Lifestyle Medicine for Depression: A Meta-Analysis of Randomized Controlled Trials

Abstract

Background: Lifestyle medicine (LM), which involves the therapeutic use of lifestyle interventions, is gaining increasing attention for managing diseases with a lifestyle-based etiology such as depression.

Aims: To determine the effects of LM interventions on depressive and anxiety symptoms and health-related quality of life (HRQoL).

Method: A systematic search was conducted by two independent researchers in six electronic databases from the earliest available records up to February 2020. Study methodological quality was evaluated using the revised Cochrane risk-of-bias tool for randomized trials (RoB 2). Potential moderators and publication bias were examined.

Results: A total of 50 randomized controlled trials (RCTs) (8,186 participants; 64.5 Female; mean age 47.9 years) were included in the meta-analysis of LM interventions relative to care-as-usual (CAU), waitlist/no intervention (WL/NI), and attention control (AC). Random-effects models showed significant reduction in alleviating depressive (d = 0.20) and anxiety (d = 0.27) symptoms as compared with CAU, as well as reducing depressive symptoms (d = 0.22) and improving HRQoL (d = 0.29) relative to WL/NI comparisons. Moreover, the moderator analyses suggested that the "number of lifestyle factors employed" was a significant moderator for the effects of LM interventions on depressive symptoms. However, no significant difference was found in depressive symptoms when LM interventions were compared with attention control (AC). No publication bias was detected.

Conclusion: LM interventions appeared to be effective in mitigating depressive symptoms. The potential moderators of LM were explored. Further studies are warranted to confirm the effects of LM on clinical depression.

Keywords: Lifestyle, depression, meta-analysis, randomized controlled trial.

Introduction

Depression is a debilitating mental health condition that is primarily characterized by persistent depressed mood and loss of interest or pleasure in usual activities (APA, 2013). Despite effective treatments for depression are present, the prevalence of depression has been increasing rapidly in recent decades (WHO Mental Health Atlas, 2017). Previous reviews suggested that the rise was likely posed by changes in lifestyle related to modernity in the past few decades (Sarris et al., 2014). Apart from biochemical, genetic, and psychological factors, there is compelling evidence indicated a cascade of unhealthy lifestyle behaviors, such as physical inactivity, sleep impairment, and pro-inflammatory nutrients rich diet, were related to the increased risk of depression (Kraus et al., 2019; Park et al., 2019; Sarris et al., 2014). Most importantly, previous evidence demonstrated that the pathogenesis and progression of depression depend on the multiplicative interactions between different determinants related to depression (Ripoll, 2012). For example, a prospective cohort study with 15,000 Spanish university graduates investigated the relationship between ultra-processed food consumption and the risk of depression for a median of 10.3 years. The findings suggested that ultra-processed food consumption is positively correlated with the risk of depression. In particular, larger effects were observed for those who were physically inactive (Gómez-Donoso et al., 2019). It is therefore imperative to adopt the multifaceted approach by considering all the modifiable underlying risk factors to prevent, manage, and treat depression.

One approach that has been gaining increasing popularity for managing diseases with a lifestyle etiology is LM (Egger et al., 2009). According to the American College of Lifestyle Medicine (2019), LM is the adoption of nutrition, physical activity, sleep and stress management as a therapeutic modality for the treatment and reversal of disease with a lifestyle etiology. LM is a comprehensive, multifaceted approach that considers several levels of causality of a given disease and focuses on both prevention and therapeutic management (Ripoll, 2012). A recently published meta-analytic review has evaluated the effect of universal multiple-risk LM interventions in improving depressive symptoms (Gómez-Gómez et al., 2020). The review pooled 20 RCTs which employed nutrition, physical activity, and/or smoking cessation as LM interventions. The findings revealed that LM interventions had a small preventive effect on depressive symptoms in non-clinically depressed adults relative to CAU/WL/NI/AC comparisons. However, because of high heterogeneity and generally low study quality, the authors concluded

that there was insufficient evidence to conclude the effect of universal multiple-risk LM interventions in reducing depressive symptoms. Moreover, their review has intentionally excluded the clinically depressed population to study the preventive effect of LM intervention on depressive symptoms. Given LM interventions could potentially be applied as a practice for managing clinical depression, the examination of LM interventions for clinical depression is thus warranted. Besides, the limited inclusion of lifestyle factors (i.e., nutrition, physical activity, and smoking cessation) in their review may restrict the effect size observed; therefore, other strong determinants of depression should be considered in LM interventions.

Taken together, there is a need to examine the effects of LM interventions, which consider a range of strong lifestyle factors that are involved in the pathogenesis and progression of depression in reducing depressive symptoms. This meta-analytic review aimed to determine the effect of LM interventions in reducing depressive symptoms relative to a CAU, WL/NI, and AC comparison. The effects of LM interventions in reducing anxiety symptoms and improving HRQoL as secondary outcomes were also examined. Potential moderators for the effect of LM intervention on depressive symptoms were explored.

Method

Protocol registration

This meta-analytic review followed the PRISMA guidelines for reporting (Liberati et al., 2009). The study protocol has been registered in the International Prospective Register of Systematic Reviews (PROSPERO; registration no.: CRD42019131729), which is an open-access online database of systematic review protocols on health-related topics.

Identification and selection of studies

We included studies that (1) were RCTs; (2) employed LM as the intervention; (3) measured depressive symptoms as either a primary or secondary outcome; and (4) compared with care as usual (CAU), waiting list (WL), no intervention (NI), and attention control (AC) as the control group. An intervention is defined as LM if it consisted of at least two of the following lifestyle elements, including physical activity, nutrition, sleep management, and/or stress management (e.g., relaxation physical activity, mindfulness, yoga). Non-English studies were excluded.

The first author (W.H.W.) systematically searched PubMed, PsycINFO, Embase, Cochrane Central Register of Controlled Trials, Medline, and CINAHL from inception to February 2020 for the terms [depression OR depressive symptom* OR depressive disorder OR major depressive disorder OR depress*] AND [lifestyle intervention OR risk reduction behavio* OR healthy lifestyle OR sedentary lifestyle OR life style OR lifestyle medicine OR lifestyle modification OR lifestyle therapeutic approach OR lifestyle education program OR interdisciplinary lifestyle intervention] AND [randomized clinical trial OR clinical trial OR controlled trial]. References obtained from the 6 electronic databases were imported into the EndNote software, X9. Duplications were discarded. Potentially relevant studies were extracted on the basis of title and abstract by two independent reviewers (W.H.W. and N.K.S.), thereafter full-text articles of potentially relevant studies were reviewed to determine the relevance. Disagreements of study selection were resolved through a discussion with a senior researcher (F.Y.H.) until a consensus was reached.

One author (WHW) recorded the following information of each study, included the first author, year of publication, country, type of participant, recruitment method, mean age, gender

distribution, study design, sample size, lifestyle factors employed, treatment duration, follow-up assessment (if any), outcome measures for depressive and anxiety symptoms and health-related quality of life (HRQoL) and major findings. Another reviewer (N.K.S.) was responsible for assuring information transposed by W.H.W. was accurate. The revised Cochrane risk-of-bias tool for randomized trials (RoB 2) was used to assess the methodological quality of RCTs included (Sterne et al., 2019).

Quality assessment

The RoB 2 evaluates RCTs in five domains, including bias arising from the randomization process; bias due to deviations from the intended interventions; bias due to missing outcome data; bias in measurement of the outcome; and bias in selection of the reported result. For cluster RCTs, an additional domain (i.e., bias arising from identification or recruitment of individual participants within clusters) is required. The possible judgment of each domain can be rated as '-' (high risk of bias, '?' (some concern), or '+' (low risk of bias). A total score ranging from 0 to 5 was calculated for each individually randomized trial to represent the total risk of bias. For cluster RCTs, the total score varied from 0 to 6. The methodological quality assessment was conducted by W.H.W. and N.K.S. independently. Inter-rater reliability calculated by Kappa statistic on the methodological quality assessment was substantial (Cohen's Kappa = 0.82). Disagreements of study selection were resolved through a discussion with F.Y.H. until a consensus was reached.

Statistical analysis

The Comprehensive Meta-Analysis Version 3 software (Biostat Inc.) was used to examine the overall effect size if there were two or more studies assessing the outcome concerned (Higgins et al., 2019). Continuous outcomes were presented as standardized mean differences (SMDs) with 95% confidence intervals (CIs). The Cohen's *d* was used to calculate between-group effect sizes, with magnitudes of 0.2, 0.5, and 0.8 considering as small, moderate and large, respectively (Hedges et al., 1985).

Since considerable heterogeneity is expected, the random-effects model was employed to estimate the overall effect size (Hedges & Vevea, 1998). Heterogeneity was measured by the I^2 statistic, which was derived from the percentage of the total variability of effect sizes due to between-studies variability. Moderator analysis using subgroup analyses was conducted to explore potential moderators when the I^2 was larger than 50%, indicating a moderate amount of

heterogeneity was detected (Higgins et al., 2003). Based on the existing literature, five potential moderators were explored including the "number of lifestyle factors adopted", "disease condition", "employment of cognitive behavioral elements", "mode of delivery", and "risk of bias". Independent sample *t*-test was used to examine if there was any significant between-group difference in the mean study attrition rate. The possibility of publication bias was examined by visual inspection of a funnel plot and Egger's regression test (Egger et al., 1997) if there were ten studies or more in the meta-analytic comparison. A two-tailed *p*-value of less than 0.05 in the Egger's regression test indicated publication bias. In case of missing data, data requests were sought from the study author(s) for a maximum of four consecutive weekly emails. A study was considered 'unable to retrieve' if no response was received from the authors.

Results

Study selection

A flowchart detailing the study selection process is summarized in Figure 2. A total of 5,495 records were identified through the database search. After removed 2,101 duplicates, 3,394 records were assessed based on title and abstract. Subsequently, 3,054 records that did not fulfill the eligibility criteria were excluded. Full-text articles of potentially relevant studies were then reviewed, of which 265 records were further excluded for various reasons (Figure 2). Among the 75 records that fulfilled all the eligibility criteria, 41 records did not provide sufficient data in the published paper. Therefore, a total of 41 study requests were made for a maximum of four consecutive weeks. In sum, 16 authors provided the study data after requests were made, and a total of 50 RCTs were included in the meta-analysis.

Study characteristics

Characteristics of the included RCTs are summarized in Table 1. The included RCTs were published from the year between 2005 to 2019. The RCTs were originated from the United States (k = 14), Australia (k = 7), China (k = 5), South Korea (k = 3), the Netherlands (k = 3), the United Kingdom (k = 3), Brazil (k = 2), Germany (k = 2), Greece (k = 2), Iran (k = 2), Spain (k = 2), Denmark (k = 1), New Zealand (k = 1), Norway (k = 1), and Singapore (k = 1). Most of the RCTs employed a two-arm trial design, except that three RCTs used three-arm, four-arm, and five-arm trial designs, respectively. Among the 50 RCTs included, there were 33 LM vs. CAU comparisons, 15 LM vs. WL/NI comparisons, and the remaining two studies were LM vs. AC comparisons.

The included RCTs targeted at a variety of populations, which included healthy individuals (k = 8), individuals with cardiac problems (k = 8), individuals with mental health problems (major depressive disorder, k = 2; depressive symptoms, k = 1; psychosis, k = 1; posttraumatic stress disorder, k = 1; schizophrenia, k = 1), individuals with diabetic problems (k = 5), individuals with cancer (k = 4), individuals with overweight and obesity (k = 4), individuals with lung problems (k = 2), and a study each targeted at individuals with increased risk of cognitive decline, Hashimoto's thyroiditis, dwelling elderly, pre-frail and frail elderly, physical disability, and metabolic syndrome. In addition, there were seven studies with multiple populations, which included first-ever stroke or transient ischemic attack, overweight/type I obesity and hypertension, overweight or obese with type 2 diabetes and depressive symptoms, coronary artery disease with depressive and anxiety

symptoms, acute coronary syndrome and depressive symptoms, type 2 diabetes with overweight or obesity paired with a family partner with overweight or obesity, and overweight or obesity with bipolar disorder.

The sample size at baseline was unable to be determined in two studies because of insufficient information in the published papers. In total, 8,186 participants were included (range: 19 to 779), of which 4,392 were randomly assigned to the LM groups and 3,866 were assigned to the control groups. Of the participants in the control groups, 428 were randomized to AC, 680 to NI/WL, and 2,758 to CAU groups. The mean age of the participants was 47.9 years (range: 10.3 to 79.4), with 64.5% of the samples were female. The majority of studies included both genders except nine included female participants only, and one included male participants only. The eligibility criteria of included RCTs are summarized in Table 2.

Of the 50 RCTs included, four RCTs used two measures to assess depressive symptoms, while the remaining used single measure only. For RCTs with two depressive symptoms measurements, only data of the primary measurement was included in the meta-analysis. The self-reported questionnaires that were used to assess depressive symptoms included the Hospital Anxiety and Depression Scale (HADS; $k = 10$), the Center for Epidemiologic Studies Depression Scale (CES-D; $k = 8$), the Depression Anxiety Stress Scale (DASS; $k = 5$), the Geriatric Depression Scale (GDS; $k = 4$), the Beck Depression Inventory- II (BDI-II; $k = 3$), the Beck Depression Inventory (BDI; $k = 3$), the Beck Youth Inventory (Second Edition; BYI-II; $k = 2$), the Patient Health Questionnaire-9 (PHQ-9; $k = 6$), the Cardiac Depression Scale (CDS; $k = 3$), the Edinburgh Postnatal Depression Scale (EPDS; $k = 2$), the Nurses Observation Scale for Geriatric Patients (NOSGER; $k = 1$), the Patient Health Questionnaire-8 (PHQ-8; $k = 1$), the State-Trait Personality Inventory (STPI; $k = 1$), the Brief Symptoms Inventory (BSI-18; $k = 1$), the Children's Depression Inventory (CDI; $k = 1$), the Short Children's Depression Inventory (SCDI; $k = 1$), the Montgomery-Åsberg Depression Rating Scale (MADRS; $k = 1$), and the Clinical Global Impressions-Bipolar Scale (CGI-BP; $k = 1$).

The level of anxiety symptoms was reported in 15 RCTs with available data. The self-reported questionnaires that were used to measure anxiety symptoms included HADS ($k = 8$), DASS ($k = 3$), BYI-II ($k = 1$), BSI-18 ($k = 1$), the STPI ($k = 1$), and the Generalized Anxiety Disorder-7 (GAD-7; $k = 1$). The HRQoL was measured in 16 RCTs with available data.

The instruments used to assess HRQoL included the Short-Form Health Survey (SF-36; $k = 3$), the Medical Outcome Study Short Form-12 (SF-12; $k = 2$), the European Organization for the Research and Treatment of Cancer Quality-of-Life Questionnaire– Core 30 (EORTC QLQ-C30; $k = 2$), the World Health Organization Quality of Life Scale (WHOQOL-BREF; $k = 2$), the Qualidem; $k = 1$), the Juniper's valid and reliable 16-item mini-asthma QOL survey ($k = 1$), the Spanish Version Quality of Life Index ($k = 1$), MacNew Heart Disease Health-related Quality of Life Questionnaire (MacNew; $k = 1$), Short Form (SF-8^{TM}) Health Survey ($k = 1$), EuroQol quality of life questionnaire ($k = 1$), and the Longitudinal Interval Follow-Up Evaluation-Range of Impaired Functioning Tool (LIFE-RIFT; $k = 1$).

Intervention characteristics

Details of treatment content are summarized in Table 3. There were 25 included RCTs combined two lifestyle factors as LM interventions (nutrition and physical activity, $k = 23$; physical activity and stress management, $k = 1$; nutrition and stress management, $k = 1$), 21 RCTs combined three lifestyle factors as LM interventions (nutrition, physical activity, and stress management, $k = 19$; nutrition, physical activity, and sleep, $k = 2$), and four RCTs combined nutrition, physical activity, stress management, and sleep as LM interventions. The majority of LM interventions were delivered face-to-face ($k = 25$), while the remaining were delivered online ($k = 5$), by telephone contact ($k = 5$), face-to-face and telephone contact ($k = 11$), by text message with internet support ($k = 1$), online and telephone contact ($k = 1$), and face-to-face, telephone contact, and online ($k = 1$). Most RCTs were delivered by health specialists, except that seven were self-help, six were delivered by trained personnel, and four studies did not report relevant information. Treatment duration varied from 4 weeks to 26 weeks ($M = 16$ weeks). All included RCTs conducted an immediate posttreatment assessment, while there were 21 RCTs conducted follow-up assessments with a range from one month to two years. Sixteen out of 50 RCTs adopted cognitive behavioral elements, and four RCTs used antidepressants during the intervention.

Attrition rate

The study attrition rate was defined as the number of participants withdrawn from the RCTs throughout the intervention period, posttreatment and posttreatment follow-up assessments. Of the 50 RCTs included, 47 RCTs provided sufficient information to determine the study attrition rate.

The mean study attrition rate was 20.6% (*SD* = 18.03%) in the intervention group and 20.1% (*SD* = 15.95%) in the control group.

Methodological quality

The methodological quality of the included RCTs assessed by RoB 2 is summarized in Table 4. Of the 50 RCTs included, four RCTs adopted a cluster design. The majority of RCTs (*k* = 30) had a low risk of bias arising from the randomization process because random components (e.g., computer-generated random numbers and reference to a random number table) were employed, and the process of randomization was conducted by an independent unit or organization. For the domain of "bias due to deviations from the intended interventions", participants and individuals delivering the interventions among the RCTs included were in general aware of the group assignment during the trial. As a result, the risk of bias of this domain was high among the RCTs included. For the risk of bias due to missing outcome data, it was rated as low risk in 41 RCTs because data were available for nearly all participants, and bias was corrected using statistical methods. Twenty-seven RCTs were rated with some concern on the bias of outcome measurements because outcome assessors were not blinded to the interventions received by participants, and thus the results might be influenced by knowledge of intervention received. For the risk of bias in the selection of the reported results, 44 RCTs were rated as low risk of bias because data were analyzed according to a pre-specified plan, and the results reported in the published papers were unlikely to have been selected. In sum, the average score of risk of bias of the included RCTs was 3.54, indicating the methodological quality was at an acceptable level.

Meta-analysis

Depressive symptoms. The pooled meta-analysis employing a random-effects model yielded a significant difference in favor of LM intervention compared with CAU (standardized mean difference = -0.20, 95% CI: -0.29, -0.10, $p < .001$, $I^2 = 61\%$, *d = 0.20, k* = 33; Figure 3) and WL/NI (standardized mean difference = -0.22, 95% CI: -0.36, -0.08, $p < .01$, $I^2 = 36\%$, $d = 0.22$; $k = 15$; Figure 4) in reducing depressive symptoms at immediate posttreatment assessment. However, the preliminary results pooled by two RCTs revealed no statistically significant reduction in depressive symptoms for LM vs. AC comparison at immediate posttreatment assessment (standardized mean difference = 0.11, 95% CI: -0.04, 0.26, $p > .05$, $I^2 = 0\%$, $d = 0.11$, $k = 2$; Figure 5).

Anxiety symptoms. The pooled meta-analysis employing a random-effects model yielded a significant difference in favor of LM intervention compared with CAU in reducing anxiety symptoms at immediate posttreatment assessment (standardized mean difference = -0.27, 95% CI: -0.41, -0.14, $p < .001$, $d = 0.27$, $k = 9$; Figure 6). However, no statistically significant reduction in anxiety symptoms was found for LM intervention vs. WL/NI in reducing anxiety symptoms at immediate posttreatment assessment (standardized mean difference = -0.24, 95% CI: -0.57, 0.09, $p > .05$, d = 0.24, $k = 5$; Figure 7). Only one study that compared with an AC group had measured the level of anxiety symptoms, thus no meta-analytic comparison was conducted.

HRQoL. The pooled meta-analysis employing a random-effects model obtained a non-significant result for LM vs. CAU in improving HRQoL at immediate posttreatment assessment (standardized mean difference = 0.11, 95% CI: -0.07, 0.29, $p > .05$, $d = 0.11$, $k = 10$; Figure 8). However, a significant improvement was found in the comparison of LM vs. WL/NI at immediate posttreatment assessment (standardized mean difference = 0.29, 95% CI: 0.04, 0.55, $p < .05$, $d = 0.29$, $k = 6$; Figure 9)

Moderator analyses

Given there was a moderate amount of inter-study homogeneity when LM was compared with CAU in reducing depressive symptoms at immediate posttreatment assessment, moderator analyses were conducted to investigate the dispersion further. Overall, the moderator analysis conducted using subgroup analysis indicated that the intervention effect varied as a function of the number of lifestyle factors employed. Other proposed moderators, including disease conditions, adoption of cognitive behavioral components, mode of delivery, and risk of bias, were not a significant moderator for the effect of LM intervention on depressive symptoms relative to a CAU comparison. Statistical summary of the moderator analysis conducted using subgroup analysis are shown in Table 5.

Publication bias

Publication bias was determined by funnel plot inspection and Egger's test (Egger et al., 1997). The funnel plot of LM vs CAU and LM vs WL/NI were close to symmetrical, suggesting publication bias was not obvious (Figure 10 and 11). Moreover, the Egger's test revealed a non-significant result for both LM vs CAU ($p = 0.21$) and LM vs WL/NI ($p = 0.94$), indicating

publication bias was unlikely. No funnel plot analysis was performed for LM vs AC because less than ten RCTs were available.

Discussion

Our meta-analysis determine the effect of LM interventions (nutrition, physical activity, stress and/or sleep management) on depression. Also, the effects of LM interventions on anxiety symptoms and HRQoL were evaluated for the first time in the literature. In sum, we included 50 RCTs that fulfilled the eligibility criteria. Most of the RCTs employed nutrition and physical activity as intervention components, with face to face being the most common mode of delivery. The majority of participants were non-depressed adults suffering from one kind of physical problem.

The overall analysis found that LM interventions had a favorable effect on depressive symptoms when compared with CAU and WL/NI as the control groups at immediate posttreatment assessment. However, the preliminary results pooled by two RCTs suggested that LM vs. AC on depressive symptoms was not significant. The current findings were consistent with the results of the sole systematic review and meta-analysis that investigated the effectiveness of universal multiple-risk LM interventions (physical activity, healthy diet, and/or smoking cessation) in reducing depressive symptoms relative to a CAU/WL/NI/AC control group (Gómez-Gómez et al., 2020). Although the types of lifestyle factors and the comparators included in this study were different from their review, the effect sizes obtained in the overall analysis of LM vs. CAU (d = 0.20) and LM vs. WL/NI (d = 0.22) in our study were similar to their review (d = 0.18).

Furthermore, the effect of LM on anxiety symptoms in contrast with CAU was significant. Such finding was commensurate with the systematic review conducted by Sarris et al. (2012) that lifestyle modifications (moderate activity level, mindfulness meditation, healthy diet) may be beneficial to the management of anxiety symptoms. Future studies may verify this finding by conducting meta-analysis with a primary interest in anxiety symptoms. Besides, our results also found significant improvement in HRQoL at immediate posttreatment assessment. However, to date, there has been no similar meta-analysis or review study that has investigated the effect of LM intervention on HRQoL. As such, we were unable to compare our results with the current literature.

As a moderate amount of heterogeneity was observed in the comparison of LM interventions and CAU in reducing depressive symptoms, we thus conducted a moderator analysis by using the subgroup analyses to identify potential moderators. The results revealed that the

number of lifestyle factors employed significantly moderated the effect of LM interventions on depressive symptoms. Specifically, LM interventions employing three lifestyle factors tended to have a larger effect size. It should be noted that the findings of LM interventions with four lifestyle factors on depressive symptoms were indeed restricted by the limited number of RCTs available (k = 3). As such, the findings only provided preliminary evidence that LM interventions with two and three lifestyle factors outperformed LM interventions with four lifestyle factors in reducing depressive symptoms. Nevertheless, this finding was also consistent with the review conducted by Gómez-Gómez et al. (2020). Their results suggested that the effect size of LM interventions with three lifestyle factors (d = 0.17) was slightly larger than LM with two lifestyle factors (d = 0.15) in reducing depressive symptoms. Notably, our results demonstrated slightly larger effect sizes for LM interventions with three lifestyle factors (d = 0.27) and two lifestyle factors (d = 0.17) in contrast to their review. One possible explanation for the larger intervention effect might be the addition of sleep and stress management as lifestyle components in the current study, such that more comprehensive coverage of the risk factors closely related to depression was included. Another possible explanation might be because we had included more than double the amount of RCTs and a larger sample size. As a result, the statistical power to detect the true difference between-group has increased.

Another moderator analysis was conducted to examine if the disease condition moderated the effect of LM interventions on depressive symptoms. Our results have provided encouraging preliminary evidence that LM interventions may be effective for individuals with depressive symptoms and major depressive disorder. Remarkably, there was a tendency for larger effect size in individuals with more severe depression condition, suggesting LM may be an effective approach for the clinical management of depression (Sarris et al., 2014). Moreover, our findings have provided favorable results for LM intervention on depressive symptoms. Future studies may explore the application of LM interventions as an entry-level step in preventing depression in community settings. The LM approach for depression may be particularly acceptable in places with considerable mental health stigma, in particular, the oriental culture (Tai, 2012). LM provides a perfect modality to overcome the barrier of perceived stigma present in conventional treatments by empowering an individual to modify universal basic lifestyle behaviors. As suggested by previous studies, the acceptability of LM was high and was sometimes preferred for their lack of perceived stigma, low cost, and fewer side effects and complications when compared with

psychotherapy and pharmacotherapy (Amminger, Schäfer, Schlögelhofer, Klier, & McGorry, 2015; Donovan & Anwar-McHenry, 2016).

We have also conducted a moderator analysis to examine if the employment of cognitive behavioral elements moderated the effect of LM interventions for depression. Existing RCTs only designed LM interventions based on the cognitive behavioral framework or included very limited cognitive behavioral components in the intervention. As such, the effect of integrating cognitive behavioral components into LM for depressive symptoms may not be prominent enough to reach a statistically significant difference in our moderator analysis. Because LM aims to act as a complementary treatment with conventional treatments, future studies are needed to investigate the applicability and effectiveness of LM intervention as an adjunction to the current first-line treatments for depression.

Our findings also revealed that the mode of delivery was not a moderator for the comparison of LM intervention and CAU. It is worth noting that, despite the rapid development of mobile technology, no RCT has taken the advantages of smartphones in delivering LM interventions. A previous review found that the utilization of smartphones to deliver mental health interventions may overcome the barriers towards traditional mental health services, such as high cost, low utilization rate, and mental health stigma (Radovic et al., 2016; Weisel et al., 2019). In terms of efficacy, a systematic review and meta-analysis of 18 RCTs found that smartphone-delivered self-management interventions (e.g., CBT, mindfulness, cognitive training) are efficacious and promising in managing depressive symptoms as compared with active (g = 0.56) and inactive control groups (g = 0.22) (Firth et al., 2017). Given that LM requires individuals to actively participate in and comply with effective lifestyle modifications (Egger et al., 2009), future interventions may adopt push notification and text-message functions in smartphones to remind and encourage depressed individuals who are typically not motivated to engage in lifestyle modifications.

Our results also suggested that the risk of bias was not a significant moderator of the effect of LM interventions on depressive symptoms. Nevertheless, more RCTs with high methodological quality are warranted to determine the effectiveness of LM for depression. Considering that the domain of 'bias due to deviations from intended interventions' was in general rated as high risk among the RCTs included, blinding of participants and research personnel to intervention

assignment in future research is desirable. This will minimize the performance and ascertainment bias, thereby a more conclusive result can be achieved (Altman and Schulz, 2001).

While heterogeneous findings were reported from individual RCTs, this meta-analysis provided a deeper understanding of the effect of LM interventions for depression by considering lifestyle factors that are related to the psychopathology of depression. The findings reinforced the existing literature that the clinical implications of LM for depression could be potent, suggesting that major clinical guidelines and mental health professionals may put greater emphasis on the potential value of LM in preventing, managing, and treating depressive symptoms (Sarris et al., 2014; Walsh, 2011; Young et al., 2018). In addition, this review was a pioneering attempt to elucidate the preliminary effectiveness of LM interventions on anxiety symptoms and HRQoL. Future review studies may conduct a systematic search with the primary interest in anxiety symptoms and HRQoL to further clarify the effectiveness. The significant moderating effect of the number of lifestyle factors employed also provided important insights into developing future LM interventions for depressive symptoms.

Several limitations should be considered when interpreting the current findings. First, although a relatively large amount of studies was included in the meta-analysis (k = 50), the number of studies comparing LM vs. CAU in some subgroup analysis were limited. The relatively low number of RCTs available in the subgroups may not have sufficient statistical power to detect meaningful effects, thereby hindering the investigation of potential moderators. Second, since we have only included LM interventions compared with CAU, WL/NI, and AC, the impact of LM interventions relative to an active comparison group remains unclear in the current literature.

In conclusion, this meta-analysis provided preliminary evidence for the effectiveness of LM interventions in reducing depressive symptoms. The potential moderators of LM were explored. We have also found initial evidence for the effect of LM interventions on anxiety symptoms and HRQoL.

Figure 1. Selection flow of studies for inclusion in the meta-analysis.

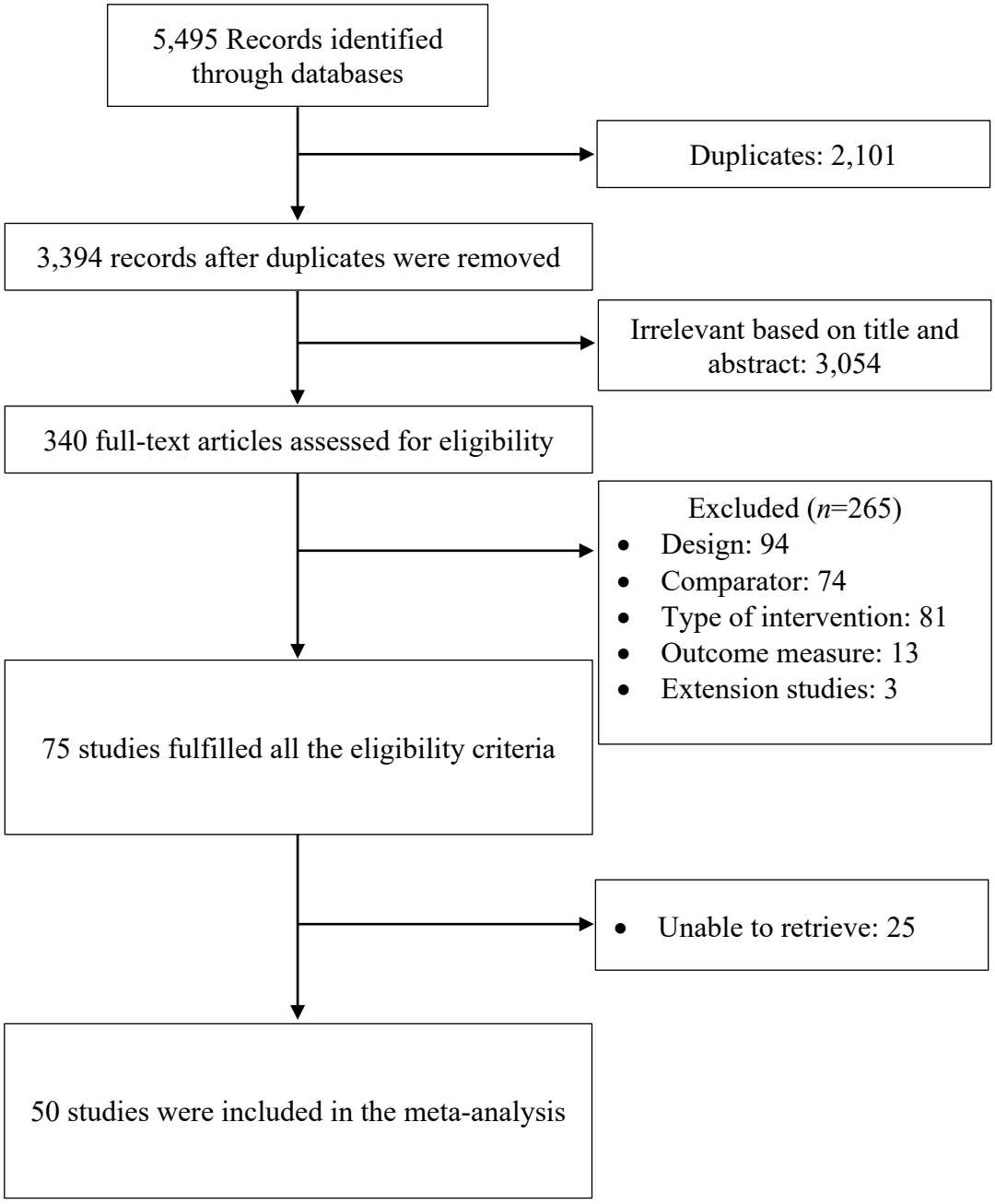


Figure 2. Forest plot comparing LM interventions vs. CAU on depressive symptoms at immediate posttreatment assessment (k = 33).

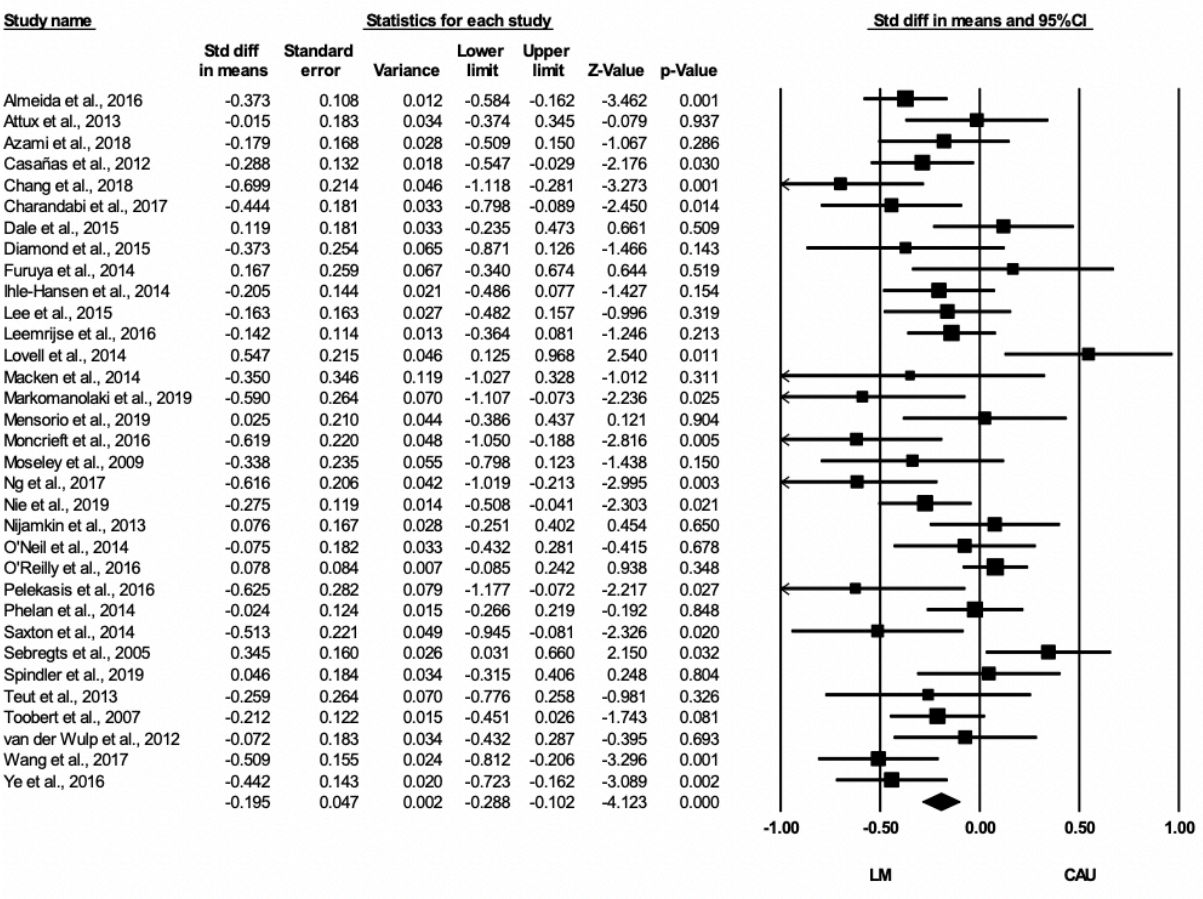
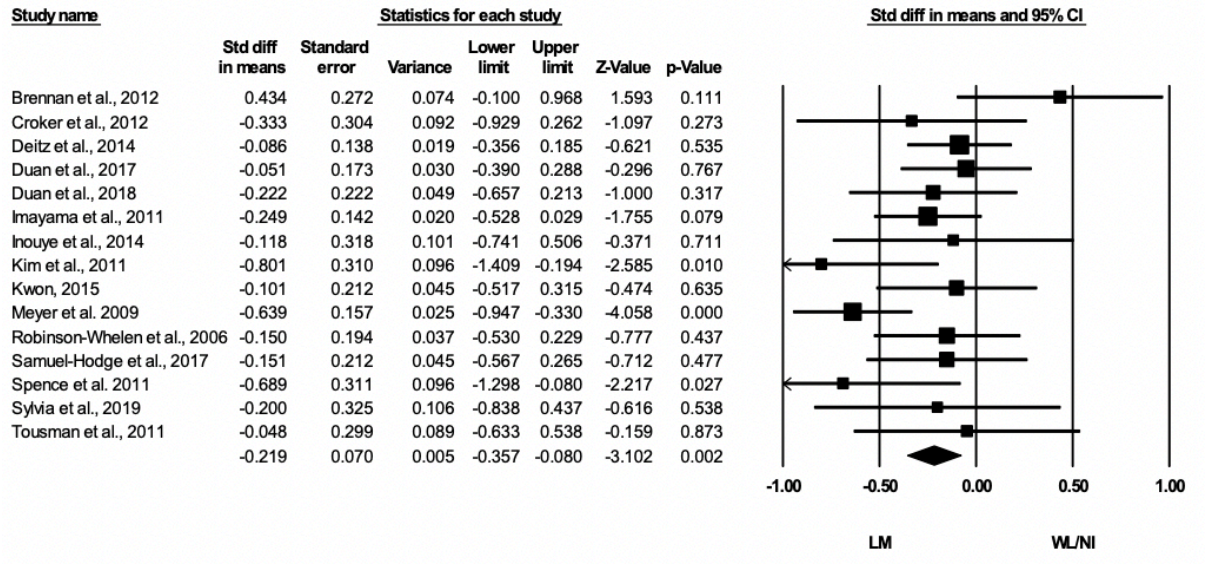


Figure 3. Forest plot comparing LM interventions vs. WL/NI on depressive symptoms at immediate posttreatment assessment (k = 15).



Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Brennan et al., 2012	0.434	0.272	0.074	-0.100	0.968	1.593	0.111
Croker et al., 2012	-0.333	0.304	0.092	-0.929	0.262	-1.097	0.273
Deitz et al., 2014	-0.086	0.138	0.019	-0.356	0.185	-0.621	0.535
Duan et al., 2017	-0.051	0.173	0.030	-0.390	0.288	-0.296	0.767
Duan et al., 2018	-0.222	0.222	0.049	-0.657	0.213	-1.000	0.317
Imayama et al., 2011	-0.249	0.142	0.020	-0.528	0.029	-1.755	0.079
Inouye et al., 2014	-0.118	0.318	0.101	-0.741	0.506	-0.371	0.711
Kim et al., 2011	-0.801	0.310	0.096	-1.409	-0.194	-2.585	0.010
Kwon, 2015	-0.101	0.212	0.045	-0.517	0.315	-0.474	0.635
Meyer et al. 2009	-0.639	0.157	0.025	-0.947	-0.330	-4.058	0.000
Robinson-Whelen et al., 2006	-0.150	0.194	0.037	-0.530	0.229	-0.777	0.437
Samuel-Hodge et al., 2017	-0.151	0.212	0.045	-0.567	0.265	-0.712	0.477
Spence et al. 2011	-0.689	0.311	0.096	-1.298	-0.080	-2.217	0.027
Sylvia et al., 2019	-0.200	0.325	0.106	-0.838	0.437	-0.616	0.538
Tousman et al., 2011	-0.048	0.299	0.089	-0.633	0.538	-0.159	0.873
	-0.219	0.070	0.005	-0.357	-0.080	-3.102	0.002

Figure 4. Forest plot comparing LM interventions vs. AC on depressive symptoms at immediate posttreatment assessment ($k = 2$).

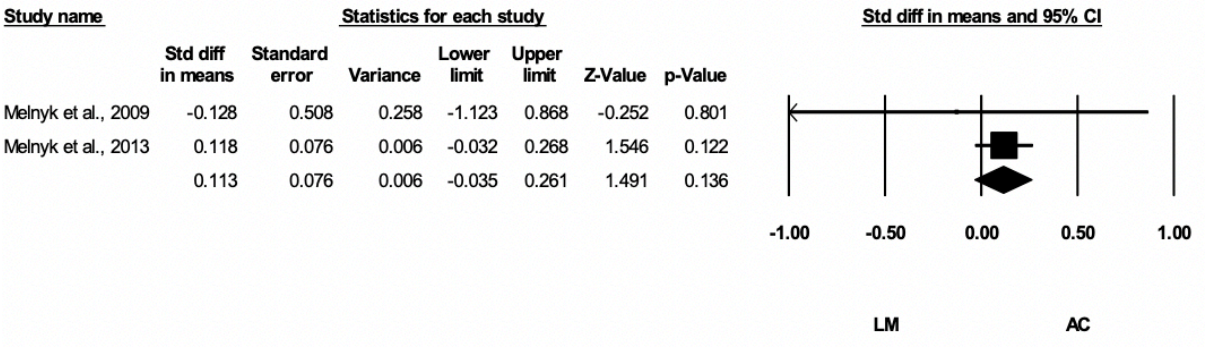


Figure 5. Forest plot comparing LM interventions vs. CAU on anxiety symptoms at immediate posttreatment assessment ($k = 9$).

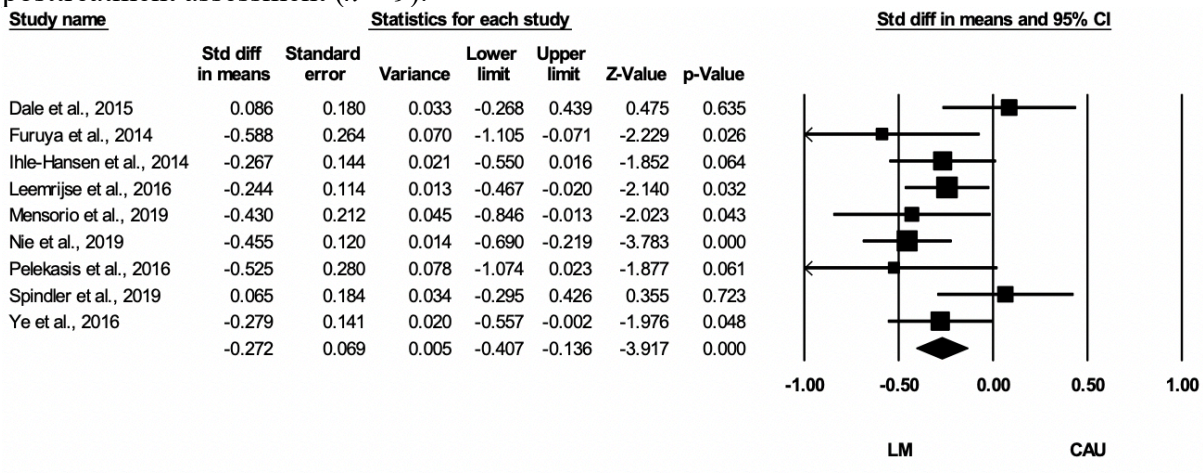


Figure 6. Forest plot comparing LM interventions vs. WL/NI on anxiety symptoms at immediate posttreatment assessment ($k = 5$).

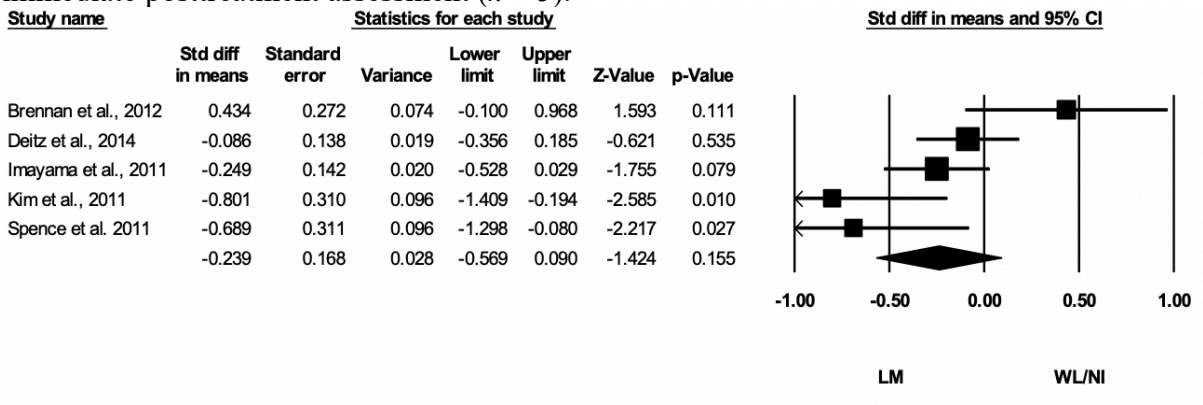


Figure 7. Forest plot comparing LM interventions vs. CAU on HRQoL at immediate posttreatment assessment (k = 10).

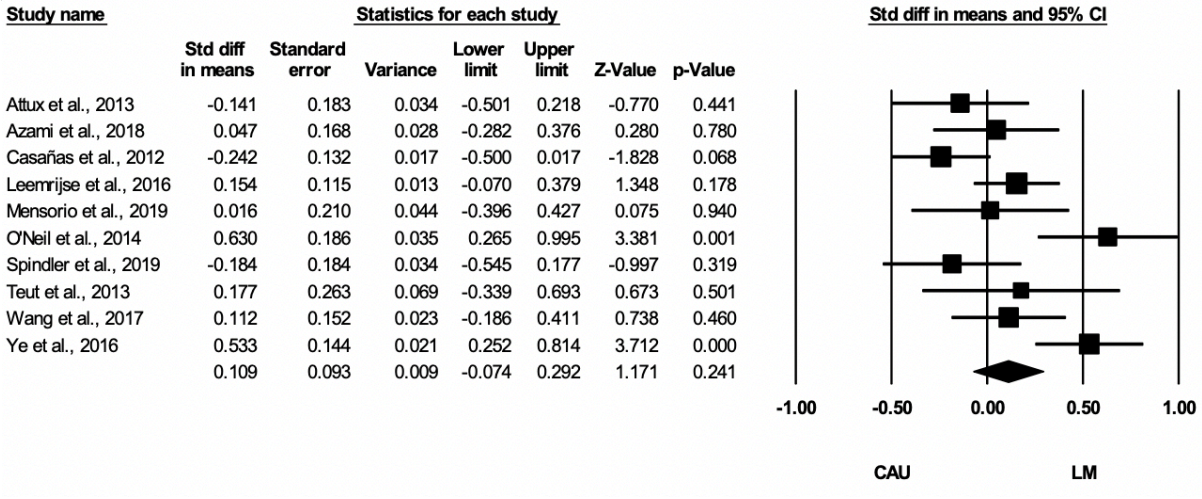


Figure 8. Forest plot comparing LM interventions vs. WL/NI on HRQoL at immediate posttreatment assessment ($k = 6$).

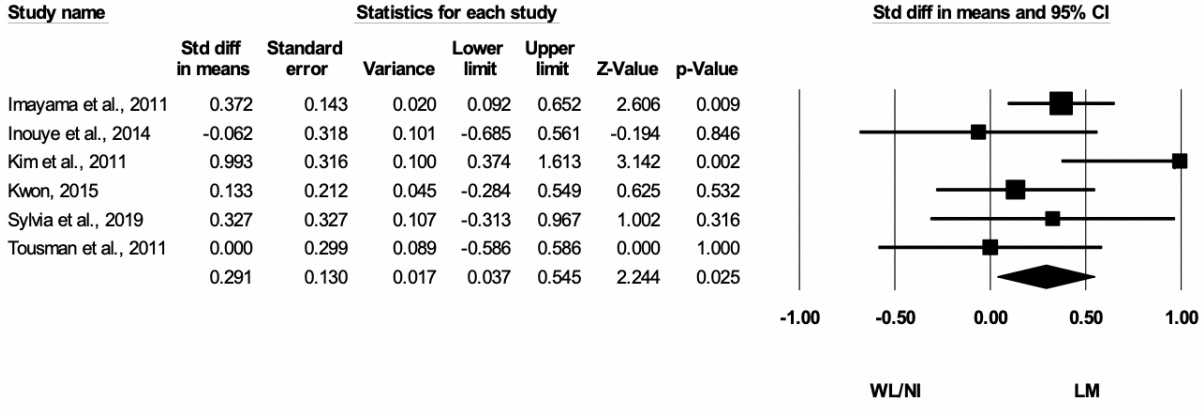


Figure 9. Funnel plot of LM intervention vs. CAU on depressive symptoms at immediate posttreatment assessment (k = 33).

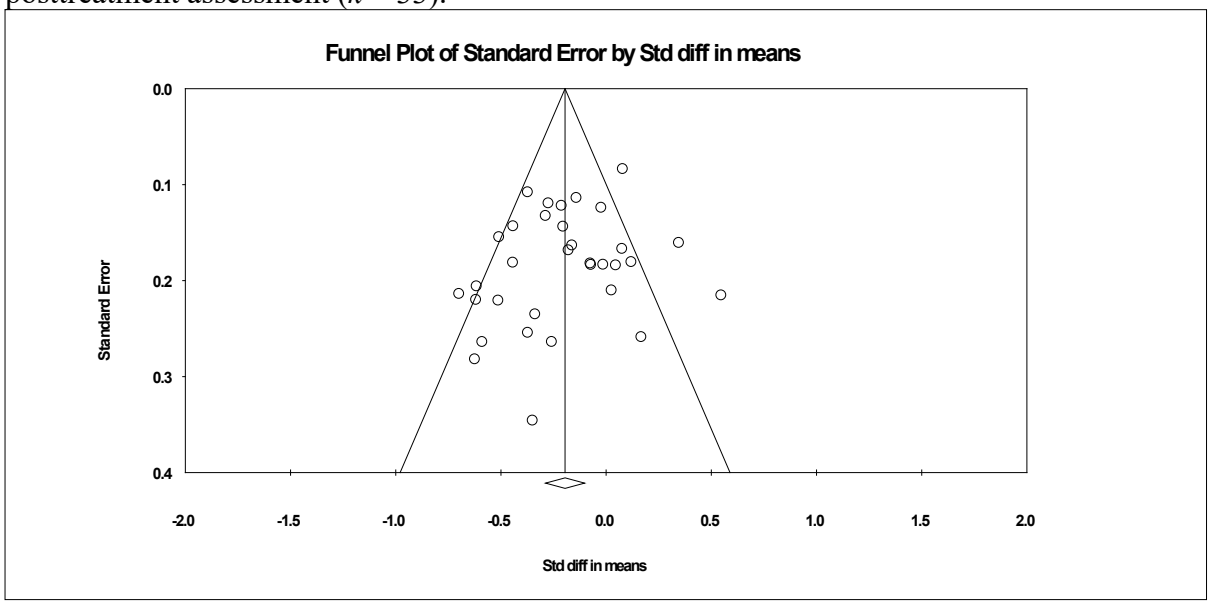


Figure 10. Funnel plot of LM intervention vs. WL/NI on depressive symptoms at immediate posttreatment assessment (k = 15).

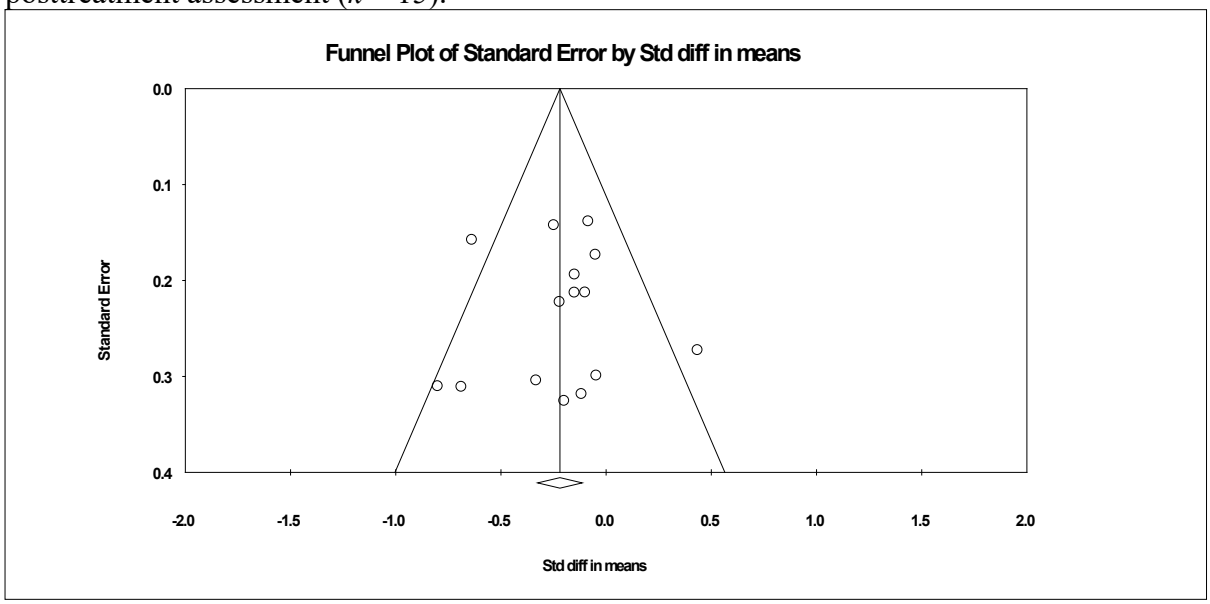


Table 1. Characteristics of randomized controlled trials of LM on depressive symptoms.

No.	Reference, year, country	Population, mean age, y (range), % female	Design	Lifestyle factors included	Treatment Duration (mo)	Follow-up assessment (mo)	Sample size (subgroup)	Depression assessment	Result reported
1	Almeida et al., 2016, Australia	Menopausal transition woman, 50.7 (NR), 100%	2-parallel arms (LM, CAU)	Nutrition, physical activity	6.5	6.5	351 (180, 171)	PHQ-9, HADS	NR
2	Attux et al., 2013, Brazil	Schizophrenia, 37.2 (NR), 40%	2-parallel arms (LM, CAU)	Nutrition, physical activity, stress management	3	6	160 (81, 79)	CDS	NR
3	Azami et al., 2018, Iran	Type 2 Diabetes, 56 (22-69), 65.5%	2-parallel arms (LM, CAU)	Nutrition, physical activity	3	6	142 (71, 71)	CES-D	No significant difference between LM and CAU in CES-D.
4	Brennan et al., 2012, Australia	Overweight or obese, 14.3 (11.5-18.9), 54%	2-parallel arms (LM, WL)	Nutrition, physical activity	6	3, 6	63 (42, 21)	DASS-21	No significant difference between LM and WL in DASS-21.
5	Casañas et al., 2012, Spain	Major depression, 53.4 (NR), 89.2%	2-parallel arms (LM, CAU)	Nutrition, physical activity, stress management, sleep management	3	3, 6	231 (119, 112)	BDI	LM significantly > CAU in BDI.
6	Chang et al., 2018, South Korea	Major depression, 77.8 (NR), 87.1%	2-parallel arms (LM, CAU)	Nutrition, physical activity, stress management	3	NA	93 (47, 46)	GDS	LM significantly > CAU in GDS.
7	Charandabi et al., 2017, Iran	Spouses of pregnant women with gestational ages of 24 to 28 weeks, 31.9 (NR), 0%	2-parallel arms (LM, CAU)	Nutrition, physical activity, sleep	2	1.5 month after childbirth	126 (63, 63)	EPDS	LM significantly > CAU in EPDS.
8	Croker et al., 2012, United Kingdom	Overweight or obese, 10.3 (8-12), 69.4%	2-parallel arms (LM, WL)	Nutrition, physical activity	6	6	72 (37, 35)	CDI	NR
9	Dale et al., 2015, New Zealand	Coronary heart disease, 59.5 (NR), 18.7%	2-parallel arms (LM, CAU)	Nutrition, physical activity (social cognitive theory)	6	NA	123 (61, 62)	HADS	No significant difference between LM and CAU in HADS.
10	Deitz et al., 2014, United States	At risk for cardiovascular disease, NR (21-72), 86%	2-parallel arms (LM, WL)	Nutrition, physical activity, stress management	1.5	NA	NR (NR, NR)	STPI (trait depression)	LM significantly > WL in STPI.
11	Diamond et al., 2015, Australia	At risk of cognitive decline, NR (NR), NR	2-parallel arms (LM, CAU)	Nutrition, physical activity	1.75	NA	90 (45, 45)	GDS	NR
12	Duan et al., 2017, China	Healthy university students, 19.2 (15-24), 54.3%	2-parallel arms (LM, NI)	Nutrition, physical activity	2	1	493 (270, 223)	CES-D	No significant difference between LM and NI in CES-D.

No.	Reference, year, country	Population, mean age, y (range), % female	Design	Lifestyle factors included	Treatment Duration (mo)	Follow-up assessment (mo)	Sample size (subgroup)	Depression assessment	Result reported
13	Duan et al., 2018, China	Coronary heart disease, 48.5 (20-75), 54%	2-parallel arms (LM, WL)	Nutrition, physical activity	2	NA	114 (60, 54)	CES-D	No significant difference between LM and WL in CES-D.
14	Furuya et al., 2014, Brazil	Preparing for the first percutaneous coronary intervention, NR (NR), NR	2-parallel arms (LM, CAU)	Nutrition, physical activity, stress management	6	NA	90 (45, 45)	HADS	No significant difference between LM and CAU in HADS.
15	Ihle-Hansen et al., 2014, Norway	First-ever stroke or transient ischemic attack, 71.6 (NR), 46.7%	2-parallel arms (LM, CAU)	Nutrition, physical activity	12	NA	195 (98, 97)	HADS	No significant difference between LM and CAU in HADS.
16	Imayama et al., 2011, United States	Overweight or obese postmenopausal women, 57.9 (NR), 100%	4-parallel arms (Diet, Exercise, *LM, *NI)	Nutrition, physical activity	12	NA	439 (118, 117, *117, *87)	BSI-18	LM significantly > NI in BSI-18.
17	Inouye et al., 2014, United States	At risk of diabetes, NR (NR), NR	2-parallel arms (LM, WL)	Nutrition, physical activity, stress management	6	6	40 (22, 18)	CES-D	No significant difference between LM and WL in CES-D.
18	Kim et al., 2011, South Korea	Breast cancer survivor, 45.8 (26-69), 100%	2-parallel arms (LM, NI)	Nutrition, physical activity	3	NA	45 (23, 22)	HADS	LM significantly > NI in HADS.
19	Kwon, 2015, South Korea	Dwelling elderly, NR (NR), NR	2-parallel arms (LM, NI)	Nutrition, physical activity, stress management	1	NA	93 (49, 44)	PHQ-9	LM significantly > NI in PHQ-9.
20	Lee et al., 2015, South Korea	Chronic obstructive pulmonary disease, 66.1 (NR), 8.6%	2-parallel arms (LM, CAU)	Nutrition, physical activity, stress management, sleep (CBT)	6	NA	151 (78, 73)	CES-D	No significant difference between LM and CAU in CES-D.
21	Leemrijse et al., 2016, Netherlands	Acute myocardial infarction or (un)stable angina pectoris, 60.4 (NR), 19%	2-parallel arms (LM, CAU)	Nutrition, physical activity	6	NA	374 (173, 201)	HADS	No significant difference between Hartcoach and CAU in HADS.
22	Lovell et al., 2014, United Kingdom	Psychosis, 25.7 (NR), 40%	2-parallel arms (LM, CAU)	Nutrition, physical activity	12	NA	105 (54, 51)	CDS	No significant difference between LM and CAU in CDS.

No.	Reference, year, country	Population, mean age, y (range), % female	Design	Lifestyle factors included	Treatment Duration (mo)	Follow-up assessment (mo)	Sample size (subgroup)	Depression assessment	Result reported
23	Macken et al., 2014, United States	Underwent coronary artery bypass surgery, NR (33-77), 17.6%	2-parallel arms (LM, CAU)	Nutrition, physical activity, stress management	NR	3	35 (18, 17)	PHQ-9	NR
24	Markomanolaki et al., 2019, Greece	Hashimoto's thyroiditis, *46.3 (25-76), 100%	2-parallel arms (LM, CAU)	Nutrition, stress management	2	NA	60 (30, 30)	DASS-21	LM significantly > CAU in DASS-21.
25	Melnyk et al., 2009, United States	Healthy adolescent, 15.5 (14-16), 68.4%	2-parallel arms (LM, AC)	Nutrition, physical activity, stress management (CBT)	2.25	NA	19 (12, 7)	BYI-II	NR
26	Melnyk et al., 2013, United States	Healthy adolescent, 14.7 (14-16), 51.6%	2-parallel arms (LM, AC)	Nutrition, physical activity, stress management (CBT)	3.75	6-mo	779 (358, 421)	BYI-II	No significant difference between COPE and AC in BYI-II.
27	Mensorio et al., 2019, Spain	Overweight/type I obesity and hypertension, 53 (28-69), 44.3%	2-parallel arms (LM, CAU)	Nutrition, physical activity	3	6, 12	106 (55, 51)	DASS-21	No significant difference between IG and CAU in DASS-21.
28	Meyer et al. 2009, Germany	Depressive symptoms, 34.8 (18-72), 76%	2-parallel arms (LM, WL)	Nutrition, physical activity, stress management (CBT)	2.25	2.25	396 (320, 76)	BDI	LM significantly > WL in BDI.
29	Moncrieft et al., 2016, United States	Overweight or obese with type 2 diabetes and depressive symptoms, 54.8 (NR), 71.2%	2-parallel arms (LM, CAU)	Nutrition, physical activity, stress management (CBT and social learning approaches)	12	NA	111 (57, 54)	BDI-II	CALM-D significantly > CAU in BDI-II.
30	Moseley et al., 2009, Australia	Healthy adolescent, 15.6 (NR), 66.7%	2-parallel arms (LM, CAU)	Nutrition, physical activity, sleep (CBT)	1	1.5	81 (41, 40)	DASS-21	No significant difference between LM and CAU in DASS-21.
31	Ng et al., 2017, Singapore	Pre-frail and frail elderly, 70 (NR), 61.4%	5-parallel arms (Nutrition, Cognitive training, Exercise *LM, *CAU)	Nutrition, physical activity	6	6	246 (49, 50, 48, *49, *50)	GDS-15	LM significantly > CAU in GDS-15.

No.	Reference, year, country	Population, mean age, y (range), % female	Design	Lifestyle factors included	Treatment Duration (mo)	Follow-up assessment (mo)	Sample size (subgroup)	Depression assessment	Result reported
32	Nie et al., 2019, China	Coronary artery disease with depressive and anxiety symptoms, NR (NR), 27.5%	2-parallel arms (LM, CAU)	Nutrition, physical activity	12	NA	284 (142, 142)	HADS	LM significantly > CAU in HADS.
33	Nijamkin et al., 2013, United States	Gastric bypass for morbid or severe obesity, 44.5 (NR), 83%	2-arms (LM, CAU)	Nutrition, physical activity, stress management (CBT, It provided strategies for cognitive behavior change)	6	NA	144 (72, 72)	BDI-II	LM significantly > CAU in BDI-II.
34	O'Neil et al., 2014, Australia	Acute coronary syndrome and depressive symptoms, 60 (NR), 24.8%	2-arms (LM, CAU)	Nutrition, physical activity, stress management, sleep (CBT)	6	NA	121 (61, 60)	CDS, PHQ-9	LM significantly > CAU in CDS and PHQ-9.
35	O'Reilly et al., 2016, Australia	Gestational diabetes mellitus, 33.8 (NR), 100%	2-parallel arms (LM, CAU)	Nutrition, physical activity, stress management, sleep	12	NA	573 (284, 289)	PHQ-9	No significant difference between LM, and CAU in PHQ-9.
36	Pelekasis et al., 2016, Greece	Breast cancer, NR (NR), 100%	2-parallel arms (LM, CAU)	Nutrition, physical activity, stress management (CBT)	2	NA	61 (30, 31)	DASS-21	LM significantly > CAU in DASS-21.
37	Phelan et al., 2014, United States	Pregnant women, *28.7 (NR), 100%	2-parallel arms (LM, CAU)	Nutrition, physical activity	12	6 and 12 month postpartum	401 (201, 200)	EPDS	NR
38	Robinson-Whelen et al., 2006, United States	Physical disabilities, 58.6(45-83), 100%	2-parallel arms (LM, WL)	Nutrition, physical activity, stress management, sleep	2	3	137 (NR, NR)	CES-D-10	NR
39	Samuel-Hodge et al., 2017, United States	Type 2 diabetes with overweight or obesity paired with a family partner with overweight or obesity, 51 (NR), 81%	2-parallel arms (LM, WL)	Nutrition, physical activity, stress management	5	NA	108 (72, 36)	PHQ-8	LM significantly > WL in PHQ-8.

No.	Reference, year, country	Population, mean age, y (range), % female	Design	Lifestyle factors included	Treatment Duration (mo)	Follow-up assessment (mo)	Sample size (subgroup)	Depression assessment	Result reported
40	Saxton et al., 2014, United Kingdom	Breast cancer, *55.6 (NR), 100%	2-parallel arms (LM, CAU)	Nutrition, physical activity	6	NA	85 (44, 41)	BDI-II	LM significantly > CAU in BDI-II.
41	Sebregts et al., 2005, Netherlands	Acute myocardial infarction and/or coronary artery bypass grafting, NR (NR), NR%	2-parallel arms (LM, CAU)	Nutrition, physical activity, stress management	2	3, 6, 9	204 (106, 98)	SCDI, BDI	No significant difference between LM and CAU in SCDI or BDI.
42	Spence et al. 2011, Australia	PTSD, 42.6 (21-68), 81%	2-parallel arms (LM, WL)	Nutrition, physical activity	2	3	44 (23, 21)	PHQ-9	LM significantly > WL in PHQ-9.
43	Spindler et al., 2019, Denmark	Cardiac Patients, 62.3 (NR), NR	2-parallel arms (LM, CAU)	Nutrition, physical activity	3	6, 12	136 (69, 67)	HADS	No significant difference between LM and CAU in HADS.
44	Sylvia et al., 2019, United States	Overweight or obese with bipolar disorder, 42.0 (NR), 65.8%	2-parallel arms (LM, WL)	Nutrition, physical activity	5	NA	38 (19, 19)	MADRS, CGI-BP	LM significantly > WL in CGI-BP; No significant difference between LM and WL in MADRS.
45	Teut et al., 2013, Germany	Older adults living in shared apartment communities, *79.4 (48-102), 67.2%	2-parallel arms (LM, CAU)	Nutrition, physical activity	12	NA	58 (29, 29)	NOSGER	LM significantly > CAU in NOSGER.
46	Toobert et al., 2007, United States	Postmenopausal women with type 2 diabetes, 60.9 (NR), 100%	2-parallel arms (LM, CAU)	Nutrition, physical activity, stress management	6	NA	279 (163, 116)	CES-D	No significant difference between LM and CAU in reducing depressive symptoms.
47	Tousman et al., 2011, United States	Asthma, 53.3 (NR), 68.9%	2-parallel arms (LM, NI)	Physical activity, stress management	1.75	2	45 (21, 24)	GDS	No significant difference between LM and NI in GDS.
48	van der Wulp et al., 2012, Netherlands	Type 2 diabetes, NR (NR), NR	2-parallel arms (LM, CAU)	Nutrition, physical activity (Social cognitive theory)	3	6	133 (68, 65)	CES-D	No significant difference between LM and CAU in CES-D.
49	Wang et al., 2017, China	Metabolic syndrome, 55.6 (24-78), 50.9%	2-parallel arms (LM, CAU)	Nutrition, physical activity, stress management	3	NA	173 (86, 87)	HADS	LM significantly > CAU in HADS.
50	Ye et al., 2016, China	Breast cancer survivors, NR (NR), 100%	3-parallel arms (*LM, NG, *CAU)	Nutrition, physical activity, stress management	12	NA	306 (*101, 112, *103)	HADS	LM significantly > CAU in HADS.

Notes. AC = Attention control; BDI = The Beck Depression Inventory; BDI-II = The Beck Depression Inventory- II; BSI-18 = The Brief Symptoms Inventory; BYI-II = The Beck Youth Inventory (Second Edition); CAU = Care-as-usual; CBT = Cognitive behavioral therapy; CDS = The Cardiac Depression Scale; CDI = The Children's Depression Inventory;

CES-D = The Center for Epidemiologic Studies Depression Scale; CGI-BP = The Clinical Global Impressions-Bipolar Scale ; DASS = The Depression Anxiety Stress Scale; EPDS = The Edinburgh Postnatal Depression Scale; GDS = The Geriatric Depression Scale; HADS = Hospital Anxiety and Depression Scale; LM = Lifestyle Medicine Intervention; MADRS = The Montgomery-Åsberg Depression Rating Scale; mo = Month; NA = Not applicable; NG = Norm group; NI = No Intervention; NOSGER = The Nurses Observation Scale for Geriatric Patients; NR = No Report; PHQ-8 = The Patient Health Questionnaire-8; PHQ-9 = The Patient Health Questionnaire-9; SCDI = The Short Children's Depression Inventory; STPI = The State-Trait Personality Inventory; wk = Week; WL = Wait-list; y = Year.

Table 2. Major eligible criteria.

Study no.	Author, year	Major eligibility criteria
1	Almeidaa et al., 2016	Incl: Aged 45-55 y, <5 y of irregular menstrual cycles, 2 or more skipped cycles and at least one interval of amenorrhea of 60 or more days, Amenorrhea < 12 mo Excl: History of gynecological treatment or surgery that could influence the assignment of menopausal status, either pre or post-menopausal, reported illness that could influence on 12 mo survival, PHQ-9 ≥ 15 or MDD at the time of assessment, evidence of alcohol abuse or dependence, past or current history of schizophrenia, delusional, schizoaffective of bipolar disorder, severe hearing impairment that could influence telephone communication, not fluent in written or spoken English, planning to move away from Western Australia over the future 12 mo, did not have a treating GP, and did not provide informed consent
2	Attux et al., 2013	Incl: Aged 18-65 y, using any antipsychotic in the past 3 mo, diagnosis on the schizophrenia spectrum confirmed by SCID I-P, PANSS <60, motivated to lose weight or concerned weight gain. Excl: Clinically unstable, currently having DM, history of an eating disorder, drug and alcohol abuse, and restricted to take any medication with the intention of controlling or reducing weight.
3	Azami et al., 2018	Incl: Iranian aged ≥ 18 y, clinically diagnosed with T2DM ≥ 6 months, medical record showing HbA1c ≥ 8%, willing to participate in follow-up care (≥ 2 visits per year), and without serious medical illness. Excl: Had cognitive dysfunction, pregnancy, blood pressure ≥ 180/110 mmHg, vision or hearing impairment, haemolytic anaemias, hemoglobinopathies, illiterate, acute or chronic diabetes complications, or major difficulties in daily activities.
4	Brennan et al., 2012	Incl: Aged 11-19 y, overweight or obese based on the international cut-off points for BMI in children and living with a parent or adult caregiver who was willing to participate in this study. Excl: Had an intellectual or physical disability that precluded from participation.
5	Casañas et al., 2012	Incl: Aged > 20 y of both sexes, had MDD based on ICD-10, BDI ≥ 10 and <30, and provided signed informed consent. Excl: Other diagnosed associated psychiatric disorders, current presence of suicidal ideation or suicide attempts, using secondary mental health services, acute or terminal medical illness, inability to speak and understand Spanish and/or Catalan language, sensory or cognitive disabilities, illiteracy, temporary residents, or non-provision of consent.
6	Chang et al., 2018	Incl: Had non-psychotic, unipolar MDD based on DSM-IV diagnosis assessed by MINI, MADRS ≥ 17, and taking antidepressants at stable dosage ≥ 6 wk prior to study entry without any medical recommendation for medication change for the next 3 mo. Excl: Had other Axis I psychiatric disorder, acute or severe medical illness, taking drugs known to cause depression, had advanced dementia, aphasia or inability to speak Korean.
7	Charandabi et al., 2017	Incl: Spouses of pregnant women with gestational ages of 24–28 wk, single and uncomplicated pregnancy, the first or second pregnancy, being registered at health centers in Bukan city-Iran, education ≥ secondary school, not participating in other similar studies, having a telephone number for follow-up, and willingness to take part in this study, training classes and telephone counselling. Excl: Spouses of pregnant women with the risk of preterm labour, history of depression, hospitalization records for mental problems, addiction or the regular use of alcohol and drugs by husband and wife, history of infertility, history of using assisted reproductive techniques in either husband or wife, participated in childbirth preparation classes (for wife only), history of a close relative's death, divorce, and other serious emotional problems during the last month.
8	Croker et al., 2015	NR
9	Dale et al., 2015	Incl: English-speaking adults, documented diagnosis of CHD, and able to access to the Internet Excl: Untreated ventricular tachycardia, severe heart failure, life-threatening coexisting disease with life expectancy < 1 y, or significant physical activity limitations for reasons other than CHD.
10	Deitz et al., 2014	Incl: At least one risk for cardiac disease or with a known condition. Excl: Pregnancy.
11	Diamond et al., 2015	Incl: Aged ≥ 50 y, adequate English for neuropsychological assessment, stabilization on medication regimes, HDRS < 20, and willingness to attend twice-weekly therapy for 7 wk. Excl: History of stroke, neurological disorder, head injury with loss of consciousness ≥ 30-min, medical condition known to affect cognition, dementia or MMSE <24.
12	Duan et al., 2017	NR
13	Duan et al., 2018	Incl: Aged 18-75 y, no restriction of physical mobility under the cardiac function at entry, no restriction of other relevant diseases, sufficient Chinese reading and writing skills, internet access via a computer at home, and mobile access.

Study no.	Author, year	Major eligibility criteria
14	Furuya et al., 2014	Incl: Aged ≥ 18 y, undergoing first PCI, and had telephone access. Excl: Being clinically unable for telephone contact, having sequelae affecting daily activities, participated in another educational programme, or having cognitive impairment as assessed by MMSE adapted to the Brazilian population.
15	Ihle-Hansen et al., 2014	Incl: Able to perform TMT A or RBANS or both. Excl: Currently with subarachnoid hemorrhage, cognitive decline, history of stroke or TIA, unable to speak Norwegian, and with a life expectancy < 12 mo.
16	Imayama et al., 2011	Incl: Age 50-75 y, BMI ≥ 25.0 kg/m^2 (≥ 23.0 kg/m^2 for Asian-American), moderate or vigorous intensity physical activity < 100 min/wk, postmenopausal, not taking hormone replacement therapy for the past 3 mo, no history of breast cancer, heart disease, diabetes mellitus, or other serious medical conditions, fasting glucose < 126 mg/dL, currently not smoking, alcohol intake < 2 drinks per day, able to attend diet or PA sessions at the intervention site, and passed the PA tolerance test.
17	Inouye et al., 2014	Incl: Filipino aged ≥ 30 y, risk score > 9 on the American Diabetes Association "Are you at risk for diabetes?" screening questionnaire. Excl: Diagnosis of diabetes, uncompensated cardiac disease, respiratory disease, or musculoskeletal disease that would preclude from PA.
18	Kim et al., 2011	Incl: Women aged ≥ 20y, stage 0–III breast cancer, primary treatment completed, and unmet behavioral goals or DQI ≥ 6. Excl: Currently progressive disease, additional primary tumors, being treated for cancer, a condition that precluded unsupervised PA, a condition that could interfere with a high vegetable and fruit diet, or serum platelets < 100,000/mm^3, serum hemoglobin < 10 g/dl, body temperature ≥ 37.8°C, or white blood cell count ≥ 11,000/mm^3.
19	Kwon, 2015	Excl: Aged ≤ 64 y and K-MMSE <24.
20	Lee et al., 2015	Incl: Aged 40–80 y, diagnosed with COPD by a physician based on Vmax 22 system and the Ultima PFX system, and stable condition and expected to live ≥ 6 mo as determined by a doctor who specialised in respiratory medicine.
21	Leemrijse et al., 2016	Incl: Aged 18–80 y and had been hospitalised < 8 wk before due to an acute myocardial infarction, STEMI, non- STEMI, UAP, or CAP. Excl: Planned surgery or other interventions, life-expectancy < 2 y based on the judgment of the treating cardiologist, moderate to severe heart failure, previous or current similar lifestyle interventions, no telephone, or communication disorders.
22	Lovell et al., 2014	Incl: Aged 16-35 y, diagnosis of schizophrenia, schizophreniform disorder, schizoaffective disorder, delusional disorder, brief reactive psychosis, or psychosis not otherwise specified, first episode of psychosis occurring within the 3 y preceding the trial, current user of an early intervention service, stable accommodation, ability to give informed consent, and BMI ≥ 25 or ≥ 24 for South Asian. Excl: Diagnosis of substance dependence or abuse that would preclude from participation, a serious history of organic factors implicated in the etiology of psychotic symptoms, or pregnancy.
23	Macken et al., 2014	Incl: Aged ≥ 19 y, diagnosis of CABS, enrollment in outpatient CR, married or living with spouse/partner for more than 1 y, spouse/partner willing to participate, no history of psychiatric illness, and had low to moderate risk for occurrence of cardiac events during PA. Inclusion criteria for partners were the same except for the CABS diagnosis and they needed permission from their primary care physician to participate. Excl: Orthopedic problems that would prevent walking on a treadmill.
24	Markomanolaki et al., 2019	Incl: Women aged ≥ 18 y, with Hashimoto's thyroiditis, residents of Athens and literate in Greek. Excl: Suffered from mental illness, received any medication or participated in other program for stress management.
25	Melnyk et al., 2013	Incl: Teens of any gender, ethnicity/race, or SES, teens who agreed to participation, a custodial parent who provided informed consent for their teen's participation, and able to read and speak English. Excl: Medical condition that would prevent from PA.
26	Melnyk et al., 2009	Incl: Enrolled in 1 of 2 sections of a required health course.
27	Mensorio et al., 2019	Incl: Aged 18–65 y, participating in clinical medical treatment for preventing metabolic syndrome or cardiac complications, and overweight or type I obesity (BMI>25 and<35). Excl: No Internet access, taking more than 3 antihypertensive drugs, having diabetes or eating disorder, having a disability that precluded from PA, or receiving any treatment for weight loss.
28	Meyer et al. 2009	Incl: Aged ≥ 18, provided consent, and completed at least half of the baseline depression questionnaire.

Study no.	Author, year	Major eligibility criteria
29	Moncrieft et al., 2016	Incl: Aged 18-70 y, BMI ≥ 27 kg/m^2, self-reported Type 2 diabetes confirmed by medical records, current treatment, or verified by study physician, and BDI-II ≥ 11. Excl: Limited life span or adherence to intervention, unsafe for participation (e.g., advanced renal disease, inability to walk, and severe mental illness). BDI-II scores ≥ 35 and considered as likely to prevent from effective participation.
30	Moseley et al., 2009	Incl: Delayed sleep timing based on the discrepant out of bedtimes (school vs. weekend mornings > 2 hr) and an insufficient amount of sleep on school nights.
31	Ng et al., 2017	Incl: Aged ≥ 65, able to ambulate without personal assistance, and living at home. Excl: MMSE ≤ 23, major depression, severe audio-visual impairment, progressive, degenerative neurologic disease, terminal illness with life expectancy < 12 mo, or participation in other interventions research study.
32	Nie et al., 2019	Incl: Aged 18-80 y, diagnosed as CAD by coronary angiography (one coronary artery having a stenosis ≥ 50%), underwent percutaneous coronary intervention or coronary artery bypass graft surgery previously, HADS-A ≥ 8 and HADS-D ≥ 8, and could be followed up regularly. Excl: At imminent risk of suicide, received antianxiety or antidepressant treatment ≤ 3 mo before enrolment, had complication with other mental disorders, other neurological diseases, uncontrolled hypertension, cardiac arrhythmia, unstable angina pectoris, disabled on vision, hearing, language, or comprehension, history of pulmonary and renal comorbidities, heart failure, tumors, or other life-threatening diseases, life expectancy < 1 y, and pregnant women or lactating women.
33	Nijamkin et al., 2013	Incl: Hispanic American, able to speak Spanish and English bilingually and proficiently, undergone a laparoscopic Roux-en-Y gastric bypass surgery 24 ± 2 weeks before recruitment. Excl: Physical inability that prevent from participation, medical conditions (such as thyroid, kidney, or heart disease), having antidepressant medication, or pregnancy.
34	O'Neil et al., 2014	Incl: Age 21–85 y, clinical diagnosis of ACS, fluency in English, availability via the telephone throughout the study, and PHQ-9 between 5–19. Excl: Having regular psychological therapy with a mental health professional at the time of admission for ACS, psychiatric condition or cognitive impairment that could impact involvement, diagnosis with a terminal illness, or inability to participate in this study as assessed by the treating clinician.
35	O'Reilly et al., 2016	Incl: Women aged ≥18 y, diagnosis of GDM in their most recent pregnancy. Excl: Pre-existing diabetes, cancer (not in remission), severe mental illness, substance abuse (illicit drugs), myocardial infarction in the preceding 3 mo, difficulty with English, involvement in another postnatal intervention research study, pregnancy at baseline or during the 12 mo of study involvement.
36	Pelekasis et al., 2016	Incl: Aged 18-75 y, history of breast cancer, receiving chemotherapy for ≥ 8 wk after entering the study, resident of Attica. Excl: Diagnosis of mental disorder, use of antipsychotics, anxiolytics, or antidepressants, practice stress management technique during the past 6 mo regularly.
37	Phelan et al., 2014	Incl: Aged > 18 y, gestational aged between 10-16 wk, singleton pregnancy, BMI between 19.8-40 kg/m^2, non-smoker, fluent in English, and have telephone access. Excl: Self-reported major health or psychiatric diseases, history of miscarriages ≥ 3, or early pregnancy weight loss due to a great concern of inadequate weight gain.
38	Robinson-Whelen et al., 2006	Incl: Aged ≥ 45 y, had a physical limitation of ≥ 1 y that influenced mobility or self-care. Excl: Had severe cognitive impairments, psychotic symptoms, current suicidal ideation, or current drug or alcohol problems that prevent from group participation, or unable to speak and understand English to provide consent, participate in a group health promotion workshop.
39	Samuel-Hodge et al., 2017	Incl: For participants: African American aged 21–75 y, self-reported diagnosis of type 2 diabetes, BMI 25–47 kg/m^2, inclusive, hemoglobin A1c value ≤ 11%, currently under the care of a health care provider, able to participate in moderate intensity PA, and willing to participate in this study with a family partner without diabetes. For family members: without a diagnosis of diabetes, self-described blood relatives or lived with or were married (≥ 1 y) to the index person. Excl: Medical contraindication to weight loss, cardiovascular event ≤ 6 mo, active cancer diagnosis, pregnant or lactating, history of renal disease except kidney stones, gastric bypass surgery or scheduled bariatric surgery, weight loss >20 lbs. in the past 3 mo, having weight loss medications, or receiving psychosis or manic-depressive treatment.
40	Saxton et al., 2014	Incl: BMI >25 kg/m2, completed surgery, chemotherapy and radiotherapy for stage I to III breast cancer 3-18 mo before. Excl: Receiving concomitant HRT or oral contraceptives, metastatic or active loco-regional disease, physical or psychiatric impairment that impaired physical mobility, severe nausea, anorexia or other conditions precluding from PA, adoption of alternative/complementary diets or high-dose antioxidant supplements, engaged in PA regularly.

Study no.	Author, year	Major eligibility criteria
41	Sebregts et al., 2005	Incl: Aged < 70 y, admitted to the University Hospital Maastricht with a diagnosis of AMI, CABG, or both, and able to participate in the regular physiotherapy PA intervention starting early after discharge. Excl: Non-Dutch speaker, illiterate, or having any psychiatric disorder that could precluding from participation severely.
42	Spence et al. 2011	Incl: Australia resident aged ≥ 18 y, had access to a computer, the Internet, and use of a printer, not currently participating in CBT having a psychotic mental illness, PHQ-9 > 22 or PHQ-9 question nine response >2, or DES>40, stable medication for ≥ 1 mo (if needed) and throughout the intervention period, and principal diagnosis of PTSD based on DSM-IV
43	Spindler et al., 2019	Incl: Aged ≥ 18 y, diagnosis of coronary artery bypass, valve surgery, heart failure or artery sclerosis, and able to understand Danish and use digital technology.
44	Sylvia et al., 2019	Incl: Aged 18-65 y, primary diagnosis of Type I Bipolar Disorder or Bipolar Disorder II, currently symptomatic, and BMI ≥ 25 kg/m^2. Excl: Had a diagnosis of anorexia nervosa, bulimia nervosa, or substance dependence 1 mo before study entry, actively suicidal, pregnancy, regular PA, had a neurologic disorder, history of head trauma, or had other conditions that precluded from participation in this study.
45	Teut et al., 2013	Incl: Older adults. Excl: Health condition that absolutely precluded from participation.
46	Toobert et al., 2011	Incl: Having type 2 diabetes ≥ 6 months, being postmenopausal, living independently, telephone user, able to read English, non-developmentally disabled, and living within 30 miles of the intervention site. Excl: Aged > 75 y or planning to move from the area within the study period.
47	Tousman et al., 2011	NR
48	van der Wulp et al., 2012	Incl: Diagnosed with Type 2 diabetes < 12 mo
49	Wang et al., 2017	Incl: Chinese citizens aged ≥18 y, with IDF-MetS, and able to communicate in Chinese and to complete the questionnaires. Excl: Psychiatric illnesses assessed by physician, terminal illnesses, impaired bilateral hearing or vision, or had difficulty in performing moderate-intensity aerobic PA.
50	Ye et al., 2016	Incl: Women aged 18-60 y, clinical diagnosis of breast cancer stratified by stage of cancer (0, I, and II), fluent speaker of Mandarin or Cantonese, on active treatment, and no schizophrenia symptoms. Excl: Male, history of suicidal behavior, unable to complete the questionnaires, and unwilling to participate in this study.

Note. ACS = Acute Coronary Syndrome; Ami = Acute Myocardial Infarction; BDI = Beck Depression Inventory; BDI-II = The Beck Depression Inventory- II; BMI = Body mass index; CABG = Coronary artery bypass grafting; CABS = Coronary Artery Bypass Surgery; CAD = coronary artery disease; CAP = Community-acquired pneumonia; CBT = Cognitive behavioral therapy; CHD = Congenital heart disease; COPD = Chronic obstructive pulmonary disease; CR = complete remission; DES = Dissociative Experiences Scale; DQI = The Dermatology Life Quality Index questionnaire; DSM-IV = Diagnostic and Statistical Manual of Mental Disorders 4th edition; GRT = Hormone-replacement therapy; HDRS = The Hamilton Rating Scale for Depression; IDF-MetS = International Diabetes Federation- metabolic syndrome; MDD = Major depressive disorder; MINI = Mini International Neuropsychiatric Interview Medical, Psychiatry, Diagnostic; MMSE = Mini-Mental State Examination; Mo = Month; PA = Physical activity; PANSS = The Positive and Negative Syndrome Scale; PCI = Percutaneous Coronary Intervention; PTSD = Post-traumatic stress disorder; RBANS = Repeatable Battery for the Assessment of Neuropsychological Status; SCID I-P = Structured Clinical Interview for DSM-IV; SES = Socioeconomic Status; STEMI = ST-Elevation Myocardial Infarction; T2DM = Type 2 diabetes; TMT A = Treadmill test; UAP = Unlicensed assistive personnel; Wk = Week; y = Year.

Table 3. Source of treatment content, brief descriptions of treatment and comparator content, and recruitment methods.

No.	Author, year	Treatment and comparator content	Recruitment
1	Almeidaa et al., 2016	Intervention: Based on the stages of change model and 'patient-centred' approach to care. MI and PS were used. Consisted of 6 health coaching telephone sessions delivered by psychologists over a period of 26 wk (2 additional sessions were provided to address obvious unmet needs). Comparator: Clinically relevant information was passed onto the treating physician	Post
2	Attux et al., 2013	Intervention: Developed by Eli Lilly Laboratories for controlling weight gain for individuals with schizophrenia under antipsychotic use. Consisted of 1 hr weekly discussion session combined with behavioural techniques and psychoeducation for 12 wk (relatives were welcomed to join), regular visits to the psychiatrist and regular sessions of other psychosocial interventions Comparator: Regular visits to the psychiatrist and regular sessions of other psychosocial interventions similar to the intervention group.	Outpatient programs
3	Azami et al., 2018	Intervention: Developed by a multidisciplinary team including endocrinologists, nutritionists, nurses, and pharmacists according to the AADE defined self-care behaviours for diabetes self-management. Based on self-efficacy theory and MI. Consisted of usual diabetes care and a 12 wk intervention, one self-management education booklet, four 10 min weekly movie clips to provide verbal encouragement, four weekly group education sessions (120 min each; relatives were welcomed to join), weekly follow-up telephone call two month after the end of group discussion sessions (15 – 20 min each) to encourage continued performance (based on MI). Comparator: Usual diabetes care similar to the intervention group and educational booklet and movie clips were provided at the end of the intervention.	Advertisement on the message boards of the clinic
4	Brennan et al., 2012	Intervention: Developed by the first author and a postgraduate psychology student. Based on CBT and the nutritional component was developed according to the Australian Guide to Healthy Eating (Smith, Kellett, and Schmerlaib, 1998), and physical activity component was according to the Australian Physical Activity Guidelines for Children and Young People (Department of Health and Ageing, 2004). Consisted of treatment phase (twelve 1 hr face-to face individual treatment sessions and 1 phone call) and maintenance phase (two 60 min clinic sessions and seven 15 min phone calls). The first 6 treatment sessions were accompanied by parents, subsequence sessions were then given the choice of attending the remaining sessions alone, or with the support of a parent. Received a programme workbook. Comparator: Offered treatment after the 6 mo waiting period.	Radio and newspaper advertisement, school staffs, health care professionals, health and fitness professionals, and university
5	Casañas et al., 2012	Intervention: Contained CBT principles. Consisted of 12 weekly, 90 min health education sessions. Homework were given and continued pharmacological treatment if needed. Comparator: GP and nurse visits (10 – 20 min each) and continued pharmacological treatment if needed.	Primary care centers
6	Chang et al., 2018	Intervention: Developed by the research group according to the SIGN guidelines for non-pharmaceutical management of depression. Prize-based contingency management was applied. Consisted of lifestyle modification information, weekly telephone-check and monthly visit check during the follow-up period of 12 weeks. Comparator: Weekly telephone and monthly home-delivered supportive psychotherapy.	Community mental health centers
7	Charandabi et al., 2017	Intervention: 2 weekly training sessions (60-90 min between 24-28 wk), received a training booklet, 10 min weekly telephone counselling were offered in the intervals between and after sessions, during postpartum period Comparator: No details.	Health centers
8	Croker et al., 2012	Intervention: Based on learning theory and uses behaviour modification techniques. Parents are instructed in behaviour management principles and Cognitive components to motivation child's lifestyle change. Comparator: No details.	NR

No.	Author, year	Treatment and comparator content	Recruitment
9	Dale et al., 2015	Intervention: Developed and refined the Text4Heart intervention by the research group according to the mHealth Development and Evaluation Framework. Based on social cognitive theory, the key mediator of self-efficacy (perceived self-efficacy), and the Common Sense Model. Consisted of a 24 wk intervention delivered through text messages (7 per wk for the first 12 wk, 5 per wk for wk 13 to 24), a supporting website, and a pedometer to self-monitor was also given. Comparator: Encouraged to attend traditional center-based cardiac rehabilitation.	Hospital
10	Deitz et al., 2014	Intervention: Consisted of a 6 wk self-paced web intervention with 5 modules (risk factors and reducing risk, diet and nutrition, getting advice, stress and cardiovascular disease, and tobacco free). Reminders were sent every 2 weeks and to those who viewed the program < 20 min. Comparator: No details.	Hospitals
11	Diamond et al., 2015	Intervention: Developed by a group of specialists based on Naismith et al. (2011). The program consisted of a 7 wk twice weekly psychoeducation and computer based cognitive training. Comparator: Standard clinical care from usual health-care professionals during the waiting period.	Specialist early intervention clinic
12	Duan et al., 2017	Intervention: Developed based on HAPA theory and targeted at the social cognitive variables of PA and FVC and self-efficacy. Consisted of an 8 wk web-based intervention (PA in the first 4 wk and FVC in the later 4 wk), selected behaviour change techniques, criterion-based feedback and examples of role models were given. Comparator: No intervention.	University
13	Duan et al., 2018	Intervention: Developed based on HAPA theory and targeted at the social cognitive variables of PA and FVC and self-efficacy. Consisted of an 8 wk web-based intervention (PA in the first 4 wk and FVC in the later 4 wk), selected behaviour change techniques, criterion-based feedback and examples of role models were given. Comparator: No details.	Hospital
14	Furuya et al., 2014	Intervention: Developed by the research group. Based on the construct of self-cognitive theory (Bandura 2004) and contents were based on literature, the manuals *My heart, My Life* ((National Heart Foundation of Australia 2008) and *The Heart Manual* (Lothian Health Board 2007). Consisted of information routinely delivered by the institution at discharge, an education programme (3 booklets), and telephone follow-ups after hospital discharge (questioned on self-care) Comparator: Received the usual instructions given by healthcare providers at the hospital.	Hospital
15	Ihle-Hansen et al., 2014	Intervention: Developed based on recommendations regarding secondary prevention after stroke (Smith, Jr. et al., 2006). Consisted of consultations with study stroke nurse and physician, health education, medical treatment, pharmacological intervention if needed, and promotion of a healthy lifestyle. The patients' carers were included as needed. Comparator: Routine care by GPs.	Hospital
16	Imayama et al., 2011	Intervention: Individual sessions with the dietitians ≥ 2/wk and met weekly in groups until wk 24, and contacted with the dietitians ≥ 2/mo either in group sessions or via email/phone contact. Had 45 min PA session ≥ 5 days/wk. Comparator: No intervention during the intervention and were offered 4 groups diet sessions and 8 wk of supervised PA sessions after the data collection at 12 mo.	Mass mailing and media placements
17	Inouye et al., 2014	Intervention: Developed based on the DPP interventions. Consisted of 8 group sessions within a 6 wk to 6 mo period. Comparator: Received the intervention after the 6 mo waiting period.	Catholic church
18	Kim et al., 2011	Intervention: Developed based on TTM (Prochaska and DiClemente, 1983), guidelines for cancer survivors (Doyle et al., 2006; Jones and Demark-Wahnefried, 2006), guidelines of the Korean Nutrition Society (2007), and food tables from the Korean Nutrition Society (1995, 2007). Consisted of a 12 wk stage-matched telephone counselling (30 min), a workbook, individualized prescription for regular PA, a balanced diet program, a portable heart rate monitor (Polar® F4, Polar Electro), and a workbook of stage matched PA and diet- related information were given. Comparator: No intervention.	Cancer Centers

No.	Author, year	Treatment and comparator content	Recruitment
19	Kwon, 2015	Intervention: Adopted from the Wheel of Wellness model and counselling methods proposed by Myers et al. (1998). Consisted of an individually four weekly, 1 hr, face to face counselling. Comparator: No intervention.	Senior welfare center and posters advertising
20	Lee et al., 2015	Intervention: Developed by the research group. Individualised telephone counselling for every two wk. Comparator: CAU from their physicians.	Outpatient clinics
21	Leemrijse et al., 2016	Intervention: Employed MI. Consisted of a 6 mo telephone-based intervention with the coach contacted participants every 4-6 wk (lasted for 20-30 min). Comparator: Visited the cardiologist, cardiac nurse, GP, physical therapist, dietician, and/or cardiac rehabilitation.	Hospital
22	Lovell et al., 2014	Intervention: Developed based on the Leventhal's Common Sense Model. Consisted of 7 individual face-to-face sessions over 6 mo and a booster session at 9 to 10 mo. Contents included motivational and behavioural components, psychoeducation, optional group activities, a booklet, and a website. Comparator: Received individualized early intervention services, enhanced-care coordination, specific care plan, and support from case managers for PA if needed.	Early intervention services
23	Macken et al., 2014	Intervention: Individualized PA plans (3 days/wk for 6 to 12 wk). Group education on diet, PA, smoking cessation, cardiac knowledge, stress management, medications, and lifestyle change. Partners received the individualized treatment plan and counselling as well. Comparator: No details.	NR
24	Markomanolaki et al., 2019	Intervention: Consisted of 8 weekly sessions, including stress management and lifestyle counselling. Comparator: Received standard care by their physicians.	NR
25	Melnyk et al., 2013	Intervention: Developed by the first author according to the Cognitive Theory. Consisted of 15 weekly sessions, including educational and cognitive behavioural skill building, 15-20 min group PA/session, provided with pedometers and a COPE manual with homework activities, and 4 parent newsletters were given. Comparator: Consisted of a 15 wk attention control intervention, provided with a pedometer for use only during the first week and post-intervention week, focused on safety and common health topics, provided with a manual with homework activities, and 4 parent newsletters were given.	High schools
26	Melnyk et al., 2009	Intervention: Developed by the first author according to the cognitive behavioural principle. Consisted of 15 sessions delivered over 9 wk (each session lasted for 50 min), including educational and cognitive behavioural skill building, 15-20 min group PA in each session, provided with pedometers and a COPE manual with homework activities. Comparator: Received instructions in health topics that were different from the intervention program and pedometers were given.	High schools
27	Mensorio et al., 2019	Intervention: Developed based on the cognitive behavioural perspective. Consisted of a web page with 9 modules focusing on behavioural therapy techniques, promotion of eating habits, and PA. Homework were provided. Comparator: Received usual medical consultations aimed at reducing cardiovascular risk factors.	Hospital
28	Meyer et al. 2009	Intervention: Based on cognitive behavioural perspective. Consisted of 10 modules and 1 introductory module (lasted for 10-60 min). Content includes behavioural activation, cognitive modification, mindfulness and acceptance, interpersonal skills, relaxation, PA and lifestyle modification, PS, childhood experiences and early schemas, positive psychology interventions, dreamwork and emotion focused interventions, and psychoeducation. Comparator: Accessed the program after the 9 wk waiting period.	Internet advertisements

No.	Author, year	Treatment and comparator content	Recruitment
29	Moncrieft et al., 2016	Intervention: Developed based on Diabetes Prevention Program and adopted the cognitive behavioural and social learning approach. Consisted of a 12 mo intervention containing 17 sessions (each session lasted for 1.5 – 2 hr, two individual sessions followed by two weekly and four bi-weekly group sessions, and 9 monthly group session. The first 6 mo focused on achieving activity and diet goals, the second half focused on problem solving and maintenance of behaviors. Materials were provided to track progress. Received laboratory results at all assessment time point and were encouraged to share results with their primary care providers. Comparator: Received laboratory results at all assessment time point and were encouraged to share results with their primary care providers	Community health clinics and referred by word of mouth
30	Moseley et al., 2009	Intervention: Developed by the researcher and based on CBT framework. A 4-lesson program consisted of psychoeducation, class discussion, peer and personal reflection, lifestyle education, role play, and group discussion Comparator: Continued with regular classes.	Secondary school
31	Ng et al., 2017	Intervention: Developed based on American College of Sports Medicine Guidelines for older adults and a neuropsychologist. Consisted of 12 wk group PA and 12 wk twice weekly 90 min home-based session, provided daily supplement for 24 wk, and cognitive training (2 hr weekly session for the first 12 wk, attended fortnightly 2 hr "booster session) Comparator: Accessed CAU, rehabilitation services, and were given placebo liquid capsules and tablet formulations.	House-to-house survey
32	Nie et al., 2019	Intervention: Developed by the research group. Consisted of health education (weekly in the first mo, twice a mo for subsequent 11 mo), 30 min emotional support in each session, and lifestyle improvement (monitor every 2 wk) Comparator: Guidance on using the medicines for CAD, regular examinations, and usual advice of CAD self-management.	Hospital
33	Nijamkin et al., 2013	Intervention: Developed based on preoperative data and the literature. Delivered based on non-judgmental and non-confrontational approach. Consisted of six 90 min educational sessions every other wk and post-bariatric standard care. The educational sessions focused on motivation, and contained CBT principle, group nutrition counselling, stress relief without food, self-motivation, and obesity relapse prevention. The comprehensive intervention targeted on lifestyle change and motivational tactics. Comparator: Received preoperative medical, psychological, and nutritional evaluation. Regular meeting with the bariatric surgeon and the registered dietitian for medical and nutritional follow-up after surgery. Consulted with a psychologist after surgery if needed, gradually increase PA level to 30 minutes per day,	Flyers
34	O'Neil et al., 2014	Intervention: Consisted of 10 telephone structured sessions with a handbook for 6 mo except target recovery was achieved prior to program completion. Employed MI and CBT principles. Received a brief National Heart Foundation of Australia education pamphlet on myocardial infarction recovery. Comparator: Received a brief National Heart Foundation of Australia education pamphlet on myocardial infarction recovery and medical care through their health care providers.	Hospital
35	O'Reilly et al., 2016	Intervention: Informed by Health Action Process Approach and social cognitive and self-regulation theory and based on GGT-DPP. Consisted of 1 individual session with a handbook, five 2 hr group sessions delivered every 2 wk, and two follow-up maintenance telephone calls delivered at 3 and 6 mo. Comparator: Received usual care and were offered the intervention program after their 12 mo data collection.	Antenatal clinic

No.	Author, year	Treatment and comparator content	Recruitment
36	Pelekasis et al., 2016	Intervention: Developed by the research group based on three RCTs (Cho et al., 2014; Walker et al., 1999; Yoo et al. 2005). Consisted of an 8 wk stress management and health promotion program (6 weekly 30 min sessions for the first 6 sessions, no intervention for the subsequent sessions). Verbal and written information about PA and diet, step pedometer was given, CBT session, phone reminder to increase treatment compliance at the spare week, audio CDs about diaphragmatic breathing, progressive muscle relaxation, and guided imagery (recommended to practice twice a day). Comparator: 15 min placebo-effect group meeting with researchers at each oncology unit visit for chemotherapy. Educational on cancer-specific topics were offered during the meeting.	Hospital
37	Phelan et al., 2014	Intervention: Attended regularly scheduled visits with prenatal care provider. Received standard nutrition counselling, a 15 min face-to-face visit with study interventionist, and received study newsletters at 2 mo intervals during pregnancy and postpartum, and a behavioural lifestyle intervention according to the 1990 IOM guidelines (one face-to-face visit with an interventionist at the start of treatment, discussion related to weight gain during pregnancy, PA, and diet), body weight scales, food records, and pedometers were provided, weekly postcards were sent to promote healthy dietary change and increase physical activity, personalized graphs of weight gain with feedback, and at least three 10-15 min supportive phone calls. Comparator: CAU same as the intervention group.	Obstetric provider offices
38	Robinson-Whelen et al., 2006	Intervention: Modified based on the health promotion program developed by Hughes et al. (2003). Developed based on social learning theory (Bandura, 1977; Lorig and Holman, 1993) and the principles of feminism, empowerment, peer modelling and support, and advocacy (Currie and Wiesenberg, 2003; Hurdle, 2001; Nosek, 1996). Consisted of 8 sessions, focus on disability-sensitive action planning, PS, peer support, and role modelling. Contacted with a "buddy" ≤ 1/wk. Comparator: A mini workshop was offered after all data collection.	Flyers, newspaper advertisement, and on-site recruitment at health care, and community service centers
39	Samuel-Hodge et al., 2017	Intervention: Developed by the researchers according to the social interdependence and social support theories. Consisted of a 20, 120 min weekly group sessions for family dyads, contents include participant weigh-in, group sharing and PS; discussion of a weight control topic (diet, PA, or behavioral change), had the chance to try a different PA and/or taste-test a new food or recipe, and goal setting Comparator: Received one newsletter with program updates and were offered a 6 wk program after immediate posttreatment assessment	TV advertisements, email messages, flyers, and a clinical diabetes registry with referrals from diabetes care providers
40	Saxton et al., 2014	Intervention: Consisted of a 24 wk lifestyle intervention and 3 supervised physical activity sessions per week (each session lasted for 40-45 mins), an individualized hypocaloric healthy eating programme and written information, weekly small-group nutrition education seminars Comparator: Received a healthy eating booklet about keeping active, 3 PA sessions, general PA, and dietary advice were offered after the final follow-up.	Hospital, local cancer support services, local media, and word of mouth
41	Sebregts et al., 2005	Intervention: Developed by the research group based on 3 major long-term clinical trials the Recurrent Coronary Prevention Project, Project New Life, and the Lifestyle Heart Trial. Consisted of usual medical care, post-discharge PA training sessions, a 8 weekly 2.5 hr each stress management and health education program (partners were encouraged to join), audiocassette tape of breathing and relaxation and PA and homework assignments were offered Comparator: Usual medical care and post-discharge PA training sessions were offered.	Hospital
42	Spence et al. 2011	Intervention: Developed based on CBT and existing iCBT programs. Consisted of 7 online sessions, a summary/homework assignment, an online discussion forum, moderated by the therapist, regular automatic reminder and notification emails, instant messaging with a clinician, additional written resources, and telephone and email contact Comparator: Intervention similar to the intervention group was offered after immediately posttreatment	A website, newspaper advertisement, email newsletter

No.	Author, year	Treatment and comparator content	Recruitment
43	Spindler et al., 2019	Intervention: Provided with non-formalized personalized feedback, a Teledialog toolbox containing technology for the Teledialog project, access to an interactive web portal called ActiveHeart for 12 wk, one monitor visit, and contacted with the healthcare staff if needed Comparator: Offered a non-technology-based conventional cardiac rehabilitation program for 12 wk	Healthcare centers and hospitals
44	Sylvia et al., 2019	Intervention: Developed by the research group based on CBT principles. Consisted of 18 sessions with three modules (nutrition, physical activity, and wellness) Comparator: Received CAU and was offered the intervention after the waitlist period is completed	NR
45	Teut et al., 2013	Intervention: Developed by doctors, naturopath, and sport therapist. Consisted of a weekly 1 hr physical activity group, naturopathic care, freshly prepared fruit or vegetable juices, individualised homeopathic treatment, and conventional usual care was continued (modification of conventional medication if needed) Comparator: Received CAU by family physicians, specialists, nurses, physiotherapists, and occupational therapists	Apartment-sharing communities
46	Toobert et al., 2011	Intervention: Developed based on combined Social Cognitive Theory, Goal Systems, Social Ecological Theory and included social-environmental and multiple system factors. Consisted of a 2.5 days non- residential retreat and 4 hr weekly meetings. Comparator: Received usual care from their physicians	Primary care clinics
47	Tousman et al., 2011	Intervention: Developed by a research psychologist with lifelong asthma. 7 meetings (1 hr individual status report and 1 hr discussion topic except wk 1) and self-management behaviour homework assignments Comparator: No intervention	NR
48	van der Wulp et al., 2012	Intervention: Developed by means of intervention mapping. MI skills were used. Three 1 hr monthly home visits by the expert patients, telephone contact within 2 wk after each visit, received usual medical care from GP, practice nurse or dietician, and phone or email contacted with the expert patients if necessary. Comparator: Received same medical care as the intervention group	Referred by GP
49	Wang et al., 2017	Intervention: Received medical investigation and treatment, treatment-related nursing practices, and a 10-min brief discharge guide, one 30-40 min individualized face-to-face education, a lifestyle modification booklet, and six 20-30 min bi-weekly telephone follow-up contacts Comparator: Received CAU similar to the intervention group	Hospital
50	Ye et al., 2016	Intervention: 8 weekly sessions in the first 2 mo, 3 sessions at 2 mo, 6 mo, and 12 mo after intervention (3 hr for each session).Consisted of 3 weekly group discussion, 150 min individual sessions with a CP and 4 follow-up telephone sessions delivered by project nurses, and telephone contact from mentors ≤ 1/wk Comparator: Received any other treatment during the study, recommended medical therapies, received 8 weekly telephone contacts in the first 2 mo, 3 times at 2 mo, 6 mo, and 12 mo	Hospital

Note. CAD = Coronary Artery Disease; CAPE = Clifton assessment procedure for the elderly; CAU = Care-as-usual; CBT = Cognitive behavioral therapy; CP = Clinical psychologyist; FVC = Food value chain; hr = Hour; GP = General practitioner; iCBT = Internet-delivered cognitive behavioral therapy; MI = Motivational Interviewing; min = Minute; mo = Month; PA = Physical activity; PS = Problem sovling; TTM = The transtheoretical model; wk = Week.

Table 4. Risk of bias assessment performed by the revised Cochrane risk-of-bias tool for randomized trials (RoB 2).

No.	Author, year	Bias arising from the randomization process	Bias due to deviations from intended interventions	Bias due to missing outcome data	Bias in measurement of the outcome	Bias in selection of the reported result	Bias arising from identification or recruitment of individual participants within cluster	Overall risk of bias (total score)
1	Almeidaa et al., 2016	+	+	+	+	+	NA	+ (5)
2	Attux et al., 2013	+	+	+	?	?	NA	? (3)
3	Azami et al., 2018	+	+	+	+	+	NA	+ (5)
4	Brennan et al., 2012	+	-	+	-	+	NA	- (3)
5	Casañas et al., 2012	+	+	+	?	+	NA	? (4)
6	Chang et al., 2018	?	+	+	?	+	NA	? (3)
7	Charandabi et al., 2017	+	+	+	+	+	NA	+ (5)
8	Croker et al., 2012	+	+	+	+	+	NA	+ (5)
9	Dale et al., 2015	+	+	+	+	+	NA	+ (5)
10	Deitz et al., 2014	+	-	+	?	+	NA	- (3)
11	Diamond et al., 2015	+	?	+	+	+	NA	? (4)
12	Duan et al., 2017	?	-	+	?	+	NA	? (2)
13	Duan et al., 2018	?	-	+	?	+	NA	? (2)
14	Furuya et al., 2014	+	?	?	?	+	NA	? (2)
15	Ihle-Hansen et al., 2014	+	+	+	+	+	NA	+ (5)
16	Imayama et al., 2011	+	-	+	+	+	NA	- (3)
17	Inouye et al., 2014	?	-	+	-	+	NA	- (2)
18	Kim et al., 2011	-	-	+	?	+	NA	- (2)
19	Kwon, 2015	+	-	+	?	+	NA	- (3)
20	Lee et al., 2015	?	?	-	?	+	NA	? (1)
21	Leemrijse et al., 2016	?	?	+	+	+	NA	? (3)
22	Lovell et al., 2014	+	+	+	+	+	NA	+ (5)
23	Macken et al., 2014	?	?	+	+	+	NA	? (3)
24	Markomanolaki et al., 2019	+	+	+	+	+	NA	+ (5)
25	Melnyk et al., 2013	+	+	+	+	+	+	+ (6)
26	Melnyk et al., 2009	+	+	+	+	+	+	+ (6)
27	Mensorio et al., 2019	?	+	+	?	+	NA	? (3)
28	Meyer et al. 2009	+	-	+	?	+	NA	- (3)
29	Moncrieft et al., 2016	+	+	+	+	+	NA	+ (5)
30	Moseley et al., 2009	?	+	+	?	+	NA	? (3)

No.	Author, year	Bias arising from the randomization process	Bias due to deviations from intended interventions	Bias due to missing outcome data	Bias in measurement of the outcome	Bias in selection of the reported result	Bias arising from identification or recruitment of individual participants within cluster	Overall risk of bias (total score)
31	Ng et al., 2017	+	+	+	+	+	NA	+ (5)
32	Nie et al., 2019	+	+	+	+	+	NA	+ (5)
33	Nijamkin et al., 2013	?	+	+	?	+	NA	? (3)
34	O'Neil et al., 2014	+	+	+	?	+	NA	? (4)
35	O'Reilly et al., 2016	+	+	+	?	+	NA	? (4)
36	Pelekasis et al., 2016	+	?	-	?	+	NA	? (2)
37	Phelan et al., 2014	+	+	+	+	+	NA	+ (5)
38	Robinson-Whelen et al., 2006	?	-	+	?	+	NA	- (2)
39	Samuel-Hodge et al., 2017	?	?	+	?	+	NA	? (2)
40	Saxton et al., 2014	+	?	+	+	+	NA	? (4)
41	Sebregts et al., 2005	+	?	+	+	+	NA	? (4)
42	Spence et al. 2011	+	-	+	-	+	NA	- (3)
43	Spindler et al., 2019	+	?	+	?	+	NA	? (3)
44	Sylvia et al., 2019	-	-	+	+	+	NA	- (3)
45	Teut et al., 2013	+	+	+	+	+	+	+ (6)
46	Toobert et al., 2011	?	+	+	?	+	+	? (4)
47	Tousman et al., 2011	?	-	-	-	+	NA	- (1)
48	van der Wulp et al., 2012	+	?	+	?	+	NA	? (3)
49	Wang et al., 2017	+	?	-	+	+	NA	- (3)
50	Ye et al., 2016	?	?	+	?	+	NA	? (2)

Note. '-' = high risk of bias; '+' = low risk of bias; '?' = some concern.

Table 5. Moderator analyses performed by the subgroup analysis of the effect of lifestyle medicine intervention on depressive symptoms relative to a care as usual comparison at immediately posttreatment.

Moderator	Subgroups	Pooled standardized mean difference (95% CI)	*p*-value	*k*	Homogeneity
Number of lifestyle factors	Two lifestyle factors	-0.17 (-0.30, -0.05)	< .01**	16	$X^2 = 7.54$, df = 2, *p*
	Three lifestyle factors	-0.27 (-0.43, -0.12)	< .01**	14	< .05
	Four lifestyle factors	0.01 (-0.12, 0.15)	.85	3	
Disease condition	With major depressive disorder	-0.45 (-0.82, -0.09)	< .05*	2	$X^2 = 2.79$, df = 2, *p*
	With depressive symptoms	-0.30 (-0.60, -0.00)	< .05*	3	> .05
	Non-depressed	-0.16 (-0.26, -0.06)	< .01**	28	
Adoption of cognitive behavioral component	Yes	-0.24 (-0.36, -0.11)	< .001***	10	$X^2 = 0.38$, df = 1, *p* > .05
	No	-0.18 (-0.29, -0.06)	< .01**	23	
Mode of delivery	Face to face meeting	-0.21 (-0.37, -0.05)	< .05*	17	$X^2 = 3.12$, df = 5, *p* > .05
	Telephone contact	-0.22 (-0.36, -0.09)	< .01**	4	
	Face to face meeting, telephone contact	-0.23 (-0.42, -0.04)	< .05*	9	
	Website	0.03 (-0.39, 0.44)	.90	1	
	Face to face meeting, website	-0.21 (-0.45, 0.03)	.08	1	
	Face to face meeting, telephone contact, website	0.05 (-0.32, 0.41)	.80	1	
Risk of bias	Low	-0.17 (-0.39, -0.04)	< .05*	11	$X^2 = 4.37$, df = 2, *p*
	Some concerns	-0.22 (-0.28, -0.05)	< .01**	21	> .05
	High	-0.51 (-0.81, -0.21)	< .01**	1	

Note. ***p<.001, **p<.01, *p<.05.

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