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Review Article

Effectiveness of universal multiple-risk lifestyle interventions in reducing depressive symptoms: Systematic review and meta-analysis

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ABSTRACT

Though many studies have explored the association between single-risk lifestyle interventions and depression, unhealthy lifestyle factors often co-occur, with adults engaging in two or more risk behaviours. To date, little is known about the effectiveness of universal multiple-risk lifestyle interventions to reduce depressive symptoms. We conducted a SR/MA to assess the effectiveness of universal multiple-risk lifestyle interventions (by promoting a healthy diet, physical activity and/or smoking cessation) to reduce depressive symptoms in adults. We searched MEDLINE, Scopus, CENTRAL, PsycINFO, WOS, OpenGrey, the ICTRP and other sources from inception to 16 September 2019. We selected only randomized controlled trials, with no restrictions on language or setting. Our outcome was the reduction of depressive symptoms. We calculated the standardized mean difference using random-effect models. Sensitivity, sub-group and meta-regression analyses were performed. Of the 9386 abstracts reviewed, 311 were selected for full-text review. Of these, 23 RCTs met the inclusion criteria, including 7558 patients from four continents. Twenty RCTs provided valid data for inclusion in the meta-analysis. The pooled SMD was -0.184 (95% CI, -0.311 to -0.057; $p = 0.005$). We found no publication bias, but heterogeneity was substantial ($I^2 = 72\%$; 95% CI: 56% to 82%). The effectiveness disappeared when only studies with a low risk of bias were included. The quality of evidence according GRADE was low. Although a small preventive effect was found, the substantial heterogeneity and RCTs with lower risk of bias suggested no effectiveness of universal multiple-risk lifestyle interventions in reducing depressive symptoms in a varied adult population. Further evidence is required.

1. Introduction

The latest estimates from the Global Burden of Disease study 2017 indicate that depressive disorders rank third for women and fifth for men in global disease burden regarding years lived with disability (James et al., 2018). After the first episode, subsequent episodes are frequent in patients with depression (Fombonne et al., 2001; Conradi et al., 2017). However, pharmacological and psychological treatments for depression only reduce disease burden by < 30% (Chisholm et al., 2004). Another method to decrease the burden of depressive disorders

is prevention through the reduction of new episodes in populations that have not already been given a diagnosis of depression (Bellón et al., 2015; Conejo-Cerón et al., 2017; van Zoonen et al., 2014) or the reduction of depressive symptoms (Deady et al., 2017; Tan et al., 2014) in clinical and nonclinical populations.

Compelling evidence proposes that depression has a significant lifestyle-driven component (Jacka and Berk, 2013; Sarris et al., 2014; Ruiz-Estigarribia et al., 2019). Thus, there is a need to consider lifestyle perspective as a strategy to promote, prevent and manage depression (Sarris et al., 2014). It is estimated that physical inactivity, unhealthy diet and smoking contribute to millions of deaths and disability-adjusted life years around the world (World Health Organization, 2014). Specifically, 3.2, 11 and 6 million deaths are attributed directly or indirectly to physical inactivity, unhealthy diet and smoking, respectively (World Health Organization, 2014). Furthermore, evidence suggests that physical inactivity, unhealthy diet and smoking present the highest prevalence rates among lifestyle risk factors (Mokdad et al., 2004; Galán et al., 2006; Mozaffarian et al., 2012; Zhang et al., 2017) in the general population. Regarding depression, these risk factors have been associated with depressive disorders (Almeida et al., 2011; Choi et al., 2019; Lopresti et al., 2013; Sanchez-Villegas et al., 2009; Schuch et al., 2018). Studies indicate that dietary interventions, physical activity or exercise, and smoking cessation programs can reduce symptoms of depression (Taylor et al., 2014; Rodríguez-Cano et al., 2016; Firth et al., 2019a; Rosenbaum et al., 2014; Schuch et al., 2016). Single-risk lifestyle interventions for reducing depressive symptoms are more numerous (ie, (Sánchez-Villegas et al., 2013; Van Der Meer et al., 2013; Daley et al., 2015; Dalgas et al., 2015; Herring et al., 2012; Brown et al., 2012; Mammen and Faulkner, 2013; Psaltopoulou et al., 2013)) than multiple-risk lifestyle interventions (Cezaretto et al., 2016; Coventry et al., 2013) in both depressed and non-depressed populations. Nevertheless, adults often engage in two or more risk behaviours (Galán et al., 2006; Mozaffarian et al., 2012; Poortinga, 2007; Silva et al., 2013). Multiple-risk lifestyle interventions are complex interventions (Craig et al., 2013; Prochaska et al., 2008a; Prochaska et al., 2008b) which can be defined as "efforts to treat two or more risk behaviours effectively within a limited time period simultaneously or sequentially" (Prochaska et al., 2013), which may be able to reduce depressive symptoms.

To the best of our knowledge only two systematic reviews and/or meta-analyses (SR/MA) of multiple-risk lifestyle interventions and depression have been published (Cezaretto et al., 2016; Coventry et al., 2013), but these present several restrictions mainly regarding the target populations included. The first SR/MA (Cezaretto et al., 2016) assessed lifestyle interventions focused on diet only and diet plus physical activity in patients at risk of or with type 2 diabetes mellitus until March 2015. The second SR/MA (Coventry et al., 2013) reviewed psychological and/or lifestyle interventions for adults with chronic obstructive pulmonary disease until January 2011. None of the previous SR/MA explored the effect of multiple-risk lifestyle interventions including smoking cessation, nor the combination of the three risk factors (healthy diet, physical activity, and smoking cessation), on the reduction of depression symptoms in a varied adult population. Additionally, several trials have been published since then.

The aim of this SR/MA was to evaluate the effectiveness of universal multiple-risk lifestyle interventions to reduce depressive symptoms in a varied adult population that included at least two of the following three factors: healthy diet, physical activity, and smoking cessation.

2. Methods

We performed an SR/MA of RCTs examining universal multiple-risk lifestyle interventions for reducing depressive symptoms, in accordance with the PRISMA guidelines (Moher et al., 2009). The protocol of this SR/MA was previously registered at PROSPERO on 18 September 2018 (registration number CRD42018100253) and has been published elsewhere (Gómez-Gómez et al., 2019).

2.1. Search strategies

We searched eight relevant electronic databases including MEDLINE (via Ovid and PubMed), Scopus, Cochrane Central Register of Controller Trial (CENTRAL), PsycINFO, Web of Science (WOS), OpenGrey Repository (System for Information on Grey Literature in Europe) and the International Clinical Trials Registry Platform (ICTRP) from database inception to 16 September 2019. We manually reviewed references of included articles and references from relevant SR/MA of multiple- or single-risk lifestyle interventions focused on healthy diet, physical activity, and/or smoking cessation. We also contacted experts in the field to identify other relevant articles. The search strategy comprised a combination of keywords and text words related to "healthy diet", "physical activity", "smoking cessation" and "depression". There were no language, year or setting restrictions. Searches were piloted in MEDLINE then adapted to run across the other databases. The specific search strategy in MEDLINE (PubMed) is showed in the Appendix 1.

2.2. Eligibility criteria

The rationale for our inclusion criteria was to have an extensive assessment of all universal multiple-risk lifestyle interventions focused on the acquisition of at least two habits including healthy diet, physical activity, and/or smoking cessation to reduce depressive symptoms in a varied adult population. Single-risk lifestyle interventions were excluded. As comparators, we considered usual care, non-intervention, waiting list, or attention controls (active control or placebo). Regarding attention controls, we only included interventions with no evidence of their effectiveness in reducing depressive symptom.

In purely preventive intervention studies, baseline depression must be ruled out using a standardized diagnostic tool or a threshold in a validated scale, and incidence must be examined at follow-up. However, due to the characteristics of multiple-risk lifestyle interventions, it is often more practical to implement universal interventions in an entire unscreened population. Thus, the outcome (as primary or secondary) was the reduction of depressive symptoms measured using validated rating scales for depression. Studies in which the target population included only patients meeting the diagnostic criteria for clinical depression were excluded as these are considered treatment rather than preventive interventions.

Only studies with adults over 18 years of age were included. No other demographic, clinical, language or setting restrictions were imposed.

2.3. Selection of studies

Two researchers (DMR and IGG) independently screened all abstracts and full texts to assess eligibility. Disagreements were resolved by consensus between both reviewers (DMR and IGG) and in case of disagreement, a third reviewer (EM) made the final decision. The degree of agreement between the initial reviewers was very good (Cohen $\kappa = 0.84$; 95% CI, 0.69 to 0.99).

2.4. Data extraction

Two researchers (DMR and IGG) independently extracted all the relevant characteristics of the included studies. Discrepancies were resolved by consensus between both reviewers (DMR and IGG). Authors, publication year and country, target population, target lifestyle factors (healthy diet and/or physical activity and/or smoking cessation), characteristics of the multiple-risk lifestyle interventions (total duration of the intervention, framework, and delivery format), conditions, sample size (control/intervention), percentage of depressive patients at

baseline, provider, outcome (measuring instrument and cut-off), setting, follow-up time and outcome were extracted. In case of incomplete data, we contacted the authors for further information.

2.5. Assessment of risk of bias

The risk of bias of the studies included was measured independently by two researchers (DMR and IGG) with five of the six criteria proposed by the Cochrane Collaboration's tool version 1 for assessing risk of bias (Higgins, 2008). The item "selective reporting" was excluded from the assessment because our only outcome of interest was the reduction of depressive symptoms. From a qualitative point of view, RCTs that scored high for risk of bias in "generation of the sequence", "blinding of evaluators of outcomes", "allocation concealment" or "incomplete outcome data" were considered to have a high overall risk of bias. Those RCTs that scored low for risk of bias in all the criteria cited previously were considered to have a low overall risk of bias. The criterion "blinding of participants and personnel" was excluded because the nature of multiple-risk lifestyle interventions makes them difficult to blind. Furthermore, to manage risk of bias as a quantitative variable in the meta-regressions, each of the five items of the Cochrane Collaboration tool included were assigned 0 points for low risk of bias, 1 for unclear risk, and 2 for high risk; hence, the lowest risk of bias score was 0 and the highest 10. We considered a score of ≤ 3 points as low risk, between 4–5 points as moderate risk and ≥ 6 points as high risk. Discrepancies were resolved by consensus between both reviewers (DMR and IGG). In case of disagreement, a third reviewer (EM) was consulted. The level of agreement between reviewers was excellent (intraclass correlation coefficient = 0.84; 95% CI, 0.60 to 0.94).

2.6. Statistical analysis

Quantitative data were analysed using Comprehensive Meta-Analysis version 2.2.021 (Biostat, Inc) and STATA version 14.2 (Stata Corporation, College Park, TX, USA). For each study, when more than one outcome measure (depressive symptoms) was reported, we calculated the standardized mean difference (SMD) by combining the SMD at different post-test follow-up times into a single estimate as the average, as well as its 95% confidence interval (CI). Negative SMDs indicated an improvement in the reduction of depressive symptoms in the intervention group. Cohen proposed the following interpretation for this effect size: 0.20 as a small effect size, 0.50 as a medium effect size and, 0.80 as a large effect size (Cohen, 1988). Random-effects models were used for pooling effect sizes.

Heterogeneity was assessed through visual inspection of the forest plot, the Q statistic and its *p*-value, and the I^2 index and its 95% CI. The I^2 index was expressed as percentages and we interpreted it as follows: unimportant heterogeneity (0–40%), moderate heterogeneity (30–60%), substantial heterogeneity (50–90%), and considerable heterogeneity (75–100%) (Higgins, 2011).

To assess publication bias, we examined the funnel plot and the trim-and-fill procedure (Duval and Tweedie, 2000). We also performed Begg and Mazumdar rank correlation (Begg and Mazumdar, 1994) and the Egger test (Stuck et al., 1998). We conducted sensitivity analyses in advance at the first and last follow-up using Hedges'g, the fixed-effects model, and excluding the RCT that most increased heterogeneity. Furthermore, we excluded RCTs with a high risk of bias and included only RCTs with a low risk of bias in both cases from both perspectives (qualitative and quantitative).

We performed subgroup analysis for categorical moderators according to target lifestyle, comparator, mean age, length of intervention, publication year, continent, follow-up, risk of bias (quantitative and qualitative criteria), sample size, target population, setting, deliverer, session format, outcome and percentage of depressive patients at baseline. We also performed random-effect meta-regression analyses to try to explain the heterogeneity. We verified the normality of the

quantitative variables that were included in the meta-regression using the skewness-kurtosis normality test (D'agostino et al., 1990), performing the pertinent transformations to approximate normality when necessary. We forced the variable risk of bias in the meta-regression models for adjustment. The variable sample size was not forced because we did not find evidence of publication bias. We performed bivariate meta-regression of each of the covariates considered for subgroup analysis. Covariates with a $p < 0.15$ in bivariate meta-regression, which were not excluded because of collinearity, were candidates for inclusion in the final meta-regression model.

2.7. Quality of evidence

The GRADE system (Balshem et al., 2011) was used to determine the overall quality of evidence.

3. Results

3.1. Study selection

A total of 14,770 records were identified (9386 after duplicate removal). Of these, 311 were examined for full-text inspection. As a result, 23 RCTs reported in 24 articles met criteria for inclusion in the systematic review. For meta-analysis calculations, we used 20 RCTs reported in 21 articles because three RCTs (Allison et al., 2000; Milani and Lavie, 2009; Siddiqui et al., 2019) of the 23 RCTs included in the systematic review did not report the necessary data after contacting the authors (see Fig. 1).

3.2. Study characteristics

A total of 7558 patients were included across 23 RCTs (see Table 1 for study characteristics). Fifteen RCTs included patients with or at high risk of cardiac diseases (Allison et al., 2000; Brotons et al., 2011; Pfaeffli Dale et al., 2015; Duan et al., 2018; Hofman-Bang, 1999; Jørstad et al., 2016; Lisspers et al., 1999; Shariful Islam et al., 2019) or diabetes (Siddiqui et al., 2019; Azami et al., 2018; Davies et al., 2016; Moore et al., 2011; Ruusunen et al., 2012; Wang et al., 2014; Rosal et al., 2005) or both (Gallagher et al., 2014), three included obese pregnant women (Poston et al., 2013; Molyneaux et al., 2018; Bogaerts et al., 2013) and one postpartum women (Surkan et al., 2012), one obese and hypertensive patients (Mensorio et al., 2019), one university students (Duan et al., 2017), one breast cancer survivors (Kim et al., 2011), and one studied employees and spouses (Milani and Lavie, 2009). Available percentages of depressive patients at baseline ranged from 13.2% to 66.7%. Age ranged between 19 and 67 years. Concerning continent, ten RCTs were conducted in Europe (Siddiqui et al., 2019; Brotons et al., 2011; Hofman-Bang, 1999; Jørstad et al., 2016; Lisspers et al., 1999; Davies et al., 2016; Ruusunen et al., 2012; Poston et al., 2013; Molyneaux et al., 2018; Bogaerts et al., 2013; Mensorio et al., 2019), five in Oceania (Milani and Lavie, 2009; Pfaeffli Dale et al., 2015; Shariful Islam et al., 2019; Moore et al., 2011; Gallagher et al., 2014), four in North America (Allison et al., 2000; Wang et al., 2014; Rosal et al., 2005; Surkan et al., 2012), and four in Asia (Duan et al., 2018; Azami et al., 2018; Duan et al., 2017; Kim et al., 2011). Sixteen used usual care as the comparator (Allison et al., 2000; Siddiqui et al., 2019; Brotons et al., 2011; Pfaeffli Dale et al., 2015; Hofman-Bang, 1999; Jørstad et al., 2016; Lisspers et al., 1999; Shariful Islam et al., 2019; Azami et al., 2018; Davies et al., 2016; Wang et al., 2014; Rosal et al., 2005; Poston et al., 2013; Molyneaux et al., 2018; Bogaerts et al., 2013; Surkan et al., 2012; Mensorio et al., 2019), whilst seven used others comparators (four waiting-list (Duan et al., 2018; Moore et al., 2011; Gallagher et al., 2014; Kim et al., 2011), two non-intervention (Milani and Lavie, 2009; Duan et al., 2017), and one attention control (Ruusunen et al., 2012). Sixteen RCTs were conducted in healthcare settings (hospital, primary or community health centre, etc.) (Allison
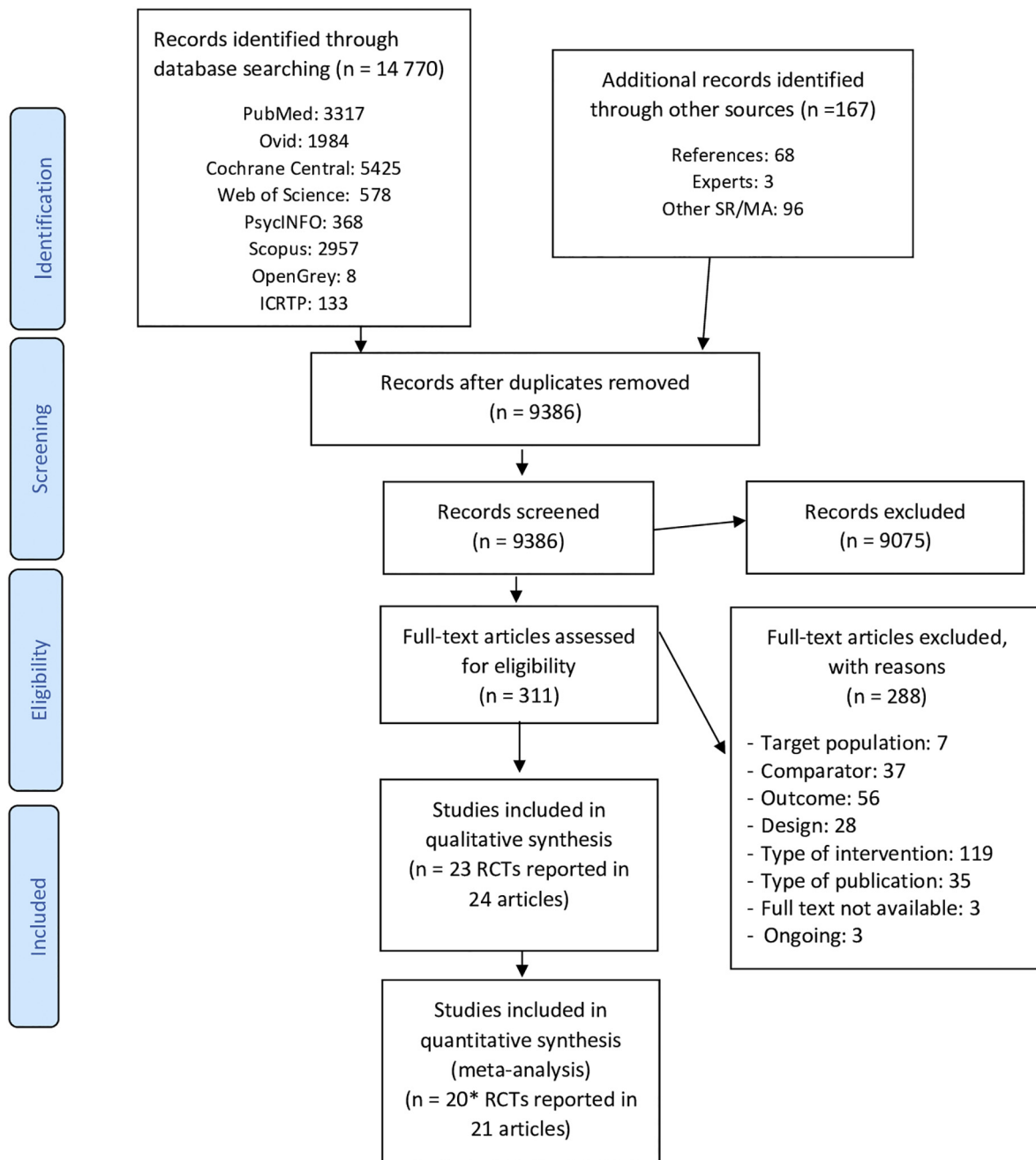
Fig. 1. PRISMA flowchart of the RCTs included.

et al., 2000; Siddiqui et al., 2019; Brotons et al., 2011; Hofman-Bang, 1999; Jørstad et al., 2016; Lisspers et al., 1999; Azami et al., 2018; Davies et al., 2016; Moore et al., 2011; Ruusunen et al., 2012; Wang et al., 2014; Rosal et al., 2005; Gallagher et al., 2014; Poston et al., 2013; Molyneaux et al., 2018; Bogaerts et al., 2013; Kim et al., 2011), five online (Pfaeffli Dale et al., 2015; Duan et al., 2018; Shariful Islam et al., 2019; Mensorio et al., 2019; Duan et al., 2017), one in the workplace (Milani and Lavie, 2009), and one in the home (Surkan et al., 2012). With respect to delivery, six were administered by nurses (Brotons et al., 2011; Hofman-Bang, 1999; Jørstad et al., 2016; Lisspers et al., 1999; Azami et al., 2018; Bogaerts et al., 2013; Kim et al., 2011), nine by other healthcare professionals (Davies et al., 2016; Moore et al., 2011; Ruusunen et al., 2012; Wang et al., 2014; Rosal et al., 2005; Gallagher et al., 2014; Poston et al., 2013; Molyneaux et al., 2018; Surkan et al., 2012), and five were online (Pfaeffli Dale et al., 2015; Duan et al., 2018; Shariful Islam et al., 2019; Mensorio et al., 2019;

Duan et al., 2017).

Treatment duration and follow-up periods ranged from 2 months to 36 months. The session format varied across studies. Six RCTs used individual and group sessions (Milani and Lavie, 2009; Hofman-Bang, 1999; Lisspers et al., 1999; Moore et al., 2011; Rosal et al., 2005; Gallagher et al., 2014; Bogaerts et al., 2013), and five used individual sessions (Allison et al., 2000; Brotons et al., 2011; Jørstad et al., 2016; Ruusunen et al., 2012; Surkan et al., 2012). Eighteen RCTs included face-to-face sessions (Allison et al., 2000; Milani and Lavie, 2009; Siddiqui et al., 2019; Brotons et al., 2011; Pfaeffli Dale et al., 2015; Hofman-Bang, 1999; Jørstad et al., 2016; Lisspers et al., 1999; Azami et al., 2018; Davies et al., 2016; Moore et al., 2011; Ruusunen et al., 2012; Wang et al., 2014; Rosal et al., 2005; Gallagher et al., 2014; Poston et al., 2013; Molyneaux et al., 2018; Bogaerts et al., 2013; Surkan et al., 2012) whereas five included non−face-to-face sessions (internet, SMS, book or/and telephone sessions) (Duan et al., 2018;

Table 1
Characteristics of the studies included in the systematic review.

First authors/year/country	Target population	Depressive patients at baseline n, (%)	Sample size (control/intervention)	Conditions	Target lifestyles	Intervention duration (weeks)	Framework	Session format	Deliverer	Setting	Depression symptomatology assessment
Allison et al. (2000) USA	Patients with UA	Don't provide data	326 (168/158)	1.Usual care 2.Nurse risk factor modification intervention	PA, HD, SC	24	Don't provide data	Face-to-face individual sessions	Nurses	Cardiovascular health clinic	SCL-90-R (baseline and 24 weeks)
Azami et al. (2018) Iran	Adults with T2DM	Don't provide data	142 (71/71)	1. Usual care 2. Usual diabetes care plus 24 weeks of the nurse-led DSME intervention	PA, HD	12	SET, MI	Book, telephone, video, and face to face group sessions	Nurses	Hospital	CES-D (baseline, 12 and 24 weeks)
Bogaerts et al. (2013) Belgium	Obese pregnant women	C: 9 (14.5) I: 16 (22.2)	197 (63/76)	1.Usual care 2.Lifestyle brochure plus lifestyle intervention[a]	PA, HD	36	TTM, MI	Face-to-face individual and group sessions	A midwife	Hospital	EPDS (baseline, before 15 weeks of gestation, between 18 and 22 weeks and between 30 and 34 weeks) ≥ 13
Brotons et al. (2010) Spain	Patients with IC, AMI, UA or ACS	C: 277 (46.5) I: 280 (45.2)	1224 (600/624)	1. Usual care 2. Secondary prevention intervention	PA, HD, SC	128	Don't provide data	Face-to-face individual sessions	Nurses	Primary care Centre	GADS (baseline and 132 weeks) Symptomatology
Pfaeffli Dale et al. (2015) New Zealand	Adults with CHD	Don't provide data	123 (62/61)	1. Usual care 2. mHealth program	PA, HD, SC	24	SCT, CSM	Internet and face-to-face individual sessions	Internet	Hospital and internet	HADS (baseline and 24 weeks)
Davies et al. (2016) UK	People at high-risk of prediabetes or T2DM	Don't provide data	880 (433/447)	1.Usual care 2.Let's prevent diabetes intervention	PA, HD	96	PE	Book and face-to-face group sessions	Trained educators	Primary care Centre	HADS (baseline, 24, 48, 96, and 144 weeks)
Duan et al. (2017) China	University students	Don't provide data	142 (54/88)	1.No intervention 2.Web-based intervention	PA, HD	8	HAPA	Internet sessions	Internet	Internet	CES-D (baseline, 8, and 12 weeks)
Duan et al. (2018) China	Cardiac patients	OS: 56(68%)	114 (54/60)	1.Wait-list 2.Web-based intervention	PA, HD	8	HAPA	Internet sessions	Internet	Internet	CES-D (baseline and 8 weeks)
Gallagher et al. (2014) Australia	Overweight/obese patients diagnosed with CHD and/or T2DM	C: 23 (28) I: 23 (35)	147 (65/83)	1.Wait-list 2.Lifestyle intervention	PA, HD	16	CBT P; PS	Face-to-face individual and group sessions	Exercise physiologist and a multidiscipli-nary group	Hospital and home	HADS (baseline and 8 weeks) ≥ 5
Islam et al. (2019) Australia	Patients with CHD	C: 62 (17.7) I: 44 (13.2)	683 (333/350)	1. Usual care 2. Tobacco, Exercise and dieT MEssages	PA, HD, SC	24	BCT	Mobile messages[b]	Internet	Internet	History of depression, PHQ-9 (baseline and 24 weeks)
Jørstad et al. (2016) The Netherlands	Patients with ACS	C: 14 (21) I: 15 (28)	120 (66/54)	1. Usual care 2. Nurse-coordinated prevention program	PA, HD, SC	24	Don't provide data	Face-to-face individual sessions	Nurses	Hospital	BDI (baseline and 48 weeks) ≥ 10
Kim et al. (2011) South Korea	Breast Cancer survivors	Don't provide data	45 (22/23)	1. Wait-list 2. Stage-matched exercise and diet (SSED) intervention	PA, HD	12	TTM	Book and telephone sessions	Nurses	National Cancer Centre	HADS (baseline and 12 weeks)
Lisspers et al. (1999); Hofman-Bang (1999) Sweden	Patients recently treated with PTCA	Don't provide data	87 (41/46)	1.Usual care 2.Multifactorial lifestyle behaviour change intervention	PA, HD, SC	48	Don't provide data	Face-to-face individual and group sessions	Nurses	Home and rehabilitation Centre	BDI (baseline, 48, and 96 weeks)
			106 (51/55)		PA, HD	12	CBT		Internet	Internet	

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Table 1 (*continued*)

First authors/year/country	Target population	Depressive patients at baseline n, (%)	Sample size (control/intervention)	Conditions	Target lifestyles	Intervention duration (weeks)	Framework	Session format	Deliverer	Setting	Depression symptomatology assessment
Mensorio et al. (2019) Spain	Obese and hypertensive patients	Don't provide data		1. Usual care 2. Internet-based intervention				Internet sessions			DASS-21 (baseline, 12, 24 and 48 weeks)
Milani and Lavie (2009) Australia	Employees and spouses	Don't provide data	339 (154/185)	1. No intervention 2. Comprehensive worksite intervention	PA, HD, SC	24	Don't provide data	Face-to-face individual and group sessions	Health educators, dieticians, nurses, exercise physiologists	Workplace	SQ (baseline and 24 weeks)
Molyneaux et al. (2018) UK	Obese pregnant women	C: (13.2) I: (13.5)	1526 (757/769)	1. Usual care 2. Lifestyle interventions for obese pregnant women	PA, HD	8	CT, SCT	Face-to-face group sessions	Health trainers	Hospital	EPDS (baseline and 12 weeks) ≥13
Moore et al. (2011) Australia	Participants with risk of T2DM	Don't provide data	274 (91/183)	1. Wait-list 2. Diabetes prevention intervention	PA, HD	24	TTM	Face-to-face individual and group sessions	Multiple facilitators	Hospital	DASS-21 (baseline and 24 weeks)
Poston et al., 2013 UK	Obese pregnant women	C: 25 (29) I: 28 (30)	181 (87/94)	1. Usual care 2. Lifestyle interventions for obese pregnant women	PA, HD	8	CT, SCT	Face-to-face group sessions	Health trainers	Hospital	EPDS (baseline and 12 weeks)
Rosal et al. (2005) USA	Latinos with T2DM	Don't provide data	25 (10/15)	1. Usual care 2. Diabetes self-management intervention	PA, HD	24	SCT	Face-to-face individual and group sessions	Nutritionist, nurse, intervention assistant	Community health centres	CES-D (baseline, 12, and 24 weeks)
Ruusunen et al. (2012) Finland	People with IGT	C: 16 (23) I: 14 (20)	140 (71/69)	1. Attention control 2. Lifestyle intervention group (Finnish Diabetes Prevention Study)	PA, HD	144	Don't provide data	Face-to-face individual sessions	A nutritionist	Multicentre	BDI (baseline and 144 weeks) ≥11
Siddiqui et al., 2019 Sweden	Immigrants at increased risk for T2D	C: 11 (26.2) I: 8 (20)	82 (42/40)	1. Usual care 2. Culturally adapted lifestyle intervention	PA, HD	16	DPP	Face-to-face group sessions	Nutritionists, diabetes nurses, physiothera-pists and health coaches	Primary care Centre	MADRS-S; HADS (baseline, 2 and 4 months)
Surkan et al. (2012) USA	Low-income, postpartum women	Don't provide data	403 (200/203)	1. Usual care 2. Usual WIC Care plus the 12-month JFY (Just for You) program.	PA, HD	48	SEM	Face-to-face individual session	Nutrition paraprofes-sionals, intervention staff	Home	CES-D (baseline and 60 weeks postpartum)
Wang et al. (2014) USA	Latinos with T2DM	OS: 168 (66.7)	252 (124/128)	1. Usual care 2. Diabetes self-management intervention	PA, HD	48	SCT	Face-to-face group sessions	Professional, trained lay workers	Community health centres	CES-D (baseline, 16, and 48 weeks)

Target Population: Unstable angina (UA), Coronary heart disease (CHD), Ischaemic cardiopathy (IC), acute myocardial infarction (AMI), acute coronary syndrome (ACS), type 2 diabetes mellitus (T2DM), percutaneous transluminal coronary angioplasty (PTCA), impaired glucose tolerance (IGT).

Depressive patients at baseline n, (%): Control group (C), Intervention group (I), Overall sample (OS).

Target lifestyle: Physical Activity (PA); Healthy Diet (HD); Smoking Cessation (SC).

Framework: Self-Efficacy Theory (SET); Social cognitive theory (SCT); Social Ecological Model (SEM); Transtheoretical Model (TTM); Cognitive behavioural principles (CBT); Behavioural Change Techniques (BCT); Problem-solving (PS); Control Theory (CT); Health Action Process Approach (HAPA); Patient empowerment (PE); Common-Sense Model (CSM); Motivational interviewing (MI); Diabetes Prevention Perspective (DPP).

Depression assessment: Symptom Checklist-90-Revised (SCL-90-R); The Center for Epidemiologic Studies Depression Scale (CES-D); Edinburgh Postnatal Depression Scale (EPDS); The Goldberg Anxiety and Depression Scale (GADS); Hospital Anxiety Depression Scale (HADS); Beck Depression Inventory (BDI); Depression Anxiety and Stress Scale (DASS-21); Kellner Symptoms Questionnaire (SQ); The Montgomery-Asberg Depression Rating Scale–Self (MADRS-S).

[a] This intervention contains three arms, but only those meeting inclusion criteria have been reported.

[b] Text messages sent weekly four times a week by web message programme.

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Shariful Islam et al., 2019; Mensorio et al., 2019; Duan et al., 2017; Kim et al., 2011). Seventeen RCTs were focused on healthy diet and physical activity (Siddiqui et al., 2019; Pfaeffli Dale et al., 2015; Duan et al., 2018; Azami et al., 2018; Davies et al., 2016; Moore et al., 2011; Ruusunen et al., 2012; Wang et al., 2014; Rosal et al., 2005; Gallagher et al., 2014; Poston et al., 2013; Molyneaux et al., 2018; Bogaerts et al., 2013; Surkan et al., 2012; Mensorio et al., 2019; Duan et al., 2017; Kim et al., 2011), and six were focused on healthy diet, physical activity, and smoking cessation (Allison et al., 2000; Milani and Lavie, 2009; Brotons et al., 2011; Pfaeffli Dale et al., 2015; Hofman-Bang, 1999; Jørstad et al., 2016; Lisspers et al., 1999). There were no interventions focused on smoking cessation and physical activity or smoking cessation and healthy diet. Regarding physical activity, eighteen RCTs recommended at least ≥ 30 min of moderate intensity physical activity at least 5 times a week (Allison et al., 2000; Milani and Lavie, 2009; Siddiqui et al., 2019; Brotons et al., 2011; Duan et al., 2018; Jørstad et al., 2016; Shariful Islam et al., 2019; Azami et al., 2018; Davies et al., 2016; Moore et al., 2011; Ruusunen et al., 2012; Poston et al., 2013; Molyneaux et al., 2018; Bogaerts et al., 2013; Surkan et al., 2012; Mensorio et al., 2019; Duan et al., 2017; Kim et al., 2011), two recommended 120–150 min of moderate-to-vigorous intensity physical activity per week (Pfaeffli Dale et al., 2015; Gallagher et al., 2014), two recommended 10,000 steps per day (Wang et al., 2014; Rosal et al., 2005) and one recommended 9 sessions of physical exercise per week (60,62). Concerning healthy diet, twelve recommended < 10% of daily energy intake from saturated fat (Siddiqui et al., 2019; Hofman-Bang, 1999; Lisspers et al., 1999; Davies et al., 2016; Moore et al., 2011; Ruusunen et al., 2012; Wang et al., 2014; Rosal et al., 2005; Gallagher et al., 2014; Poston et al., 2013; Molyneaux et al., 2018; Mensorio et al., 2019; Kim et al., 2011), whereas nine recommended at least 5 servings of fruit and vegetables per day (Allison et al., 2000; Pfaeffli Dale et al., 2015; Duan et al., 2018; Jørstad et al., 2016; Shariful Islam et al., 2019; Azami et al., 2018; Bogaerts et al., 2013; Surkan et al., 2012; Duan et al., 2017) and two recommended the Mediterranean diet (Milani and Lavie, 2009; Brotons et al., 2011). All of the RCTs promoting smoking cessation consisting of smoking cessation counselling (Allison et al., 2000; Brotons et al., 2011; Pfaeffli Dale et al., 2015; Hofman-Bang, 1999; Jørstad et al., 2016; Lisspers et al., 1999; Moore et al., 2011).

Finally, ten RCTs measured depression as the primary outcome (Milani and Lavie, 2009; Siddiqui et al., 2019; Jørstad et al., 2016; Azami et al., 2018; Ruusunen et al., 2012; Wang et al., 2014; Gallagher et al., 2014; Bogaerts et al., 2013; Surkan et al., 2012; Kim et al., 2011) and thirteen as the secondary outcome (Allison et al., 2000; Siddiqui et al., 2019; Brotons et al., 2011; Pfaeffli Dale et al., 2015; Duan et al., 2018; Hofman-Bang, 1999; Lisspers et al., 1999; Davies et al., 2016; Moore et al., 2011; Rosal et al., 2005; Poston et al., 2013; Molyneaux et al., 2018; Mensorio et al., 2019; Duan et al., 2017).

3.3. Risk of bias of the included studies

The risk of bias for each study is detailed in Table 2. From the qualitative criteria, five (Brotons et al., 2011; Shariful Islam et al., 2019; Moore et al., 2011; Ruusunen et al., 2012; Gallagher et al., 2014) and seven (Pfaeffli Dale et al., 2015; Duan et al., 2018; Azami et al., 2018; Davies et al., 2016; Bogaerts et al., 2013; Mensorio et al., 2019; Duan et al., 2017) RCTs had a high and low overall risk of bias, respectively. Of the 20 RCTs included in the MA, of 10 points, nine RCTs had ≤ 3 points (Pfaeffli Dale et al., 2015; Duan et al., 2018; Jørstad et al., 2016; Azami et al., 2018; Davies et al., 2016; Bogaerts et al., 2013; Mensorio et al., 2019; Duan et al., 2017; Kim et al., 2011), eight had a risk of 4–5 points (Brotons et al., 2011; Hofman-Bang, 1999; Lisspers et al., 1999; Shariful Islam et al., 2019; Wang et al., 2014; Rosal et al., 2005; Poston et al., 2013; Molyneaux et al., 2018; Surkan et al., 2012) and three had a risk of ≥ 6 points (Moore et al., 2011; Ruusunen et al., 2012; Gallagher et al., 2014).

3.4. Effectiveness of universal multiple-risk lifestyle interventions to reduce depressive symptoms

Meta-analysis calculations were based on 20 comparisons reported in 21 articles. The pooled SMD was −0.184 (95% CI, −0.311 to −0.057; $p = 0.005$). There was substantial heterogeneity across studies ($I^2 = 72\%$; 95% CI, 56% to 82%), and this was significant ($Q_{19} = 67.37$; $p < 0.001$). These results showed universal multiple-risk lifestyle interventions had a small but statistically significant effect in reducing depressive symptoms. Fig. 2 presents the forest plot.

3.5. Publication bias

The Egger (bias, 0.77; 95% CI, −1.33 to 2.88; $p = 0.452$) and Begg and Mazumdar (z = −0.84; $p = 0.417$) tests indicated no significant publication bias. The trim-and-fill procedure imputed two studies, and the SMD adjusted for publication bias was −0.215 (95% CI, −0.338 to −0.092; $p = 0.001$).

3.6. Sensitivity analyses

The pooled SMDs revealed little change between the first and last evaluation with the fixed-effects model, Hedges'g, and when only the RCTs with a high risk of bias were excluded (quantitative and qualitative criteria). When the RCT that most increased heterogeneity was excluded, heterogeneity decreased substantially ($I^2 = 36\%$) and the pooled SMD slightly (−0.14; 95% CI,-0.23 to −0.05). However, when we included only RCTs with a low risk of bias from both perspectives (quantitative and qualitative criteria), heterogeneity [$I^2 = 14.9\%$ (quantitative criteria); $I^2 = 0\%$ (qualitative criteria)] and the pooled SMD [−0.09; 95% CI, −0.210 to 0.029 (quantitative criteria); −0.073; 95% CI, −0.178 to 0.032 (qualitative criteria)] decreased substantially with no significant differences between groups. See Table 3.

3.7. Subgroup analyses

There was a tendency for greater effectiveness in interventions targeting three risk factors, in people over age 55, with studies conducted outside of Europe, with a moderate risk of bias from a quantitative perspective, with a high risk of bias from a qualitative perspective, delivered by nurses, and with < 20% of depressive patients at baseline. The effectiveness was not associated with the comparator or target population among others. See Table 4.

3.8. Meta-regression analyses

The final meta-regression model including three variables explained 61.39% of the heterogeneity. There was a tendency towards greater effectiveness when studies were conducted outside of Europe ($\beta = -0.235$ [95% CI, −0.416 to −0.009]; $p = 0.042$). No significant association was found between effectiveness and risk of bias from a quantitative perspective ($\beta = -0.149$ [95% CI, −0.360 to 0.060]; $p = 0.149$) and percentage of depressive patients at baseline ($\beta = -0.235$ [95% CI, −0.510 to 0.040]; $p = 0.089$).

3.9. Quality of evidence

Because we only included RCTs, the initial quality of the body of evidence was high. We reduced the rating from high to moderate because the heterogeneity was substantial, although 61.39% of this was explained by meta-regression analysis. There was no publication bias. Precision was adequate since we included a sufficient number of studies to calculate SMD, and the total number of participants was high. Indirectness was low since the target population, the interventions and our outcome did not differ from those of primary interest. We reduced the rating from moderate to low because there were few studies with a

Table 2
Risk of bias.

	Selection bias		Performance bias	Detection bias	Attrition bias	Score
	Random sequence generation (0–3)	Allocation concealment (0–3)	Blinding of participants and personnel (0–3)	Blinding of outcome assessment (0–3)	Incomplete outcome data (0–3)	Range (0 − 10)
Allison et al., 2000	Low (0)	Low (0)	High (2)	Low (0)	Low (0)	2
Azami et al., 2018	Low (0)	Low (0)	High (2)	Low (0)	Low (0)	2
Bogaerts et al., 2013	Low (0)	Low (0)	High (2)	Low (0)	Low (0)	2
Brotons et al., 2011	Low (0)	Low (0)	High (2)	High (2)	Low (0)	4
Pfaeffli Dale et al., 2015	Low (0)	Low (0)	High (2)	Low (0)	Low (0)	2
Davies et al., 2016	Low (0)	Low (0)	High (2)	Low (0)	Low (0)	2
Duan et al., 2017	Low (0)	Low (0)	High (2)	Low (0)	Low (0)	2
Duan et al., 2018	Low (0)	Low (0)	High (2)	Low (0)	Low (0)	2
Gallagher et al., 2014	Low (0)	High (2)	High (2)	Low (0)	High (2)	6
Lisspers et al., 1999; Hofman-Bang, 1999	Unclear (1)	Unclear (1)	High (2)	Low (0)	Unclear (1)	5
Islam et al. 2019	Low (0)	Low (0)	High (2)	High (2)	Low (0)	4
Jørstad et al., 2016	Low (0)	Low (0)	High (2)	Low (0)	Unclear (1)	3
Kim et al., 2011	Low (0)	Unclear (1)	High (2)	Low (0)	Low (0)	3
Mensorio et al., 2019	Low (0)	Low (0)	High (2)	Low (0)	Low (0)	2
Milani and Lavie, 2009	Unclear (1)	Unclear (1)	High (2)	Low (0)	Low (0)	4
Molyneaux et al., 2018	Low (0)	Unclear (1)	High (2)	Unclear (1)	Low (0)	4
Moore et al., 2011	Low (0)	Unclear (1)	High (2)	Unclear (1)	High (2)	6
Poston et al., 2013	Low (0)	Unclear (1)	High (2)	Unclear (1)	Low (0)	4
Rosal et al., 2005	Low (0)	Low (0)	High (2)	Unclear (1)	Unclear (1)	4
Ruusunen et al., 2012	Unclear (1)	Unclear (1)	High (2)	Low (0)	High (2)	6
Siddiqui et al., 2019	Low (0)	Unclear (1)	High (2)	Low (0)	High (2)	5
Surkan et al., 2012	Unclear (1)	Unclear (1)	High (2)	Low (0)	Low (0)	4
Wang et al., 2014	Low (0)	Unclear (1)	High (2)	Unclear (1)	Low (0)	4
Average risk	0.15[a]/0.17[b]	0.5[a]/0.52[b]	2.0[a]/2.0[b]	0.39[a]/0.39[b]	0.39[a]/0.48[b]	3.55[a]/3.56[b]

[a] With 20 RCTs included in meta-analysis.
[b] With 23 RCTs included in systematic review and meta-analysis.

low risk of bias, and when only these studies were included in the analyses, the effect size substantially decreased with no significant differences between groups. To conclude, the overall quality of evidence according to the GRADE system was low.

4. Discussion

To the best of our knowledge, this is the first SR/MA to assess the effectiveness of universal multiple-risk lifestyle interventions in reducing depressive symptoms through the promotion of physical activity, healthy diet and/or smoking cessation in the entire adult population. We included a total of 23 RCTs in the systematic review and 20 RCTs in the meta-analysis, including 7558 participants from 12 countries and four continents. Universal multiple-risk lifestyle interventions had a small and statistically significant effect (SMD -0.184 (95% CI, − 0.311 to − 0.057; $p = 0.005$)) on reducing depressive symptoms in varied adult populations by the acquisition of two (healthy diet and physical activity) or three (the previous two plus smoking cessation) healthy habits. We should note that universal interventions are never expected to produce large pooled effect sizes (Tan et al., 2014). There was substantial heterogeneity, of which about 60% was explained by a meta-regression model including three variables: continent, risk of bias, and percentage of depressive patients at baseline. There were few RCTs with a low risk of bias, and including only these in the meta-analysis, both the pooled SMD and heterogeneity considerably decreased with no statistically significant differences. According to GRADE, the overall quality of evidence was low.

The primary analysis of this SR/MA is consistent with that of the comparable review of the effectiveness of psychological and lifestyle interventions on depression in people with or at risk of type 2 diabetes mellitus (Cezaretto et al., 2016). This SR/MA has shown that overall lifestyle interventions reduce depression but the effects are small. In addition, our SR/MA differs from those conducted previously because we focused on lifestyle interventions with at least two components

(healthy diet, physical activity, and/or smoking cessation), and we excluded RCTs with psychological interventions. Future SR/MA should explore the effect of multi-risk lifestyle interventions in patients with clinical depression.

We only found statistically significant associations for continent when adjusted for risk of bias in meta-regression. Studies conducted outside of Europe presented greater effectiveness. Previous SR/MA have not reported results for continent in moderator analysis (Cezaretto et al., 2016; Coventry et al., 2013). Concerning the association between lifestyles and depression, current evidence based on SR/MA found that certain healthy dietary patterns characterized by high intakes of vegetables, fruits, fish, and whole grains decreased risk of depression (Lai et al., 2014; Li et al., 2017; Molendijk et al., 2018). However, some SR/MAs reported weak evidence showing that unhealthy dietary patterns increase risk of depression (Li et al., 2017; Molendijk et al., 2018), and a recent RCT did not find a multinutrient supplementation intervention (Bot et al., 2019) effective in reducing the incidence of depression Regarding dietary interventions, recent SR/MA showed symptoms of depression could be significantly reduced by dietary interventions (Firth et al., 2019a). With respect to smoking and depression, recent SR/MA have shown that smoking increases depression risk (Luger et al., 2014), and depression can be reduced after smoking cessation (Taylor et al., 2014; Stepankova et al., 2017). Furthermore, the evidence related to physical activity and/or exercise as a treatment for reducing depression symptoms is quite clear (Rosenbaum et al., 2014; Schuch et al., 2016). Exercise interventions are found to be effective in reducing depressive symptoms when implemented alone (Carter et al., 2016; Kvam et al., 2016; Pritchett et al., 2017; Balchin et al., 2016) or in combination with other pharmacological or psychological treatment (Kvam et al., 2016). Future trials should explore the combined effect of multiple-risk interventions in combination with other psychological interventions to prevent depression. In this line, novel interventional approaches are emerging regarding lifestyle and mental disorders such as mindfulness, yoga, breathing techniques and e-health lifestyle
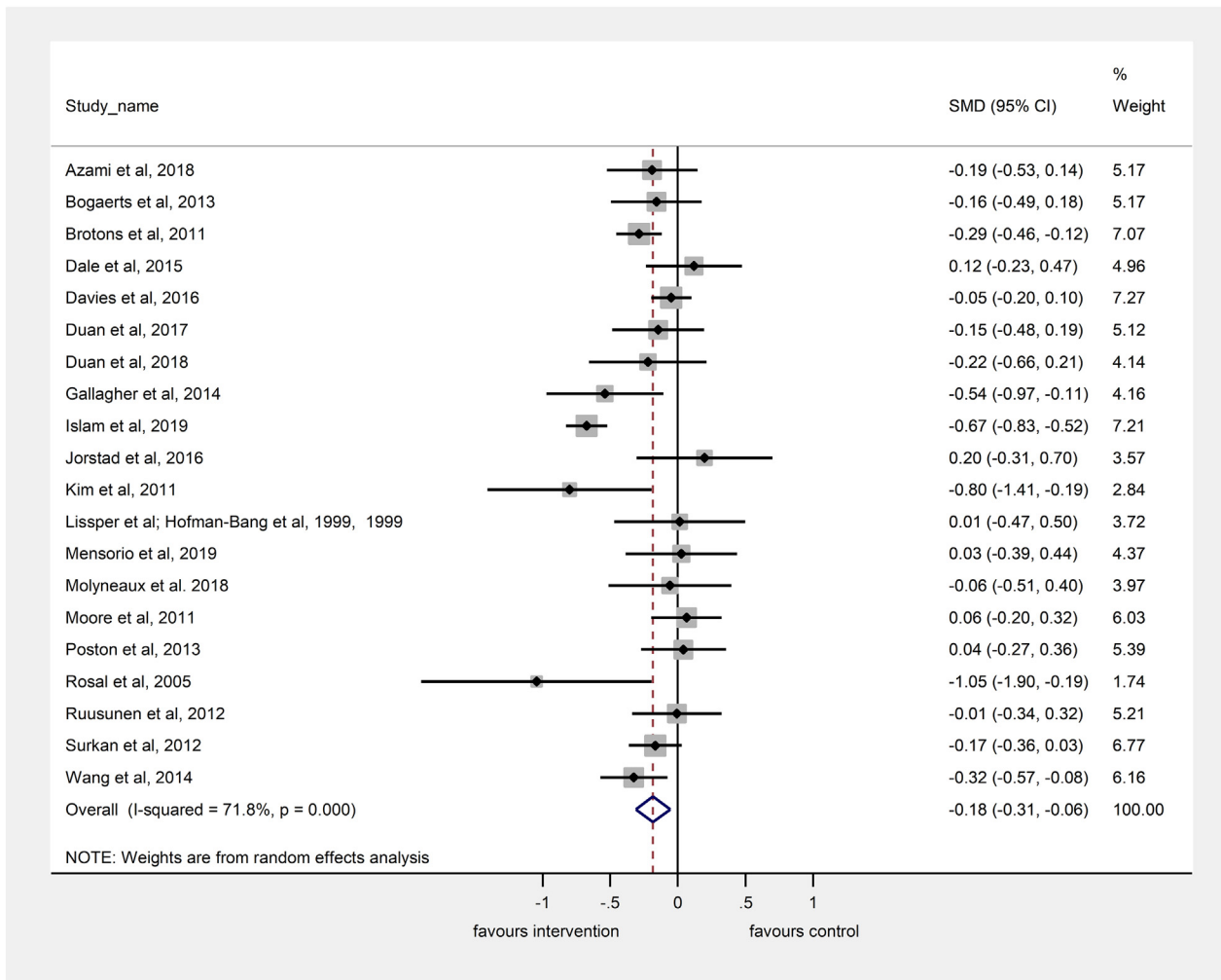
Fig. 2. Forest plot: Average standardized mean differences (SMD) for multiple-risk intervention versus control conditions for depression outcomes.

Table 3
Effectiveness of multiple-risk lifestyle interventions to reduce depressive symptoms.

Effectiveness	N	SMD	95% CI	P	I^2 (95% CI)
Primary analysis	20	−0.184	(−0.311 to −0.057)	0.005	72% (56%–82%)
Sensitivity analyses					
At first evaluation	20	−0.166	(−0.295 to −0.038)	0.011	73% (57%–82%)
At last evaluation	20	−0.167	(−0.299 to −0.035)	0.013	74% (59%–83%)
Fixed-effects model	20	−0.222	(−0.283 to −0.161)	0.000	72% (56%–82%)
Hedges'g	20	−0.183	(−0.309 to −0.056)	0.005	72% (56%–82%)
[a]RCT that most increased heterogeneity excluded	19	−0.138	(−0.230 to −0.047)	0.003	36% (0%–63%)
[b]RCTs excluded because of high risk of bias	15	−0.125	(−0.224 to −0.025)	0.014	25% (0%–60%)
[c]Including only RCTs with low risk of bias	7	−0.073	(−0.178 to 0.032)	0.173	0% (0%–71%)
[d]RCTs excluded because of high risk of bias	17	−0.195	(−0.333 to −0.056)	0.006	73% (56%–83%)
[e]Including only RCTs with low risk of bias	9	−0.091	(−0.210 to 0.029)	0.137	14.9% (0%–57%)

Abbreviations: RCTs, randomized controlled trials; SMD, standardized mean difference.

[a] The RCT that most increased heterogeneity: Shariful Islam et al., 2019.

[b] Qualitative criteria for exclusion (studies that scored high risk of bias for sequence generation, allocation concealment, blinding of evaluators of outcomes, or incomplete outcome data): Brotons et al., 2011; Gallagher et al., 2014; Shariful Islam et al., 2019; Moore et al., 2011; Ruusunen et al., 2012.

[c] Qualitative criteria for inclusion (RCTs that scored low risk of bias for sequence generation, allocation concealment, blinding of evaluators of outcomes, and incomplete outcome data): Azami et al., 2018; Bogaerts et al., 2013; Pfaeffli Dale et al., 2015; Davies et al., 2016;Duan et al., 2017; Duan et al., 2018; Mensorio et al., 2019.

[d] Quantitative criteria for exclusion (studies that scored ≥ 6 points, score range 0–10): Gallagher et al., 2014; Moore et al., 2011; Ruusunen et al., 2012.

[e] Quantitative criteria for inclusion (RCTs that scored ≤3 points, score range 0–10): Azami et al., 2018; Bogaerts et al., 2013; Pfaeffli Dale et al., 2015; Davies et al., 2016; Duan et al., 2017; Duan et al., 2018; Jørstad et al., 2016; Kim et al., 2011; Mensorio et al., 2019.

Table 4

Subgroup analysis of the effectiveness of multiple-risk lifestyle interventions to reduce depressive symptoms.

Subgroup analysis	N	SMD	95% CI	P	I^2	Between-group heterogeneity
Target lifestyles						
Physical activity and healthy diet	14	−0.150	−0.251 to −0.049	0.004	33%	Q = 16.02, df(Q) = 1, p < 0.001
Physical activity, healthy diet and smoking cessation	5	−0.173	−0.505 to 0.159	0.307	87%	
Comparator						
Usual care/no intervention	14	−0.171	−0.316 to −0.026	0.021	75%	Q = 1.89, df(Q) = 2, p = 0.389
Active control	1	−0.007	−0.339 to 0.324	0.965	0%	
Waiting list	4	−0.321	−0.701 to 0.059	0.098	70%	
Age						
Mean ≤ 55 years	9	−0.080	−0.203 to 0.043	0.204	0%	Q = 6.34, df(Q) = 1, p = 0.012
Mean age > 55 years	10	−0.260	−0.472 to −0.049	0.016	85%	
Length of intervention						
≤ 24 weeks	14	−0.186	−0.413 to 0.042	0.110	80%	Q = 3.99, df(Q) = 1, p = 0.046
> 48 weeks	6	−0.182	−0.288 to −0.076	0.001	32%	
Publication year						
Within the last 5 years	11	−0.188	−0.385 to 0.008	0.060	79%	Q = 2.77 df(Q) = 1, p = 0.096
Over 5 years ago	9	−0.156	−0.307 to −0.005	0.043	51%	
Continent						
Europe	9	−0.100	−0.188 to −0 0.011	0.027	5%	Q = 14.17, df(Q) = 1, p < 0.001
Others	11	−0.335	−0.419 to −0.250	< 0.001	78%	
Follow-up						
1 to 40 weeks	14	−0.206	−0.404 to −0.008	0.041	77%	Q = 3.99, df(Q) = 1, p = 0.046
> 40 weeks	6	−0.163	−0.274 to −0.052	0.004	32%	
Risk of bias (quantitative)						
Low	9	−0.091	−0.210 to 0.029	0.310	15%	Q = 19.11, df(Q) = 2, p < 0.001
Moderate	8	−0.280	−0.488 to −0.071	< 0.001	79%	
High	3	−0.124	−0.450 to 0.203	0.058	68%	
Risk of bias (qualitative)						
Low/moderate	15	−0.117	−0.196 to −0.039	0.140	25%	Q = 16.95, df(Q) = 1, p < 0.001
High	5	−0.380	−0.477 to −0.283	0.055	87%	
Risk of bias (qualitative)						
Low	7	−0.073	−0.178 to 0.032	0.833	0%	Q = 11.84, df(Q) = 1, p = 0.001
Moderate/high	13	−0.240	−0.416 to −0.063	< 0.001	77%	
Sample size						
≤ 200	11	−0.135	−0.277 to 0.007	0.090	37%	Q = 4.99, df(Q) = 2, p = 0.083
201–880	7	−0.235	−0.515 to 0.045	< 0.001	91%	
> 1000	2	−0.260	−0.417 to −0.102	0.352	0%	
Target population						
Universal[a]	1	−0.145	−0.485 to 0.194	0.401	0%	Q = 3.18, df(Q) = 2, p = 0.204
At risk[b]	7	−0.151	−0.412 to 0.110	0.255	85%	
Clinical[c]	12	−0.195	−0.336 to −0.053	0.007	85%	
Setting						
Online	5	−0.198	−0.566 to 0.169	0.290	85%	Q = 17.16, df(Q) = 3, p = 0.001
Home/hospital and home	3	−0.220	−0.475 to 0.035	0.090	38%	
Hospital	7	−0.078	−0.250 to 0.093	0.371	33%	
Primary/community health centre	5	−0.210	−0.395 to −0.025	0.026	63%	
Deliverer						
Online	5	−0.198	−0.566 to 0.169	0.290	85%	Q = 17.09, df(Q) = 2, p < 0.001
Nurse	6	−0.202	−0.384 to −0.020	0.029	36%	
Other health professionals	9	−0.135	−0.269 to −0.001	0.048	48%	
Session format						
Individual	10	−0.202	−0.402 to-0.002	0.047	79%	Q = 9.78, df(Q) = 1, p = 0.002
Group/individual and group	10	−0.141	−0.273 to −0.008	0.038	41%	
Outcome						
Primary	8	−0.217	−0.365 to −0.069	0.004	36%	Q = 0.07, df(Q) = 1, p = 0.795
Secondary	12	−0.156	−0.342 to 0.030	0.100	81%	
% Depressive patients at baseline						
Missing	10	−0.104	−0.232 to 0.025	0.102	38%	Q = 30.26, df(Q) = 2, p < 0.001
≤ 20	3	−0.331	−0.764 to 0.103	0.002	84%	
> 20	7	−0.188	−0.344 to −0.033	0.114	42%	

Abbreviation: SMD, standardized mean difference.

[a] Participants with no disease.

[b] Participants at risk of developing a disease.

[c] Participants with established disease.

interventions (Firth et al., 2019b).

The most frequent healthy habit combinations were healthy diet and physical activity. This result was found in one of the SR/MA aiming to test the effectiveness of multiple-risk lifestyle interventions (Meader et al., 2017). Furthermore, unhealthy diet and physical inactivity tend to cluster (Poortinga, 2007; Silva et al., 2013), and they present the highest prevalence rates of risk factor co-occurrence (Poortinga, 2007). It is of note that we found no interventions based on healthy diet or physical activity and smoking cessation. Future trials should explore the combined effects of healthy diet or physical activity and smoking cessation on depression.

4.1. Study limitations and strengths

Our study has some limitations. First and foremost were the low number of RCTs with a low risk of bias and the high heterogeneity.

From qualitative and quantitative criteria, seven and nine RCTs, respectively, were considered to have a low risk of bias. Subgroup analyses indicated that RCTs with a lower risk of bias had a tendency to report a smaller effect size. However, risk of bias was not significant in meta-regression analysis. The same limitations were found in other SR/MAs evaluating the effectiveness of physical activity interventions on postpartum depressive symptoms (Daley et al., 2015; Pritchett et al., 2017). Regarding heterogeneity, the RCT by Shariful Islam et al. (2019) could be considered an outlier because it decreased heterogeneity the most (I2 = 36%; 95% CI: 0% to 63%) when it was excluded. Comparing it with the included studies, it comprised a text messages intervention during 6 months, and depression was measured at baseline with clinical records. Second, the majority of RCTs reduced depression symptoms as a secondary outcome, which might explain why depressive patients were not excluded at baseline. In addition, many of the RCTs did not report information about the intake of anti-depressants and/or their role in the effect size. Third, this study included varied adult populations and interventions, so this might have contributed to the increased clinical heterogeneity. Nevertheless, we found no significant result according to target population (universal, at risk, clinical) in subgroup analysis. Fourth, more than half of the RCTs included target populations at risk of or with cardiac diseases or diabetes. This may be because a large portion of these diseases are closely associated with unhealthy habits: smoking, unhealthy diet, and physical inactivity (World Health Organization, 2014). Therefore, our conclusions apply exclusively to this population profile. Fifth, many of the studies did not report information about participants' intervention adherence at the end of the intervention. Consequently, this variable was not analysed in this SR/MA. Sixth due to the characteristics of lifestyle interventions, all the RCTs presented a high risk of bias regarding blinding of participants and personnel. Seventh, only six RCTs had > 40 weeks of follow-up. It is therefore difficult draw conclusions on long-term effectiveness. Eighth, no RCT excluded depressed patients at baseline. Thus, no conclusion can be drawn regarding primary prevention of depression. Caution is required when interpreting these results.

In spite of these limitations, our SR/MA explored a large number of reports from the most relevant databases in this area combined with extensive supplementary hand searching. Furthermore, the broad range of search terms used and no restrictions on study publication language, publication year, or settings contributed to achieving a highly sensitive search. This SR/MA included a large number of participants with different characteristics from diverse settings and countries. These aspects give the study a wide scope, which supports its external validity. Study selection, data extraction, and risk of bias assessment were performed by trained and independent reviewers, with good inter-observer reliability. We applied rigorous methodology (PRISMA and GRADE) to the SR/MA process and evaluation of the quality of evidence.

5. Conclusion

We found that universal multiple-risk lifestyle interventions had a small and statistically significant effect on the reduction of depressive symptoms in a varied adult population. However, due to the high heterogeneity and low quality of evidence, we conclude that at present there is insufficient evidence of the effectiveness of universal multiple-risk lifestyle interventions to reduce depressive symptoms. Further long-term RCTs evaluating universal multiple-risk lifestyle interventions to reduce depressive symptoms as the primary outcome, with a low risk of bias are needed. Given that unhealthy diet, physical inactivity, and smoking are associated with risk of depression (Lai et al., 2014; Li et al., 2017; Molendijk et al., 2018; Luger et al., 2014; Carter et al., 2016; Kvam et al., 2016; Martínez-González and Sánchez-Villegas, 2016), the profile of co-occurrence of lifestyle risk factors in the adult population (Galán et al., 2006; Mozaffarian et al., 2012; Poortinga, 2007; Silva et al., 2013) and the potential for multiple-risk lifestyle interventions to be low cost, provide greater health benefits,

and optimise the promotion of healthy habits, multiple-risk interventions might be considered.

Declaration of competing interest

The authors declare they have no conflicts of interest.

Appendix 1. Database searched: MEDLINE (PubMed)

((((((((((((((((((((Smoking[MeSH Terms]) OR "tobacco products"[MeSH Terms]) OR "smoking cessation"[MeSH Terms]) OR "tobacco use"[MeSH Terms]) OR tobacco[Title/Abstract]) OR "cigarette smoking"[Title/Abstract]) OR cigar*[Title/Abstract]) OR smok*[Title/Abstract])) AND ((((("healthy diet"[MeSH Terms]) OR "diet, mediterranean"[MeSH Terms]) OR "healthy eating"[Title/Abstract]) OR "healthy food"[Title/Abstract]) OR diet*[Title/Abstract]))) OR ((((((((((Smoking[MeSH Terms]) OR "tobacco products"[MeSH Terms]) OR "smoking cessation"[MeSH Terms]) OR "tobacco use"[MeSH Terms]) OR tobacco[Title/Abstract]) OR "cigarette smoking"[Title/Abstract]) OR cigar*[Title/Abstract]) OR smok*[Title/Abstract])) AND ((((((((((("physical activity"[Title/Abstract]) OR "physical activities"[Title/Abstract]) OR exercise*[Title/Abstract]) OR "motor activity"[Title/Abstract]) OR "sedentary lifestyle"[Title/Abstract]) OR sedentary[Title/Abstract]) OR "motor activity"[MeSH Terms]) OR "sedentary lifestyle"[MeSH Terms]) OR fitness[Title/Abstract]) OR sport[Title/Abstract]) OR "leisure activities"[Title/Abstract]))) OR (((((("healthy diet"[MeSH Terms]) OR "diet, mediterranean"[MeSH Terms]) OR "healthy eating"[Title/Abstract]) OR "healthy food"[Title/Abstract]) OR diet*[Title/Abstract])) AND ((((((((((("physical activity"[Title/Abstract]) OR "physical activities"[Title/Abstract]) OR exercise*[Title/Abstract]) OR "motor activity"[Title/Abstract]) OR "sedentary lifestyle"[Title/Abstract]) OR sedentary[Title/Abstract]) OR "motor activity"[MeSH Terms]) OR "sedentary lifestyle"[MeSH Terms]) OR fitness[Title/Abstract]) OR sport[Title/Abstract]) OR "leisure activities"[Title/Abstract]))) OR (((((((((((Smoking[MeSH Terms]) OR "tobacco products"[MeSH Terms]) OR "smoking cessation"[MeSH Terms]) OR "tobacco use"[MeSH Terms]) OR tobacco[Title/Abstract]) OR "cigarette smoking"[Title/Abstract]) OR cigar*[Title/Abstract]) OR smok*[Title/Abstract])) AND ((((("healthy diet"[MeSH Terms]) OR "diet, mediterranean"[MeSH Terms]) OR "healthy eating"[Title/Abstract]) OR "healthy food"[Title/Abstract]) OR diet*[Title/Abstract])) AND ((((((((((("physical activity"[Title/Abstract]) OR "physical activities"[Title/Abstract]) OR exercise*[Title/Abstract]) OR "motor activity"[Title/Abstract]) OR "sedentary lifestyle"[Title/Abstract]) OR sedentary[Title/Abstract]) OR "motor activity"[MeSH Terms]) OR "sedentary lifestyle"[MeSH Terms]) OR fitness[Title/

Abstract]) OR sport[Title/Abstract]) OR "leisure activities"[Title/Abstract])))) OR (((((("life style"[MeSH Terms]) OR "life style"[Title/Abstract]) OR lifestyle[Title/Abstract]) OR lifestyles[Title/Abstract]) OR "life styles"[Title/Abstract])) OR "behaviour change"[Title/Abstract])) AND ((((((depress*[Title/Abstract]) OR "depressive disorder"[Title/Abstract]) OR Psycho*[Title/Abstract]) OR Mood disorder*[Title/Abstract]) OR depression[MeSH Terms]) OR "depressive disorder"[MeSH Terms])) AND ((((((Randomized controlled trial [Publication Type]) OR random*[Title/Abstract]) OR controlled[Title/Abstract]) OR trial[Title/Abstract]) OR clinical trial[Title/Abstract]) OR controlled clinical trial[Publication Type]))

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