stress-management (yoga, meditation, progressive deep relaxation, and directed or receptive imagery), social support (support groups) and physical activity.	- An initial 3 day retreat - 6 months of weekly, 4-h meetings - 2 months weekly meetings - 4 meetings over the remaining 18 months - Dietitian + exercise physiologist + stress-management instructor	Decrease % daily calories from saturated fat. 1 h of moderate aerobic activity at least 3 days/week. At least 1 h/day of stress management (yoga, meditation, directed or receptive imagery and progressive deep relaxation).
[49] U.S.A.	58.7	5129 (40.5%)	DM confirmed by physician	BDI	12	Intensive behaviorally-oriented diet and physical activity counseling. First 4 months consumed a diet of 1200–1800 kcal/d and replaced 2 meals and 1 snack per day with liquid shakes and meal bars.	- 3 group +1 individual meeting each month during months 1–6 - 2 group and 1 individual session per month during months 7–12 - Dietitian + Physical educator + stress-management instructor	Mean weight loss ≥7% of initial weight. Increase physical activity to ≥175 min/week
[50] U.S.A.	57.4	214 (43%)	DM confirmed by HbA1C	SCL-20	24	Nurse care managers helped identify clinical goals and develop individualized care plans and strategies for self-care activities	- Initial individual visit - Phone calls 2–3 times/month during the maintenance - Phone calls every 4–6 weeks - Nurses trained and supervised by physicians and psychiatrists	Depression improvements Medication adherence, diet, exercise regimens, monitoring blood pressure

[51] Germany	58.7	223 (52%)	DM confirmed by physician and HbA1C	WBQ22	6	Instruction for a blood glucose device, documentation of daily blood glucose levels and eating/exercise habits, and state of well-being. During counseling, questions based on self-perception, self-reflection and self-regulation were discussed.	- Visits once every 4 weeks - Family practitioner	Daily diary to become more familiar with their diabetes in terms of eating habits, well-being and the significance of self-monitoring of blood glucose. Promotion of self-reflection and enhancement of self-regulation.
[52] U.S.A.	52.6	163 (49.7%)	DM confirmed by physician	PHQ-9	12	Patients receive coaching via Smartphone and enter their blood glucose, carbohydrates consumed, and diabetes medication taken. From this, real time feedback is provided. Primary care providers have access to patients' online logbook. Physicians are provided with data analysis reports and treatment recommendations and all received American Diabetes Association Guideline for diabetes care.	- Contact every 2–3 months - Physician + Diabetes educator	N/A
[53] U.S.A.	53.5	40 (47.5%)	DM confirmed by physician	CES-D	6	Individuals were placed on a tailored low-glycemic index (GI) diet and received comprehensive education on following a low-GI diet.	- 2 group sessions - 1 individual session - 3 telephone counseling sessions (with 1 contact occurring each month) - Dietitians	Obtain 55% of daily energy intake from carbohydrates. Reduction of daily GI score to 55. Consume <10% daily calories from saturated fat and <300 mg/d of dietary cholesterol.
[38] Japan	72	1173 (46.3%)	DM confirmed by physician	Short form of GDS-15	36	Non-reported	- Frequency non-reported - Physician	HbA1c < 6.9%, BMI < 25 kg/m^2 Systolic blood pressure <130 mmHg Diastolic blood pressure <85 mmHg HDL-C > 40 mg/dL Serum triglycerides <150 mg/dL Serum total cholesterol <180 mg/dL (or LDL-C <100 mg/dL if patients had CHD) or <200 mg/dL (or LDL-C <120 mg/dL if patients did not have CHD).
[45] Australia	61.3	307 (41%)	At-risk of DM confirmed by OGTT	Short form of DASS-21	6	Sessions encouraging healthy lifestyle change including, weight-loss goals, self-management and problem-solving skills.	- 1 session per month - General practitioner	Increase physical activity and healthy eating to lose weight.
[54] U.S.A.	62.6	25 (20%)	DM confirmed by physician	CES-D	6	Diabetes-related knowledge and attitudes were assessed and strategies to improve diabetes self-management skills were initiated.	- 1 h individual session - 10 weekly 2.5–3 h group sessions - Two-15 min individual sessions - Nutritionist + Nurse + Intervention assistant	Healthy diet, increase physical activity and improve adherence to daily blood glucose self-monitoring and all medications.

(*continued on next page*)

Table 2 (*continued*)

Reference number, Country	Age[a] (yrs)	Sample size n (%male)	Population with or at-risk of diabetes mellitus (DM)	Depression assessment	Intervention: Duration (months)	Type and strategies	Frequency and consultant	Goals
[55] U.S.A.	58.02	336 (46.7%)	DM confirmed by physician	Short form of CES-D	3	Phone calls to reinforce education and self-management skills learned in standard diabetes disease management programs.	- Weekly phone call (initially 15–20 min and subsequently 5–7 min in length) - Nurse + Nutritionist + Primary Care Provider	Glycemic control Prevention of diabetes complications.
[56] U.S.A.	66.7	345 (33.9%)	DM confirmed by physician	PHQ-9	6	Action planning and problem solving in the areas of healthy eating, fitness, stress management and relaxation techniques.	- 2.5 h of group education during 6 weeks to implement DSMP (Diabetes Self-Management Program) - Trained 2 peer leaders + diabetes educators	Decrease weight and fatigue, and increase exercise and healthy eating.
[57] U.S.A.	52	62 (41.9%)	DM confirmed by physician	PHQ-9	6	Coaches provided information on nutrition, physical activity, stress management, blood sugar testing and medication management.	- 1 phone call per week for the first 3 months (15 min) - 1 bi-weekly phone call for the final 3 months - Coaches trained and supervised by Psychologist	Increase physical activity, healthy eating, and Glycemic control Medication management.
[46] Brazil	55.4	177 (32.2%)	At-risk of DM confirmed by impaired FBS or OGTT	BDI	9	Counseling and print materials on dietary habits, physical activity and stress management.	- 3 medical visits - 1 counseling session with a Dietitian - 2-h group sessions (4 in month 1, 2 in month 2, and 1 each month until month 9) - Endocrinologist + Nutritionist + Physical educator + Psychologist	Weight loss ≥5%, dietary fiber intake ≥20 g/d, saturated fat ≤10% of total energy, and moderate physical activity ≥150 min per week.
[58] U.S.A.	58	549 (43%)	DM confirmed by physician	CES-D	24	Diabetes self-management and lifestyle change counseling through motivational interviewing.	- 1-h individual visit at week 2 and 6 - 1-h individual visit month 3, 6, and 12 - 1-h individual visit every 6 months thereafter - Primary care provider + Nurse	Glycemic control Blood pressure control Stress management
[59] South Korea	55.6	43 (62.8%)	DM confirmed by physician	CES-D	4	Exercise, diet, and process of change and self-efficacy counseling.	- One 1-h counseling every 2 months - 1 (10–30 min) telephone counseling every week during intervention - Nurse	Complete 150 min moderate exercise/week; 200–300 kcal reduction in daily calories.
[60] USA	56.8	44 (50.6%)	DM confirmed by physician	MADRS	12	Self-monitoring of blood glucose, lifestyle counseling (exercise, diet), and cognitive behavioral therapy (CBT) for adherence and depression.	- 3 counseling session with Dietitian and 1 with Nurse - 12 CBT group sessions	Diabetes self-care. Individualized goals of nutrition and activity.

OGTT = Oral Glucose Tolerance Test; FBS = Fasting Blood Sugar; BDI = Beck Depression Inventory; CES-D = Centre for Epidemiological Studies-Depression Scale; PHQ-9 = Patient Health Questionnaire-9; GDS-15 = 15-item Geriatric Depression Scale; SCL-20 = Hopkins Symptom Checklist-20; WBQ22 = patient Well-Being Questionnaire; DASS-21 = Depression, Anxiety and Stress Scale; HbA1C = glycosylated hemoglobin A1.

[a] Mean age in years.

Difference (SMD) calculation was used to combine the results from the different tools used to measure depression.

We chose a fixed- or random-effects model to estimate the combined effects based on the results of the heterogeneity test (Cochrane-Q). Stratified analyses were conducted according to key features of study design including methods of the lifestyle intervention (group or individual face-to-face sessions, telephone, and internet), duration (≤6 months, 7–12 months, and >12 months), frequency of intervention (4×/month, 1×/month, and <1×/month), age (≤60 years, >60 years), and sex, as well as T2DM status (at-risk of and with T2DM). We estimated I^2 as the indicator of heterogeneity using the restricted likelihood method. The significance levels of $P < 0.10$ and $I^2 > 50\%$ were considered as heterogeneity. For subgroup analysis, we tested for interaction using a chi-square significance test [41]. For subgroups with more than two variables and seven observations, we performed meta-regression. A sensitivity analysis was performed to assess the contribution of each study to the overall effect. We evaluated publication bias by qualitatively assessing a funnel plot of the impact of lifestyle interventions on depression in participants at-risk of or with T2DM and by using Begg's rank correlation test and Egger's regression method [42]. The statistical analyses were performed using Stata version 11.

Results

The search identified 609 potentially relevant articles (Fig. 1). After assessing titles and abstracts, 504 publications were considered irrelevant. Following full review of the remaining 105 articles, 16 duplicates, 26 studies with incomplete depression data and 33 non-interventional studies were excluded. We identified 30 eligible studies that evaluated the effect of lifestyle interventions on depression in individuals at-risk of or with T2DM. Of these, 11 studies (Table 1) did not present sufficient information for meta-analysis, leaving 19 studies for the final analyses. These randomized trials evaluated the impact of lifestyle interventions on depression in participants at-risk of [43–46] or with [38,47–60] T2DM (Table 2).

The meta-analyses included 9107 individuals (4687 receiving an intervention and 4420 control) aged between 18 and 84 years at baseline. One study included only women [48]. The studies were conducted in North American [44,47–50,52–58,60], European [43,51], Asian [38,59], Australian [45], and Brazilian [46] populations. Ten studies showed that lifestyle interventions improved depression scores [47,49–54,56,57,59]. Antidepressant use was assessed in four studies [43,46,49,50].

Seventeen interventional studies focused on both diet and physical activity, one study implemented only dietary interventions [53], and one did not report intervention features [38]. Ten studies showed that lifestyle interventions had a positive impact reporting changes on dietary habits, such as saturated fat [48,53,54], fiber and energy intake [43,46,53,54], improvements in healthy eating [44,45,56,57,59], and/or higher fruit and vegetable consumption [47]. One study demonstrated a correlation between reduced energy intake and reduced depression scores

Table 3 Pooled results of the point estimates (95% confidence intervals) of the depression improvements after lifestyle intervention in at-risk of, or with T2DM individuals.

	Pooled effect estimate (95%CI)	P Heterogeneity	I^2 (%)	No. of studies
Effect on depression				
Overall	−0.165 (−0.265; −0.064)	<0.001	67.9	19
By age				
Mean age <60 years	−0.201 (−0.323; −0.080)	0.001	57.6	13
Mean age ≥60 years	−0.105 (−0.288; 0.079)	0.263	72.1	6
By disease condition				
At-risk of T2DM	0.004 (−0.163; 0.171)	0.905	0.0	4
Diagnosed with T2DM	−0.202 (−0.317; −0.087)	<0.001	72.5	15
By methods of intervention				
Group sessions	−0.209 (−0.378; −0.039)	0.002	68.7	8
Individual sessions	−0.241 (−0.403; −0.078)	0.058	50.8	7
Individual sessions by phone or internet[a]	0.061 (−0.177; 0.299)	0.259	26.0	3
By duration of intervention				
≤6 months	−0.203 (−0.381; −0.026)	0.008	59.9	10
7–12 months	−0.152 (−0.358; 0.055)	0.086	67.9	3
>12 months	−0.148 (−0.366; 0.070)	<0.001	81.1	5
By frequency of intervention				
Less than once a month	0.061 (−0.112; 0.234)	0.807	0.0	3
Once a month	−0.201 (−0.345; −0.057)	0.156	34.1	7
Four times a month	−0.247 (−0.441; −0.053)	<0.001	76.3	7
Effect on energy intake				
Overall	−1.191 (−2.243; −0.139)	<0.001	93.9	4
By T2DM				
At-risk of T2DM	−0.326 (−0.565; −0.087)	0.380	0.0	2
Diagnosed with T2DM	−2.440 (−6.949; 2.069)	<0.001	97.3	2

P for interactions are as follows: for T2DM status (at-risk of and with T2DM = 0.342; for age = 0.881, and for sex = 0.682.

[a] Software installed in the mobile phone.

Please cite this article in press as: Cezaretto A, et al., Impact of lifestyle interventions on depressive symptoms in individuals at-risk of, or with, type 2 diabetes mellitus: A systematic review and meta-analysis of randomized controlled trials, Nutrition, Metabolism & Cardiovascular Diseases (2016), http://dx.doi.org/10.1016/j.numecd.2016.04.009

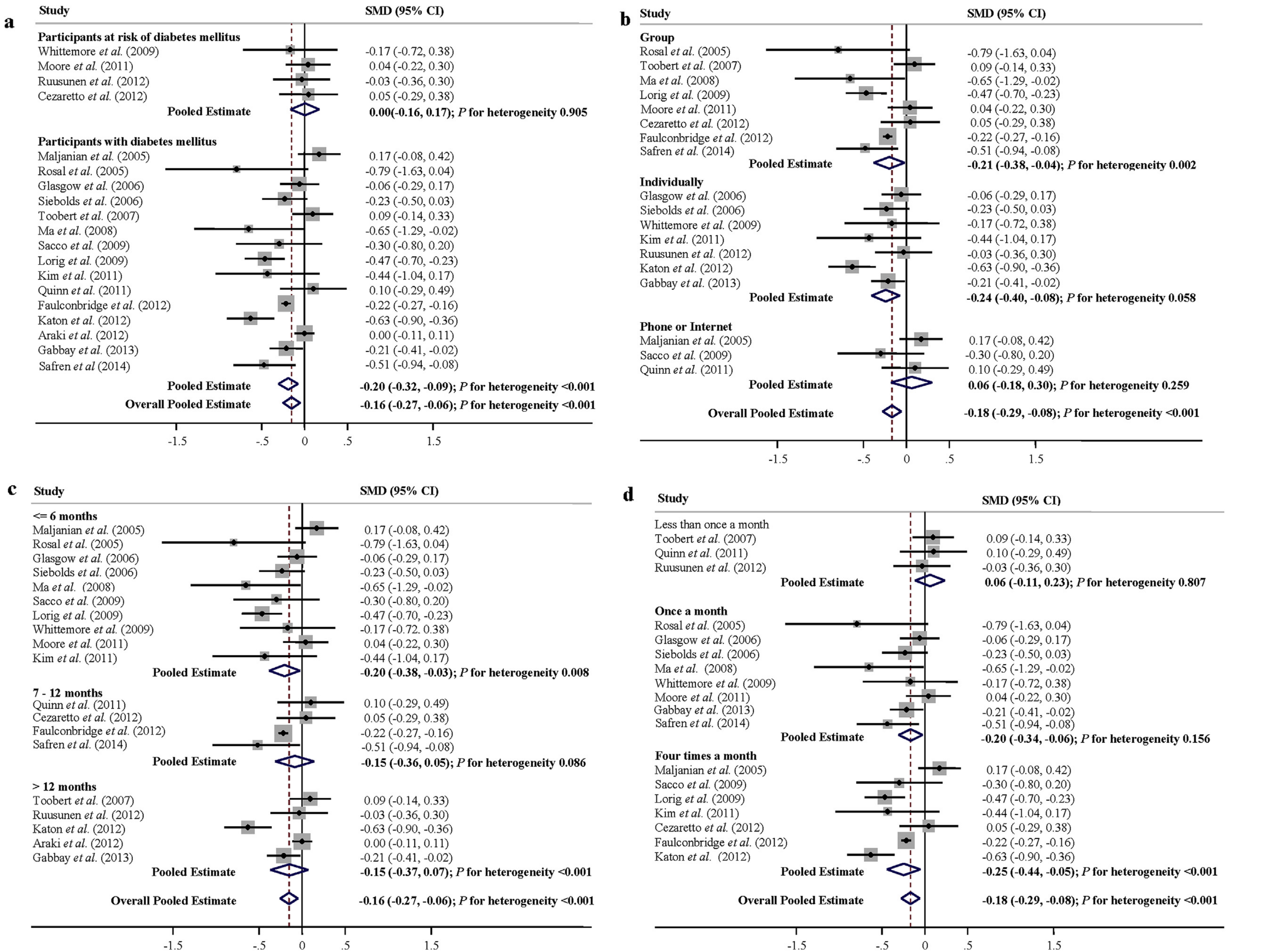


Figure 2 Forest plots of the effect of dietary and lifestyle interventions on depression 2a) in individuals at-risk or diagnosed with type 2 diabetes mellitus, stratified by 2b) methods 2c) duration and 2d) frequency of interventions. The center of each square indicates the standardized mean differences (SMD) of that study, and the horizontal lines indicate 95%CIs; the area of the square is proportional to the amount of data from that study; diamonds indicate pooled estimates.

Please cite this article in press as: Cezaretto A, et al., Impact of lifestyle interventions on depressive symptoms in individuals at-risk of, or with, type 2 diabetes mellitus: A systematic review and meta-analysis of randomized controlled trials, Nutrition, Metabolism & Cardiovascular Diseases (2016), http://dx.doi.org/10.1016/j.numecd.2016.04.009

[43]. In all of the studies, trained healthcare professionals applied behavioral strategies to help participants achieve their desired lifestyle changes. Three studies reported the presence of a psychiatrist or psychologist during the interventions [46,50,57]. In other studies, interventions were supervised by trained nurses, physicians and/or nutritionists (Table 2). Eight studies structured the interventions as group sessions [45,46,48,49,53,54,56,60] and four performed individual consultations [46,49,53,54]. Seven studies relied on individual, face-to-face consultations [43,44,47,50,51,58,59], four used telephone or internet orientations [44,52,55,57], and one did not describe the lifestyle intervention [38].

The duration of the interventions ranged from two to 36 months (median: six months). One study examined three components of the intervention (coaches, primary care providers, and personal decision-making process) [52]; only the results of including all three components in the intervention was considered in this meta-analyses. The sessions were commonly most frequent during the first six months of the intervention (mean = 2.08, SD = 1.41 sessions/month). Computer or mobile phone software was utilized by health coaches for diabetes management in four studies [47,52,55,57]. Among the included studies, six studies analyzed the interventions at various time points [44,48,50,54,58,60]. From these, one study showed that benefits in the short term were lost after the completion of the intervention [54]. Contrarily, one study found that the benefit of the intervention was maintained over 24 months [50].

The overall pooled analysis of 19 studies [38,43–59] showed a significant small effect of lifestyle interventions on improved depression scores (SMD: −0.165; 95%CI: −0.265, −0.064; I^2:67.9%). Stratified analysis revealed a robust effect on depression in individuals with T2DM (SMD: −0.202; 95%CI: −0.317, −0.087; I^2:72.5%). However, no effect was found in individuals at-risk of T2DM (SMD: 0.004; 95%CI: −0.163, 0.171; I^2:0.0%) (Table 3; Fig. 2a).

The stratified analyses by method of intervention showed that both individual (SMD: −0.241; 95%CI: −0.403, −0.078; I^2: 50.8%) and group (SMD: −0.209; 95%CI: −0.378, −0.039; I^2:68.7%) sessions had a significant beneficial effect on depression. However, depression scores were unaffected by internet and telephone interventions (SMD: 0.061; 95% CI: −0.177, 0.299; I^2:26.0%) (Table 3; Fig. 2b).

In stratified analyses by intervention duration, the *≤6-months* category had the strongest effect (SMD: −0.203; 95%CI: −0.381, −0.026; I^2:59.9%) compared to the *7-12-months* or *>12-months* categories (Table 3; Fig. 2c). Analyses by frequency of the interventions showed a significant beneficial effect on depression in association with sessions provided *four times a month* (SMD: −0.247; 95%CI: −0.441, −0.053; I^2:76.3%) and *once a month* (SMD: −0.201; 95%CI: −0.345, −0.057; I^2:34.1%). Depression was not affected by a less frequent intervention (Table 3; Fig. 2d).

In the meta-regression model, the effects of lifestyle intervention methods (SMD: 0.09; 95%CI: −0.09, 0.27; I^2:62.3%), duration of intervention (SMD: 0.028; CI: −0.12, 0.17; I^2: 68.6%), and frequency of intervention (SMD: −0.11; 95%CI −0.29, 0.07; I^2: 64.0%) were investigated on the mean difference in depression scores. In subgroup analyses, we did not find any differences by T2DM status (at-risk of and with T2DM; p for interaction = 0.342), age (p for interaction = 0.881), and sex (p for interaction = 0.682).

Meta-analysis of four studies [43,46,53,54] assessed the effect of interventions on energy and fiber intake. A statistically significant reduction in energy intake was found (SMD: −1.191; 95%CI: −2.243, −0.139; *P* for heterogeneity <0.001; I2:93.9%). Interventions had no effect on fiber intake (data not shown).

Five studies did not control for bias [43,44,51,53,58]. Some studies did not report about blinding and randomization (Appendix 1). Details about loss to follow-up were unclear in three studies [43,44,53] and absent in two studies [51,58]. In sensitivity analysis, excluding the women-only study [48] and studies reporting antidepressant medication use [43,46,49,50] did not change the overall pooled effect. Similarly, exclusion of the study considering only depressed individuals with diabetes did not alter both the overall pooled effect of lifestyle interventions and the effect of depression in the analyses of the with-T2DM subset. Publication bias was not apparent in the analyzed studies, as the funnel plot of the impact of lifestyle interventions on depression was close to symmetrical. Egger's regression method (P for bias = 0.974) and Begg's rank correlation test (P for bias = 0.184) also did not confirm the hypothesis of publication bias (Appendix 2).

Discussion

Promoting healthy diets and physical activity have been considered key strategies for diabetes prevention [61–63]. However, lifestyle modification is more challenging among patients with diabetes who have psychiatric comorbidities, such as depression [64,65]. Interdisciplinary interventions focused on behavioral change are being utilized effectively to control depression symptoms, improve quality of life, and enhance self-care by maintaining a healthy lifestyle [66,67]. This systematic review assessed the impact of dietary and lifestyle interventions on depression scores in individuals at risk of or diagnosed with T2DM. In general, interventions resulted in decreased depression scores regardless of the intensity and duration of intervention. In the meta-analysis, the interventions using individualized person-centered or group-session approaches were associated with significant depression score improvements. Results were null for telephone interventions. Presence of psychosocial-trained health professionals during face-to-face interventions might be facilitating the remission of depressive symptoms.

The diverse nature of various interventions paired with the wide range of study durations should prompt caution in the interpretation of pooled data. To partially address this issue, the meta-analyses included different subsets to analyze intervention methods. For interventions that used face-to-face methods a significant reduction in depression was found. Among short, intermediate, and longer-term intervention durations, it was evident, upon meta-analysis,

Please cite this article in press as: Cezaretto A, et al., Impact of lifestyle interventions on depressive symptoms in individuals at-risk of, or with, type 2 diabetes mellitus: A systematic review and meta-analysis of randomized controlled trials, Nutrition, Metabolism & Cardiovascular Diseases (2016), http://dx.doi.org/10.1016/j.numecd.2016.04.009

that all durations were useful in reducing depression scores. Furthermore, when the frequency of interventions was considered, substantial depression score improvement was found within the weekly frequency subset. These findings further validate previous studies [28,68] that demonstrate providing increased attention to individuals with chronic diseases could result in a greater sense of care and in turn improvements in depression outcomes.

Improving physical activity may reduce symptoms of depression [32,69,70] but the impact of changes in dietary habits on depression outcomes is unclear. In this study, it was not possible to analyze the effect of diet on depression because studies investigated different dietary parameters. Some studies, however, did demonstrate decreased depression scores in participants with improved dietary habits [47,53,56,57,59]. Previous studies have shown that dietary intakes of certain nutrients [71,72] may contribute to improved mental health. These findings indicate that adopting a healthy diet could result in reduced symptoms of depression. Just as obesity is widely acknowledged as a major risk factor in the development of diabetes, researchers have found an association between obesity and depression [73]. Despite some controversial reports [74], foods rich in simple carbohydrates have been associated with developing a negative mood [75]. Furthermore, adopting a healthy and conscious diet may lead to physical fitness, which in turn may result in an enhanced sense of well-being, consequently decreasing depressive symptoms. However, interventions considering younger individuals were shown to be more effective at reducing depression symptoms than interventions focusing on elderly populations. The studies included in this review did not consider the potential for co-morbidities in older individuals, which could prevent lifestyle interventions from resulting in improved depression symptoms. The relationship between depression and diabetes is complex. In addition to the association between unhealthy life habits and depression and diabetes, there is extensive literature speculating on a link between depression, diabetes, and subclinical inflammation [76]. Changes in the hypothalamic-pituitary-adrenal axis, present in depression, could impair glucose metabolism, ultimately contributing to the generation or deterioration of the pro-inflammatory state and in turn raise cardiovascular risk [77]. Several studies support the association between depression and activation of the immune-inflammatory system [78]. A recent meta-analysis revealed that inflammatory markers have a small but significant association with the subsequent development of depression [76]. Furthermore, specific nutrients, such as omega-3 fatty acids [72] and methylfolate [79], may be linked to the reduction of depression and the attenuation of inflammation. This suggests a physiological link between diet and both depression and T2DM.

The ever-increasing burden of chronic diseases such as depression and T2DM continue to be a challenge to global health. The increased frequency of T2DM paired with a considerable impact on psychosocial factors, health care, and costs have made depression and T2DM priorities for policy makers around the world [80]. Individuals with both conditions may have a reduced life expectancy by 5–6 years, mainly due to cardiovascular complications [81]. A recent meta-analysis found that individuals with diabetes who are depressed have a 1.5-fold increased risk of mortality compared to those who are not depressed [26]. Even those individuals with diabetes who have subclinical depression (not a clinically diagnosed condition like Major Depression Disorder) exhibit an increased risk of mortality [14]. In this review, we found that lifestyle interventions to manage T2DM were also effective in decreasing depression scores. Overall healthy lifestyles can contribute to improvements in depression, and vice-versa [82].

The current study has some limitations. First, the assessment of depression was of secondary interest to most studies. Second, it is possible that the Hawthorne effect played a role in measuring depression scores and overestimating the true impact of lifestyle interventions on reducing depression in many studies. Moreover, most studies did not assess antidepressant use, which could have had an influence on the results; some antidepressant classes such as the tricyclic may trigger cardiovascular complications and interfere with the effectiveness of lifestyle interventions. Therefore, some studies failed to provide necessary information, such as details on the randomization process, assessment of bias, and intervention designs, and may raise concerns about the quality of studies included in this review. Also, due to differing methods of analysis or types of variables presented among studies, a meta-analysis could only be conducted on 18 of the 29 studies; nevertheless, the number of studies is considered satisfactory and added new results to literature. One study was excluded from the meta-analysis as it focused on only one nutrient rather than the total diet, and this may misrepresent our results [83]; this report suggested that low protein intake was associated with increased depression.

Despite considering methodologically robust trials for this meta-analysis, our results show a small effect in favor of lifestyle interventions in depression among individuals with T2DM. It is important to note that there was significant heterogeneity across different study types; this could be due to the fact that the majority of studies considered weight loss as a main outcome and changes in depression scores as a secondary result of the interventions. The confounding effect of obesity and weight loss on depression might have influenced the results of our study. However, studies included in this review utilized various depression assessment tools; most of them have a high sensitivity. Those tools can examine different aspects of depression beyond somatic symptoms and are widely used to assess emotional and social depressive symptoms in individuals with chronic diseases such as T2DM. Investigating the impact of various types of intervention (e.g. diet and physical activity) on depression was beyond the scope of our review. Future studies should evaluate whether different lifestyle intervention strategies have different

Please cite this article in press as: Cezaretto A, et al., Impact of lifestyle interventions on depressive symptoms in individuals at-risk of, or with, type 2 diabetes mellitus: A systematic review and meta-analysis of randomized controlled trials, Nutrition, Metabolism & Cardiovascular Diseases (2016), http://dx.doi.org/10.1016/j.numecd.2016.04.009

impacts on depression among individuals at risk for, or with, T2DM.

Conclusion

Overall, the meta-analyses suggested that lifestyle interventions intended to manage T2DM, delivered face-to-face and with a high degree of frequency, are effective in improving depression.

Negative consequences of depression in individuals at risk of or with T2DM are known to include poor dietary intake, low physical activity levels, increased mortality, and health care costs. Consequently, it is essential that these vulnerable groups be screened regularly for depression. Once diagnosed, these individuals may benefit from treatment and management involving healthy lifestyles by an interdisciplinary team. Future studies need to investigate if different strategies used in lifestyle interventions for individuals at risk of or with T2DM can help improve or prevent depression.

Ethical standards

The manuscript does not contain clinical studies or patient data, and therefore ethical approval was not necessary.

Author's contributions

AC: performed the review and meta-analyses, and drafted the manuscript.

SRGF and SS: critically reviewed the manuscript.

BS: contributed to data analyses and critically reviewed the manuscript.

FK: developed the conception and methodology of the Review, oversaw the meta-analyses, and drafted and finalized the manuscript.

Declaration of interest

This work was supported by São Paulo Research Foundation. The authors declare they have no conflicts of interest.

Acknowledgment

The authors acknowledge Simone Enns for her contribution in data extraction.

Appendix 1

Risk-of-bias of the randomized controlled trials.

Author, Country	Sequence generation	Allocation concealment	Blind outcome assessor	Incomplete outcome data	Reporting to loss to follow up	Selective outcome reporting	Other bias	Comment
[43] Finland	Unclear	Unclear	Unclear	Low	Unclear	Low	Low	Good quality study; concise data analysis
[44] U.S.A.	Low	Low	Unclear	Low	Unclear	Low	Low: small sample	Good quality study; analysis difficult to interpret
[47] U.S.A.	Low	Low	Unclear	Low	Low	Low	Low	Good quality study
[48] U.S.A.	Low	Low	Unclear	Low	Low	Low	Low	Good quality study; methods concisely described
[49] U.S.A.	Unclear	Unclear	Low	Low	Low	Low	Low	Good quality study; very concise description of non-completers
[50] U.S.A.	Unclear	Unclear	Low	Low	Low	Low	Low	Good quality study
[51] Germany	Unclear	Unclear	High	Unclear	High	Low	Unclear	Possibly a good quality; Non reported missing on follow-up
[52] U.S.A.	Low	Low	Low	Low	Low	Low	Low	Good quality study; methods concisely described
[53] U.S.A.	Low	Low	Unclear	Low	Unclear	Low	Low	Good quality study
[38] Japan	High	High	Unclear	High	Low	High	Unclear	Possibly a good quality; methods not concisely described.
[45] Australia	Low	Low	High	Low	Low	Low	Unclear	Good quality study
[54] U.S.A.	Low	Low	Unclear	Low	Low	Low	Low: small sample	Good quality study; methods concisely described
[55] U.S.A.	Low	Low	Unclear	Low	Low	Low	Low	Good quality study
[56] U.S.A.	Unclear	Unclear	High	Low	Low	Low	Low	Good quality study; concise data analysis
[57] U.S.A.	Low	Low	Unclear	Low	Low	Low	Low: small sample	Good quality study; concise data analysis

(*continued on next page*)

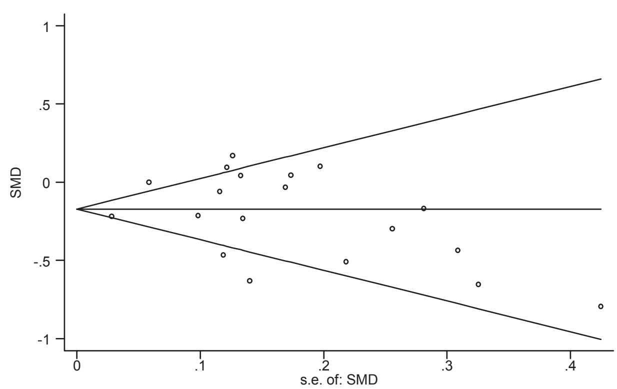
Please cite this article in press as: Cezaretto A, et al., Impact of lifestyle interventions on depressive symptoms in individuals at-risk of, or with, type 2 diabetes mellitus: A systematic review and meta-analysis of randomized controlled trials, Nutrition, Metabolism & Cardiovascular Diseases (2016), http://dx.doi.org/10.1016/j.numecd.2016.04.009

(*continued*)

Author, Country	Sequence generation	Allocation concealment	Blind outcome assessor	Incomplete outcome data	Reporting to loss to follow up	Selective outcome reporting	Other bias	Comment
[46] Brazil	Unclear	Unclear	High	Low	Low	Low	Low	Good quality study
[58] U.S.A.	Unclear	Unclear	High	High	High	Low	Low	Possibly a good quality; Non reported missing on follow-up
[59] South Korea	Unclear	Unclear	Unclear	Low	Low	Low	Low: small sample	Good quality study; methods concisely described
[60] U.S.A	High	High	High	Low	High	Unclear	Unclear	Good quality study; methods concisely described

Appendix 2

Funnel plot with pseudo 95% confidence limits.



References

[1] World Health Organization. The global burden of disease: 2004 update. Health Statistics and Information Systems, World Health Organization; 2008. 11-6-2013. Ref Type: Report.

[2] Kessler RC, Ustun TB. The World Mental Health (WMH) survey initiative version of the World Health Organization (WHO) Composite International Diagnostic Interview (CIDI). Int J Methods Psychiatr Res 2004;13:93–121.

[3] Marcus M, Yasamy MT, van Ommeren M, Chisholm D, Saxena S. Depression: a global public health concern. Mental Health: Depression, World Health Organization; 2012 [Ref Type: Online Source], Remain: Online Source, [accessed 05.02.16], URL: http://www.who.int/mental_health/management/depression/who_paper_depression_wfmh_2012.pdf.

[4] Demyttenaere K, Bruffaerts R, Posada-Villa J, Gasquet I, Kovess V, Lepine JP, et al. Prevalence, severity, and unmet need for treatment of mental disorders in the World Health Organization World Mental Health Surveys. JAMA 2004;291:2581–90.

[5] Simon GE. Long-term prognosis of depression in primary care. Bull World Health Organ 2000;78:439–45.

[6] Lecrubier Y. Depressive illness and disability. Eur Neuropsychopharmacol 2000;10(Suppl. 4):S439–43.

[7] Spitzer RL, Williams JB, Kroenke K, Linzer M, deGruy 3rd FV, Hahn SR, et al. Utility of a new procedure for diagnosing mental disorders in primary care. The PRIME-MD 1000 study. JAMA 1994;272:1749–56.

[8] Kessler RC, Chiu WT, Demler O, Merikangas KR, Walters EE. Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication. Arch Gen Psychiatry 2005;62:617–27.

[9] McQuaid JR, Stein MB, Laffaye C, McCahill ME. Depression in a primary care clinic: the prevalence and impact of an unrecognized disorder. J Affect Disord 1999;55:1–10.

[10] Chisholm D. Dollars, DALYs and Decisions: economic aspects of the mental health system. Mental Health: Evidence and Research, Department of Mental Health and Substance Abuse, World Health Organization; 2006 [Ref Type: Online Source], Remain: Online Source, [accessed 05.02.16], URL: http://www.who.int/mental_health/management/depression/who_paper_depression_wfmh_2012.pdf.

[11] Alberti KG, Zimmet P, Shaw J. International Diabetes Federation: a consensus on type 2 diabetes prevention. Diabet Med 2007;24:451–63.

[12] Laatikainen T, Dunbar JA, Chapman A, Kilkkinen A, Vartiainen E, Heistaro S, et al. Prevention of type 2 diabetes by lifestyle intervention in an Australian primary health care setting: greater Green Triangle (GGT) Diabetes Prevention Project. BMC Public Health 2007;7:249.

[13] Tuomilehto J, Lindstrom J, Eriksson JG, Valle TT, Hämäläinen H, Ilanne-Parikka P, et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. N Engl J Med 2001;344:1343–50.

[14] Cuijpers P, Smit F. Excess mortality in depression: a meta-analysis of community studies. J Affect Disord 2002;72:227–36.

[15] World Health Organization. Definition, diagnosis and classification of diabetes mellitus. Part 1: diagnosis and classification of diabetes mellitus. Department of Noncommunicable Disease Surveillance, World Health Organization; 1999 [Ref Type: Online Source], Remain: Online Source, [accessed 05.02.16], URL: http://apps.who.int/iris/bitstream/10665/66040/1/WHO_NCD_NCS_99.2.pdf.

[16] Katon W, Russo J, Lin EH, Heckbert SR, Ciechanowski P, Ludman EJ, et al. Depression and diabetes: factors associated with major depression at five-year follow-up. Psychosomatics 2009;50:570–9.

[17] Strine TW, Kroenke K, Dhingra S, Balluz LS, Gonzalez O, Berry JT, et al. The associations between depression, health-related quality of life, social support, life satisfaction, and disability in community-dwelling US adults. J Nerv Ment Dis 2009;197:61–4.

[18] Williams R, Van Gaal L, Lucioni C. Assessing the impact of complications on the costs of Type II diabetes. Diabetologia 2002;45:S13–7.

[19] Schwarz PE, Gruhl U, Bornstein SR, Landgraf R, Hall M, Tuomilehto J. The European perspective on diabetes prevention: development and Implementation of A European Guideline and training standards for diabetes prevention (IMAGE). Diab Vasc Dis Res 2007;4:353–7.

[20] Renn BN, Feliciano L, Segal DL. The bidirectional relationship of depression and diabetes: a systematic review. Clin Psychol Rev 2011;31:1239–46.

[21] Knol MJ, Twisk JW, Beekman AT, Heine RJ, Snoek FJ, Pouwer F. Depression as a risk factor for the onset of type 2 diabetes mellitus. A meta-analysis. Diabetologia 2006;49:837–45.

[22] Mezuk B, Eaton WW, Albrecht S, Golden SH. Depression and type 2 diabetes over the lifespan: a meta-analysis. Diabetes Care 2008;31:2383–90.
[23] Nouwen A, Winkley K, Twisk J, Lloyd CE, Peyrot M, Ismail K, et al. Type 2 diabetes mellitus as a risk factor for the onset of depression: a systematic review and meta-analysis. Diabetologia 2010;53:2480–6.
[24] Egede LE, Hernandez-Tejada MA. Effect of comorbid depression on quality of life in adults with Type 2 diabetes. Expert Rev Pharmacoecon Outcomes Res 2013;13:83–91.
[25] Simon GE, Katon WJ, VonKorff M, Unützer J, Lin EH, Walker EA, et al. Cost-effectiveness of a collaborative care program for primary care patients with persistent depression. Am J Psychiatry 2001;158:1638–44.
[26] Park M, Katon WJ, Wolf FM. Depression and risk of mortality in individuals with diabetes: a meta-analysis and systematic review. Gen Hosp Psychiatry 2013;35:217–25.
[27] Bogner HR, Morales KH, Post EP, Bruce ML. Diabetes, depression, and death: a randomized controlled trial of a depression treatment program for older adults based in primary care (PROSPECT). Diabetes Care 2007;30:3005–10.
[28] Bogner HR, Morales KH, de Vries HF, Cappola AR. Integrated management of type 2 diabetes mellitus and depression treatment to improve medication adherence: a randomized controlled trial. Ann Fam Med 2012;10:15–22.
[29] Pibernik-Okanovic M, Begic D, Ajdukovic D, Andrijasevic N, Metelko Z. Psychoeducation versus treatment as usual in diabetic patients with subthreshold depression: preliminary results of a randomized controlled trial. Trials 2009;10:78.
[30] Nimalasuriya K, Compton MT, Guillory VJ. Screening adults for depression in primary care: a position statement of the American College of Preventive Medicine. J Fam Pract 2009;58:535–8.
[31] Kodner DL, Spreeuwenberg C. Integrated care: meaning, logic, applications, and implications–a discussion paper. Int J Integr Care 2002;2:e12.
[32] Silveira H, Moraes H, Oliveira N, Coutinho ES, Laks J, Deslandes A. Physical exercise and clinically depressed patients: a systematic review and meta-analysis. Neuropsychobiology 2013;67:61–8.
[33] van der Heijden MM, van Dooren FE, Pop VJ, Pouwer F. Effects of exercise training on quality of life, symptoms of depression, symptoms of anxiety and emotional well-being in type 2 diabetes mellitus: a systematic review. Diabetologia 2013;56:1210–25.
[34] Higgins JPT, Green S. Cochrane handbook for systematic reviews of interventions. Chichester: John Wiley and Sons; 2006.
[35] Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JP, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. BMJ 2009;339:b2700.
[36] Diagnosis and classification of diabetes mellitus. Diabetes Care 2013;36(Suppl. 1):S67–74.
[37] Anderson DR, Christison-Lagay J, Villagra V, Liu H, Dziura J. Managing the space between visits: a randomized trial of disease management for diabetes in a community health center. J Gen Intern Med 2010;25:1116–22.
[38] Araki A, Iimuro S, Sakurai T, Umegaki H, Iijima K, Nakano H, et al. Long-term multiple risk factor interventions in Japanese elderly diabetic patients: the Japanese Elderly Diabetes Intervention Trial–study design, baseline characteristics and effects of intervention. Geriatr Gerontol Int 2012;12(Suppl. 1):7–17.
[39] Kempf K, Kruse J, Martin S. ROSSO-in-praxi: a self-monitoring of blood glucose-structured 12-week lifestyle intervention significantly improves glucometabolic control of patients with type 2 diabetes mellitus. Diabetes Technol Ther 2010;12:547–53.
[40] Dupont WD. Statistical modeling for biomedical researchers: a simple introduction to the analysis of complex data. Cambridge, UK: Cambridge University Press; 2009.
[41] Altman DG, Bland JM. Interaction revisited: the difference between two estimates. BMJ 2003;326:219.
[42] Publication bias in meta-analysis: prevention, assessment and adjustments. New York, NY: Wiley; 2005.
[43] Ruusunen A, Voutilainen S, Karhunen L, Lehto SM, Tolmunen T, Keinänen-Kiukaanniemi S, et al. How does lifestyle intervention affect depressive symptoms? Results from the Finnish Diabetes Prevention Study. Diabet Med 2012;29:e126–32.
[44] Whittemore R, Melkus G, Wagner J, Dziura J, Northrup V, Grey M. Translating the diabetes prevention program to primary care: a pilot study. Nurs Res 2009;58:2–12.
[45] Moore SM, Hardie EA, Hackworth NJ, Critchley CR, Kyrios M, Buzwell SA, et al. Can the onset of type 2 diabetes be delayed by a group-based lifestyle intervention? A randomised control trial. Psychol Health 2011;26:485–99.
[46] Cezaretto A, Siqueira-Catania A, de Barros CR, Salvador EP, Ferreira SR. Benefits on quality of life concomitant to metabolic improvement in intervention program for prevention of diabetes mellitus. Qual Life Res 2012;21:105–13.
[47] Glasgow RE, Nutting PA, Toobert DJ, King DK, Strycker LA, Jex M, et al. Effects of a brief computer-assisted diabetes self-management intervention on dietary, biological and quality-of-life outcomes. Chronic Illn 2006;2:27–38.
[48] Toobert DJ, Glasgow RE, Strycker LA, Barrera Jr M, Ritzwoller DP, Weidner G. Long-term effects of the Mediterranean lifestyle program: a randomized clinical trial for postmenopausal women with type 2 diabetes. Int J Behav Nutr Phys Act 2007;4:1.
[49] Faulconbridge LF, Wadden TA, Rubin RR, Wing RR, Walkup MP, Fabricatore AN, et al. One-year changes in symptoms of depression and weight in overweight/obese individuals with type 2 diabetes in the Look AHEAD study. Obesity (Silver Spring) 2012;20:783–93.
[50] Katon W, Russo J, Lin EH, Schmittdiel J, Ciechanowski P, Ludman E, et al. Cost-effectiveness of a multicondition collaborative care intervention: a randomized controlled trial. Arch Gen Psychiatry 2012;69:506–14.
[51] Siebolds M, Gaedeke O, Schwedes U. Self-monitoring of blood glucose–psychological aspects relevant to changes in HbA1c in type 2 diabetic patients treated with diet or diet plus oral antidiabetic medication. Patient Educ Couns 2006;62:104–10.
[52] Quinn CC, Shardell MD, Terrin ML, Barr EA, Ballew SH, Gruber-Baldini AL. Cluster-randomized trial of a mobile phone personalized behavioral intervention for blood glucose control. Diabetes Care 2011;34:1934–42.
[53] Ma Y, Olendzki BC, Merriam PA, Chiriboga DE, Culver AL, Li W, et al. A randomized clinical trial comparing low-glycemic index versus ADA dietary education among individuals with type 2 diabetes. Nutrition 2008;24:45–56.
[54] Rosal MC, Olendzki B, Reed GW, Gumieniak O, Scavron J, Ockene I. Diabetes self-management among low-income Spanish-speaking patients: a pilot study. Ann Behav Med 2005;29:225–35.
[55] Maljanian R, Grey N, Staff I, Conroy L. Intensive telephone follow-up to a hospital-based disease management model for patients with diabetes mellitus. Dis Manag 2005;8:15–25.
[56] Lorig K, Ritter PL, Villa FJ, Armas J. Community-based peer-led diabetes self-management: a randomized trial. Diabetes Educ 2009;35:641–51.
[57] Sacco WP, Malone JI, Morrison AD, Friedman A, Wells K. Effect of a brief, regular telephone intervention by paraprofessionals for type 2 diabetes. J Behav Med 2009;32:349–59.
[58] Gabbay RA, Anel-Tiangco RM, Dellasega C, Mauger DT, Adelman A, Horn DH. Diabetes nurse case management and motivational interviewing for change (DYNAMIC): results of a 2-year randomized controlled pragmatic trial. J Diabetes 2013;5(3):349–57.
[59] Kim CJ, Kim DJ, Park HR. Effects of a cardiovascular risk reduction intervention with psychobehavioral strategies for Korean adults with type 2 diabetes and metabolic syndrome. J Cardiovasc Nurs 2011;26:117–28.
[60] Safren SA, Gonzalez JS, Wexler DJ, Psaros C, Delahanty LM, Blashill AJ, et al. A randomized controlled trial of cognitive behavioral therapy for adherence and depression (CBT-AD) in patients with uncontrolled type 2 diabetes. Diabetes Care 2014;37:625–33.
[61] Colagiuri R. A guide to National diabetes programmes. International Diabetes Federation; 2010. International Diabetes Federation. 1-8-2013. [Ref Type: Online Source], Remain: Online Source,

Please cite this article in press as: Cezaretto A, et al., Impact of lifestyle interventions on depressive symptoms in individuals at-risk of, or with, type 2 diabetes mellitus: A systematic review and meta-analysis of randomized controlled trials, Nutrition, Metabolism & Cardiovascular Diseases (2016), http://dx.doi.org/10.1016/j.numecd.2016.04.009

[accessed 05.02.16], URL: http://www.idf.org/webdata/Guide-to-NDP_web.pdf.
[62] Lindstrom J, Ilanne-Parikka P, Peltonen M, Aunola S, Eriksson JG, Hemiö K, et al. Sustained reduction in the incidence of type 2 diabetes by lifestyle intervention: follow-up of the Finnish Diabetes Prevention Study. Lancet 2006;368:1673–9.
[63] Li G, Zhang P, Wang J, Gregg EW, Yang W, Gong Q, et al. The long-term effect of lifestyle interventions to prevent diabetes in the China Da Qing Diabetes Prevention Study: a 20-year follow-up study. Lancet 2008;371:1783–9.
[64] Lustman PJ, Anderson RJ, Freedland KE, de GM, Carney RM, Clouse RE. Depression and poor glycemic control: a meta-analytic review of the literature. Diabetes Care 2000;23:934–42.
[65] Mathew CS, Dominic M, Isaac R, Jacob JJ. Prevalence of depression in consecutive patients with type 2 diabetes mellitus of 5-year duration and its impact on glycemic control. Indian J Endocrinol Metab 2012;16:764–8.
[66] Ludman EJ, Peterson D, Katon WJ, Lin EH, Von Korff M, Ciechanowski P, et al. Improving confidence for self care in patients with depression and chronic illnesses. Behav Med 2013; 39:1–6.
[67] Pazzagli C, Mazzeschi C, Laghezza L, Reboldi GP, De FP. Effects of a multidisciplinary lifestyle intervention for obesity on mental and physical components of quality of life: the mediatory role of depression. Psychol Rep 2013;112:33–46.
[68] Katon WJ, Lin EH, Von KM, Ciechanowski P, Ludman EJ, Young B, et al. Collaborative care for patients with depression and chronic illnesses. N Engl J Med 2010;363:2611–20.
[69] Dinas PC, Koutedakis Y, Flouris AD. Effects of exercise and physical activity on depression. Ir J Med Sci 2011;180:319–25.
[70] Roshanaei-Moghaddam B, Katon WJ, Russo J. The longitudinal effects of depression on physical activity. Gen Hosp Psychiatry 2009;31:306–15.
[71] Bae YJ, Kim SK. Low dietary calcium is associated with self-rated depression in middle-aged Korean women. Nutr Res Pract 2012; 6:527–33.
[72] Lin PY, Su KP. A meta-analytic review of double-blind, placebo-controlled trials of antidepressant efficacy of omega-3 fatty acids. J Clin Psychiatry 2007;68:1056–61.
[73] Faith MS, Butryn M, Wadden TA, Fabricatore A, Nguyen AM, Heymsfield SB. Evidence for prospective associations among depression and obesity in population-based studies. Obes Rev 2011;12:e438–53.
[74] Benton D, Nabb S. Carbohydrate, memory, and mood. Nutr Rev 2003;61:S61–7.
[75] Macht M. How emotions affect eating: a five-way model. Appetite 2008;50:1–11.
[76] Valkanova V, Ebmeier KP, Allan CL. CRP, IL-6 and depression: a systematic review and meta-analysis of longitudinal studies. J Affect Disord 2013;150:736–44.
[77] Burke HM, Davis MC, Otte C, Mohr DC. Depression and cortisol responses to psychological stress: a meta-analysis. Psychoneuroendocrinology 2005;30:846–56.
[78] Raison CL, Capuron L, Miller AH. Cytokines sing the blues: inflammation and the pathogenesis of depression. Trends Immunol 2006;27:24–31.
[79] Papakostas GI, Shelton RC, Zajecka JM, Bottiglieri T, Roffman J, Cassiello C, et al. Effect of adjunctive L-methylfolate 15 mg among inadequate responders to SSRIs in depressed patients who were stratified by biomarker levels and genotype: results from a randomized clinical trial. J Clin Psychiatry 2014;75: 855–63.
[80] Molosankwe I, Patel A, Jose GJ, Knapp M, McDaid D. Economic aspects of the association between diabetes and depression: a systematic review. J Affect Disord 2012;142(Suppl. S42–S55).
[81] Das-Munshi J, Stewart R, Ismail K, Bebbington PE, Jenkins R, Prince MJ. Diabetes, common mental disorders, and disability: findings from the UK National Psychiatric Morbidity Survey. Psychosom Med 2007;69:543–50.
[82] Williamson DA, Rejeski J, Lang W, Van DB, Fabricatore AN, Toledo K. Impact of a weight management program on health-related quality of life in overweight adults with type 2 diabetes. Arch Intern Med 2009;169:163–71.
[83] Ciarambino T, Ferrara N, Castellino P, Paolisso G, Coppola L, Giordano M. Effects of a 6-days-a-week low protein diet regimen on depressive symptoms in young-old type 2 diabetic patients. Nutrition 2011;27:46–9.
[84] Ockene IS, Tellez TL, Rosal MC, Reed GW, Mordes J, Merriam PA, et al. Outcomes of a Latino community-based intervention for the prevention of diabetes: the Lawrence Latino Diabetes Prevention Project. Am J Public Health 2012;102:336–42.
[85] Giel KE, Enck P, Zipfel S, Schrauth M, Bury A, Graf M, et al. Psychological effects of prevention: do participants of a type 2 diabetes prevention program experience increased mental distress? Diabetes Metab Res Rev 2009;25:83–8.
[86] Rubin RR, Knowler WC, Ma Y, Marrero DG, Edelstein SL, Walker EA, et al. Depression symptoms and antidepressant medicine use in Diabetes Prevention Program participants. Diabetes Care 2005;28:830–7.
[87] Davies MJ, Heller S, Skinner TC, Campbell MJ, Carey ME, Cradock S, et al. Effectiveness of the diabetes education and self management for ongoing and newly diagnosed (DESMOND) programme for people with newly diagnosed type 2 diabetes: cluster randomised controlled trial. BMJ 2008;336: 491–5.
[88] Steinhardt MA, Mamerow MM, Brown SA, Jolly CA. A resilience intervention in African American adults with type 2 diabetes: a pilot study of efficacy. Diabetes Educ 2009;35:274–84.
[89] Glasgow RE, Nutting PA, King DK, Nelson CC, Cutter G, Gaglio B, et al. A practical randomized trial to improve diabetes care. J Gen Intern Med 2004;19:1167–74.
[90] Katon WJ, Von KM, Lin EH, Simon G, Ludman E, Russo J, et al. The Pathways Study: a randomized trial of collaborative care in patients with diabetes and depression. Arch Gen Psychiatry 2004; 61:1042–9.

Please cite this article in press as: Cezaretto A, et al., Impact of lifestyle interventions on depressive symptoms in individuals at-risk of, or with, type 2 diabetes mellitus: A systematic review and meta-analysis of randomized controlled trials, Nutrition, Metabolism & Cardiovascular Diseases (2016), http://dx.doi.org/10.1016/j.numecd.2016.04.009