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Physical activity during pregnancy and postpartum depression: systematic review and meta-analysis

Short title: Physical activity and postpartum depression

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Abstract

Background It is still largely unknown whether physical activity (PA) during pregnancy may be useful to avert subsequent postpartum depression (PPD). We conducted a systematic review and meta-analysis to determine the preventive effects of PA during pregnancy on PPD.

Methods A systematic review of English and non-English articles was conducted using CINAHL, Cochrane Controlled Trials Register, PsycINFO, MEDLINE, SportDiscuss and Web of Science databases. Studies which tested the effect of any type of PA measured during pregnancy on depression or depressive symptoms in the first year postpartum were included. Relevant articles were extracted independently by 2 authors using predefined data fields, including study quality indicators. The protocol was registered on PROSPERO (CRD42018087086).

Results Twenty one studies, fit our selection criteria. Among them, seventeen studies were included in the meta-analysis, representing 93 676 women. Robust Variance Estimation random-effects meta-analysis indicated a significant reduction in postpartum depression scores (Overall SMD = -0.22 [95% CI -0.42 to -0.01], $p=0.04$; $I^2 = 86.4\%$) for women physically active during pregnancy relative to those who were not active. This association was reinforced in intervention studies (SMD = -0.58 [9% CI -1.09 to -0.08]).

Limitations Overall meta-analysis showed important heterogeneity in PA assessment, suggesting the existence of potential moderators such as intensity, frequency, trimester of pregnancy or type of physical activity practiced.

Conclusions PA during pregnancy appears to reduce the risk of PPD symptoms. High quality studies addressing the role of PA in the perinatal period and its impact on new mother's mental health remain necessary.

Keywords: depression, exercise, pregnancy, postpartum, systematic review, meta-analysis

Introduction

Postpartum depression (PPD) is defined as the occurrence of a minor or major depression up to one year after giving birth and is estimated to affect 5 to 25% of new mothers (O'Hara and McCabe, 2013). The consequences of PPD may be severe and far-reaching, negatively affecting women who suffer from it as well as their partners and relatives (Kerstis et al., 2014). Moreover, PPD may have important consequences for children's physical and emotional development (Field, 2010; Goodman et al., 2011). Importantly, the occurrence of PPD is also a risk factor for future depressive episodes (Robertson et al., 2004). In terms of the treatment of PPD, recommended treatment options are antidepressant medication as well as cognitive behavioral therapy (CBT) (Gelenberg et al., 2010). However, women who are breastfeeding might be concerned by the effects of antidepressants on their child (Pearlstein et al., 2006). Time, transportation and access to childcare are the most commonly reported barriers to undertaking psychotherapy during the postpartum period (Goodman, 2009). The primary prevention of PPD could therefore help new mothers avoid a long, costly and hard-to-access process of recovery (Katon and Ludman, 2003).

One potentially promising method for preventing PPD is physical activity (PA). PA can be defined as any bodily movement produced by skeletal muscles that require energy expenditure (WHO, 2010). Overall, findings from meta-analyses, reviews, and recent randomized trials demonstrate encouraging results for the use of PA in the treatment and prevention of depression in the general population (Mammen and Faulkner, 2013; Rosenbaum et al., 2014). PA has been shown to improve the mood of persons with mild to moderate depression just as well as antidepressant medication, CBT or social support (Kvam et al., 2016). Although mechanisms explaining this phenomenon are not yet fully understood, several hypotheses have been suggested. PA could reduce depressive symptoms through biological mechanisms, for example by increasing beta-endorphins levels, which are associated with improved mood, euphoria and enthusiasm but also pain reduction (Stathopoulou et al., 2006) and increasing levels of brain neurotransmitters (including dopamine, serotonin and noradrenaline) associated with feelings of satisfaction and euphoria (Schuch et al.,

2017). Besides these biochemical and physiological pathways for the positive influence of PA on depression, several psychosocial mechanisms have been proposed as well, including changes in self-efficacy, self-esteem and mastery, distraction and behavioral activation (Craft, 2005; Peluso and de Andrade, 2005). PA performed in a group-based format can lead to reduced depressive symptoms via social mechanisms, such as increased social support (Armstrong and Edwards, 2003). For healthy pregnancies without contraindications, the current guidelines of the American Congress of Obstetricians and Gynecologists (ACOG) recommend that pregnant women accumulate 150 minutes of moderate-intensity aerobic activity per week (American College of and Gynecologists, 2015). This may improve their health and that of their unborn child through gestational weight management, sleep cycle improvement and gestational diabetes risk reduction (Nascimento et al., 2012). However, less is known about the mental health effects of women's PA during the perinatal period. An emerging body of work, including some systematic reviews and meta-analyses, provides evidence supporting the benefits of PA on perinatal depression. Daley et al. (2015) detected a significant reduction in antenatal depressive symptoms for women who undertook PA before and during pregnancy. Likewise, Pritchett et al. (2017) and McCurdy et al. (2017) established that PA after giving birth significantly reduces postpartum depressive symptoms. These results, albeit based on a small number of trials, give reason to believe that PA during pregnancy may plausibly protect against PPD and could be used as an accessible means of preventing mental health problems in new mothers. This was also the conclusion from two previous review studies focusing on the effects of perinatal PA on postnatal depression. Teychenne and York (2013) reported five studies examining this association, two of which (Sexton et al., 2012; Songøygard et al., 2012) found an inverse relationship between PA and the presence of postnatal depressive symptoms. More recently, Poyatos-Léon et al. (2017) assessed the effectiveness of PA interventions on preventing and controlling postpartum depressive symptoms in a meta-analysis. They included two interventions (Huang et al., 2011; Mohammadi et al., 2015) specifically targeting PA during pregnancy. The conclusion of this study was

that there was a decrease in postpartum depressive symptom scores for women participating in PA interventions during pregnancy and the postpartum period.

Yet, these encouraging conclusions should be observed carefully due to the small number of studies taken into consideration as well as methodological concerns. Consideration of potential biases was not systematic with for instance some of the primary studies including women who met depressive symptoms criteria at baseline (i.e. during pregnancy), potentially obscuring an effect of PA on postnatal depressive symptoms. Moreover, the interventions included in the meta-analysis conducted by Poyatos-Léon et al. (2017) comprised both prenatal and postnatal activities, preventing firm conclusions regarding the beneficial effects of prenatal activities.

To our knowledge, no published meta-analysis has exclusively examined the association between PA during pregnancy and PPD. Thus, the aim of the present systematic literature review and meta-analysis is to assess whether physical activity performed during pregnancy reduces the risk of depression in the postpartum period. Furthermore, the identification of potential moderators of change and their associations with postnatal depressive symptoms is likewise important. We still know little about which dose (frequency, duration, intensity) or domain (leisure-time, occupational, domestic, transport) of PA is most effective in reducing the risk of postnatal depression, as well as the pregnancy trimesters during which activity should preferably be performed. Results have the potential to give precious information for the refinement of clinical guidelines and intervention design in the primary prevention of postpartum depression.

Methods

This review follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The protocol was registered on PROSPERO (CRD42018087086).

Information sources and searches

Relevant studies were identified by searching the CINAHL, Cochrane Central Register of Controlled Trials, PsycINFO, Medline, SportDiscuss and Web of Science databases in October 2017. The search strategy combined the following groups of keywords: physical activity; pregnancy; postpartum; depression, as well as keywords for specific types of physical activity (e.g. walking, yoga) and was not restricted by date or language. Searches were specified for both MeSH terms and text words and were modified to meet the requirements of each database. A sample MEDLINE search strategy used to identify trials for this review is included in **Table 1**. The reference lists of studies that met search criteria were also examined to identify additional studies, as well as forward citation and examination of relevant review articles.

Inclusion and exclusion criteria

Both intervention and observational studies were considered, specifically: Randomized Controlled Trials (RCT), retrospective and prospective cohorts, case-control and cross-sectional studies. To be included, studies had to test the effect of any type of PA measured at least once during pregnancy on depression or depressive symptoms in the first year after birth. For our main outcome, study subjects had to be diagnosed using a structured clinical interview, screened for probable depression using a validated tool (e.g. Edinburgh Postnatal Depression Scale, EPDS)(Cox et al., 1987) or diagnosed according to the judgment of a health professional (e.g. GP, health visitor or psychiatrist). The following studies were excluded: (1) qualitative studies, comments, editorials and studies on animals, (2) studies that did not measure PA during pregnancy, (3) studies that combined PA with other interventions or treatment (including diet, behavioral therapy or antidepressant medication), and (4) studies in which depression was measured exclusively before/during pregnancy or more than one year after delivery.

Study selection and data extraction

The identification of potentially eligible articles according to our inclusion and exclusion criteria was conducted in subsequent steps by five authors (AN, CB, FEK, JW, LP). First, titles and abstracts of retrieved studies were independently screened by two people. A paper was included if at least one of them judged it to be relevant. Full articles of potentially relevant studies were then retrieved for detailed evaluation by all authors, using a standardized eligibility form. In case of disagreement between reviewers regarding a study's eligibility, a decision was mutually agreed upon after discussion. If a study fulfilled our inclusion criteria, two authors independently extracted data using a form that included detailed descriptions of the following elements: publication type, participant characteristics, study design, number of cases, frequency, duration, intensity and domain of physical activity, potential sources of bias and relevant confounders and main outcome indicators. Incongruities were discussed and checked against the original article to reach agreement. Study authors were contacted if additional information was required to adequately complete the data extraction form.

Assessment of study quality

The evaluation of study quality and possible bias for each article was performed by the same five authors using forms adapted from the Cochrane risk of bias tool (Higgins and Green, 2011) for intervention studies and the Newcastle-Ottawa Scale (Wells et al., 2011) for observational studies. These assessments take into account the quality of the exposure and outcome measurements, the representativeness of the study population, and the treatment of missing values. Additionally, for intervention studies, we assessed whether: a) studies were randomized, b) a randomization sequence was generated, c) outcome assessment was blinded, and d) an intention to treat analysis was performed. For observational studies, we evaluated: a) sample selection, b) response rate and loss-to-follow up and c) adjustment for confounders. Factors that are associated with both physical activity during pregnancy and postpartum depression should be considered as important confounders to be taken into account when studying this association. They can be classified as socio-

demographic (maternal age, socioeconomic status); health/ pregnancy related (pregnancy complications, delivery type, parity) and psychological factors (lack of social support, maternal mental health antecedents (Beck, 2001; Myers and Johns, 2018; Symons Downs et al., 2008). To limit bias, quality assessment of the study conducted by van der Waerden et al. (van der Waerden et al., submitted) was performed by two authors (CB and MM) who were not associated with that study. Possible scores for quality assessment ranged from zero to seventeen for intervention studies and from zero to eighteen for observational studies. To calculate a mean quality score across studies, Risk of bias scores for intervention studies were converted to a score out of 18.

Studies with quality scores lower than 7 (< 25% quintile) were considered to present a “high risk of bias”, those ranging 7 to 11 a “moderate risk of bias”, and those with a score greater than or equal to 12 (> 75% quintile) a “low risk of bias”.

Data synthesis

To summarize the effects of physical activity on postpartum depression scores in the meta-analysis, we calculated the Standardized Mean Difference (SMD) and its 95% confidence intervals using the Practical Meta-Analysis Effect Size Calculator (Wilson). To combine effect sizes from different studies into a weighted mean effect size, each effect size was weighted by the inverse of its variance and then averaged (Lipsey and Wilson, 2001). Effect sizes are assumed independent in standard meta-analytical procedures (Gleser and Olkin, 2009). However, it is not uncommon for primary studies to provide multiple correlated effect size estimates for the same underlying outcome construct of interest (e.g. depressive symptoms measured with two different scales, or effects measured at 6 and 12 months follow-up). Non-independence of outcomes is usually dealt with by computing a mean outcome within a study or by selecting one of the effect size estimates, but these approaches leave out potentially relevant information (Tanner-Smith and Tipton, 2014). A newly proposed method for handling statistically dependent effect sizes in meta-analysis is Robust Variance Estimation (RVE) (Hedges et al., 2010). A main advantage compared with other methods is that it does not require

having information on the covariance structure of effect sizes, information that is typically hard to acquire (Moeyaert et al., 2017). A fixed effect meta-analysis was undertaken in the absence of heterogeneity, otherwise a random effects model was used (Borenstein et al., 2010). To test for homogeneity, the Q statistic was computed to determine whether each set of effect sizes shared a common population effect size (Lipsey and Wilson, 2001). The I^2 statistic was used to aid the interpretability of between-study heterogeneity; an $I^2 > 50\%$ was considered as an indicator of important heterogeneity (Higgins et al., 2003).

A priori hypothesized subgroup analyses were performed according to the year of publication (≤ 2008 vs. > 2008 , the year the ACOG guidelines were published), domain of PA (leisure vs. other domains), pregnancy trimester of PA, control for depression at study baseline (yes vs. no), time of depression assessment (within 16 weeks postpartum vs. later), as well as study quality (low, moderate or high risk of bias). Due to the low number of studies per subgroup, RVE could not be applied. However, subgroup analyses through standard mixed effect models yield results that are not too biased if relatively few studies report more than one effect size, which was the case here (Tipton and Pustejovsky, 2015).

Finally, the results of a meta-analysis may be biased because studies with non-significant results are less likely to be published than those with significant results. To detect publication bias, a funnel plot was examined both graphically and using Egger's linear regression method (Sterne et al., 2005). A p-value of $< .05$ indicates a significant association between the effect size and precision, and is indicative of the possibility of publication bias. The meta-analysis was performed using the Review Manager statistical program (Cochrane, 2008) and STATA 14.0 using the *robumeta* macro (StataCorp, 2015).

Results

Search results

Our database search resulted in the identification of 2602 potentially relevant articles. After removing duplicate titles, we were left with 2427 articles. An additional 10 articles were found when scanning article reference lists, yielding a total of 2437 initial titles. Following the steps outlined above, 408 abstracts and then 68 full publications were screened for eligibility for this review. Main reasons for exclusion of publications were absence of a PA measure during pregnancy, absence of a PPD measure or exclusive focus on antenatal depression. Finally, we identified 20 publications, describing 21 different studies that fit our criteria for inclusion in the systematic review (**Figure 1**).

Characteristics of the included studies and participants

Table 2 and **Table 3** show the characteristics of intervention and observational studies that were selected. All were published between 1993 and 2018 as peer-reviewed articles or dissertations, or are currently under review. Six studies were conducted in the USA (Bershinsky et al., 2014; Campolongo et al., 2017; Demissie et al., 2013; Ersek and Brunner Huber, 2009; Guida et al., 2012; Symons Downs et al., 2008), eleven in Europe (Denmark, France, Norway, Poland, Spain, Sweden and United Kingdom) (Aguilar-Cordero et al., 2018; Claesson et al., 2014; Kowalska et al., 2014; Nordhagen and Sundgot-Borgen, 2002; Rankin, 2008; Shakeel et al., 2018; Songøygard et al., 2012; Strøm et al., 2009; van der Waerden et al., submitted; Vargas-Terrones et al., 2018) and four elsewhere (Australia, Canada, Iran and South Korea) (Abraham et al., 2001; Jeon and Yang, 2013; Mohammadi et al., 2015; Stephenson, 1993). Six studies were interventional trials (Aguilar-Cordero et al., 2018; Bershinsky et al., 2014; Mohammadi et al., 2015; Rankin, 2008; Shakeel et al., 2018; Songøygard et al., 2012; Vargas-Terrones et al., 2018) and fifteen studies were observational, including in total 100 494 women. Women were on average aged between 25 and 32 years old. PPD was mainly assessed by the Edinburgh Postnatal Depression Scale (EPDS), with other frequent measures being the Center for Epidemiologic Studies Depression Scale (CES-D) (Bershinsky et al., 2014; Symons Downs et al., 2008), the Hospital Anxiety and Depression Scale (HADS) (Nordhagen and Sundgot-Borgen, 2002), prescription of antidepressant medications or hospitalization for depression

(Strøm et al., 2009), items from the PRIME-MD scale (Ersek and Brunner Huber, 2009; Guida et al., 2012) or Zung's depression scale (Jeon and Yang, 2013). Antenatal depression was taken into account in thirteen studies, either by excluding participants with current mood disorder in the study, or by controlling for maternal antenatal emotional distress, EPDS or CES-D scores.

Physical activity characteristics

Across the different studies, 41.6% of women were classified as being physically active in pregnancy. The duration of PA ranged from 30 minutes per week to 150 minutes or more per week. Studies diverged as to their recommendations on the frequency. For the intervention studies, one study recommended practicing 90 minutes at least once a week (Bershinsky et al., 2014). Two studies (Rankin, 2008; Songøygard et al., 201) recommended practicing 30 to 60 minutes twice a week and three studies (Aguilar-Cordero et al., 2018; Mohammadi et al., 2015; Vargas-Terrones et al., 2018) 30 to 60 minutes three times a week. Observational studies were less specific in their description of PA frequency, but generally recommended at least 30 minutes 1 to 4 times per week. Exercise intensity varied from low to high, and was in most studies adapted to the exercise capacities of pregnant women. Types of PA reported were diverse. In intervention studies they included yoga, aerobic exercise, stretching and strength training exercises on floor and in an aquatic environment. In observational studies, PA was generally defined as leisure-time activities or all movements contributing to the total daily energy expenditure (both exercise and other activities of daily living). Trimester during which PA was evaluated varied across studies from all three pregnancy trimesters, to the second and third or third trimester only. Only van der Waerden et al. and Shakeel et al (2018) respectively studied the impact of PA in the first and second only. Part of this variation probably is due to study design and participant recruitment for the different studies under consideration. However, it does indicate that maintaining PA across pregnancy, including the last trimester is generally feasible for women.

Association between physical activity during pregnancy and postpartum depression

Intervention studies

Three small intervention studies reported a statistically significant reduction in postpartum depressive symptoms among women participating in a prenatal Hatha yoga intervention (Bershadsky et al., 2014), an aerobic exercise program (Rankin, 2008) and in a prenatal aerobic, strength and endurance intervention in an aquatic environment (Aguilar-Cordero et al., 2018). The other three intervention studies reported non-significant differences between intervention and control groups in terms of postnatal depression rates. However, the study by Vargas-Terrones et al. (2018) reported a close to significant ($p= 0.067$) reduction in CES-D scores among women in the aerobic exercise intervention compared to the control group.

Observational studies

Among the observational studies, five found a statistically significant negative association between PA during pregnancy and postpartum depressive symptoms (Abraham et al., 2001; Claesson et al., 2014; Kowalska et al., 2014; Nordhagen and Sundgot-Borgen, 2002; Symons Downs et al., 2008). Two additional studies found statistically significant associations for specific doses of PA or PPD assessment. Guida et al. (2012) reported that pregnant women who were physically active for ≥ 5 days/week had fewer postpartum depressive symptoms compared to those who were active ≤ 1 day/week (OR = 0.66 [0.26-0.96]), but not in comparison with women who were moderately active (1-4 days/week; OR = 0.82 [0.47-1.08]). Shakeel et al. (2018) found that women who performed at least 150 minutes of moderate to vigorous PA in bouts of at least 10 minutes, three times a week, had significant lower risk of PPD in comparison to physically inactive women or women who were active below this threshold. Strøm et al. (2009) found that prenatal physical activity significantly reduced antidepressant prescription but not hospital admissions for depression during the first postpartum year. Further, one study evaluating physical activity as a composite measure of household, occupational, sports and transportation activities, found that higher levels of overall and

domestic activities during the third trimester increased the risk for postpartum depression (OR = 1.17 [95% CI 1.07-1.29])(van der Waerden et al., submitted)). The other studies considered (Campolong et al., 2017; Demissie et al., 2013; Ersek and Brunner Huber, 2009; Stephenson, 1993; van der Waerden et al., submitted) found no statistically significant associations between PA during pregnancy and PPD.

Study quality

Risk of bias was variable with an average score of quality of 9.8/18 (sd=3.0, median = 10.0) across all studies included.

Intervention studies

In intervention studies, quality scores ranged from 8 to 14/17 (mean=12.0, sd=2.6, median=12.2), corresponding to low to moderate risk of bias. In particular, only two studies described whether PA was assessed using validated questionnaires or objective tools (Aguilar-Cordero et al., 2018; Vargas-Terrones et al., 2018). Furthermore, current or prior depression was controlled for in only three of the studies (Bershinsky et al., 2014; Mohammadi et al., 2015; Vargas-Terrones et al., 2018). **(Table 1; supplement)**

Observational studies

Quality was highly variable for observational studies and quality scores ranged from 4 to 13/18 (mean=8.9, sd=2.7, median=10.0), corresponding to low to high risk of bias. These quality scores were mainly influenced by the fact that only eight studies (Campolong et al., 2017; Claesson et al., 2014; Demissie et al., 2013; Jeon and Yang, 2013; Shakeel et al., 2018; Symons Downs et al., 2008; van der Waerden et al., submitted) ascertained the exposure using either a pedometer or a validated questionnaire. Further, missing values were imputed in three studies (Shakeel et al., 2018; van der Waerden et al., submitted), complete observations only were analyzed in seven studies and missing

value treatment was not described in two studies (Abraham et al., 2001; Kowalska et al., 2014). Finally, five studies did not control for important confounders (Campolong et al., 2017; Jeon and Yang, 2013; Kowalska et al., 2014; Nordhagen and Sundgot-Borgen, 2002; Stephenson, 1993), in particular the presence of depression at study baseline. (**Table 2, supplement**)

Meta-analysis

Overall meta-analysis

Four studies (Abraham et al., 2001; Guida et al., 2012; Nordhagen and Sundgot-Borgen, 2002; Symons Downs et al., 2008) lacked information for calculating standardized mean differences. Thus, seventeen studies were eligible for inclusion in the meta-analysis (six interventional, and eleven observational), providing twenty four standardized mean effect sizes. **Figure 2** shows the Forest plot for the individual and overall mean effect sizes with 95% confidence intervals. The RVE random-effects meta-analysis indicated a significant reduction in postpartum depression scores (Overall SMD = -0.22 [95% CI -0.42 to -0.01], p=0.04; I² = 86.4%) for PA during pregnancy relative to women who were not classified as physically active.

Intervention studies meta-analysis

Intervention studies showed a significant inverse association between PA during pregnancy and PPD (SMD = -0.58 [95% CI -1.09 to -0.08], p=0.02, I²=90.7%), indicating that being physically active during pregnancy might prevent PPD. (**Figure 2**)

Observational studies meta-analysis

Observational studies also showed an inverse, but not significant, association between PA during pregnancy and PPD (SDM = -0.07 [95% CI -0.20 to 0.06], p=0.24, I²=74.4%). (**Figure 2**)

Subgroup analyses

As substantial heterogeneity was present in the primary analysis subgroup comparisons were conducted (**Table 4**). None of the subgroups taken into consideration were significantly related to the estimated effect size. Although we aimed to evaluate effect size differences according to PA characteristics such as intensity, frequency and trimester of pregnancy of PA, we were often limited by lack of information on primary studies or too much variation in moderator types to run statistically meaningful subgroup analyses. Focusing on intervention studies only, we could perform a sensitivity analysis for PA intensity, after exclusion of the one low intensity PA intervention (i.e. Mohammadi and colleagues). The overall effect of PA on PPD symptoms was even stronger (SMD = -0.70 [95%CI -1.19 to -0.22], p=0.005) for studies with moderate to high intensity.

Publication bias

Visual inspection of the funnel plot (**Figure 3**) for the overall weighted mean effect size showed no apparent asymmetry, supported by the results of Egger's regression intercept ($b=-0.58$ [95%CI -2.32 to 1.16], $p=0.50$), indicating publication bias was not likely.

Discussion

Main findings

To our knowledge, this is the first systematic review and meta-analysis to investigate the effectiveness of PA during pregnancy to prevent PPD. Overall, eleven studies showed significant associations, indicating that antenatal PA has moderately beneficial effects on PPD. One study reported that higher levels of PA were associated with increased levels of PPD and nine studies found no significant associations. With a small, but significant, overall mean effect size and in particular a significant medium effect size for intervention studies, the results of our meta-analysis indicate that PA during pregnancy could prevent the occurrence of postpartum depressive symptoms.

Subgroup analyses

The overall effect size was mainly driven by the overall larger effects we found for intervention studies compared to outcomes from observational studies. One possible explanation for this difference according to study type is that despite recommendations most women drastically decrease their regular PA levels over the course of pregnancy (Gaston and Cramp, 2011; Pereira et al., 2007). We cannot rule out the possibility that habitually active participants in the observational studies were simply no longer sufficiently physically active during the course of pregnancy for us to be able to distinguish them from non-active women. On the other hand, in the Randomized Trials the dose and frequency of PA is controlled for and generally follows the recommendations outlined by the American College of Obstetrics and Gynecology. It should be noted though that in five out of six interventions the exercise was performed in a group, which could be an additional source of support for pregnant women by reducing their symptoms through social mechanisms.

We further sought to conduct subgroup analyses to elucidate factors associated with the potentially beneficial effects of physical activity. We observed significant heterogeneity in the main analyses, suggesting the existence of moderating factors which influence the relationship between prenatal PA and postnatal depression. However, many studies described the exposure only in general terms restricting us to crude comparisons between overall versus leisure-time activity to assess the impact of exercise domain. As these outcomes were not significant, it is difficult for us to comment on what type of exercise might be most effective. Generally, literature on domain specific effects of PA suggests that leisure-time activities in particular are beneficial for mental health (White et al., 2017). It has to be confirmed whether this also applies to pregnant women. Information on duration, intensity and timing was either lacking or too diverse to make meaningful comparisons. It may be the case that a dose effect exists, but we were not able to explore this question due to a lack of precision in the primary studies. It would be important for future research to be more rigorous in assessing and reporting PA exposure.

Comparison with previous work

Previously, Teychenne and York (2013) presented outcomes of a systematic review of four observational studies and one randomized controlled trial studying PA during pregnancy and PPD. Among these studies, four (Demissie et al., 2013; Ersek and Brunner Huber, 2009; Songøygard et al., 2012; Symons Downs et al., 2008) were also included our meta-analysis. We did not include the fifth study (Sexton et al., 2012) because its study population was composed of women recovering from perinatal depressive symptoms. More recently, Poyatos-Leon et al. (2017) examined the effect of PA interventions in controlling postpartum depressive symptoms. Two of these interventions (Huang et al., 2011; Mohammadi et al., 2015) were conducted in the prenatal period, but we only retained one because the other (Huang et al., 2011) tested the effect of a combined dietary and exercise program. Based on this limited number of primary studies, both reviews concluded that PA during pregnancy is associated with a lower incidence of postpartum depressive symptoms. By presenting a comprehensive review and meta-analysis of published and unpublished studies, our work considerably extends this evidence. Our results find support for the suggested preventive effect of antenatal physical activity on postpartum depression. Past meta-analyses also suggest that PA during pregnancy has beneficial effects on the management of antenatal depression (Daley et al., 2015), as does postpartum PA in the prevention and treatment of PPD (Daley et al., 2009; McCurdy et al., 2017; Pritchett et al., 2017). It should be noted that the studies we included all considered non-symptomatic women recruited from the general population. Depressive symptoms in pregnant and postpartum women are usually found to be associated with socio demographic and psychiatric risk factors, including income, relationship and employment status, years of education, prior history of mental disorders, stressful life events, poor social support, domestic violence, and pregnancy/obstetric complications (Norhayati et al., 2015). Thus, our results could be underestimated due to the fact that the studied populations were not particularly at risk of future

PPD. Indeed, preventive interventions may be particularly useful among women who have characteristics predisposing them to postnatal distress (Fontein-Kuipers et al., 2014).

Strengths and limitations

This study has several strengths. First, publication bias was minimized by our systematic exploration of six databases in the fields of biomedicine, psychology and physical activity. With 21 studies totaling 100 494 participants, we included more than three times as many studies as in previous systematic analyses and we were able to provide more precision in our effect size estimates. In addition, using Robust Variance Estimation for our meta-analytic estimates we were able to take into account *all* reported outcomes, thereby avoiding the loss of information that is associated with effect size estimates based solely on one overall mean score.

However, we were not able to adequately explain the observed heterogeneity in our main analysis. Although we aimed to evaluate effect size differences according to several a-priori determined moderators, we were often limited by lack of information on primary studies or too much variation in moderator types to run statistically meaningful subgroup analyses. Some additional moderator analyses were run for intervention studies only, but these results should be interpreted with caution because of the limited number of primary studies on which they are based on. Further, many studies in this review were limited by methodological weaknesses, resulting in overall moderate quality ratings. First, most of the time we were not able to distinguish between objective and self-reported measures of PA, which are potentially subject to recall problems, bias, and socially desirable responses. Moreover, some primary studies did not correct for important confounders such as past mental health problems or presence of depression during pregnancy to exclude the possibility of reverse causality (pregnant women who are already depressed are less likely to engage in PA). Past depression is also one of the most important predictors of PPD (Seimyr et al., 2013). Finally, a number of studies were undertaken in group settings and therefore it is not known whether the

mental health benefits were produced by the PA or other nonspecific factors such as increased social contacts and support.

Implications for practice

We found a potential small to moderate preventive effect of prenatal physical activity on postnatal depressive symptoms. Results of the current study are informative and could give some clinical guidance to health professionals. Firstly, PA promotion efforts targeting this period are necessary because PA during pregnancy has been shown to reduce risk of antenatal depression, which is predictive of postnatal depression (Teychenne and York, 2013). Furthermore, exercise provides benefits in terms of maternal health and quality of life and may also have positive effects on fetal growth and fetal adaptation (Nascimento et al., 2012). Third, pregnant women are generally inclined to reduce their physical activity PA levels due to pregnancy related barriers such as tiredness, pain, and a growing belly. However, despite these factors not being counter indications for physical activity PA during a healthy pregnancy, many care providers still advise women to lessen their PA when they feel stressed or tired (Merx et al., 2017). Our results suggest that, after elimination of contraindications and taking into accounts women's exercise habits before pregnancy, engaging in at least 30 minutes of moderate intensity PA once to four times a week could contribute to reducing PPD risk. No conclusions could be drawn from our study regarding exercise domains, although aerobic and strength based PA appear to be equally effective. Overall, these recommendations are in line with many of the existing guidelines for physical activity during pregnancy across different countries and can be applied in routine medical practice (Evenson et al., 2014). We were not able to determine if PA is more effective in preventing PPD during specific trimesters of pregnancy, but given the fact that pregnant women are generally inclined to reduce their physical activity levels we recommend to support their engagement in PA from the first trimester onwards. From a public health perspective, pregnancy is a period that is documented as one wherein women may be more apt to incorporate changes into their routine and offers a window of opportunity to prevent or to

limit any negative outcomes (Edvardsson et al., 2011). Therefore, changes in PA habits - often difficult to make in the general adult population - may be more readily incorporated by women during the pregnancy period (Cioffi et al., 2010). Targeted information on the role of PA in conferring mental health benefits may be useful in promoting physical activity among pregnant women (Currie et al., 2013). An alternative option is to refer pregnant women to locally accessible and enjoyable moderate-intensity PA programs (e.g., pregnancy courses, walking, and swimming). Group-based PA in particular could provide additional social support, which has been shown to protect against PPD (Craft and Perna, 2004; McCurdy et al., 2017). Given the current popularity and availability of prenatal yoga classes, the positive effects of yoga on prenatal depression (Gong et al. 2015) and indications that it can contribute to the prevention of PPD (Bershadsky et al. 2014), more studies in this domain seem warranted.

Conclusion

In this systematic review and meta-analysis we found a small to moderate reduction in postpartum depressive symptoms among women who were physically active during their pregnancy, especially when regarding the outcomes of intervention studies. It highlights the continuing need for further research to address the major gap in the literature concerning the role of PA in the perinatal period and its impact on new mother's mental health. More studies are needed, distinguishing frequency and domain of physical activity and the role timing of physical activity in pregnancy or postpartum. The development and rigorous evaluation of PA interventions may be particularly relevant considering that the majority of pregnant women do not meet the recommended PA guidelines. Thus, physical activity during the pregnancy, if recommended by a physician, might contribute to long-term benefits for mothers' overall health and well-being.

Competing interests

The authors declare that they have no competing interests

Author's contributions

JW and LP developed the initial idea for the study; AN conducted the database searches. AN, CB, FEK, JW and LP initially screened the title and abstracts of identified studies, independently assessed the methodological quality of each included study and conducted the final selection of studies to be included in the review. AN, CB, FEK, MM, JW and LP extracted information and data from the studies; AN and JW performed the meta-analysis and drafted the manuscript. All authors have read and approved the final manuscript.

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Figure 1 Flowchart and selection of studies

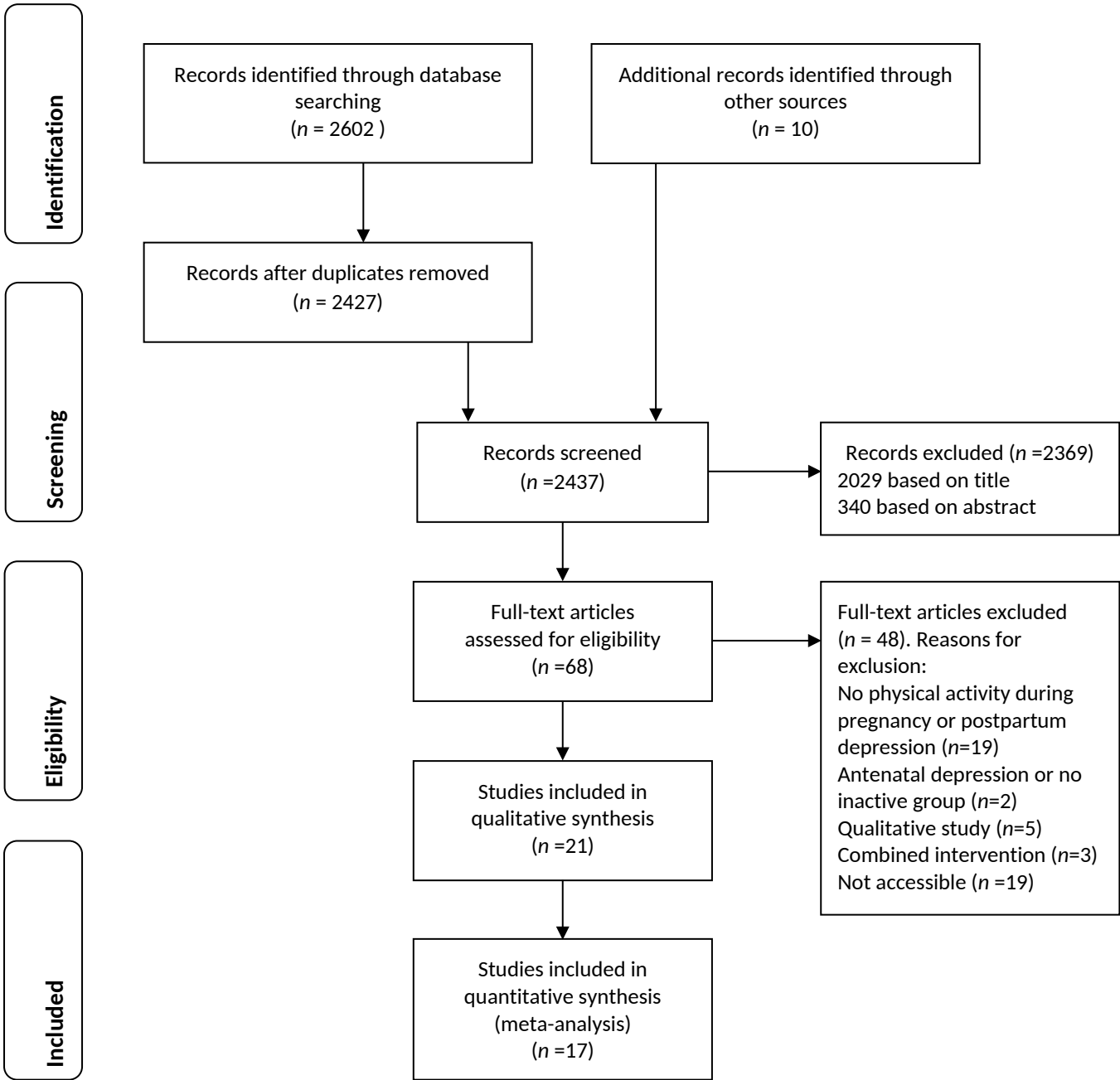


Figure 2 Standardized mean difference (SMD), 95% confidence interval and forest plot for physical activity in pregnancy

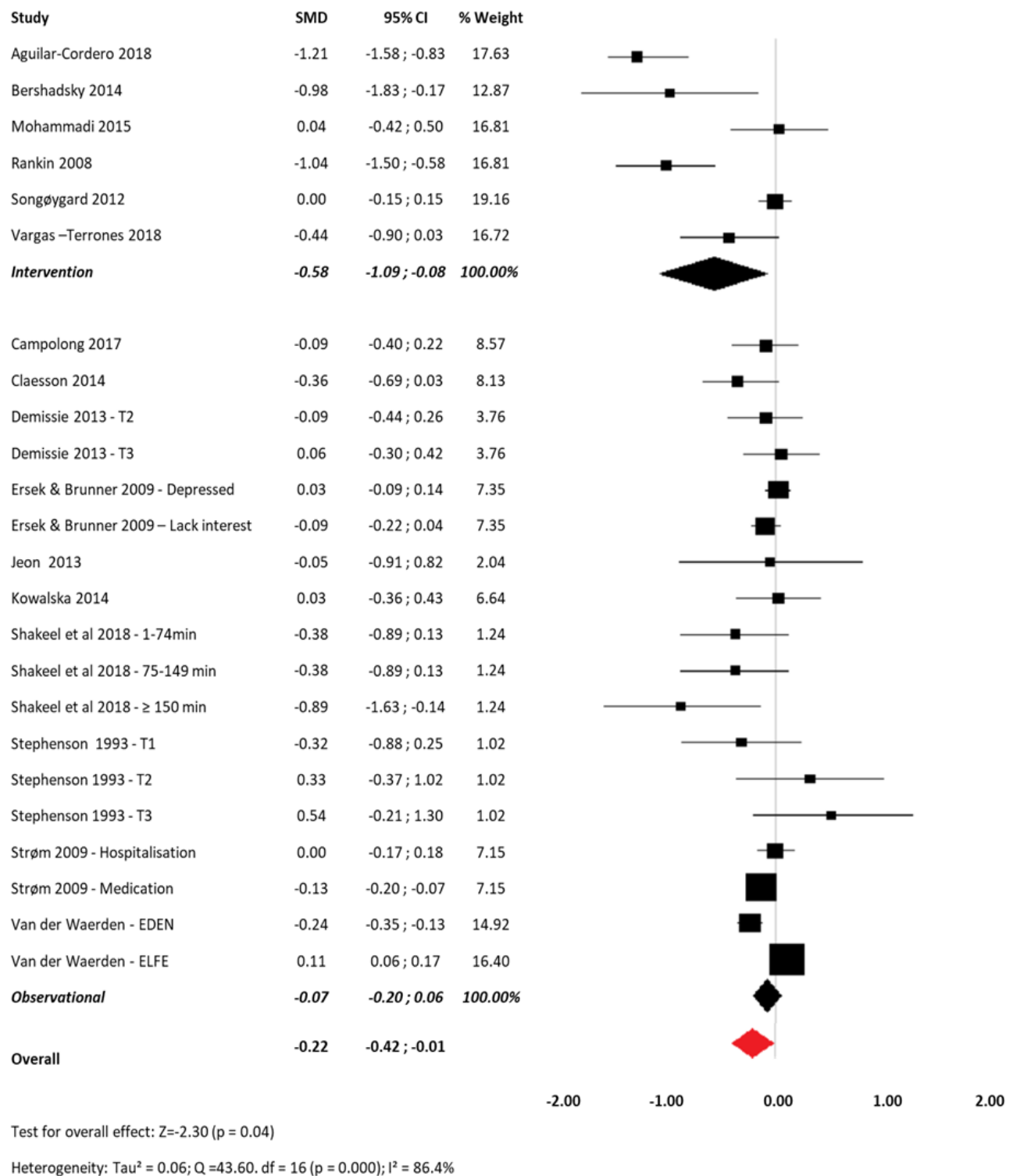


Figure 3 Funnel plot with pseudo 95% confidence limits

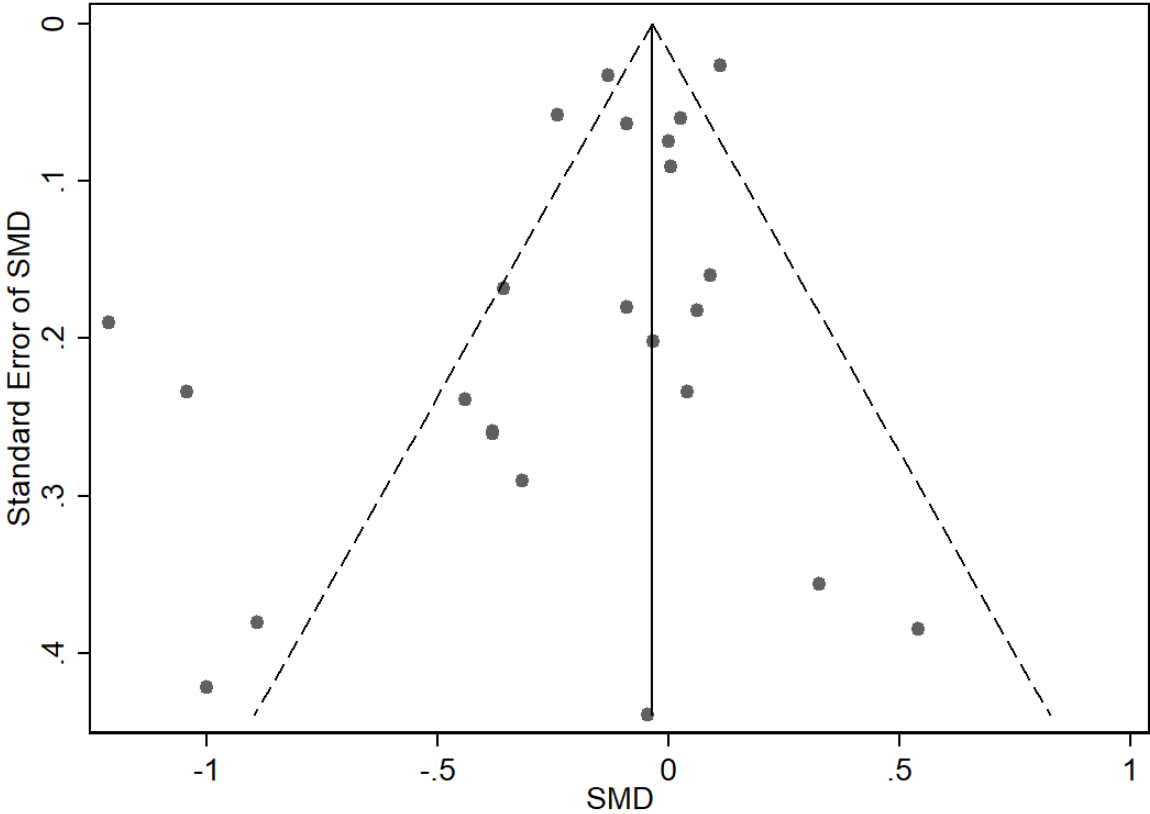


Table 1 Search strategy

DATABASE: Ovid MEDLINE(R) 1946 to October week 4 2017

Search Strategy:

((physical activ* OR exercis* OR physical training OR physical exerc* OR physical fitness OR walking OR running OR jogging OR swimming OR *cycl* OR weight lifting OR yoga OR shopping OR working OR sedentary behav* OR clean* OR (domestic OR household) AND activ*))

AND (pregnant women OR preganc* OR during pregnancy OR prenatal OR perinatal))

AND ((postpartum OR post-partum OR postnatal OR post-natal)

AND (depress* OR mood OR mental health OR depressive disorder*))

OR well-being [ti ab] OR "baby blues")

NOT rats [ti ab]

Table 2 Summary table of intervention studies examining the association between prenatal physical activity and postpartum depression									
Study	Subjects (n) PA/ PIA	Domain of PA	Frequency/ duration	Intensity	Trimester	<u>Antenatal depression accounted for</u>	<u>Outcome and timing of PPD assessment</u>	<u>Association with PPD</u>	<u>Quality score (0-17)</u>
*Aguilar-Cordero et al Spain 2018	65/64	Warm-up, aerobic and strength and endurance exercises in an aquatic environment	60 min/3x week	Moderate	2-3	<u>No</u>	EPDS (<u>continuous</u>) 6 weeks	Regular antenatal PA in an aquatic environment was associated with a lower risk of PPD	13
*Bershadsky et al USA 2014	26/8	Prenatal Hatha yoga	90 mins/ at least 1x week	Low to moderate	1-3	<u>Exclusion of women with self-reported depressive disorder</u> <u>Analyses adjusted for AD</u> 9-item CESD (<u>continuous</u>)	9-item CESD (<u>continuous</u>) 8 weeks	Regular yoga practice during pregnancy is associated with fewer PPD symptoms	<u>9</u>
*Mohammadi et al Iran 2015	38/35	Home-based stretching and breathing exercises	20-30 min/ 3x week	Low	3	<u>Exclusion of women with AD</u> <u>EPDS ≤14</u>	EPDS (<u>continuous</u>) 4 weeks 8 weeks	Antenatal PA did not show a positive effect on depression both 1 and 2 months postpartum	<u>8</u>
*Rankin et al UK 1999	47/37	Aerobic exercise program	30-40 min/ 2x week	Moderate to high	2-3	<u>No</u>	EPDS (<u>continuous</u>) 12-16 weeks	<u>Significant</u> difference was found between PA and PIA groups in terms of postnatal depression	<u>10</u>
*Songøygard Norway 2012	379/340	Endurance training and strength/balance exercises	60 min/week for 12 weeks and 45 min/ 2x week	Moderate to high	2-3	<u>No</u>	EPDS (<u>≥10 and ≥13</u>) 12 weeks	No difference in EPDS scores between the PA and PIA group	<u>14</u>
* Vargas-Terrones et al Spain 2018	70/54	Walking, stretching, aerobic exercise, muscular strength, coordination and balance, floor exercises, relaxation	60 min/ 3x week	Moderate	1-3	<u>Analyses adjusted for AD</u> <u>CES-D (continuous)</u>	CESD (<u>≥16</u>) 6 weeks	CESD scores not significantly reduced among PA in comparison to PIA but difference close to significant	<u>14</u>

Studies marked with * are included in the meta-analysis; PA= Physical Activity; PIA= Physical InActivity; AD= Antenatal Depression
EPDS= Edinburgh Postnatal Depression Scale; CESD= Center for Epidemiologic Studies Depression Scale

Table 3 Summary table of observational studies examining the association between prenatal physical activity and postpartum depression

Study	Study design	Subjects (n) PA/ PIA	Domain of PA	Frequency/ duration	Intensity	Trimester	<u>Antenatal depression accounted for</u>	<u>Outcome and timing of PPD assessment</u>	<u>Association with PPD</u>	<u>Quality score (0-18)</u>
Abraham et al Australia 2001	Cross sectional	181	ND	ND	Low	1-2	<u>No</u>	EPDS (<u>continuous</u>) 1 week	Women who undertook low- intensity PA early in pregnancy had lower EPDS scores	7
*Campolong et al USA 2017	Prospective cohort	157/ 52	Overall physical activity	≥150 min/week	ND	1-3	<u>Analyses adjusted for AD EPDS (continuous)</u>	EPDS (<u>continuous</u>) 6-8 weeks -	No significant differences in postpartum mean EPDS scores between PA and PIA	8
*Claesson et al Sweden 2014	Prospective cohort	74/79	ND	30 mins / 3 x week	Moderate	1-3	<u>ND</u>	EPDS (<u>continuous</u>) 11 weeks	PA had fewer postpartum depressive symptoms compared with PIA	12
*Demissie et al USA 2013	Prospective cohort	2 nd trimester: 432/ 220 3 rd trimester: 409/ 243	Work, leisure, child care, house care, gardening, transportation Overall physical activity	ND	Moderate to high	2 -3	<u>Analyses adjusted for AD CESD (≥17)</u>	EPDS (≥13) 12 weeks	No significant associations were found between total or domain-specific PA at either 2 nd or 3 rd trimester and postpartum depressive symptoms	11
*Ersek and Brunner Huber USA 2009	Cross sectional	865/1304	ND	30min/ ≥1 x/week	ND	3	<u>Analyses adjusted for AD Maternal emotional hardship during pregnancy (yes vs. no)</u>	PRIME-MD (feeling depressed; having little interest or pleasure) 6 weeks	No significant associations between PA during the third trimester and feeling Depressed or having little interest/pleasure	8
Guida et al USA 2012	Cross sectional	3726/2477	ND	30 mins / 1-4x week ≥5x week	Moderate	3	<u>No</u>	PRIME-MD (feeling depressed; having little interest or pleasure) 8-24 weeks	PIA (i.e. less than one day of PA/week) during the last three months of pregnancy were at increased odds for PPD compared to women who engaged in regular PA	7
*Jeon et al South Korea	Prospective cohort	9/13	Yoga	60min/ 2 x week	Low to moderate	1-3	<u>No</u>	Zung (<u>continuous</u>) 6 weeks	No significant difference was found	6

2013									between PA and PIA women in terms of postnatal depression	
*Kowalska et al Poland 2014	Cross sectional	46/54	ND	ND	ND	ND	<u>Exclusion of women with self-reported psychiatric disorder</u>	EPDS (≥ 10) 3 days	PA during pregnancy had better mood	4
Nordhagen and Sundgot-Borgen Norway 2012	Prospective cohort	1 st trimester: 115/38 2 nd trimester: 105/51 3 rd trimester: 85/78	ND	≥ 60 min/week	Low to high	1-3	<u>Exclusion of women with known psychiatric disorder</u>	HADS-D (≥ 8) 6 weeks	Moderate PA for more than 60min/week during the third trimester was significantly associated with lower HADS-D scores compared to PIA	7
*Shakeel et al Norway 2018	Prospective cohort	0 min/week: 138 1-74 min/week: 101 75-149 min/week: 135 ≥ 150 min/week: 196	ND	1-74 75-149 ≥ 150 min/week	Moderate to high	2	<u>Analyses adjusted for AD</u> <u>EPDS (≥ 10)</u>	EPDS (≥ 10) 12 weeks	At least 150 min of moderate to vigorous PA in bouts of ≥ 10 min associated with lower risks of EPDS in comparison to PIA or low intensity PA	12
*Stephenson Canada 1993	Prospective cohort	1 st trimester: 24/24 2 nd trimester: 16/16 3 rd trimester: 14/14	Leisure	ND	ND	1-3	<u>No</u>	EPDS (≥ 10) 6 weeks	PA during any of the three trimesters of pregnancy was not significantly associated with lower PPD scores	6
*Strøm Denmark 2009	Prospective cohort	26494/44372	Leisure	ND	Moderate to high	1-3	<u>Analyses adjusted for history of previous depression</u>	Admission to hospital or outpatient contact with diagnosis of a depressive episode Antidepressant medication prescription 1- 52 weeks	No association was observed between PA and PPD admission in the first year after birth Vigorous PA was associated with a lower risk of	11

									antidepressant prescription in the first year postpartum compared to PIA	
Symons Downs et al USA 2008	Prospective cohort	209/11	Leisure	30 mins/ 1-4 x week	Low to high	1-3	<u>Analyses adjusted for AD</u> <u>CESD (continuous)</u>	<u>CESD (continuous)</u> 6 weeks	Cumulative PA throughout the three trimesters of pregnancy was associated with lower PPD	10
*Van der Waerden et al France 2017	Prospective cohort	EDEN: 963/933	Work, leisure-time physical and locomotive activity, sports Overall physical activity	ND	Low to high	1	<u>Analyses adjusted for AD</u> <u>CESD (≥ 16)</u>	<u>EPDS (≥ 12)</u> 16 weeks 24 weeks 52 weeks	PA in the first trimester was not associated with PPD	12
*Van der Waerden et al France 2017	Prospective cohort	ELFE: 7859/ 7935	Work, leisure, domestic, transportation Overall physical activity	ND	Low to high	3	<u>Analyses adjusted for AD</u> <u>Maternal psychological distress during pregnancy (yes vs. no)</u>	<u>EPDS (≥ 12)</u> 8 weeks	Higher levels of domestic and overall PA in the third trimester were significantly associated with increased risk for PPD	13

Studies marked with * are included in the meta-analysis

PA= Physical Activity; PIA= Physical InActivity; AD= Antenatal Depression; ND= Non Described

EPDS= Edinburgh Postnatal Depression Scale; CESD= Center for Epidemiologic Studies Depression Scale; PRIME-MD=Primary Care Evaluation of Mental Disorders; HADS-D= Hospital Anxiety and Depression Scale

Table 4 Univariate moderator analyses

Variable	k	SMD	95% CI	Q	P
All studies	<u>24</u>	<u>-0.22</u>	<u>-0.42- -0.01</u>	<u>43.60</u>	<u>0.04*</u>
Intervention	6	-0.58	-1.09- -0.08	53.52	0.02*
Observational	<u>18</u>	<u>-0.07</u>	<u>-0.20- 0.06</u>	<u>66.39</u>	<u>0.24</u>
<u>Study characteristics</u>					
<u>Year of Publication</u>					<u>0.75</u>
_____ <2008	<u>4</u>	<u>-0.56</u>	<u>-1.16- 0.03</u>	<u>3.62</u>	
_____ ≥2008	<u>20</u>	<u>-0.23*</u>	<u>-0.45- -0.01</u>	<u>13.42</u>	
<u>Study quality</u>					<u>0.83</u>
_____ Low risk of bias	<u>13</u>	<u>-0.26</u>	<u>-0.54- 0.02</u>	<u>7.76</u>	
_____ Moderate risk of bias	<u>6</u>	<u>-0.37*</u>	<u>-0.74- -0.01</u>	<u>7.23</u>	
_____ High risk of bias	<u>5</u>	<u>0.04</u>	<u>-0.65- 0.72</u>	<u>0.44</u>	
<u>PA characteristics</u>					
<u>Domain of PA</u>					<u>0.83</u>
_____ Leisure	<u>10</u>	<u>-0.31</u>	<u>-0.65- 0.02</u>	<u>8.19</u>	
_____ Other	<u>14</u>	<u>-0.23</u>	<u>-0.51- 0.04</u>	<u>8.14</u>	
<u>Depression characteristics</u>					
<u>MD control at baseline</u>					<u>0.84</u>
_____ Yes	<u>9</u>	<u>-0.29</u>	<u>-0.62- 0.05</u>	<u>4.73</u>	
_____ No	<u>15</u>	<u>-0.25</u>	<u>-0.53- 0.03</u>	<u>11.43</u>	
<u>Timing of PPD assessment</u>					<u>0.82</u>
_____ <16 weeks	<u>21</u>	<u>-0.29*</u>	<u>-0.52- -0.06</u>	<u>16.18</u>	
_____ ≥ 16 weeks	<u>3</u>	<u>-0.14</u>	<u>-0.67 - 0.40</u>	<u>0.13</u>	

k = number of studies; SMD=Standardised Mean Difference; 95% CI = 95% confidence interval around the effect size; Q = test statistic assessing heterogeneity; B = point estimate of the regression slope, indicating how much the effect size increased with one unit of the variable; * p < .05; ** p < .01; *** p < .001

Competing interests

The authors declare that they have no competing interests

Author's contributions

JW and LP developed the initial idea for the study; AN conducted the database searches. AN, CB, FEK, JW and LP initially screened the title and abstracts of identified studies, independently assessed the methodological quality of each included study and conducted the final selection of studies to be included in the review. AN, CB, FEK, MM, JW and LP extracted information and data from the studies; AN and JW performed the meta-analysis and drafted the manuscript. All authors have read and approved the final manuscript.

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	Aguilar-Cordero et al 2018	Bershadsky et al 2014	Mohammadi et al 2015	Rankin et al 1999	Songøygard 2012	Vargas-Terrones et al 2018
Representativeness of the sample	***	*	**	**	***	*
Ascertainment of exposure	**	*	*	*	*	**
PPD not present at start of the study or accounted for	-	*	*	-	-	*
Assessment of outcome	**	**	**	**	**	**
Inclusion of intention-to-treat analysis?	*	**	-	*	**	**
Random sequence generation	**	-	-	**	**	**
Blinding of outcome assessment	**	*	-	**	**	**
Incomplete outcome data	*	*	**	-	**	**
Total quality score	13	9	8	10	14	14
Supplement 1 Risk of bias assessment for intervention studies						

	Abraham et al 2001	Campolong et al 2017	Claesson et al 2014	Demissie et al 2013	Ersek and Brunner Huber 2009	Guida et al 2012	Jeon et al 2013	Kowalska et al 2014	Nordhagen and Sundgot-Borgen 2012	Shakeel et al 2018	Stephenson 1993	Strøm 2009	Symons Downs 2008	Van der Waerden et al ELFE	Van der Waerden et al EDEN
Study design	-	*	*	*	-	-	-	-	-	*	*	*	*	*	*
Representativeness of the sample	**	*	*	***	**	**	*	*	**	**	*	**	*	***	**
Ascertainment of exposure	*	**	**	**	*	*	**	?	*	**	*	*	**	**	**
PPD not present at start of the study or accounted for	*	-	?	*	*	?	-	*	-	*	-	*	*	*	*
Sample size justified and satisfactory ¹	-				*	*	-	-	*						
Description of non respondents ¹	-				?	?	?	?	?						
Adequacy of follow up ²		*	**	-						*	-	*	*	*	*
Assessment of outcome	**	**	**	**	*	*	**	**	**	**	**	***	**	**	**
Comparability (control for confounders)	*	-	*	*	*	*	-	-	-	*	-	*	*	*	*
Missing data	-	*	***	*	*	*	*	?	*	**	*	*	*	**	**
Total quality score	7	8	12	11	8	7	6	4	7	12	6	11	10	13	12
Supplement 2 Risk of bias assessment for observational studies															
¹ For cross-sectional studies only															
² For cohort studies only															