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Review

Effectiveness of cognitive behavioral therapy for perinatal maternal depression, anxiety and stress: A systematic review and meta-analysis of randomized controlled trials

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ABSTRACT

Cognitive behavioral therapy (CBT) has been widely studied in prenatal or postnatal depression, with much less research on anxiety and stress. This meta-analysis aims to comprehensively evaluate CBT efficacy for perinatal depression, anxiety and stress in the short term (from baseline to immediately post-intervention) and in the long term (from baseline to the end of follow-up). Five databases were searched. We included 79 randomized controlled trials (RCTs) and quasi-RCTs assessing the efficacy of CBT during pregnancy and the first year postpartum. Primary outcome was the mean score change in depression, anxiety and stress. CBT-only and CBT plus other interventions were effective for perinatal maternal depression in the short term (SMD −0.69, 95% CI: −0.83, −0.55) and long term (SMD −0.59, 95% CI −0.75, −0.42). CBT-only had both short- and long-term efficacy for perinatal anxiety (short term: SMD −0.63, 95% CI −0.85, −0.42; long term: SMD −0.71, 95% CI −1.02, −0.39) and short-term efficacy for perinatal stress (SMD −0.96, 95% CI −1.40, −0.52). Overall, CBT was effective for perinatal maternal depression, anxiety and stress. CBT-only exhibited short-term efficacy for perinatal depression, anxiety and stress, and long-term efficacy for perinatal depression and anxiety. Subgroup analyses suggested that CBT-only was effective across a wide variety of modalities.

1. Introduction

The transition to parenthood, from conception to the first year after delivery, is a time of physical, social, financial and emotional changes that increase the risk for maternal mental health problems, such as depression, anxiety and stress (Clout & Brown, 2016; Seth, Lewis, & Galbally, 2016). Although symptoms of perinatal depression and anxiety are well known, stress is often operationalized as symptoms such as being overwhelmed or unable to relax. The present systematic review and meta-analysis looks at two forms of stress experienced by women during pregnancy: generalized stress resulting from experiences that exceed the women's ability to effectively cope, and post-traumatic stress disorder (PTSD) resulting from potentially life threatening events (e.g., traumatic childbirth). Recent epidemiological data estimated the prevalence of postnatal maternal depression, anxiety and PTSD at 17%, 15%, and 4%, respectively (Dennis, Falah-Hassani, & Shiri, 2017; Shorey et al., 2018; Yildiz, Ayers, & Phillips, 2017). During pregnancy, prevalence rates of 14.8% and 3.3% have been reported for maternal depression and PTSD, respectively (Nisar et al., 2020; Yildiz et al., 2017), and prevalence rates of maternal anxiety have been found to be 18.2% in the 1st trimester, 19.1% in the 2nd trimester and 24.6% in the 3rd trimester of pregnancy (Dennis et al., 2017). Finally, perinatal depression, anxiety, and PTSD comorbidity rates range from 2% to 3% (Agius, Xuereb, Carrick-Sen, Sultana, & Rankin, 2016). Pregnant women with depression and/or anxiety are more likely to experience mental health disorders during the postpartum period. Furthermore, women with prenatal depression and/or anxiety are at higher risk of poorer obstetric outcomes (e.g., pregnancy complications, preeclampsia) and

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suicidal behaviors (Grigoriadis et al., 2018; Kendig et al., 2017; Kim et al., 2013). Thus, various forms of distress during and after pregnancy are a significant public health concern.

Children exposed to prenatal maternal depression, anxiety and/or stress tend to have poorer birth outcomes (e.g., preterm birth, low birth weight, low APGAR scores) (Flynn, McBride, Cely, Wang, & DeCesare, 2015; Grigoriadis et al., 2018; Walsh et al., 2019). Prospectively, perinatal maternal mental health disorders have been linked to impaired physical, neurobehavioral, cognitive and emotional development during childhood that may persist into adulthood (Douros et al., 2017; Kingston & Tough, 2014; Manzari, Matvienko-Sikar, Baldoni, O'Keeffe, & Khashan, 2019; Pearson et al., 2013; Surkan, Kennedy, Hurley, & Black, 2011). Additionally, maternal mental health disorders can impact mother-infant interactions that, in turn, may hinder child development (Brummelte & Galea, 2016).

Given the high prevalence and deleterious impacts of perinatal maternal depression, anxiety and/or stress, there is great interest in identifying effective interventions. Existing research has demonstrated a wide range of therapeutic options including, but not limited to, medication, psychological interventions, mindfulness, relaxation and exercise (Davenport et al., 2018; Dennis & Dowswell, 2013; Smith, Shewamene, Galbally, Schmied, & Dahlen, 2019). Perinatal women often prefer non-pharmacological treatments like psychotherapy because of concerns about effects of medication on the child (Battle, Salisbury, Schofield, & Ortiz-Hernandez, 2013; Hagberg, Robijn, & Jick, 2018). Furthermore, there is accumulating evidence that psychotherapy is effective in treating perinatal depression (Clatworthy, 2012; Dennis, 2005; Dennis & Dowswell, 2013; Loughnan, Joubert, Grierson, Andrews, & Newby, 2019). Cognitive behavioral therapy (CBT) has been recommended as one of the first psychotherapy options for mild-to-moderate perinatal depression (Choate & Gintner, 2011; National Collaborating Centre for Mental Health UK, 2014).

CBT focuses on modifying maladaptive thoughts and cognitive distortions and changing behavioral patterns that maintain distress (Beck & Haigh, 2014). Specifically, cognitive restructuring is one component of CBT with the goal of identifying, evaluating and changing negative, distorted feelings and thoughts (Hope, Burns, Hayes, Herbert, & Warner, 2010). Behavioral activation, another component of CBT, is a functional analytical approach for increasing pleasant activities to maintain or improve psychological well-being (Cuijpers, van Straten, & Warmerdam, 2007). Relative to other therapeutic options, CBT can be provided in a wide variety of formats such as in-person group (women alone) format, in-person group (women and partners) format, in-person individual (women alone) format, in-person individual (women and partners) format, internet-based (women alone) format, telephone-based (women alone) format and workbook-based (women alone) format.

Previous systematic reviews have demonstrated the effectiveness of CBT for prenatal (Shortis, Warrington, & Whittaker, 2020) or postnatal maternal depression (Huang, Zhao, Qiang, & Fan, 2018; Nardi, Laurenzi, Di Nicolò, & Bellantuono, 2012; Perveen, Mahmood, Gosadi, Mehraj, & Sheikh, 2013; Roman, Constantin, & Bostan, 2020), but few meta-analytic studies have assessed CBT effectiveness in both prenatal and postnatal women (Sockol, 2015). Given the high prevalence of maternal depression during both pregnancy and postpartum (Rodriguez-Cabezas & Clark, 2018), and a continuum of depression from pregnancy into postpartum (Pampaka et al., 2019; Underwood, Waldie, D'Souza, Peterson, & Morton, 2016), and given accumulating CBT interventions that are delivered across this continuum (Burger et al., 2019; Milgrom, Schembri, Ericksen, Ross, & Gemmill, 2011; Ngai, Wong, Chung, Chau, & Hui, 2020), more research is needed to appraise the efficacy of CBT across both the prenatal and postnatal periods. Further, no meta-analysis has comprehensively examined both short-term (immediately post-intervention) and long-term (e.g., 3, 6 or 12 months post-intervention) efficacy of CBT. In addition, reviews of CBT for perinatal maternal mental health have mainly focused on depression, with much less attention paid to anxiety and stress. Finally, some clinical trials have integrated CBT within multimodal interventions (e.g., CBT + mindfulness; CBT + education + social support), but no meta-analysis has examined the differential efficacy of CBT combined with other interventions.

A further gap in the existing reviews of CBT for perinatal depression, anxiety and/or stress is failure to consider the variety of modalities potentially associated with the CBT effectiveness. A previous review (Sockol, 2015) demonstrated the relevance of modalities such as different intervention formats (group vs. individual) and differences in intervention timing (prenatal vs. postnatal vs. mixed) in CBT trials for perinatal depression. These factors have yet to be examined meta-analytically for perinatal anxiety and/or stress. To our knowledge, other intervention formats have not been examined, including internet-based format with women alone (Loughnan et al., 2019; Loughnan et al., 2019), workbook-based format with women alone (Austin et al., 2008; Lowndes, Egan, & McEvoy, 2019) and telephone-based format with women alone (Ngai, Wong, Leung, Chau, & Chung, 2015), which may influence the efficacy of CBT for perinatal depression, anxiety and/or stress. Delivery of interventions by specialists (e.g., psychologists) or non-specialists (e.g., nurses), number of intervention sessions and prevention or treatment interventions may also influence CBT effectiveness (Milgrom et al., 2011). Lastly, there have not been meta-analyses of CBT effectiveness specifically for perinatal depression, anxiety and/or stress in low-income women. In comparison to more affluent women, low-income women are much more vulnerable to perinatal mental health disorders, with prevalence rates of antenatal depression and anxiety as high as 41.7% (Luke et al., 2009) and 23% (van Heyningen et al., 2017), respectively, yet they are less likely to receive adequate perinatal care (Sidebottom, Hellerstedt, Harrison, & Jones-Webb, 2017).

To address the aforementioned gaps, the objectives of this systematic review and meta-analysis are to: a) review the existing literature on CBT-only and CBT + co-interventions (CBT-CI) for perinatal maternal depression, anxiety and stress, and evaluate their effectiveness; b) evaluate both short- and long-term efficacy of CBT-only and CBT-CI; c) examine the efficacy of specific types of CBT-CI; d) examine the efficacy of specific CBT-only modalities (i.e., intervention formats, intervention timing, prevention or treatment, specialists or non-specialists delivery and number of intervention sessions) and e) examine the efficacy of CBT-only among low-income perinatal women.

2. Methods

This meta-analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Moher, Liberati, Tetzlaff, & Altman, 2009) (see Supplementary S1).

2.1. Search strategy

PubMed, Embase, CINAHL, PsycINFO, and Cochrane Library electronic databases were searched from inception to April 20, 2020 using the following terms: (prenatal or maternal or pregnant or pregnancy or antenatal or prepartum or antepartum or postpartum or postnatal or puerperal or perinatal or peripartum) and (depression or anxiety or stress or distress or psychological or bereavement or partner violence or trauma) and (cognitive behavio* or CBT). Language was limited to English. An updated search was performed on November 15, 2021, using the same strategy. The detailed search strategy is presented in Supplementary S2. Additionally, we manually searched the reference lists of relevant reviews.

2.2. Inclusion and exclusion criteria

2.2.1. Participants

Trials were eligible for inclusion if they included women who 1) were pregnant or postpartum (i.e., within 12 months post-delivery) and 2) had risk factors for perinatal depression, anxiety and/or stress at

baseline (i.e., selective prevention), or exhibited early depressive, anxiety and/or stress signs that did not meet clinical diagnostic criteria or were below a cut-off indicative of significant symptoms at baseline (i.e., indicated prevention), or met clinical diagnostic criteria for depression, anxiety and/or stress or were above a cut-off indicative of significant symptoms at baseline (i.e., treatment). No limitation was placed on the symptom severity at baseline for treatment.

Trials were excluded if they included pregnant women who had a diagnosis of schizophrenia or bipolar disorder, had severe acute mental illnesses (i.e., requiring hospitalization or involving suicidal ideation), had known substance abuse problems, had an in vitro fertilization pregnancy, were overweight or obese, and/or had a high-risk pregnancy (i.e., in presence of diabetes, cancer, HIV/AIDS, or any other relevant chronic conditions).

2.2.2. Intervention group

Only trials of interventions explicitly stating the use of CBT that included a combination of cognitive and behavioral components were included. Trials of cognitive restructuring alone or behavioral activation alone were excluded. Trials on CBT-CI were also eligible. Trials were excluded if CBT was conducted during labor. No restriction was put on the intervention locations (e.g., hospital, home, clinic) or formats such as in-person group (women alone) format, in-person group (women and partners) format, in-person individual (women alone) format, in-person individual (women and partners) format, internet-based (women alone) format, telephone-based (women alone) format and workbook-based (women alone) format, or whether specialists (e.g., psychologists) delivered the intervention. Self-help guided/unguided interventions were also eligible for inclusion. Finally, both prevention interventions including selective and indicated prevention and treatment interventions (defined in Supplementary S4) were included.

2.2.3. Control group

Control groups include no-intervention control, treatment as usual (TAU), enhanced TAU, waitlist, attention controls (e.g., standard parenting education), informational booklet about TAU, or active controls. For active controls, only trials that allowed for the isolation of the effects of CBT were included. For example, a trial comparing CBT plus medication vs. medication alone was eligible, whereas CBT alone compared to medication alone was not.

2.2.4. Outcomes

The primary outcomes were short-term and long-term efficacy of CBT. Short-term efficacy was defined as mean score changes in depression, anxiety and stress symptoms from baseline (i.e., pre-intervention assessment) to immediately post-intervention. Long-term efficacy was defined as mean score changes in depression, anxiety and stress symptoms from baseline to the end of follow-up (~12 months). Depression, anxiety and stress symptoms were measured using various measurement scales. The hierarchy of symptom severity measurement scales used is listed in Supplementary Tables S1–S3. We prioritized self-rated scales over clinician-rated scales since the majority of trials included in the current meta-analysis reported maternal self-rated data.

2.2.5. Study design

Randomized controlled trials (RCTs) and quasi-RCTs (e.g., the allocation of participants to the CBT group or the control relying on methods that were not truly random) were eligible for inclusion in this systematic review and meta-analysis.

2.3. Data extraction

Two authors (XL and DPL) independently screened the full articles and then conducted the final selection of eligible trials. Data were extracted by two authors (XL and DPL). Discrepancies were resolved by discussion until consensus was reached. The extracted data included the name of the first author, publication year, country, study design, participant characteristics, diagnosis measures, intervention indication, types, formats and timing of CBT, CBT contents, intervention group, control group, and outcome measures. We contacted 15 corresponding authors for missing outcome information, and the authors of five trials replied and provided us with the missing data.

2.4. Quality assessment

Two authors (XL and VP) independently assessed the risk of bias of included trials using RevMan 5.3 (Cochrane Collaboration, London, UK) based on the Cochrane Collaboration's Risk of Bias Tool 5.1.0 (Higgins et al., 2011). The quality was assessed based on seven domains: 1) random sequence generation; 2) allocation concealment; 3) blinding of outcome assessment; 4) blinding of participants and personnel; 5) incomplete outcome data; 6) selective reporting and 7) other bias. Risk of bias was categorized as low, high or unclear. Disagreements about quality assessment were resolved by discussion until consensus was reached.

2.5. Statistical analysis

Statistical analyses were conducted using RevMan 5.3 (Cochrane Collaboration, London, UK) and STATA 15.0. Mean and standard deviation (SD) of the score changes from baseline to immediately post-intervention and to the end of follow-up were extracted directly or imputed based on the following formula: mean $= x_2 - x_1$ ($x_1$is the baseline mean score, $x_2$is immediately post-intervention or the end of follow-up mean score); SD $=\sqrt{SD_1{}^2 + SD_2{}^2 - (2 \times Corr \times SD_1 \times SD_2)}$ (SD_1 is the baseline SD, SD_2 is the immediately post-intervention or the end of follow-up SD). *Corr* (the correlation coefficient between baseline scores and final scores) was conservatively set at 0.5 as done in previous studies (Follmann, Elliott, Suh, & Cutler, 1992; Fukuta, Goto, Wakami, & Ohte, 2016). Mean difference (MD) between groups with 95% confidence interval (CI) was computed to examine CBT efficacy. Standardized mean difference (SMD) with 95% CI was calculated when different measurement scales were used for the same outcome. Differences were considered statistically significant when the 95% CI excludes 0, with significance threshold set at $p < 0.05$. When data could not be pooled, we evaluated individual trials narratively. Two of the eligible trials include more than one CBT arm (e.g., CBT delivered by nurses, CBT delivered by psychologists and TAU); data from these three arms were entered in the current meta-analysis as two separate comparisons (i.e. CBT delivered by nurses vs. TAU and CBT delivered by psychologists vs. TAU). To avoid counting the same women from the TAU arm twice, the sample size was halved in the two comparisons.

A random-effects model was used to pool trials with substantial heterogeneity (i.e., $I^2 \geq 50\%$ or $p < 0.05$). We also conducted subgroup analyses and meta-regression analyses to further identify the probable source of the heterogeneity. For CBT-only, the following subgroup analyses were performed: 1) different intervention formats including in-person group (women alone) format vs. in-person group (women and partners) format vs. in-person individual (women alone) format vs. in-person individual (women and partners) format vs. internet-based (women alone) format vs. telephone-based (women alone) format vs. workbook-based (women alone) format; 2) intervention timing (prenatal vs. postnatal vs. mixed); 3) selective prevention vs. indicated prevention vs. treatment; 4) the intervention delivered by specialists (e.g., psychologist) compared to the intervention with non-specialists (e.g., obstetrician, nurse, social worker, health visitor), mixed (both specialists and non-specialists) and unguided self-help intervention; 5) low-income women compared with women at general income levels (possibly including some low-income individuals, hereafter referred to as 'general population'); 6) depression, anxiety and stress assessed based on different measurement scales and 7) number of intervention sessions

(< 8 sessions vs. ≥ 8 sessions).

In addition, a subgroup analysis was conducted to evaluate different types of multimodal when CBT-CI was more effective than controls. Additional psycho-information (e.g., psychoeducation that introduces information about depression symptoms) provided within CBT sessions was not coded as a new intervention type. CBT-integrated intervention types such as relaxation, social support, mindfulness or antidepressant medication (ADM) were considered as multimodal.

If a trial did not provide sufficient information for classification in either subgroup, it was assigned to a third group named 'unspecified'. Tests for subgroup differences were conducted with statistical significance set at $p < 0.05$. In addition, meta-regression analyses for short-term efficacy were performed to test whether the efficacy of CBT-only or CBT-CI was related to time from baseline to the end of the intervention (i.e., the length of the intervention). Meta-regression analyses for long-term efficacy were conducted to test whether the efficacy of CBT-only or CBT-CI was related to 1) time from baseline to the end of follow-up; and 2) time from the end of the intervention to the end of follow-up. Meta-regression analyses were also conducted based on risk of bias of trials (low risk of bias was coded as "0"; unclear or high risk of bias was coded as "1") using the seven domains described in the Quality assessment section. To further test the stability of the results, sensitivity analyses were performed. Visual inspection of a funnel plot was used to assess publication bias when ≥10 trials were available (Terrin, Schmid, & Lau, 2005).

3. Results

3.1. Study selection

The flowchart of record inclusion/exclusion process is presented in Fig. 1. A total of 3348 records were identified from the databases, and 9 records were identified from the reference list of other reviews. After removal of 1595 duplicates, titles and abstracts of 1762 records were screened. After excluding 1615 irrelevant articles, full texts of 147 articles were assessed and 77 articles of these met criteria for inclusion.

3.2. Characteristics of included trials

Characteristics of the 77 articles (79 trials, n = 11,221 women) included in the current systematic review are presented in Supplementary Table S4. Among these articles, 66 articles (68 trials) (see Supplementary S3) were included in the meta-analysis while 11 were excluded due to unavailable outcome data. Most trials were RCTs, and six were quasi-RCTs. Interventions can be divided into selective prevention (10 trials), indicated prevention (8 trials) and treatment (61 trials). Forty-two trials examined CBT conducted during pregnancy only, 33 trials examined CBT conducted during the postnatal period only, and four trials examined CBT conducted during both pregnancy and the postnatal period. Intervention groups ranged from 1 to 15 sessions, and the interventions included CBT-only (59 trials) and CBT-CI (20 trials). For control groups, the most common comparator was TAU (52 trials), followed by waitlist (12 trials), attention control (5 trials), active control (4 trials), enhanced TAU (2 trials), informational booklet (3 trials) and no-

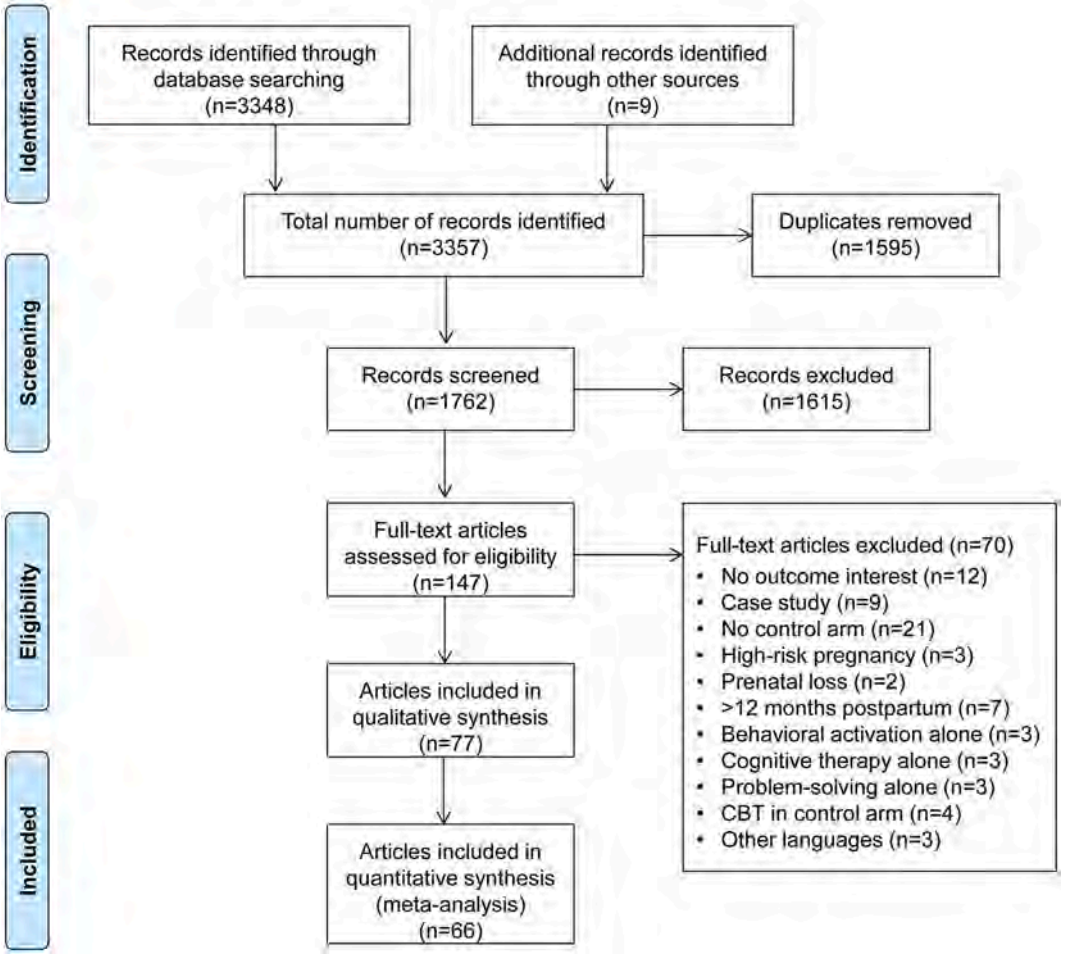

Fig. 1. Flowchart of record selection process. n indicates the number of records. CBT = cognitive behavioral therapy.

intervention control (1 trial).

3.3. Quality assessment

Risks of bias of the 79 trials are presented in Supplementary Figs. S1 and S2.

3.3.1. Selection bias

Most trials (52/79; 65.8%) had low risk of bias from the randomization process. Unclear risk of random sequence generation was found in 30.4% (24/79) of the trials because they did not mention how the randomization procedure was conducted. Three (3.8%) trials utilized inappropriate randomization (i.e., based on even or odd numbers, or receiving prenatal care before randomization). The risk of allocation concealment was low in 37 (46.8%) trials, unclear in 36 (45.6%) trials and high in 6 (7.6%) trials.

3.3.2. Performance bias

Given the nature of the CBT, participants and personnel could not be blinded to the intervention condition they were assigned (e.g., CBT vs. waitlist, CBT vs. TAU). Thus, the majority of trials (52/79; 65.8%) were subject to high risk of performance bias.

3.3.3. Detection bias

Unclear or high risk of detection bias was observed in most (51/79; 64.6%) trials in which outcomes relied on self-rated measures (participants themselves) as they were not blinded to the intervention allocation. However, in 35.4% (28/79) of trials, self-rating participants were blinded to the hypotheses, or outcomes were rated by clinicians blinded to allocation.

3.3.4. Attrition bias

The risk of attrition bias was low in more than half (47/79; 59.5%) of the trials, and high in 22.8% (18/79) of the trials. To deal with missing outcome data, nearly half (37/79; 46.8%) of the trials utilized intention-to-treat analysis, which avoided exaggerated effect estimates that typically stem from analyses restricted to intervention completers (Porta, Bonet, & Cobo, 2007).

3.3.5. Reporting bias

Forty-five (57.0%) trials in which outcomes were reported as predefined had a low-risk bias of selective reporting, while the risk was unclear in 41.8% (33/79) trials that did not provide enough information to allow a determination of bias. No high risk of bias was observed across the trials.

3.3.6. Other bias

About half (41/79; 51.9%) of the trials had unclear risk of other biases. Five trials (6.3%) exhibited high risk of bias from baseline imbalance.

3.4. Effects summary

Effect sizes for CBT-only, CBT-only modalities, CBT-CI, and main types of CBT-CI on perinatal maternal depression, anxiety and stress, are summarized in Supplementary Table S5.

3.5. Depression

3.5.1. Short-term efficacy

Overall, 54 trials ($n = 5393$) were included in the meta-analysis. CBT significantly improved symptoms of perinatal maternal depression compared to controls: SMD = −0.69, 95% CI: −0.83 to −0.55, $I^2 = 81\%$ (Fig. 2). The reduction of depression levels was larger in the CBT-only group compared to the control group (41 trials, $n = 4182$, SMD = −0.67, 95% CI -0.81 to −0.52, $I^2 = 79\%$). The CBT-CI group also had a greater improvement in depression compared to the control group (13 trials, $n = 1211$, SMD: −0.79, 95% CI −1.15 to −0.43, $I^2 = 87\%$). The estimate for subgroup differences between CBT-only and CBT-CI was nonsignificant ($p = 0.54$). Three CBT-only trials (Cooper, Murray, Wilson, & Romaniuk, 2003; Meager & Milgrom, 1996; Wozney et al., 2017) were not included in the meta-analysis due to unavailable means and SDs; these three trials reported that CBT-only was superior to controls. Specifically, a pilot RCT (Meager & Milgrom, 1996) showed that depression scores were lower in the CBT-only group compared to TAU at post-intervention, and a similar result was reported by Cooper et al. (2003). Another trial (Wozney et al., 2017) showed that participants were 1.5 times more likely to experience remission following CBT-only compared to waitlist.

3.5.1.1. Subgroup analyses. All predefined subgroup analyses on CBT-only could be conducted (see Supplementary Figs. S3–S9). Stratification by intervention formats showed that, compared to controls, in-person group (women alone), in-person group (women and partners), in-person individual (women alone), in-person individual (women and partners), workbook-based (women alone), internet-based (women alone) and telephone-based (women alone) CBT-only were more effective in reducing depression levels (Fig. S3). Selective prevention, indicated prevention and treatment CBT-only conducted during pregnancy, postpartum and both, showed significant reduction in depression levels compared to controls (Figs. S4 and S5). CBT-only delivered by specialists, non-specialists and both were all effective, whereas unguided CBT did not significantly reduce depression levels compared with controls (Fig. S6). Additionally, CBT-only significantly reduced depression symptoms relative to controls among low-income perinatal women (Fig. S7). Finally, CBT-only was associated with larger decreases in depression levels compared to controls regardless of measurement scales and number of sessions (Figs. S8 and S9). As for CBT-CI subgroups, CBT + mindfulness, CBT + third-wave approaches and CBT + education + relaxation had larger reductions in depression levels compared with controls while there were no significant differences for CBT + ADM (Fig. S10).

3.5.1.2. Meta-regression. The length of the intervention was unrelated to the efficacy of CBT-only or CBT-CI (Table S6). For risk of bias in each domain, the lower the risk of bias in the allocation concealment domain, the higher the CBT-only efficacy (regression coefficient = −0.358, 95% CI -0.705 to −0.010, $p = 0.044$). The CBT-only or CBT-CI efficacy was not affected by risk of biases in any of the other six domains (Table S7).

3.5.1.3. Publication bias. The asymmetry of the funnel plot revealed a possible publication bias (Fig. S11). We applied the "trim-and-fill" method (Duval & Tweedie, 2000) to test and adjust for the publication bias. The results of the "Trim-and-fill" analysis indicated that five trials were missing. If these five trials were included in the meta-analysis, the funnel plot would have been more symmetrical. Despite this, the filled pooled estimate based on 59 trials (SMD = −0.79, 95% CI -0.94 to −0.65) yielded a similar effect size.

3.5.1.4. Sensitivity analysis. We performed sensitivity analyses by omitting trials one by one and compared the new estimate after omitting one trial with the overall effect size (95%CI) to test the stability of each trial. Each new estimate was similar to the overall estimate and remained significant (Fig. S12).

3.5.2. Long-term efficacy

A total of 37 trials ($n = 4374$) were included in the meta-analysis (follow-up length: 4.95 ± 3.77 months). Overall, CBT led to significant long-term reductions in depression levels compared to controls: SMD = −0.59, 95% CI -0.75 to −0.42, $I^2 = 84\%$ (Fig. 3). In comparison with controls, both CBT-only (28 trials, SMD = −0.54, 95% CI -0.73 to

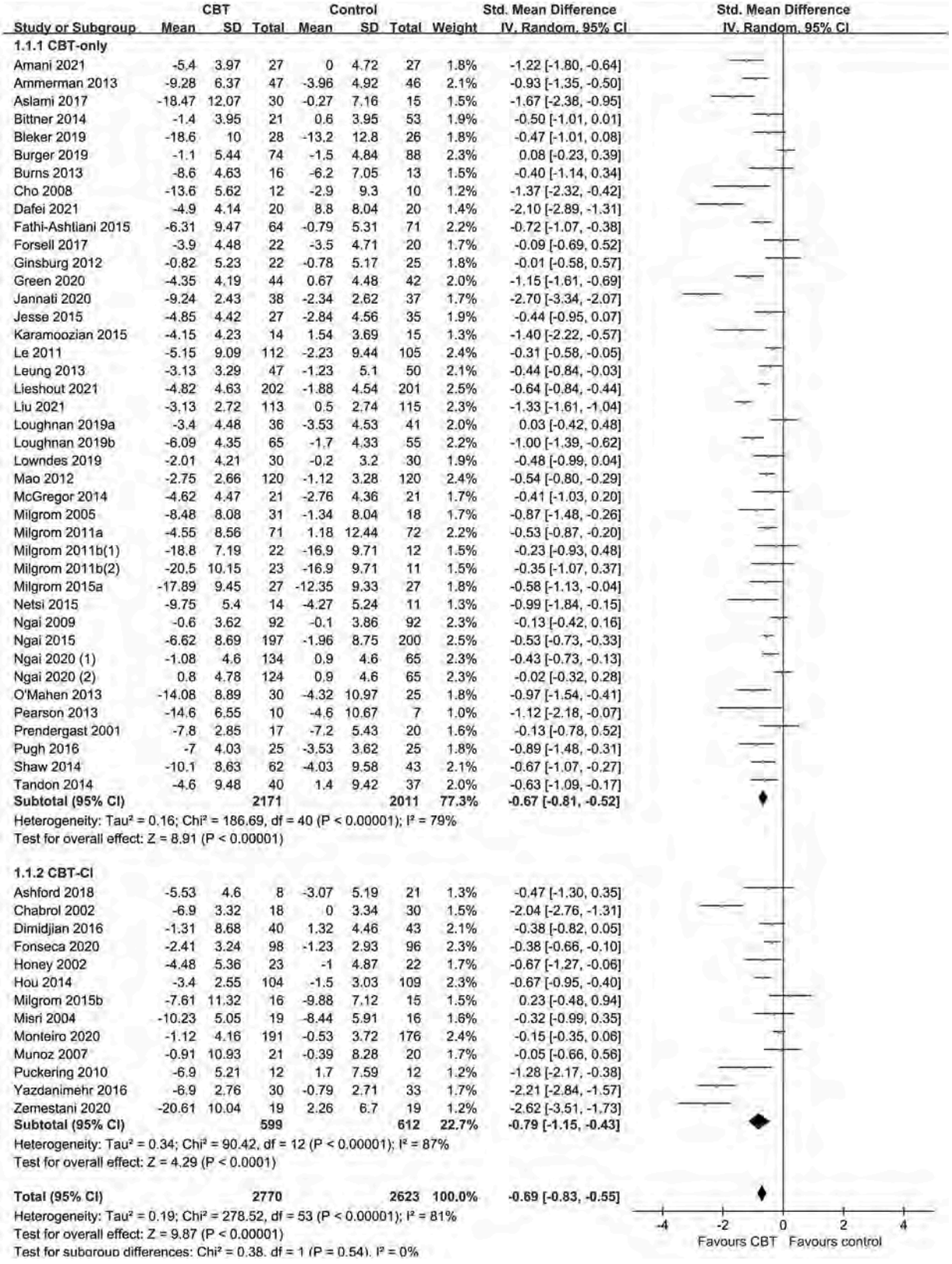

Fig. 2. Forest plot of short-term efficacy of CBT for perinatal maternal depression compared with controls. Subgroup analyses were conducted based on CBT-only and CBT-CI in random effects model. Effect sizes are Std. Mean Difference (95% CI) presented in subtotal for CBT-only, subtotal for CBT-CI and total for CBT. The negative Std. Mean Difference (−0.67) with 95% CI excluding 0 (−0.81, −0.52) indicates the superiority of CBT-only over controls. The negative Std. Mean Difference (−0.79) with 95% CI excluding 0 (−1.15, −0.43) indicates the superiority of CBT-CI over controls. The negative Std. Mean Difference (−0.69) with 95% CI excluding 0 (−0.83, −0.55) indicates an overall superiority of CBT over controls. CBT = cognitive behavioral therapy, CBT-CI = cognitive behavioral therapy + co-interventions, CI = confidence interval, IV = inverse variance, SD = standard deviation.

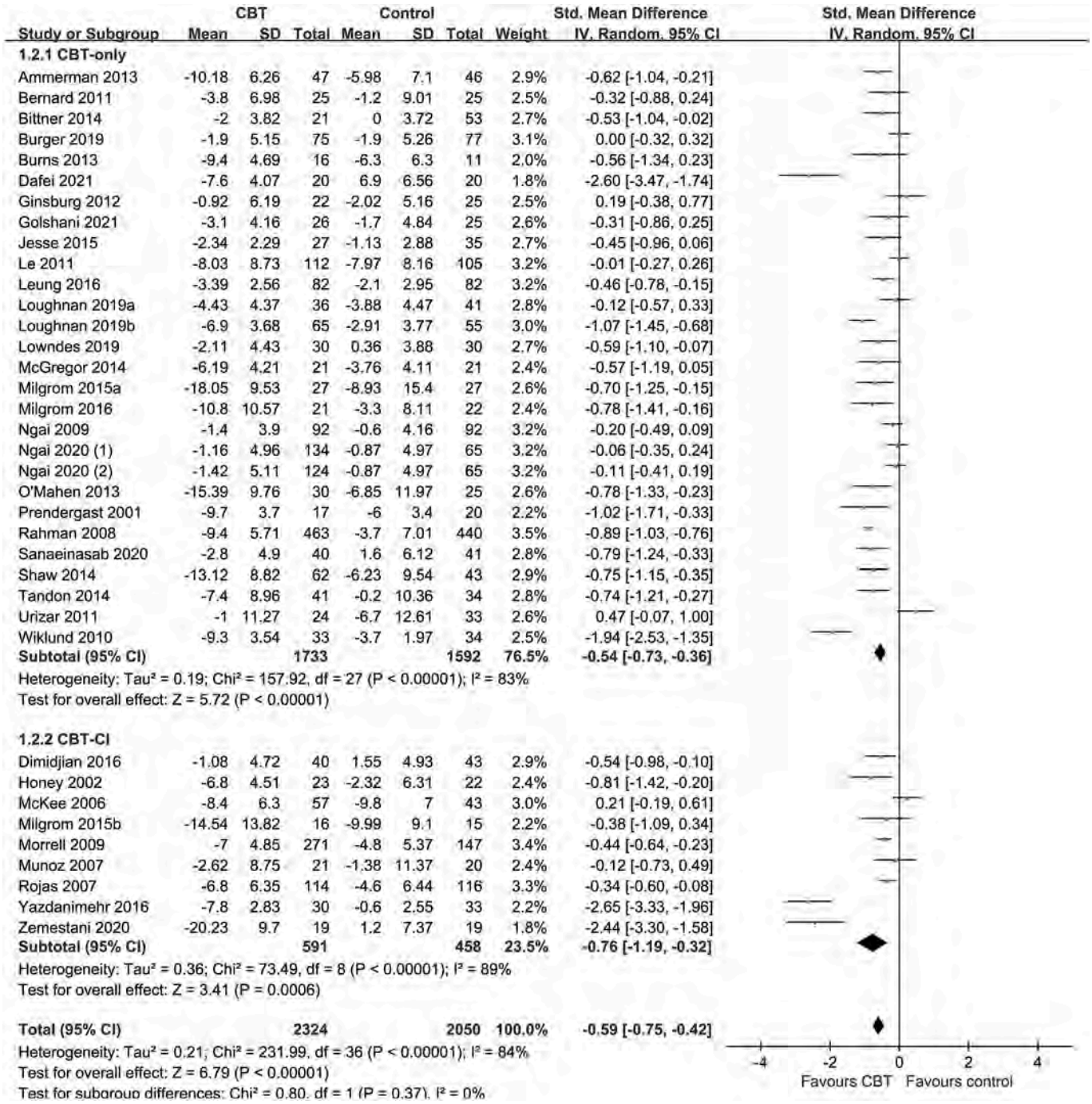

Fig. 3. Forest plot of long-term efficacy of CBT for perinatal maternal depression compared with controls. Subgroup analyses were conducted based on CBT-only and CBT-CI in random effects model. Effect sizes are Std. Mean Difference (95% CI) presented in subtotal for CBT-only, subtotal for CBT-CI and total for CBT. The negative Std. Mean Difference (−0.54) with 95% CI excluding 0 (−0.73, −0.36) indicates the superiority of CBT-only over controls. The negative Std. Mean Difference (−0.76) with 95% CI excluding 0 (−1.19, −0.32) indicates the superiority of CBT-CI over controls. The negative Std. Mean Difference (−0.59) with 95% CI excluding 0 (−0.75, −0.42) indicates an overall superiority of CBT over controls. CBT = cognitive behavioral therapy, CBT-CI = cognitive behavioral therapy + co-interventions, CI = confidence interval, IV = inverse variance, SD = standard deviation.

−0.36, I^2 = 83%) and CBT-CI (9 trials, SMD = −0.76, 95% CI -1.19 to −0.32, I^2 = 89%) were associated with greater improvement in depression symptoms. Eight trials (CBT-only: 6 trials; CBT-CI: 2 trials) could not be included in the meta-analysis due to unavailable outcome data, and the findings from these eight trials were mixed. On the one hand, two CBT-only trials (Austin et al., 2008; Hagan, Evans, & Pope, 2004) and one multimodal trial (George, Kumar, & Girish, 2020) reported that prenatal CBT did not decrease the number of women with postnatal depression. Similarly, no significant benefits of CBT-only on preventing or treating postnatal depression were observed by Barrera et al. (2015) and by Cooper et al. (2003). On the other hand, CBT-only (Ramezani, Khosravi, Motaghi, Hamidzadeh, & Mousavi, 2017) and CBT plus interpersonal psychotherapy (IPT) (Kozinszky et al., 2012) during pregnancy significantly reduced the risk for postpartum depression. Two CBT-only trials also showed long-term efficacy at postpartum (Abdollahpour, Keramat, Mousavi, & Khosravi, 2018; Wozney et al., 2017). Specifically, one trial reported the mean depression levels of the CBT-only group were lower than the control group 4 months after

delivery (Abdollahpour et al., 2018), and the other reported mothers treated with CBT only were 12.5 times as likely to experience remission at 12 months postpartum (Wozney et al., 2017).

3.5.2.1. Subgroup analyses. All predefined subgroup analyses on CBT-only could be conducted (see Supplementary Figs. S13–S19). First, in-person group (women alone), in-person individual with and without partner involvement, workbook-based (women alone) and internet-based (women alone) formats showed superiority over controls, while no significant differences were observed between the in-person group (women and partners) format and controls (1 trial only) (Fig. S13). For the remaining subgroup analyses, CBT-only showed greater reductions in depression levels compared with controls whether it occurred during pregnancy or postpartum (Fig. S14), or whether it was selective prevention, indicated prevention or treatment (Fig. S15). CBT-only delivered by specialists, non-specialists and both were all associated with greater improvements in depressive symptoms compared with controls, while the effects of unguided CBT-only did not exhibit improvements in symptoms relative to controls (Fig. S16). CBT-only did not significantly reduce depression levels in low-income perinatal women (Fig. S17). Additionally, CBT-only was associated with larger decreases in depression levels assessed by the Edinburgh Postnatal Depression Scale, Depression Anxiety Stress Scale (DASS) and Hamilton Depression Rating Scale while trials that used either the Beck Depression Inventory II or Center for Epidemiological Studies Depression Scale failed to show significant reductions in depression compared to controls (Fig. S18).

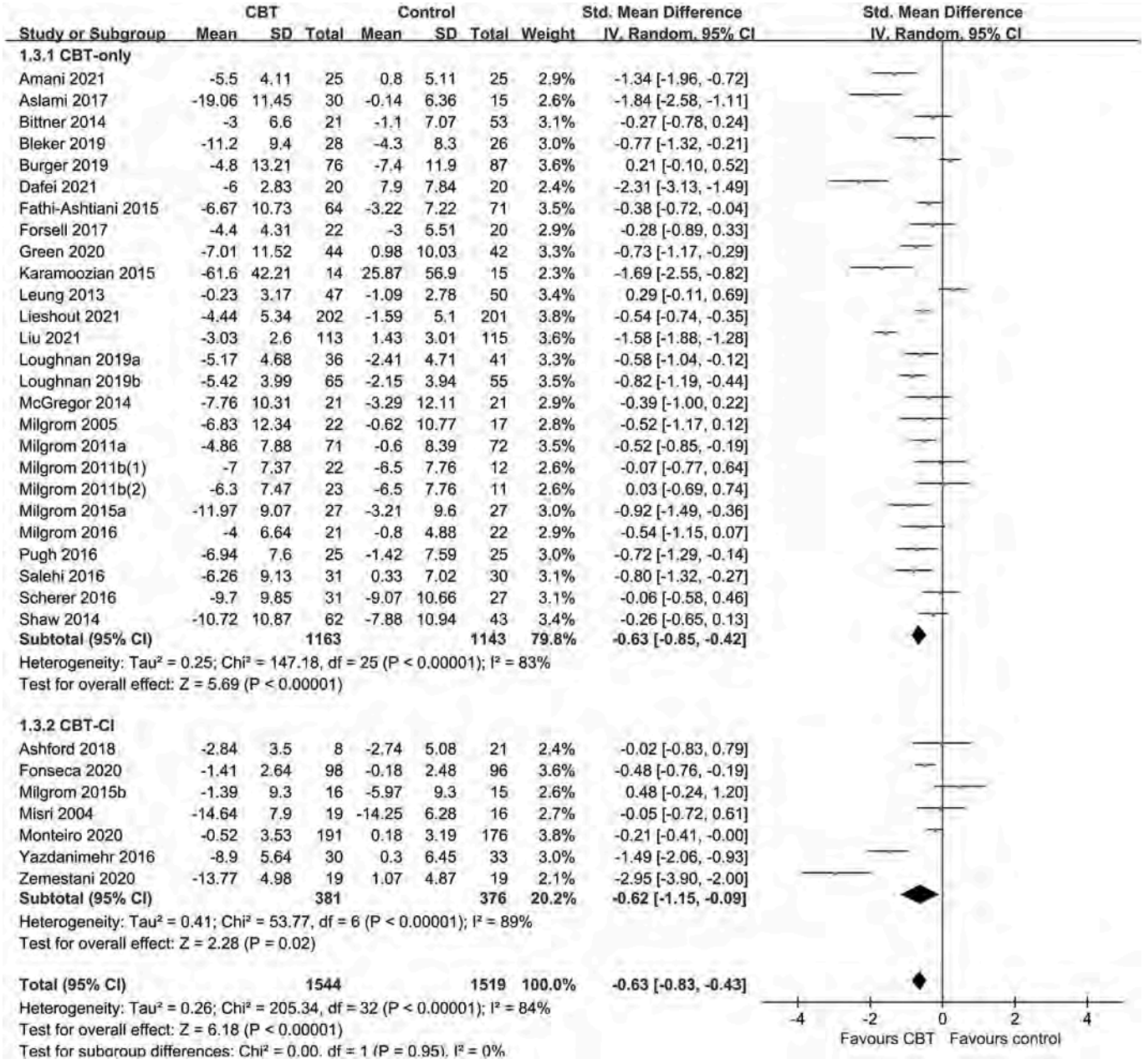

Fig. 4. Forest plot of short-term efficacy of CBT for perinatal maternal anxiety compared with controls. Subgroup analyses were conducted based on CBT-only and CBT-CI in random effects model. Effect sizes are Std. Mean Difference (95% CI) presented in subtotal for CBT-only, subtotal for CBT-CI and total for CBT. The negative Std. Mean Difference (−0.63) with 95% CI excluding 0 (−0.85, −0.42) indicates the superiority of CBT-only over controls. The negative Std. Mean Difference (−0.62) with 95% CI including 0 (−1.15, −0.09) indicates no difference between CBT-CI and controls. The negative Std. Mean Difference (−0.63) with 95% CI excluding 0 (−0.83, −0.43) indicates an overall superiority of CBT over controls. CBT = cognitive behavioral therapy, CBT-CI = cognitive behavioral therapy + co-interventions, CI = confidence interval, IV = inverse variance, SD = standard deviation.

Finally, CBT-only displayed superiority over controls regardless of number of sessions (Fig. S19). For trials of CBT-CI, CBT + mindfulness, CBT + education + relaxation and CBT + person-centered approach were superior to control conditions in reducing depression levels, while there was no significant efficacy in reducing depression levels for CBT + ADM or CBT + education + social support (Fig. S20).

3.5.2.2. Meta-regression. Neither time from baseline to the end of follow-up nor time from the end of the intervention to the end of follow-up was related to the efficacy of CBT-only or CBT-CI (Table S6). The efficacy of CBT-only or CBT-CI was not affected by risk of biases in any of the seven domains (Table S7).

3.5.2.3. Publication bias. The funnel plot appeared to be asymmetrical (Fig. S21). "Trim-and-fill" analysis indicated that nine trials were missing. If these nine trials were included in the meta-analysis, the funnel plot would have been more symmetrical. The filled pooled estimate based on 46 trials (SMD = −0.81, 95% CI -1.02 to −0.60) was similar to the original effect size.

3.5.2.4. Sensitivity analysis. The long-term efficacy of CBT for perinatal depression was also stable (Fig. S22).

3.6. Anxiety

3.6.1. Short-term efficacy

A total of 33 RCTs ($n = 3063$) were eligible for inclusion in the meta-analysis, which showed a significant reduction in anxiety levels (SMD = −0.63, 95% CI -0.83 to −0.43, $I^2 = 84\%$) for CBT compared to controls (Fig. 4). Anxiety levels were significantly reduced following CBT-only (SMD = −0.63, 95% CI -0.85 to −0.42, $I^2 = 83\%$) and CBT-CI (SMD = −0.62, 95% CI -1.15 to −0.09, $I^2 = 89\%$). Of the 10 trials that were excluded from the meta-analysis due to unavailability of outcome data, none reported outcomes for short-term anxiety symptoms.

3.6.1.1. Subgroup analyses. Six subgroup analyses on CBT-only could be conducted (see Supplementary Figs. S23–S28). In-person group (women alone), internet-based (women alone) and workbook-based (women alone) CBT-only exhibited greater improvements in anxiety symptoms compared to controls (Fig. S23). There was no difference between in-person individual (women alone) or in-person group (women and partners) CBT-only and controls whereas in-person individual (women and partners) CBT-only showed significant improvement in anxiety symptoms (Fig. S23). CBT-only delivered during prenatal and postnatal periods was more effective than controls in reducing anxiety levels (Fig. S24). Both indicated prevention and treatment interventions were associated with reduced anxiety levels compared with controls (Fig. S25). CBT-only delivered by specialists and by non-specialists, and unguided CBT-only had larger reduction in anxiety levels compared to controls (Fig. S26). CBT-only was associated with larger reductions when anxiety was assessed by the Beck Anxiety Inventory (BAI), State-Trait Anxiety Inventory-State (STAI-S), DASS-21 or General Anxiety Disorder-7 (GAD-7), however CBT-only demonstrated no advantage over controls when anxiety was assessed using the State-Trait Anxiety Inventory (STAI) or Anxiety Subscale of Hospital Anxiety and Depression Scale (Fig. S27). Finally, CBT-only displayed superiority over controls regardless of number of sessions (Fig. S28). For trials of CBT-CI, CBT + mindfulness and CBT + third-wave approaches were superior to control conditions in reducing anxiety levels, while there was no significant efficacy in reducing anxiety levels for CBT + ADM (Fig. S29).

3.6.1.2. Meta-regression. The efficacy of CBT-only or CBT-CI was not affected by the length of the intervention (Table S6). The efficacy of CBT-only or CBT-CI was not affected by risk of biases in any of the seven domains (Table S7)

3.6.1.3. Publication bias. While the funnel plot appeared to be asymmetrical (Fig. S30), Egger's test indicated no significant publication bias ($p = 0.258$). The "trim-and-fill" method indicated that four trials were missing. The filled pooled estimate based on 37 trials (SMD = −0.77, 95% CI: −0.99 to −0.55) was similar to the original estimate.

3.6.1.4. Sensitivity analysis. After omitting trials one by one, the estimate remained significant for combined CBT-only and CBT-CI (Fig. S31A), CBT-only (Fig. S31B), but not for CBT-CI (Fig. S31C), suggesting that the efficacy of overall CBT and CBT-only was stable while the efficacy of CBT-CI was not stable.

3.6.2. Long-term efficacy

In total, 13 RCTs ($n = 919$) were included in the meta-analysis of long-term efficacy (follow-up length: 2.50 ± 2.46 months). The reduction in anxiety levels was significantly larger in the CBT group than in the control group (SMD = −0.79, 95% CI -1.16 to −0.43, $I^2 = 85\%$) (Fig. 5). Of these, CBT-only was associated with greater anxiety relief than controls (SMD: -0.71, 95% CI -1.02 to −0.39, $I^2 = 77\%$) while CBT-CI did not significantly reduce anxiety levels (SMD: -1.10, 95% CI -2.87 to 0.67, $I^2 = 95\%$). One CBT-only trial that could not be included in the meta-analysis reported no difference in the incidence of postnatal anxiety between the CBT-only delivered during pregnancy and controls (Austin et al., 2008).

3.6.2.1. Subgroup analyses. Six CBT-only subgroup analyses could be conducted (see Supplementary Figs. S32–S37). Compared to controls, in-person group format with and without partner involvement, internet-based (women alone) format, but not in-person individual (women alone) format, significantly reduced anxiety levels (Fig. S32). Compared to controls, CBT-only conducted during pregnancy and postpartum was associated with anxiety score reduction compared to controls, while CBT-only conducted across both pregnancy and postpartum did not significantly reduce anxiety levels (Fig. S33). Indicated prevention interventions did not significantly reduce anxiety levels while treatment interventions were associated with reduced anxiety levels compared with controls (Fig. S34). Unguided CBT-only, but not CBT-only delivered by specialists or by non-specialists, yielded larger reduction in anxiety levels compared to controls (Fig. S35). CBT-only was associated with symptom reductions compared to controls when anxiety was assessed using BAI and GAD-7; however, no advantage of CBT-only was found when anxiety was assessed using DASS-21, STAI or STAI-S (Fig. S36). Lastly, CBT-only <8 sessions significantly reduced anxiety levels compared to controls (Fig. S37).

3.6.2.2. Meta-regression. The efficacy of CBT-only was not affected by time from baseline to the end of follow-up (Table S6). The longer the time from the end of the intervention to the end of follow-up, the higher CBT-only efficacy (regression coefficient = 0.030, 95% CI 0.005 to 0.055, $p = 0.024$). CBT-only efficacy was not affected by risk of biases in any of the seven domains (Table S7).

3.6.2.3. Publication bias. The funnel plot appeared to be symmetrical (Fig. S38), and Egger's test indicated no significant publication bias ($p = 0.246$). The "trim-and-fill" method indicated no missing trials.

3.6.2.4. Sensitivity analysis. After omitting trials one by one, the estimate remained significant for combined CBT-only and CBT-CI (Fig. S39A) and CBT-only (Fig. S39B).

3.7. Stress

3.7.1. Short-term efficacy

Eight RCTs ($n = 481$) were included in the meta-analysis. Overall, stress levels were reduced following CBT: SMD = −0.89, 95% CI: −1.30

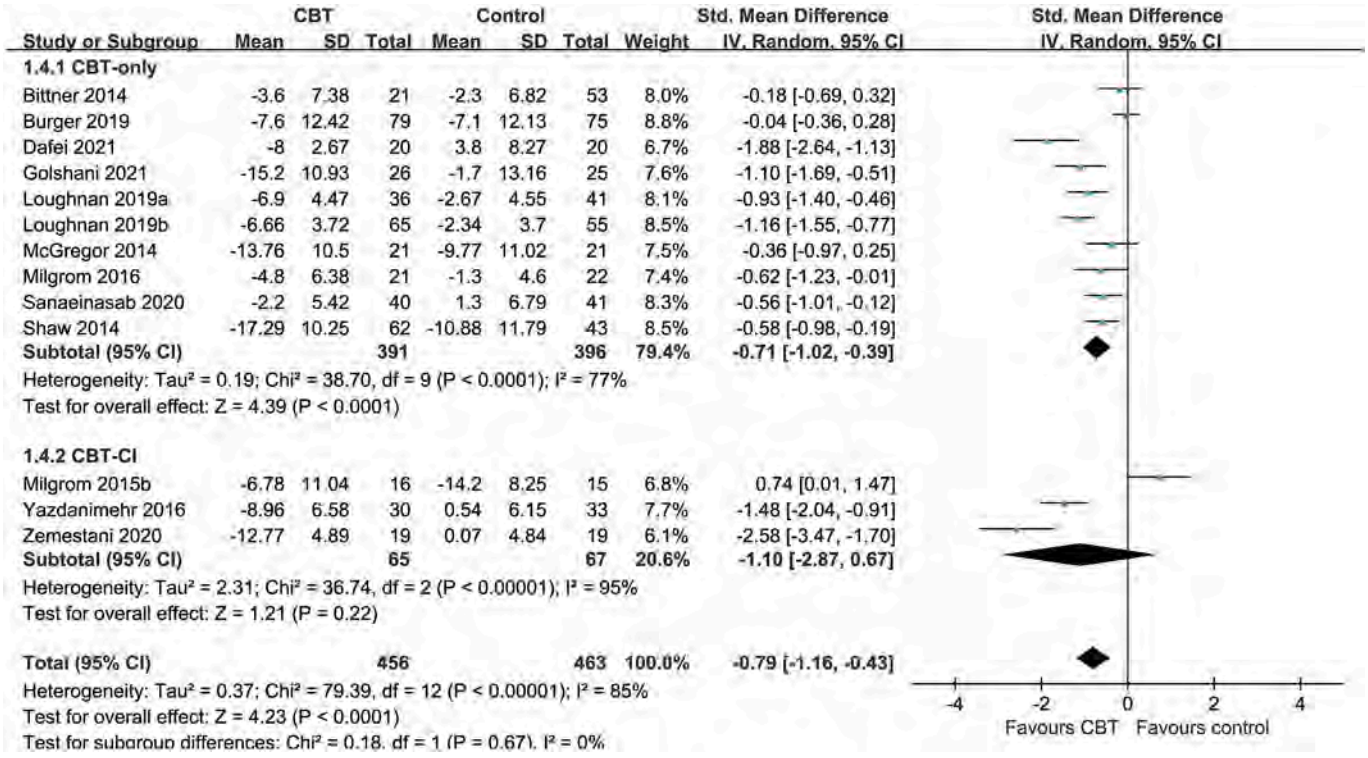

Fig. 5. Forest plot of long-term efficacy of CBT for perinatal maternal anxiety compared with controls. Subgroup analyses were conducted based on CBT-only and CBT-CI in random effects model. Effect sizes are Std. Mean Difference (95% CI) presented in subtotal for CBT-only, subtotal for CBT-CI and total for CBT. The negative Std. Mean Difference (−0.71) with 95% CI excluding 0 (−1.02, −0.39) indicates the superiority of CBT-only over controls. The negative Std. Mean Difference (−1.10) with 95% CI including 0 (−2.87, 0.67) indicates no difference between CBT-CI and controls. The negative Std. Mean Difference (−0.79) with 95% CI excluding 0 (−1.16, −0.43) indicates an overall superiority of CBT over controls. CBT = cognitive behavioral therapy, CBT-CI = cognitive behavioral therapy + co-interventions, CI = confidence interval, IV = inverse variance, SD = standard deviation.

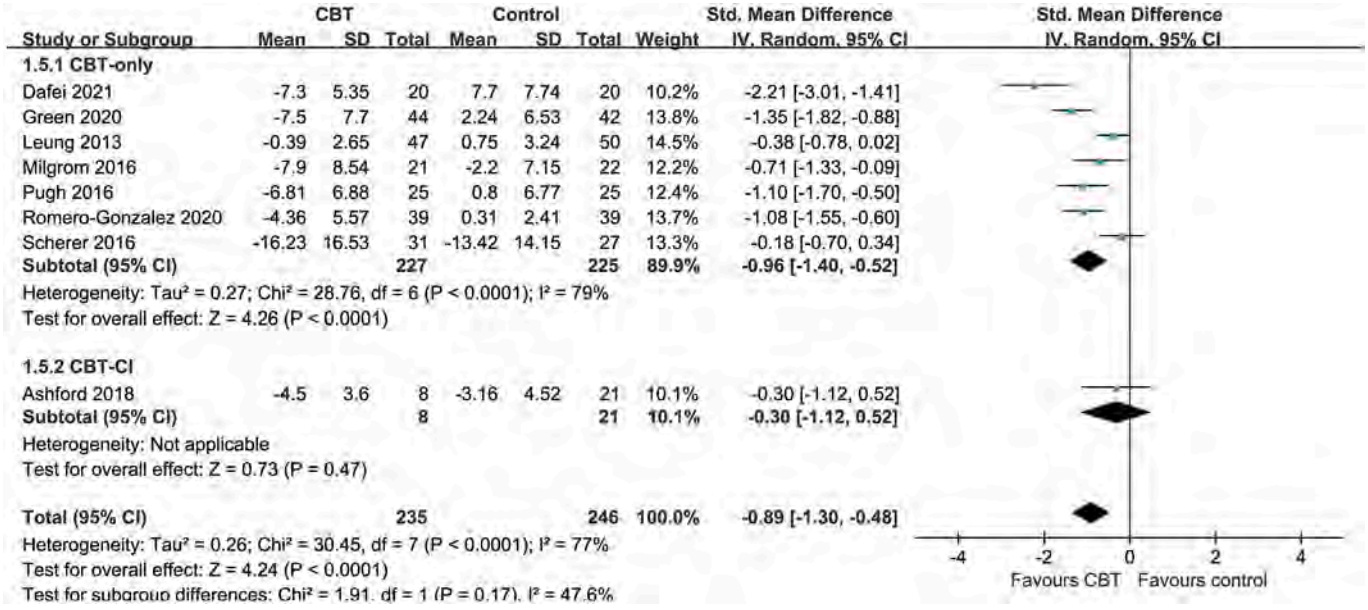

Fig. 6. Forest plot of short-term efficacy of CBT for perinatal maternal stress compared with controls. Subgroup analyses were conducted based on CBT-only and CBT-CI in random effects model. Effect sizes are Std. Mean Difference (95% CI) presented in subtotal for CBT-only, subtotal for CBT-CI and total for CBT. The negative Std. Mean Difference (−0.96) with 95% CI excluding 0 (−1.40, −0.52) indicates the superiority of CBT-only over controls. The negative Std. Mean Difference (−0.30) with 95% CI including 0 (−1.12, 0.52) indicates no difference between CBT-CI and controls. The negative Std. Mean Difference (−0.89) with 95% CI excluding 0 (−1.30, −0.48) indicates an overall superiority of CBT over controls. CBT = cognitive behavioral therapy, CBT-CI = cognitive behavioral therapy + co-interventions, CI = confidence interval, IV = inverse variance, SD = standard deviation.

to −0.48, $I^2 = 77\%$ (Fig. 6). CBT-only was associated with larger stress level reductions compared to controls (SMD = −0.96, 95% CI: −1.40 to −0.52, $I^2 = 79\%$) while no significant difference in symptom reduction was detected between CBT-CI and controls (SMD = −0.30, 95% CI: −1.12 to 0.52). One trial could not be included in the meta-analysis, although its results supported the efficacy of CBT-only intervention (Kaboli et al., 2017).

3.7.1.1. Subgroup analyses. Six CBT-only subgroup analyses were conducted (see Supplementary Figs. S40–S45). In-person group format with and without partner involvement and internet-based (women alone) format significantly reduced stress levels compared to controls (Fig. S40). CBT-only delivered during pregnancy, postpartum, across both pregnancy and postpartum periods was associated with reductions of stress levels (Fig. S41). CBT-only as selective prevention, indicated prevention and treatment reduced stress levels compared to controls (Fig. S42). CBT-only delivered by specialists, but not by non-specialists, led to greater reductions in stress levels compared to controls (Fig. S43). In comparison with controls, CBT-only was associated with significant reductions when stress was assessed with the DASS-21 and the Perceived Stress Scale (PSS) (Fig. S44). Finally, CBT-only displayed superiority over controls regardless of number of sessions (Fig. S45).

3.7.1.2. Meta-regression. The efficacy of CBT-only was not related to the length of the intervention (Table S6). The efficacy of CBT-only was not affected by risk of biases in any of the seven domains (Table S7).

3.7.1.3. Sensitivity analysis. The sensitivity analysis results showed stable efficacy of combined CBT-only and CBT-CI (Fig. S46A) and CBT-only (Fig. 46B) for perinatal stress.

3.7.2. Long-term efficacy

CBT-only was associated with larger stress level reductions compared to controls in the long term: five trials, $n = 379$, SMD = −1.14, 95% CI: −2.15 to −0.13, $I^2 = 94\%$ (Fig. S47). No CBT-CI trials assessed long-term efficacy for perinatal stress.

3.7.2.1. Subgroup analyses. Six CBT-only subgroup analyses were conducted (see Supplementary Figs. S48–S53). Internet-based (women alone) CBT-only significantly reduced stress levels compared to controls (Fig. S48). In-person group CBT-only conducted with women and partners, but not with women alone, showed superiority to controls in reducing stress levels (Fig. S48). CBT-only delivered during pregnancy was associated with reductions of stress levels, while CBT-only during postpartum was not better in reducing stress levels compared to controls (Fig. S49). CBT-only did not lead to greater reduction in stress levels compared to controls regardless of indicated prevention or treatment interventions (Fig. S50). Neither CBT-only delivered by specialists nor non-specialists was associated with greater reduction in stress levels compared to controls (Fig. S51). In comparison with controls, CBT-only was associated with significant reductions when stress was assessed with the DASS, but displayed no advantages when stress was assessed with the PSS (Fig. S52). Finally, CBT-only <8 sessions did not significantly reduced stress levels compared to controls (Fig. S53).

3.7.2.2. Meta-regression. Neither time from baseline to the end of follow-up nor time from the end of the intervention to the end of follow-up was related to the efficacy of CBT-only (Table S6). The efficacy of CBT-only was not affected by risk of biases in any of the seven domains (Table S7).

3.7.2.3. Sensitivity analysis. The long-term efficacy of CBT-only for perinatal stress was not stable (Fig. S54), such that the significant estimate became nonsignificant after omitting four trials one by one.

3.8. Post-traumatic stress disorder

3.8.1. Short-term efficacy

One trial reported that CBT-only ($n = 105$) was not effective in reducing PTSD symptoms measured with Davidson Trauma Scale (DTS) in the short term compared to controls: MD = −9.35, 95% CI −18.90 to 0.20 (Fig. S55).

3.8.2. Long-term efficacy

Two trials ($n = 155$) were included in the meta-analysis. CBT-only was associated with improvement in PTSD symptoms measured with DTS compared to controls: MD = −13.79, 95% CI −25.27 to −2.30, $I^2 = 42\%$ (Fig. S56).

4. Discussion

This is the first meta-analysis to comprehensively evaluate the short- and long-term efficacy of CBT-only and CBT-CI for perinatal depression, anxiety, stress and PTSD. Overall, there are three main findings. First, both CBT-only and CBT-CI were effective for perinatal maternal depression in the short and long term. Second, CBT-only had both short- and long-term efficacy for perinatal anxiety. Third, CBT-only was effective for women with perinatal stress in the short term and for women with perinatal PTSD in the long term. This is also the largest and the most comprehensive meta-analysis examining the efficacy of CBT-only specific to a wide variety of modalities in perinatal women.

4.1. Depression

CBT-only outperformed control conditions in short and long terms across in-person group (women alone), in-person individual (women alone or women and partners), internet-based (women alone) and workbook-based (women alone) formats, and whether delivered by specialists or non-specialists. We found that internet-based (women alone) CBT-only showed greater improvement in perinatal depression compared to controls, which was consistent with a previous review (SMD = −1.08, 95% CI: −1.74 to −0.41) (Huang et al., 2018). Another meta-analysis including 8 trials also found short-term efficacy of internet-based CBT for postnatal depression: SMD = −0.63, 95% CI: −0.77 to −0.50 (Lau, Htun, Wong, Tam, & Klainin-Yobas, 2017).

We found that both in-person group (women and partners) and in-person individual (women and partners) formats were effective to improve women's perinatal depression in the short term, supporting the feasibility of partner-inclusive CBT that focuses on couple relationships and social support form partners (Epstein & Zheng, 2017). Partners involved in CBT sessions are thought to help provide support, avoid conflict or decrease distress for women (Baucom, Belus, Adelman, Fischer, & Paprocki, 2014). In addition, both women (23.8%) and men (10.4%) can suffer from perinatal depression between the first trimester and 1 year postpartum (Paulson & Bazemore, 2010), and thus it is important to develop couple interventions to meet the stressful demands of parenthood. The efficacy of in-person individual (women and partners) CBT-only, but not in-person group (women and partners) CBT-only, was maintained in the long term. This difference may be due to the fact that the in-person group format had fewer sessions (3 vs. 8 sessions) and longer follow-up (12 vs. 9 months) compared to the in-person individual format.

Additionally, consistent with previous research (Sockol, 2015), the results of our meta-analysis indicated that CBT-only for both prevention interventions and treatment interventions during either pregnancy or the postpartum period was effective in both short and long terms. Particularly, prenatal CBT-only was effective in treating active depression and preventing the emergence of prenatal depression in the short term (Fig. S57), which was in line with previous reviews (Shortis et al., 2020; Yasuma et al., 2020). Additionally, postnatal CBT-only had long-term effectiveness in treating postnatal depression (Fig. S58), supporting

the conclusions from two previous reviews (Huang et al., 2018; Perveen et al., 2013).

This is the first meta-analysis evaluating CBT for perinatal depression with a subgroup analysis specifically for low-income women. In line with a previous narrative review (Nillni, Mehralizade, Mayer, & Milanovic, 2018), we found that CBT-only had short-term efficacy among low-income women with perinatal depression. However, in the present study, CBT-only did not exhibit long-term efficacy in low-income perinatal depressed women. A possible explanation might be due to our inclusion of one trial of CBT tailored to reduce stress rather than depression. In fact, this may well explain the negative result given that, when this one trial was omitted in the sensitivity analysis, CBT was shown to be effective for improving long-term depression in low-income perinatal women.

In terms of CBT-CI, CBT + ADM did not yield extra advantage over ADM monotherapy in either the short or long term, but this finding should be interpreted with caution due to small number of trials included in this subgroup analysis. A possible explanation is a lack of adherence in women who had to attend both CBT and ADM sessions concurrently: In one CBT + ADM trial, women in the CBT + ADM arm attended fewer CBT sessions and discontinued ADM more frequently and earlier compared to women in the CBT alone arm or the ADM alone arm (Milgrom et al., 2015). However, this finding contrasts with previous reviews for depression in the general population showing superiority of CBT + ADM over CBT alone (Dunlop et al., 2019; Keller et al., 2000), and this inconsistency might be attributed to sequential addition of CBT or ADM to the monotherapy in the two reviews. In contrast, CBT + mindfulness exhibited short- and long-term efficacy compared to wait-list or TAU, in line with documented efficacy of CBT + mindfulness relative to controls (e.g., health education, relaxation training, and supportive psychotherapy) in the general population (Goldberg et al., 2019; Hofmann & Gómez, 2017).

4.2. Anxiety

We found that, CBT-only showed overall effectiveness for perinatal anxiety in both short and long terms. In contrast, one preliminary meta-analysis (Maguire, Clark, & Wootton, 2018) showed that CBT for perinatal anxiety was effective post-intervention (SMD: 0.49, 95% CI: 0.05–0.80), but was not effective in later follow-ups (SMD: 0.40, 95% CI: −0.14–0.94). The inconsistency between studies with respect to long-term effectiveness is probably due to different number of included trials between our study (7 trials) and the previous meta-analysis (2 trials). Despite the overall efficacy of CBT-only for perinatal anxiety, the specific effectiveness differed based on various formats. We found that, for women alone, in-person group format, but not in-person individual format was superior to control conditions for short-term effects on perinatal anxiety. This apparent lack of efficacy of in-person individual (women alone) format might be due to the involvement of general practitioners (GP) in the control arms of three trials: GPs may have provided psychological care that narrowed the effect difference between CBT-only and this comparator.

In line with the findings for perinatal depression, internet-based (women alone) CBT-only showed better short- and long-term efficacy for perinatal anxiety relative to TAU. This finding is in line with previous meta-analyses for anxiety in the general population (Spek et al., 2007; Ye et al., 2015). Internet-based CBT in the perinatal population may present advantages with respect to cost-effectiveness and desirability; this format of CBT has been reported to substantially reduce costs when treating severe health anxiety (Hedman, Andersson, Ljótsson, Axelsson, & Lekander, 2016). Additionally, internet-based format may be more appealing and accessible to many perinatal women who have to look after babies at home or who have trouble traveling between home and places where in-person interventions were delivered. It is also a viable alternative during population-level upheavals such as the COVID-19 pandemic. Contrary to our findings for depression, CBT-only was not effective for perinatal anxiety when administered in-person individually (women alone), either in the short term or in the long term.

Unlike the findings for perinatal depression, a brief unguided CBT was effective for perinatal anxiety in both short and long terms. A possible explanation is that, in one of the two trials, the CBT-only intervention called "MUMentum Pregnancy" focused on addressing increased anxiety surrounding the birth and health of the baby rather than prenatal depression (Loughnan et al., 2018). Despite small sample size, this finding established preliminary efficacy of brief self-help CBT-only for perinatal anxiety symptoms that have received little attention to date.

The meta-regression result showed that the longer the time from the end of the intervention to the end of follow-up, the higher the long-term efficacy of CBT-only for perinatal anxiety. We speculate that women continued using the CBT techniques they had learned during the intervention period, and thus continued to reduce their anxiety levels across time. It might also be explained by the fact that, among the 10 trials included in this meta-regression, 5 trials included women comorbid for depression, anxiety and stress symptoms. As such, changes in anxiety levels might require longer to become evident, which is consistent with a previous review showing that psychotherapies for comorbid mental health disorders exhibited better long-term efficacy relative to their short-term efficacy (Leichsenring & Rabung, 2011). However, this finding should be interpreted with caution given the high heterogeneity and small sample size, and thus future research is needed to determine it.

4.3. Stress and PTSD

Internet-based (women alone) CBT-only was effective in treating stress symptoms in the short term, in line with meta-analysis results for stress or PTSD in the general population (Heber et al., 2017; Kuester, Niemeyer, & Knaevelsrud, 2016). This medium effect (SMD = −0.65) of the short-term efficacy for perinatal stress in our study was lower than a large effect (SMD = −0.84) reported in a previous review (Lau et al., 2017). A possible explanation is differences in target populations between this review (postnatal, pregnancy loss) and our study (perinatal, without pregnancy loss). Women with pregnancy loss were more likely to have higher levels of stress at baseline, and accordingly, they demonstrated greater reductions in symptoms. Moreover, our study addressed a gap in Lau et al. (2017) by showing long-term efficacy of internet-based (women alone) CBT-only for perinatal stress. We also observed that CBT-only was effective for perinatal stress during both pregnancy and postpartum in the short term while the long-term efficacy of CBT-only for perinatal stress was limited to pregnancy. The absence of postpartum efficacy possibly due to small sample size (two trials), and thus future meta-analyses including more trials are needed.

Given that prenatal maternal stress have long-lasting adverse effects on child outcomes (Jones et al., 2019; King, Dancause, Turcotte-Tremblay, Veru, & Laplante, 2012), the ability to prevent or mitigate stress in women exposed to stressors has potential implications for child development. We found that CBT-only was effective in preventing perinatal PTSD in the long term, in line with existing evidence of PTSD prevention in the general population (Kliem & Kröger, 2013; Qi, Gevonden, & Shalev, 2016). The only trial included in the short-term analysis did not show efficacy of CBT-only; a possible explanation was that the acute intervention phase might have been too short to detect efficacy, but was observed a few weeks post-intervention as the women continued to make use of techniques acquired during the intervention to address their PTSD symptoms.

4.4. Limitations

There are several limitations that need to be considered. First, most trials were of low-to-moderate quality. However, we performed sensitivity analyses by omitting included trials to test the robustness of our

results. Second, although some sources of heterogeneity were identified in subgroup analyses, statistical heterogeneity remained moderate-to-high within several subgroups. This residual heterogeneity might be partially attributed to the variability of scales used to measure depression, anxiety and stress. Third, our database searches were limited to English and published articles, and thus we cannot exclude the possibility that some trials in other languages or from grey literature sources might have been missed. Fourth, the number of studies included in the main meta-analysis for perinatal stress was relatively small, and the number of studies included their subgroup analyses was even smaller. The number of studies in the CBT-CI subgroup analyses (e.g., CBT + ADM) for perinatal depression was also small. Therefore, these findings should be interpreted with caution. Finally, 11 RCTs used waitlist control groups, and one trial used a no-intervention control, which possibly overestimated the efficacy when compared to other control conditions such as TAU, enhanced TAU or attention controls.

4.5. Future directions

Future network meta-analysis is needed to rank the efficacy among various CBT modalities in perinatal women and evaluate their acceptability to better inform intervention selections in the clinical practice. Furthermore, determining the most cost-effective way of delivering CBT to perinatal women is an important area for future research.

5. Conclusions

Our study extends prior reviews by demonstrating efficacy of CBT-only in treating perinatal depression and anxiety in both short and long terms and stress in the short term, as well as efficacy of CBT-only in preventing perinatal depression, anxiety and stress in the short term. Our findings also add to a growing body of literature demonstrating short- and long-term efficacy of CBT-only for perinatal depression in low-income women. CBT-only exhibited short- and long-term efficacy for perinatal depression and anxiety across a wide range of formats during prenatal and postnatal periods. Among combination therapies, CBT + mindfulness provided extra treatment benefits for perinatal depression. These findings suggest that many factors contribute to the efficacy of CBT for perinatal depression, anxiety and stress.

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Contributors

XL designed the study, conducted literature searches, extracted data, did meta-analyses, and wrote the draft of the manuscript. DPL screened and selected trials for inclusion, and DPL and VP revised early drafts of the manuscript. XL and VP performed quality assessment. SL identified instances of CBT and CBT-CI. GE assisted with high resolution of figures and with the design and statistical analyses. SK supervised the work of XL and contributed to the refinement of the manuscript. All authors contributed to and have approved the final manuscript.

Declaration of Competing Interest

All authors declare that they have no conflicts of interest.

Data availability

Data will be made available on request.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.cpr.2022.102129.

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