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Physical activity and physical exercise in perinatal depression prevention: a Systematic review and Meta-analysis

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ABSTRACT

Background: Perinatal depression, a concept that includes antenatal depression and postpartum depression, is concerning and its prevention is consensual. The American College of Obstetricians and Gynecologists (ACOG)'s guidelines recommend, for healthy pregnant and postpartum women, at least 150 minutes per week of moderate-intensity aerobic activity, spread throughout the week and adjusted as medically indicated, but the full impact of these strategies is still unknown.

Objective: To assess the effects of exercise practice and physical activity on perinatal depression prevention in pregnant and postpartum women.

Methods: Systematic review of observational and intervention studies and meta-analysis. Participants: non-depressed women either pregnant or up to twelve months postpartum. Interventions/ exposures: exercise practice or physical activity. Outcome measures: depression diagnosis/risk or measurement of depressive symptoms.

Results: We identified eleven eligible studies for inclusion: three randomized controlled trials (RCT) and eight prospective cohorts. The systematic review presented some evidence of moderate physical exercise in aquatic environment and regular exercise practice during gestation to produce a reduced risk of perinatal depression. The meta-analysis showed no evidence of the impact of exercise in perinatal depression: before and after intervention (CI95% [-0.30, 0.66]), with large heterogeneity [Q-test ($p<0.01$) and I^2 (93.4%)]; control group (CI95% [0.04; 0.42]) and intervention group (mean difference not statistically different); heterogeneity [control group: low ($p=0.61$; $I^2=0.0\%$); intervention group: high ($p<0.01$; $I^2=85.3\%$)]. About physical activity, the systematic review revealed some evidence for prevention of perinatal depression and the meta-analysis showed nonexistence of impact of physical activity in perinatal depression (CI95% [0.33; 1.41]); and large heterogeneity ($p=0.02$; I2=73.3%). Two RCT studies had unclear risk of bias and one a high risk of bias due to inadequate blinding. The quality of evidence for the other studies, using Newcastle-Ottawa nonrandomized scale was classified from good to poor.

Conclusion: According to current evidence synthesized in this review, there is no strong evidence of exercise or physical activity in the prevention of perinatal depression. Some studies reported lower perinatal depressive symptoms associated with higher exercise practice behavior. As for physical activity, some studies report lower perinatal depressive symptoms associated with physical activity. More studies are needed to evidence these findings: more RCTs, with larger samples, including non-singleton pregnant women, overweight and obese women, women in possible social risk (e.g. women that do not speak or understand the official language of the country they reside), adapting the study to the population's culture. Studies should

englobe pre-conception, as well as more assessment times, both for perinatal depression symptoms and exercise/physical activity during pregnancy and in the postpartum period. As for the assessment exercise and physical activity outcomes, more objective measures are needed, such as by using pedometers or monitors. About depression outcome assessment, although it might be expensive to do by clinicians, it would be the best way to measure perinatal depressive symptoms and make perinatal depression definitive diagnosis, in order to accurately assess effective disease incidence's decrease. Clinicians should recommend exercise practice to pre-pregnant women, pregnant women and postpartum women, as a way of improving health condition in general, but this recommendation still lacks quality evidence concerning perinatal depression prevention.

KEYWORDS: PERINATAL DEPRESSION, ANTENATAL DEPRESSION, POSTPARTUM DEPRESSION, PREVENTION, PHYSICAL ACTIVITY, PHYSICAL EXERCISE.

1. INTRODUCTION

The *International Statistical Classification of Diseases*, 11th edition (ICD11) defines that a depressive episode is characterized by a period of almost daily depressed mood or diminished interest in activities, lasting at least two weeks accompanied by other symptoms such as difficulty concentrating, feelings of worthlessness or excessive or inappropriate guilt, hopelessness, recurrent thoughts of death or suicide, changes in appetite or sleep, psychomotor agitation or retardation, and reduced energy or fatigue[1]. According to the World Health Organization (WHO) more women are affected than men. The WHO emphasizes that prevention programs have been shown to reduce depression[2].

As for the definition of perinatal depression (PND), it refers to the major and minor episodes during pregnancy (antenatal) or within the first 12 months after delivery (postpartum or postnatal)[3]. The signs and symptoms for PND are the same as for depression in general. There are still no specific diagnostic criteria for PND; diagnosis is based on the ICD11[1] or the *Diagnostic and Statistical Manual*, 5th edition (DSM5)[4]. It's not simple to recognize PND since it's signs and symptoms can be attributed to the normal changes of pregnancy and postpartum period[3]. PND affects one in seven women and is one of the most common medical complications in the perinatal period. Actually, in the United States of America, maternal suicide now exceeds hemorrhage and hypertensive disorders as a cause of maternal mortality[3].

Most of the studies concentrate in postpartum depression (PPD), rather than in antenatal depression[5]. Antenatal depression doesn't have a concrete definition on ICD11 or DSM5[1,4]

and it's prevalence is not totally known, but it's estimated to be 20%[6]. Also, it is well established that antenatal depressive symptoms are the best predictor of PPD[7].

As for PPD, according to the ICD11 it is a disorder with depressive symptoms, commencing within about 6 weeks after delivery. This designation should not be confused or used to refer to the postpartum blues, that occur soon after delivery, which are mild and transient depressive symptoms that do not meet the diagnostic requirements for a depressive episode[1]. It affects 10-15% of postpartum women[3]. Mothers at risk of postpartum depression (PPD) are seldom identified during pregnancy or at the time of delivery[8]. We should also keep in mind that PPD may also be a continuation of a depressive disorder that existed prior to pregnancy, rather than a new disorder[3]. PPD affects, globally, 0.5% to 60% women[9]. It's prevalence differs depending on the world region, for example, in Singapore, Malta, Denmark and Malaysia, the prevalence of PPD was 0.5-9%, while in Guyana, Costa Rica, Italy, Chile, South Africa, Korea and Taiwan it was 34-57.0%[9].

About the numerous consequences of maternal depression in the family: for the women, besides elevated risk of PPD, antenatal depression has been linked to poor maternal self-care, preeclampsia, birth difficulties for the mother and child, increased risk of preterm delivery and reduced breastfeeding[6]. For the newborn, maternal depression is strongly associated with lower APGAR (American Pediatric Gross Assessment Record) scores, failure to thrive, and poor physical and emotional/behavior development[10–13]. It may also affect the bonding between mother and child, which is most significant in the new born period[14]. At the end of the first year, children whose parents respond immediately to any cry or fussiness or who receive extra attention in the first 4 months, show less crying and fussiness[15]. And finally, the children of depressed mothers are also at higher risk of developing depression later in life, of sleep disturbances and irritability, lower scores on developmental scales, exhibiting reduced motor tone and activity, and have more behavioral problems[16]. It is important to acknowledge that maternal depression can influence child development, but poor infant outcomes can also affect maternal mood[6], despite this, the incidence of PPD is much higher than the incidence of babies born with poor birth outcomes[17], making clear that the poor outcome in children is not the main reason for PPD.

As for physical activity (PA), WHO defines it as any bodily movement produced by skeletal muscles that requires energy expenditure. It is not the same as exercise, as the latter is a subcategory of physical activity that is planned, structured, repetitive, and purposeful in the way that the improvement or maintenance of one or more components of physical fitness is the objective. PA includes exercise as well as other activities which involve bodily movement and are done as part of playing, working, active transportation, house chores and recreational activities. The risk of depression in adults is decreased with regular and adequate levels of

PA[18]. PA could reduce depressive symptoms through biological mechanisms, such as by increasing beta-endorphins levels[19], levels of brain neurotransmitters associated with feelings of satisfaction and euphoria[20], self-esteem and mastery[21,22], but also by decreasing pain[19]. By performing PA in a group-based format, we add to its benefits the social support[23].

ACOG's guidelines recommend that, for healthy pregnant and postpartum women, at least 150 minutes per week of moderate-intensity aerobic activity (i.e., equivalent to brisk walking), spread throughout the week and adjusted as medically indicated. The guidelines advise that pregnant women who habitually engage in vigorous-intensity aerobic activity (i.e., the equivalent of running or jogging) or who are highly active "can continue physical activity during pregnancy and the postpartum period, provided that they remain healthy and discuss with their health care provider how and when activity should be adjusted over time"[24].

A 2018 systematic review and meta-analysis about the effectiveness of exercise-based interventions for preventing or treating postpartum depression[25] concluded that exercise is effective in reducing depressive symptoms in postpartum women, but the effect size was small to moderate and was based on mostly small, low quality RCTs.

To our knowledge there are no systematic reviews to date that assess the evidence of both physical activity and exercise impact on antenatal and postpartum depression (perinatal depression) prevention.

2. METHODS

This systematic review was conducted and reported in accordance with the Preferred Reporting Items for Systematic Review and Meta-analyses (PRISMA) guidelines for systematic reviews and meta-analysis (Appendix – PRISMA 2009 Checklist). **Systematic review registration number in PROSPERO**: CRD42019117739.

2.1 Eligibility criteria

In the present review, we included randomized control trials that met the following inclusion criteria: (*a*) *design* – longitudinal interventional and observational studies were considered; (*b*) *population* – pregnant women or women up to one year postpartum without a depression diagnosis; we also included studies in which only a part of the population could fit into our study, and we analyzed such data separately; (*c*) *intervention* – assessment of intervention or exposure to physical activity or physical exercise. To be included, studies had to test the effect of any type of physical activity measured at least once during pregnancy on depression or depressive symptoms during that pregnancy or in the first year after birth; (*d*) *control* – usual

care, null control, or not exposed/less exposed to physical exercise or physical activity; (*e*) *predefined outcome* – decrease in perinatal depression incidence. This outcome was assessed in absolute number of participants with perinatal depression diagnosis or in the mean value of depressive symptoms assessed using validated assessment tools (e.g. Edinburg Postnatal Depression Scale). We included studies that directly related depressive symptoms to physical activity or exercise and studies that measured these outcomes but didn't relate them, asking the authors for missing data.

2.2 Information sources and search strategy

Comprehensive systematic online searches were conducted using the following electronic databases and a combination of keywords: the PubMed, Cochrane and Embase databases until 13th December 2018. Additionally, to identify potentially relevant studies not found in the previous search, reference lists of included studies, clinical guidelines and previous pertinent reviews were hand-searched.

The search strategy for PubMed and Cochrane databases is specified in Table I and was performed on the 3rd of December of 2018. As for Embase database, the search strategy on the 3rd of December of 2018 is in Table II. The search was restricted to articles written in either English, Portuguese, Spanish or French; no other limits were placed during this phase of the study.

#	***Searches***
1.	Postpartum depression [MeSH]
2.	Perinatal depression [MeSH]
3.	Antenatal depression [MeSH]
4.	Maternal depression [MeSH]
5.	Puerperium depression [MeSH]
6.	Postnatal depression [MeSH]
7.	Pregnant [MeSH]
8.	Pregnancy [MeSH]
9.	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8
10.	Exercise [MeSH]
11.	Physical activity [MeSH]
12.	Yoga [MeSH]
13.	Sports [MeSH]
14.	Fitness [MeSH]
15.	Physical medicine [MeSH]
16.	#10 OR #11 OR #12 OR #13 OR #14 OR #15
17.	Prevention [MeSH]
18.	Intervention [MeSH]
19.	#17 OR #18
20.	#9 AND #16 AND #19

Table I: Search syntax for PubMed and Cochrane databases.

PICO heading	Syntax set
Population	'postnatal depression'/exp OR 'depression, postpartum' OR 'depression, puerperium' OR 'maternal depression' OR 'postpartum depression' OR 'post-natal depression' OR 'postnatal depression' OR 'postpartum depression' OR 'puerperal depression' OR 'puerperium depression' OR 'perinatal depression'/exp OR 'perinatal depression' OR 'antenatal depression'/exp OR 'ante-natal depression' OR 'ante-partum depression' OR 'antenatal depression' OR 'antepartum depression' OR 'pre-natal depression' OR 'pre-partum depression' OR 'prenatal depression' OR 'prepartum depression' OR 'pregnancy'
Intervention	'exercise'/exp OR 'physical activity'/exp OR 'activity, physical' OR 'physical activity' OR 'sport'/exp OR 'competitive gymnastics' OR 'competitive sport' OR 'sport' OR 'sports' OR 'yoga'/exp OR 'hatha yoga' OR 'yoga' OR 'yogic meditation' OR 'physical medicine'/exp OR 'physical medicine' OR 'fitness'/exp OR 'fitness' OR 'fitness, physical' OR 'physical fitness'
Study	'observational study'/exp OR 'non experimental studies' OR 'non experimental study' OR 'nonexperimental studies' OR 'nonexperimental study' OR 'observation studies' OR 'observation study' OR 'observational studies' OR 'observational studies as topic' OR 'observational study' OR 'observational study as topic' OR 'prevention study'/exp OR 'prevention study' OR 'prevention trial' OR 'preventive study' OR 'preventive trial' OR 'intervention study'/exp OR 'intervention studies' OR 'intervention study' OR 'intervention trial' OR 'interventional studies' OR 'interventional study' OR 'interventional trial' OR 'randomized controlled trial/exp' OR 'controlled trial, randomized' OR 'randomized controlled study'
Strategy	Population AND Intervention AND Study

Table II: Search syntax for EMBASE database.

2.3 Data extraction and quality assessment

Two reviewers (ABP and IR) independently screened the titles and abstracts identified in the literature search to assess which did not comply with the inclusion criteria, and consensus was obtained in the union of their selections. The researchers then proceeded to review the full-texts of the remaining studies and, after an independent analysis, attempted to reach consensus regarding eligibility. Divergent opinions regarding study inclusion were settled by discussion and consensus was obtained, with no need for the dispute to be settled by a third party. Data and records management throughout the review of studies were conducted in Covidence[26], the standard production platform for Cochrane reviews selected by Cochrane.

Quality of included RCT studies was assessed by the same two reviewers using the risk of bias tools provided by the Cochrane Collaboration[27]; this tool assigns a value of high, low or unclear to the following items: sequence generation; allocation concealment; blinding of participants, personnel and outcome assessors; incomplete outcome data; selective outcome reporting; other sources of bias. Any dispute was resolved through consensus. The level of risk

for each study was then classified as *low* (all key domains presenting low risk), *unclear* (one or more key domains with unclear risk), and *high* (high risk for one or more key domains).

Risk of bias and quality of included non-RCT studies was assessed by the same two reviewers using Newcastle-Ottawa scale for nonrandomized studies[28] where a study can be awarded a maximum of one star for each numbered item within the Selection category (representativeness of the exposed cohort, selection of the non-exposed cohort, ascertainment of exposure, demonstration that outcome of interest was not present at start of study) and Outcome category (assessment of outcome, was follow-up long enough for outcomes to occur, adequacy of follow up of cohorts) and a maximum of two stars can be given for Comparability (comparability of cohorts on the basis of the design or analysis).

For each outcome, means, 95% confidence intervals (CI), and *P* values were collected for the post-intervention/exposure measurement. If relevant data was missing, the authors of the studies were contacted for additional information.

2.4 Outcomes and statistical analysis

The primary outcome assessed was decrease in PND's incidence or symptoms. We accepted the following screening tools for PND: Edinburgh Postnatal Depression Scale (EPDS), Postpartum Depression Screening Scale; Patient Health Questionnaire 9; Beck Depression Inventory; Beck Depression Inventory-II; Center for Epidemiologic Studies Depression Scale; Zung Self-rating Depression Scale; Hamilton Depression Rating Scale; The WHO-5 Well-Being Index; Structured Clinical Interview for DSM-5; and Structured Clinical Interview for DSM-IV.

Statistical analyses were conducted using the model of aleatory effects, and the impact of heterogeneity on meta-analyses was assessed through Q-test and I^2 statistic. The meta-analyses were performed using the package "metaphor" of R's platform (v. 3.3.2) and significance level adopted was 0,05.

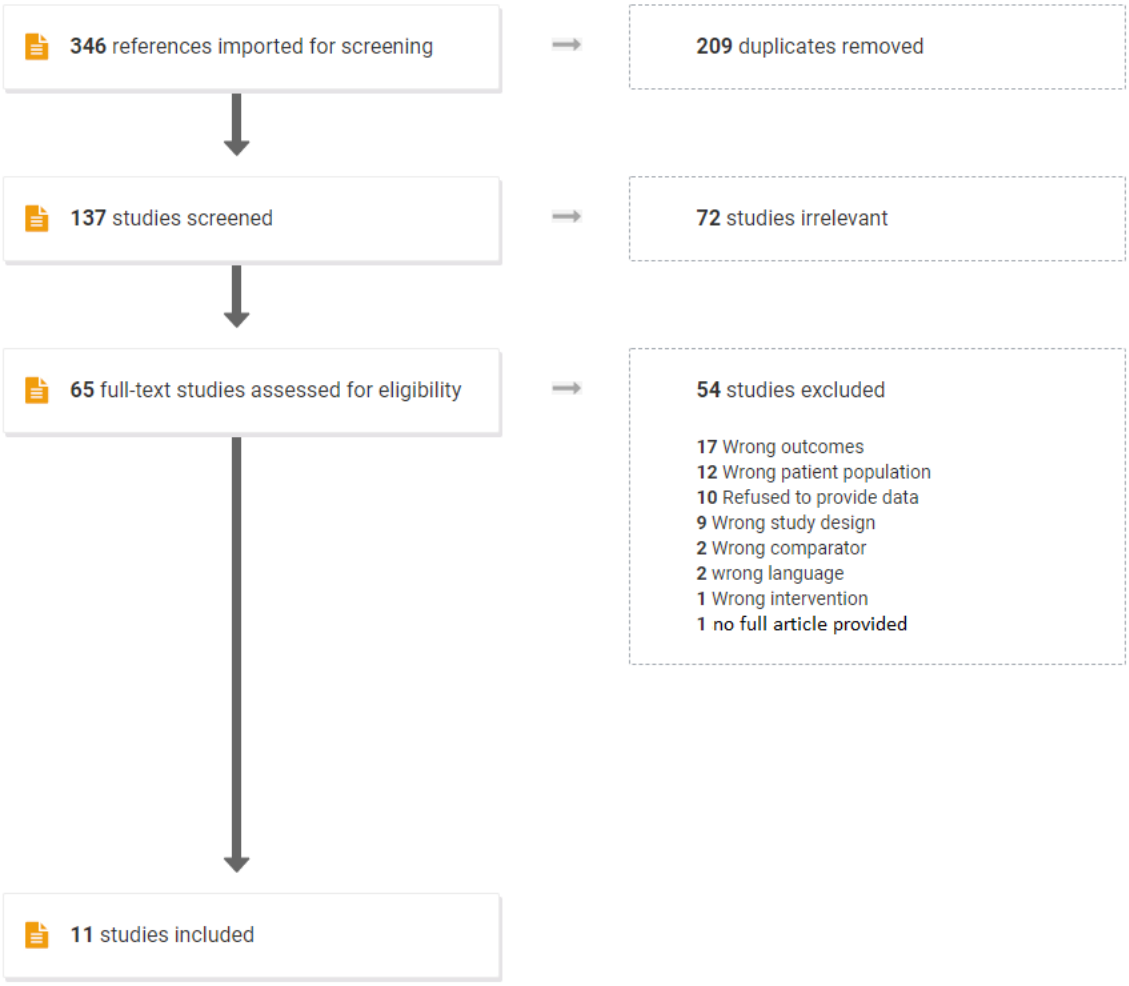
For each outcome referring to exercise practice, mean difference and the corresponding 95% confidence interval (CI) were obtained. These results were combined between each other to produce a summary measure.

To evaluate physical activity, we used odds-ratio and its confidence interval, and a summary measure was also obtained.

3. RESULTS

3.1 Study selection

As presented in **Flowchart 1**, the initial search carried out 346 references (in Embase, Cochrane and PubMed electronic databases). Of these, 209 were found to be duplicates and were therefore excluded, and 72 were found irrelevant based on review of title and abstract. The remaining 65 studies were read in full and assessed for eligibility and 54 were excluded due to wrong outcome[29,30,39–45,31–38], wrong patient population[46,47,56,57,48–55], refusal to provide data[58–67], wrong study design[68–76], wrong comparators[77,78], wrong language[79,80], wrong intervention[81] and no full article provided[81]. In the end, eleven studies were included.



Flowchart 1 – Literature search and selection process for studies included.

3.2 Study characteristics and risk of bias and quality assessment

The main characteristics and outcomes of interest of the included eleven studies were extracted for the purpose of this systematic review and are summarized in **Table V (referring to exercise practice)** and **Table VI (referring to physical activity)**.

We included a total of six exercise practice studies and five physical activity studies and, in every study, population consisted of non-depressed women either pregnant or up to twelve months postpartum.

3.2.1 Exercise practice studies

All six included studies were published between 2008 and 2018, with one being conducted in Iran, one in Taiwan, one in Spain, one in Norway and the remaining two in the United States of America. Three are RCTs, one is a quasi-experimental one group pretest-posttest, and the remaining two are prospective cohorts.

Participants/ Population

All studies recruited women from outpatient centers and hospitals except for Down *et al.*[82] that recruited women in the city. Regarding physical exercise it was assessed either before, during and after pregnancy[82] or during pregnancy and in the postpartum (PP) period[83,84] or just after pregnancy[85–87]. Three[83,85,87] of our included studies assessed perinatal depressive symptoms (DS) in the PP period and the remaining three[82,84,86] assessed DS both during pregnancy and in PP period. Sample sizes ranged from 23 to 719 participants.

Interventions/ exposure

Various types of interventions and exposure measures were employed. Concerning interventions, authors included twelve weeks of 60 minutes of low intensity exercise (yoga, pilates and aerobics class), twelve weeks of 60 minutes of moderate to high intensity exercise, recommendations of doing exercise and gestational moderate exercise in aquatic environment. Exposures included number of minutes of weekly pre-pregnancy exercise activity and number of minutes of weekly physical exercise.

Outcome measures

Analysis considered the outcome of interest reported in each of included trial, regardless they were presented as primary or secondary outcomes. The outcome measures observed were obtained with the following validated scales: CED-D and EPDS.

3.2.2 Physical activity studies

All five included studies were published between 2011 and 2018, with one being conducted in Norway, one in Sweden and the remaining three in the United States of America (USA). All of them were prospective cohorts.

Participants/ Population

All studies recruited women from prenatal clinics and health clinics. Regarding physical activity, it was assessed either just during pregnancy[88–90], or during pregnancy and in the PP period[91] or just after pregnancy[92]. One[88] of our included studies assessed DS only during pregnancy and, thus, just assessing the presence of antenatal depression, three[90–92] assessed DS in the PP period and another one[89] assessed DS both during pregnancy and in the PP period. Sample sizes ranged from 153 to 1077 participants.

Exposures

Various types of exposures were assessed, including occupational, recreational, child and adult care and indoor and outdoor household activities, total amount of moderate to vigorous physical activity (MVPA) or moderate intensity PA performed weekly.

Outcome measures

Analysis considered the outcome of interest reported in each of included trial, regardless if they were presented as primary or secondary outcomes. The outcome measures observed were obtained with the following validated scales: CED-D and EPDS.

3.2.3 Risk of Bias and Quality assessment

The results of quality assessment and risk of bias, performed such as described in Methods, are presented in **Table III and IV**.

Regarding the three RCT studies, the key domains used to assess overall level of risk were allocation concealment, blinding of outcome assessors and incomplete outcome data. All the included studies reported adequate allocation concealment and were classified as having low risk of bias on that topic. About blinding of outcome assessors, one study had low risk of bias, one had unclear risk of bias due to not having any information about the topic and one had high risk of bias since the authors acknowledged the assessors were not blind and that could produce an assessment bias. For incomplete outcome data' item, all trials were assessed as presenting unclear risk of bias regarding that no study presented information on this topic. Therefore, overall risk of performance bias was classified as unclear or high. Summary assessment of risk of bias for each included study is table III.

As for nonrandomized studies, no study had the full score on the Newcastle-Ottawa scale, which, to date, lacks to identify a threshold score distinguishing “good” and “poor” quality studies, but we used habitually used cutoffs for “good quality” (3 or 4 stars in selection domain and 1 or 2 stars in comparability domain and 2 or 3 stars in outcome/exposure domain) “fair quality” (2 stars in selection domain and 1 or 2 stars in comparability domain and 2 or 3 stars in outcome/exposure domain) and “poor quality” (0 or 1 star in selection domain or 0 stars in comparability domain or 0 or 1 stars in outcome/exposure domain). All the studies lacked to achieve an objective assessment of outcome, and, regarding the assessment of exposure only three done so objectively. Only two studies achieved good quality, four were classified as having fair quality and the remaining two as poor quality studies. Summary assessment of risk of bias for each included study is table IV.

	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessor	Incomplete outcome data	Selective outcome reporting	Other sources of bias	Overall level of risk
SONGØYGARD *et al.*, 2011[83]	+	+	?	+	?	-	-	?
Mohammadi et al., 2014[86]	+	+	-	-	?	+	-	-
Aguilar-Cordero *et al.*, 2018[85]	+	+	?	?	?	?	+	?

Table III – Risk of bias summary for RCT studies: review authors’ judgements about each risk-of-bias item (view Methods): + = low risk of bias, ? = unclear risk of bias, - = high risk of bias. Underlined domains refer to key domains used to assess overall level of risk.

Study ID	Newcastle-Ottawa scale for nonrandomized studies[a]								
	Selection				Comparability	Outcome			Total score out of 9
	Representativeness of the exposed cohort (Maximum ★)	Selection of the non-exposed cohort (Maximum ★)	Ascertainment of exposure (Maximum ★)	Demonstration that outcome of interest was not present at start of study (Maximum ★)	Comparability of cohorts based on the design or analysis (Maximum ★★)	Assessment of outcome (Maximum ★)	Was follow-up long enough for outcomes to occur (Maximum ★)	Adequacy of follow up of cohorts (Maximum ★)	
Downs, Di-Nallo and Kirner 2008[82]	★	★	-	-	★	-	★	★	(5) **fair quality**
Campolong et al., 2017[84]	-	★	-	-	★	-	★	-	(3) **poor quality**
Ko et al., 2013[87]	-	-	-	-	--	-	★	-	(1) **poor quality**
Demissie et al., 2011[92]	★	★	★	-	★	-	★	★	(6) **good quality**
Demissie et al., 2011[88]	★	★	★	-	★	-	-	★	(5) **fair quality**
Claesson et al., 2012[89]	★	★	-	-	★	-	★	★	(5) **fair quality**
Demissie et al., 2013[90]	-	★	★	-	★	-	★	★	(5) **fair quality**
Shakeel et al., 2018[91]	★	★	★	-	★	-	★	★	(6) **good quality**

Table IV – Risk of bias and quality assessment of non-RCT studies: review authors' judgements about each assessment item (view Methods).

[a]A study can be awarded a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of two stars can be given for Comparability. Yellow: studies that had no information on the topic.

3.3 Results of studies

3.3.1 Results of the exercise practice studies: results of individual studies and synthesis of results

General results of the studies are summarized in **Table V.**

Of the six studies included, three of the studies reported lower perinatal depressive symptoms (DS) associated with higher exercise practice behavior (EB)[82,85,87].

Downs, DiNallo and Kimer[82] concluded that higher pre-pregnancy exercise behavior resulted on lower DS on gestational first trimester and consequently lower DS in the third trimester of pregnancy and in the PP (postpartum). However, they defended that DS and body image satisfaction experienced during mid-pregnancy are important to predict later DS, whereas EB is less important for predicting future DS in pregnancy and PP.

Campolong *et al.*[84] concluded that there were no significant differences in DS scores between exercise groups. SONGØYGARD *et al.*[83] stated that a subgroup of women who didn't practice exercise as a regular habit before pregnancy had reduced risk of PPD by participating in the regular EB during gestation. Mohammadi *et al.*[86] defended there was no evidence of the role of EB in the prevention of PND.

Ko *et al.*[87] stated that, although the DS score decreased from pre-test to post-test, it did not reach a significant level.

Aguilar *et al.*[85] concluded that women who performed moderate physical exercise in an aquatic environment had lower risk of PPD.

Studies	Country	Design	Number of participants	Results in the control group (CG) and in the exercise practice group (EPG)	Population and sample	Assessment time points for depression and for exercise	Baseline depression score	Intervention or exposure	Control	Depression Diagnosis Criteria
Downs, DiNallo and Kirner 2008[82]	USA	Observational (prospective cohort)	230	**CG (n=113)** 1st trimester mean of 11.5 2nd trimester mean of 11.1 3rd trimester mean of 11.6 Postpartum mean of 9.9 **EPG (n=96)** 1st trimester mean of 10.2 2nd trimester mean of 8.3 3rd trimester mean of 9.4 Postpartum mean of 11.1 p value 1st trimester (0.24) p value 2nd trimester (0.04) p value 3rd trimester (0.13) p value PP (0.39)	Pregnant women from Central Pennsylvania	**Depression**: 1st, 2nd and 3rd pregnancy trimesters, and 6 weeks postpartum. **Exercise**: before, during and after pregnancy.	N/A	**Active exercise practice (n=96):** 120 minutes or more of weekly activity in pre-pregnancy	Somewhat active exercise practice (n=113): less than 120 minutes and more than 30 minutes of activity weekly in pre-pregnancy	CES-D ≥ 16
Campolong *et al.* 2017[84]	USA	Secondary analysis from a larger prospective cohort study	209	**CG (n=52)** 28 weeks mean of 4.0 6 weeks PP mean of 3.6 **EPG (n=157)** 28 weeks mean of 3.4 6 weeks PP mean of 4.1 p value 28 weeks (0.10) p value 6 weeks PP (0.99) Population divided by number of trimesters of pregnancy with sufficient exercise: 0 trimesters (n=23) mean at 28 weeks of 3.6; mean at 6 weeks PP of 3.4 1 trimester (n=34) mean at 28 weeks of 4.4; mean at 6 weeks PP of 3.7 2 trimesters (n=23) mean at 28 weeks of 3.7; mean at 6 weeks PP of 3.8 3 trimesters (n=23) mean at 28 weeks of 3.0; mean at 6 weeks PP of 4.5 p value 28 weeks (0.04) p value 6 weeks PP (0.99)	Pregnant women (ages 18–45 years) enrolled from outpatient obstetrics and family medicine clinics located at an academic medical center	**Depression**: pregnant women at 28th week, and 6-8 weeks postpartum. **Exercise**: 1st, 2nd and 3rd trimesters and at 6 weeks postpartum.	N/A	**Sufficient exercise (n=157):** at least 150 minutes weekly	Insufficient exercise (n=52): less than 150 minutes weekly	EPDS > 10

Ko *et al*. 2013[87]	Taiwan	Quasi-experimental one-group pretest-posttest	23	**EPG (n=16)** Pretest mean of 8.31 Posttest mean of 7.87	Women 6 weeks postpartum from a postpartum outpatient clinic	**Depression** and **exercise**: baseline (6 weeks postpartum) and after the 3 month's exercise program (2-6 months postpartum).	We only included women with CES-D pre-test score ≤14 Mean of 8.31	**Exercise practice (n=16):** 12 weeks of low intensity exercise – twelve 60 minutes classes of Yoga, Pilates and aerobics	None	CES-D ≥ 15
SONGØYGARD *et al.* 2011[83]	Norway	RCT	719	**CG (n=340)** EPDS<10=95.0% EPDS≥10=5.0% EPDS<13=97.6% EPDS≥13=2.4% (n=8) Mean 2.52, SD 2.90; median 2; interquartile range 0-4; p=0.35 **EPG (n=379)** EPDS<10=96.3% EPDS≥10=3.7% EPDS<13=98.1% EPDS≥13=1.1% (n=4) Mean 2.52, SD 3.30; median 1; interquartile range 0-3; p=0.35 p value EPDS ≥10 (0.46) p value EPDS ≥13 (0.25)	Pregnant women between 20 and 36 weeks, recruited when attending a routine ultrasound examination at 18th week at and hospital	**Depression**: 3 months postpartum. **Exercise**: at the end of the training period.	N/A	**Exercise practice (n=379):** 12 weeks of weekly 60 minutes moderate to high intensity exercise sessions led by physiotherapists plus instruction of completing a 45 minutes home exercise program at least twice a week (30 minute endurance training and 15 minutes strength/ balance exercises)	Usual care and written information containing advice on diet, pelvic floor muscle exercises and pregnancy-related pelvic girdle pain (n=340)	EPDS ≥ 10 (minor depression) and EPDS ≥ 13 (major depression

Mohammadi *et al*. 2014[86]	Iran	RCT	110	**CG (n=36)** 0 developed PPD: Baseline mean of 8.14. 1 month PP mean of 7.46 2 months PP mean of 6.5 **I1 n=38 (0 developed PPD):** Baseline mean of 7.77 1 month PP mean of 7.66 2 months PP mean of 6.58 **I2 n=36 (0 developed PPD):** Baseline mean of 9.07 1 month PP mean of 8.03 2 months PP mean of 6.58 p value baseline (0.24) p value 1 month PP (0.82) p value 2 months PP (0.70)	Pregnant women between 26 and 32 weeks with EPDS < 15, recruited from 14 public health centers in Tabriz	**Depression**: baseline (pregnant between 26-32 weeks), 1 month postpartum, 2 months postpartum. **Intervention**: at the end of the study – either at delivery or 2 months postpartum	CG (n=36) mean of 8.14 I1 (n=38) mean of 7.77 I2 (n=36) mean of 9.07	**Intervention 1** (I1) (n=38): a theorical and a practical educational session about exercise in pregnancy, lasting for 40 minutes: recommendation to do the low intensity stretching and breathing exercise three times per week (for 20-30 minutes each) until delivery **Intervention 2** (I2) (n=36): recommendation of doing a 2 month postnatal exercises in addition to getting the instructions of the Intervention 1 group	Control group (n=36): antenatal and postnatal ordinary educations of 40 minutes session	EPDS 11-12 and ≥ 13
Aguilar-Cordero *et al.* 2018[85]	Spain	RCT	125	**CG (n=60):** mean of 10.17 38 at risk of PPD **EPG (n=65):** mean of 6.41 14 at risk of PPD p value between groups (<0.001)	Pregnant women between 12-20 week at health centers in Granada	**Depression**: post-intervention (between the 4-6 weeks postpartum)	N/A	**Exercise practice (n=65):** moderated physical exercise in an aquatic environment from weeks 20 to 37 of gestation, three 1 hour sessions per week	Usual care (n=60)	EPDS ≥ 10 (risk) EPDS ≥ 16 (more severe risk)

Table V: Summary of exercise practice studies' characteristics; CES-D Centre for Epidemiologic Studies Depression Scale; EPDS Edinburgh Postnatal Depression Scale; N/A not applicable; RCT randomized controlled trial; PP postpartum; SD standard deviation.

The mean difference of the results in the depression measure before and after the intervention (physical exercise) is not statistically significant as one could see from the confidence interval (CI95% [-0.30, 0.66]) of the summary measure (Figure 1). Besides, from the presented values, it's possible to conclude that the impact of exercise is almost null. The studies included in the meta-analysis[82–86] reveal a large studies' heterogeneity, evidenced by the Q-test ($p<0.01$) and by the I^2 (93.4%).

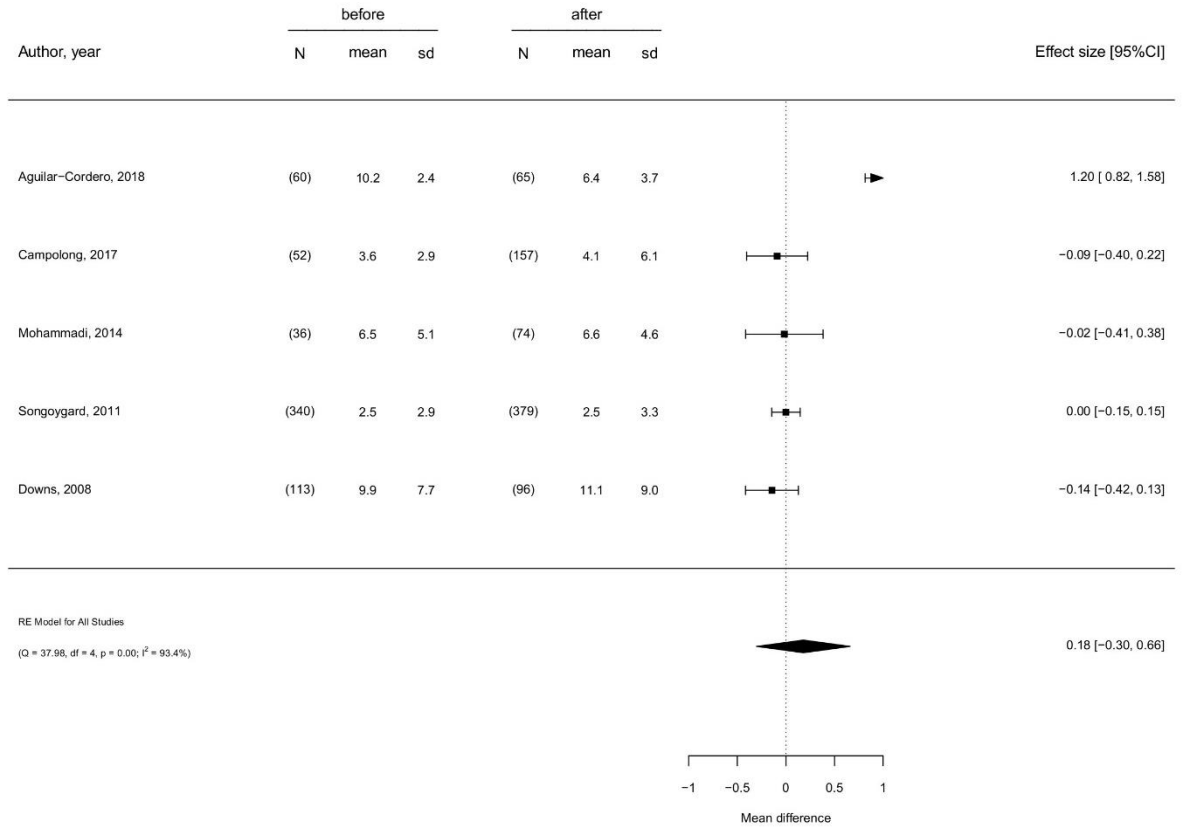


Figure 1. Forest plot of effect of exercise on depression. sd = standard; CI = confidence interval.

In the control group, regarding four studies[82,84,86,87], one was able to observe a statistically significant effect, however with a very reduced mean difference (CI95% [0.04; 0.42]). In the intervention group the mean difference was not statistically significant (Figures 2 and 3). On the other hand, the CIs between the intervention group and the control group were overlapping, thus there was no statistical evidence of the two groups having different results. In the control group heterogeneity is trifling ($p=0.61$; $I^2=0.0\%$) yet in the intervention group it is high ($p<0.01$; $I^2=85.3\%$).

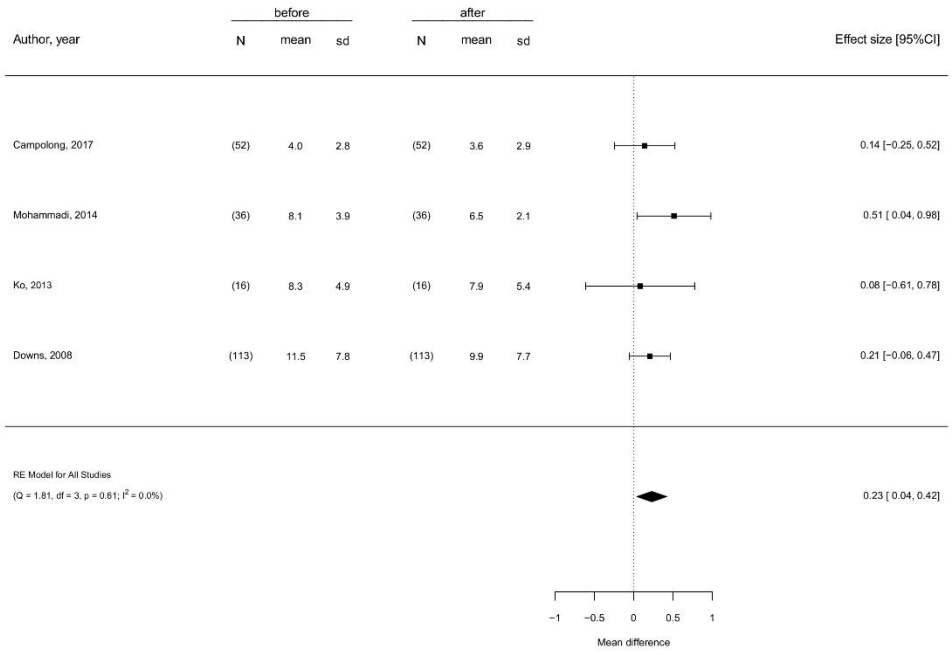


Figure 2. Forest plot of effect of exercise on depression, in the control group. sd = standard; CI = confidence interval.

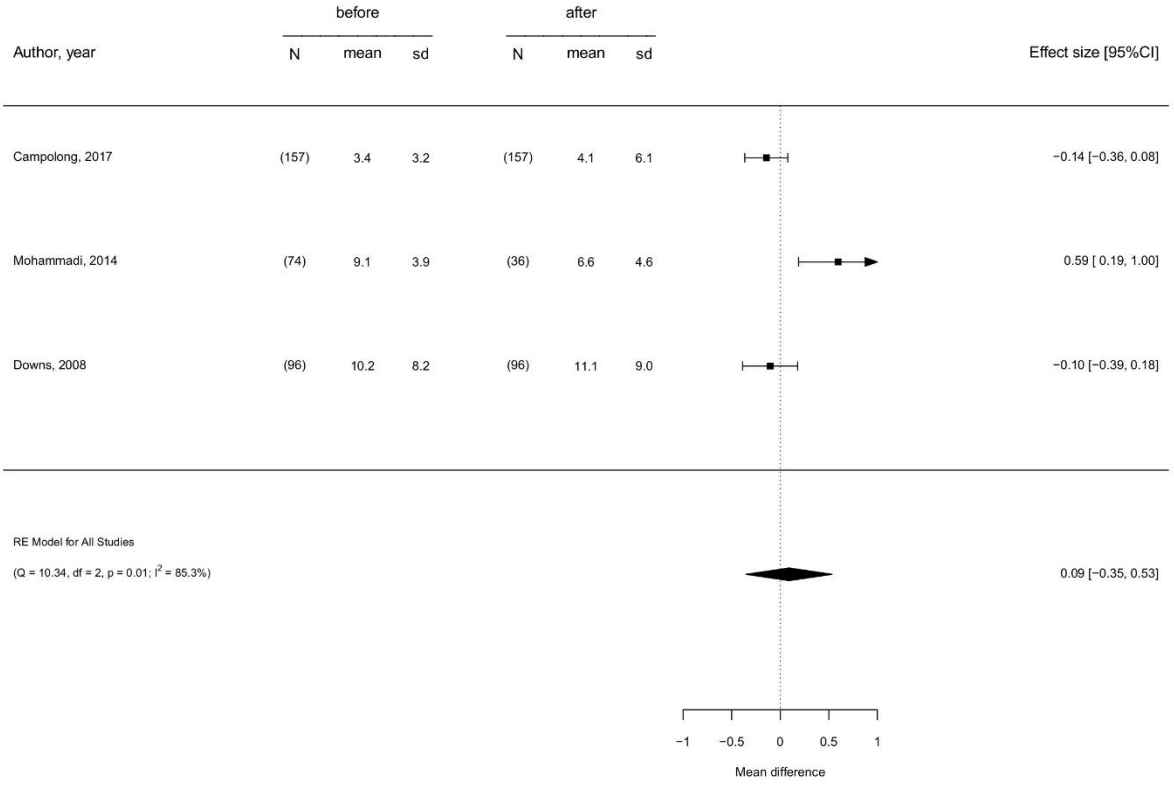


Figure 3. Forest plot of effect of exercise on depression, in the intervention group. sd = standard; CI = confidence interval.

3.3.2 Results of the physical activity studies: results of individual studies and synthesis of results

General results of the studies are summarized in **Table VI.**

One[92] of the five studies reported that women participating in MVPA (moderate-to-vigorous physical activity) had increased odds of having elevated perinatal depressive symptoms (DS). Demissie *et al.*[88], Claesson *et al.*[89] and Shakeel *et al.*[91] found lower DS associated with physical activity (PA). And one[90] reported that MVPA had no significant associations with DS.

Demissie *et al.*[92], in 2011 regarding postpartum depression (PPD), concluded that the association of MVPA and postpartum depressive symptoms varied according to the domain/type of PA. They found that participating in any MVPA was associated with having increased odds of elevated DS. Women participating in adult and child care, indoor household and work MVPA at 3 months PP had more risk of having elevated DS at 12 months PP. There was no association between recreational and outdoor household MVPA and DS.

Demissie *et al.*[88], in 2011 regarding antenatal depression, said that total and domain specific MVPA at 17-22 weeks gestation had few associations with DS at 24-29 weeks gestation. In fact, they concluded that total perceived MVPA was related to reduced odds of elevated DS, but women participating in adult and child care activity of perceived moderate to vigorous intensity, or in high amounts of indoor household, had increased odds of having high DS and recreational MVPA had null effects on DS. They also found that women who met PA recommendations and participated in more than median levels of non-elective MVPA had increased odd of elevated DS. There were no associations between outdoor household or transportation activity and DS.

Demissie *et al.*[90], in 2013 regarding PPD, found most of the associations between MVPA at 17-22 gestational weeks and DS at 3 month PP almost null. Women participating in recreational MVPA had a small decrease in the odds of having DS at 3 months PP and women participating in outdoor household MVPA had a small increase in the odds of being depressed at 3 months PP. The strongest association with 3 months postpartum depressive symptoms was work MVPA which reduced the odds in 86%. As for MVPA between 27-30 weeks of gestation and DS at 3 months PP they found that participating in work and adult and child care MVPA was related to an increase in the odds of having high DS at 3 months PP and participating in outdoor household MVPA had lower odds of having elevated 3 month PP DS.

Claesson *et al.*[89] reported significant differences between the two study groups in mean value of total score of EPDS.

Shakeel *et al.*[91] observed that women who performed weekly ≥150 minutes of MVPA in bouts ≥10 min had lower risk of PPD, compared to those who did not accumulate any MVPA.

Studies	Country	Design	Number of participants	Results in the control group (CG) and in the physically active group (PAG)	Population and sample	Assessment time points for depression and for PA	Baseline depression score	Intervention or exposure	Control	Depression Diagnosis Criteria
Demissie *et al.*, 2011[92]	USA	Observational (prospective cohort)	550	**CG (n=176):** 10 scored ≥ 13 **PAG (n=374):** 25 scored ≥ 13 qui square value of total MVPA (0.65) p value of total MVPA (0.7122) EPDS median of 4 EPDS < 13 (n=609) EPDS ≥ 13 (n=43)	Women who participated in the Pregnancy, Infection and Nutrition (PIN) postpartum study, contacted after delivery	**Depression** and **physical activity**: 3rd and 12th months postpartum.	N/A	**Physical activity (n=374):** occupational, recreational, child and adult care and indoor and outdoor household activity	Physically inactive (n=176): women who don't practice MVPA	EPDS ≥ 13
Demissie *et al.*, 2011[88]	USA	Observational (prospective cohort)	1077	**CG (n=726):** OR of 0.56 with CI 95% of (0.38- 0.83) **PAG (351):** OR of 0.63 with CI 95% (0.50-1.07)	Women who participated in the PIN3 recruited from prenatal clinics	**Depression**: pregnant women before 20 weeks and between 24-29 weeks. **Physical activity**: at 17-22 weeks gestation.	N/A	**Physical activity (n=351):** > the median of nonzero values	Physically inactive (n=726): ≤ the median of non-zero values	CES-D ≥ 17
Claesson *et al.*, 2012[89]	Sweden	Observational (prospective cohort)	153	**CG (n=79):** Gestational week 15 (n=76) mean of 7.1 Gestational week 35 (n=73) mean of 6.9 PP week 11 (n=70) mean of 5.3 **PAG (n=74):** Gestational week 15 (n=74) mean of 5.5 Gestational week 35 (n=68) mean of 4.6 PP week 11 (n=73) mean of 3.8 p value gestational week 15 (non-adjusted 0.009 and adjusted to socio demographic characteristics 0.024) p value gestational week 35 (non-adjusted 0.002 and adjusted to socio demographic characteristics 0.004) p value PP week 11 (non-adjusted 0.033 and adjusted to socio demographic characteristics 0.059)	Obese pregnant women recruited from an antenatal care clinic	**Depression**: pregnant women at 15 weeks, 35 weeks and at 11 weeks postpartum. **Physical activity:** diary during whole pregnancy.	N/A	**Physical activity (n=74):** as being habitual when performed with at least moderate intensity three times weekly or more during at least 15 weeks of pregnancy	Physically inactive (n=79): women who were recommended to practice moderated intensity activities for at least 30 minutes daily but chose, according to their diaries, to practice physical activities bellow the recommend amount regarding intensity, frequency and duration	EPDS values

Demissie *et al.* 2013[90]	USA	Observational (prospective cohort)	652	**CG (n=220):** 16 developed PPD **PAG (n=432):** 27 developed PPD p value (0.6197) OR of 1.07 with CI 95% (0.46-2.46)	Women who participated in the PIN3 recruited from prenatal clinics	**Depression**: 3 months postpartum. **Physical activity**: at 17-22 weeks and at 27-30 weeks gestation	N/A	**Physical activity (n=432):** Total MVPA > 0	Physically inactive (n=220): total MVPA of zero	EPDS ≥ 13
Shakeel *et al.*, 2018[91]	Norway	Observational (prospective cohort)	570	**CG (n=196):** 33 with depression; p value < 0.001 **PAG 1a (n=138):** 10 with depression; OR for PPD of 0.5, with CI 95% (0.21-1.32) **PAG 1b (n=101):** 10 with depression; OR for PPD of 0.5, CI 95% (0.21-1.35) **PAG 2(n=135):** 5 with depression; OR of PPD of 0.2, CI 95% (0.06-0.90)	Women who participated in STORK Groruddalen Cohort Study, based on data collected at three child health clinics	**Depression**: 3 months postpartum. **Physical activity**: at 28th week gestation and 3 months postpartum	N/A	**Physical activity (n=374):** **PAG 1** (n=239): <150 minutes of MVPA/week **PAG 1a** (n=138): 1-74 minutes of MVPA/week **PAG 1b** (n=101): 75-149 minutes of MVPA/week **PAG 2** (n=135): most active group defined as ≥ 150 minutes of MVPA/ week	Physically inactive (n=196): 0 minutes of MVPA/ week	EPDS ≥ 10

Table VI: Summary of physical activity studies' characteristics; CES-D Centre for Epidemiologic Studies Depression Scale; EPDS Edinburgh Postnatal Depression Scale; N/A not applicable; PP postpartum; SD standard deviation; OR odds ratio.

Regarding the analysis of physical activity in three studies[90–92] (Figure 4), we could deduct that the studies pointed to a nonexistence of impact of PA in perinatal depression (IC95% [0.33; 1.41]). It was seen that there was a large heterogeneity in the studies (p=0.02; I2=73.3%).

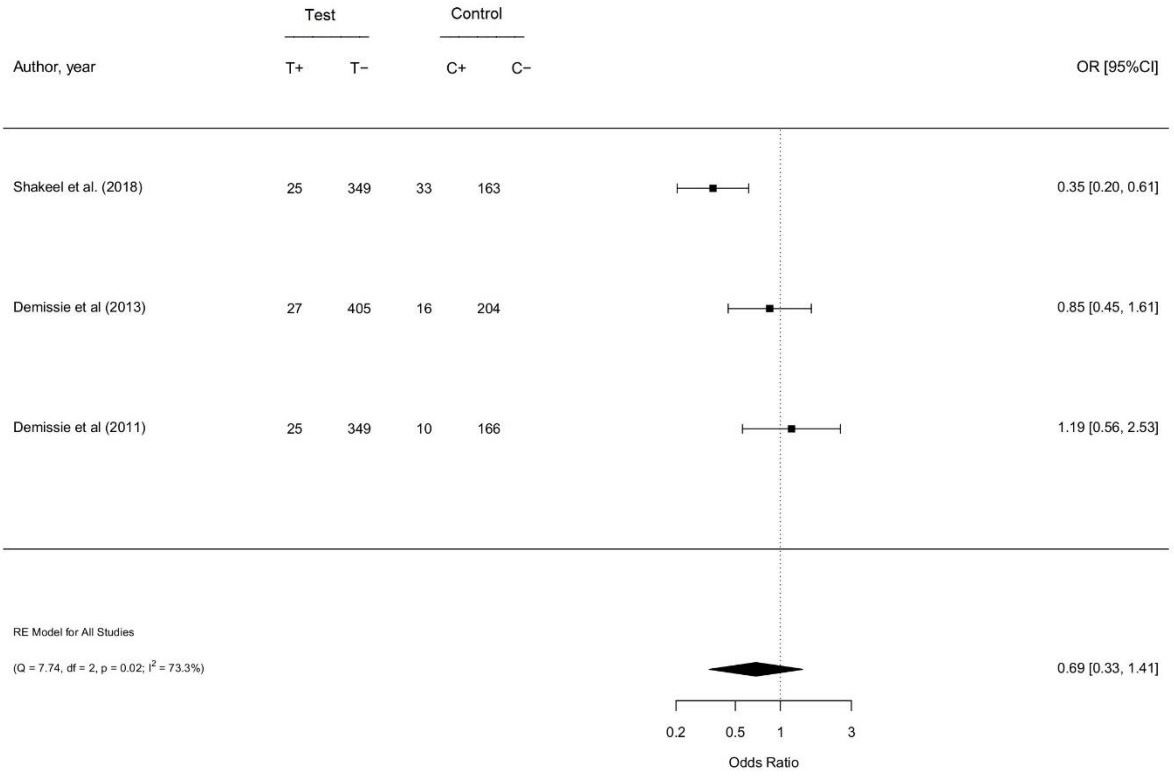


Figure 4. Forest plot of effect of physical activity on depression. OR = odds ratio; CI = confidence interval.

4. DISCUSSION

4.1 Summary of evidence

From the meta-analysis performed, in what concerns exercise practice, it's possible to conclude that the impact of exercise is almost null in the five studies adressed[82–86]. In the analysis of just the control group, regarding four studies[82,84,86,87], one observed a statistically significant effect. Addressing the control group and intervention group there was no statistical evidence of the two groups having different results.

Regarding the analysis of physical activity in three studies[90–92] we deducted that the studies pointed to a nonexistence of impact of PA in depression.

The heterogeneity observed in the different meta-analysis could be due to the variations of methodological strategies that were found either in relation to the moments of measurement or in the studied populations.

This review highlighted the importance of perinatal depression prevention. In fact, we started by reviewing the definitions of perinatal depression, antenatal depression and postpartum depression, addressing their prevalence and the lack of a concrete definition for antenatal depression and knowledge of its prevalence, realizing that postpartum depression was better studied at the time, comparing to the antenatal depression. Just one[88] of our included studies addressed only antenatal depression; all the others addressed perinatal depression or only postpartum depression.

In this review we divided studies according to the types of interventions/ exposures in "exercise practice" and "physical activity".

Although half of the six exercise practice studies acknowledged the role of EB in preventing DS both in pregnancy and the PP period[82,85,87], some of the authors defended that its role was not significant in the prevention of perinatal depression[84,86,87] or that it had a moderate role in influencing DS, when practiced before pregnancy[82].

Downs, DiNallo and Kirner's[82] was the only study in this review that accounted for exercise practice before pregnancy. They emphasize that EB and pre-pregnancy EB roles as possible moderators of body image satisfaction should not be overlooked, and this could have an impact in PND. Aguilar-Cordero *et al.*[85] studied overweight and obese pregnant women, and associated these conditions, strongly, to PPD, heightening the need to inform and promote exercise practice among these women. SONGØYGARD *et al.*[83] stated that although they concluded that there were no significant differences in DS scores between groups they found that in a subgroup of women who didn't practice exercise as a regular habit before pregnancy had

reduced risk of PPD by participating in the regular exercise during gestation. As for Campolong et al.[84] they indicated that there were no significant differences in DS scores between intervention groups, the reasons pointed by the authors for this finding were that their cohort consisted mainly of healthy, married Caucasian women with low-risk pregnancies who resided near hospitals and clinics and were motivated to participate in the cohort, suggesting the cohort had a low baseline risk of PND.

About the physical activity studies, the majority[88,89,91] associated PA with lower DS. Demissie *et al.*[90] (2013) didn't find any associations between PA and DS and they stated that one reason for this could be the need for studies assessing pre-pregnancy PA and/ or PA during the full length of pregnancy, despite this they stated that total perceived MVPA was indeed associated with lower odds of having PP at 3 months, they also pointed that specific MVPA activities, that are possible stressors, increase the risk of DS. In fact, some activities were time dependent, and the best example was work MVPA that in the earlier time point decreased substantially the odds for DS and a few weeks later it was associated with high DS. The only study that reported higher DS associated with PA was conducted by Demissie *et al.*[92] and they also attribute this finding to more stressful specific MVPA or strenuous activities or even life circumstances (i.e. adult child care MVPA associated with financial struggles).

4.2 Limitations

We reviewed a total of only eleven studies due to the lack of response to our request for data from ten authors[58–67]. Three RCT (exercise practice) studies and eight prospective cohorts (both exercise practice and physical activity).

All included RCT trials in this review were reported as having overall unclear risk of bias, mainly due to incomplete outcome data, which possibly overestimates the effects of the lifestyle activity, or high risk of bias due to blinding of outcome assessor, as no strategies were reported to address the issue of incomplete blinding. Across most of the included trials, there were some other items that were also evaluated as having high or unclear risk of bias due to unclear reporting of some information, like, for instance, the "blinding of participants and personnel" and "other sources of bias".

As for the risk of bias of nonrandomized studies, no study had the full score on the Newcastle-Ottawa scale. All the studies lacked to achieve an objective assessment of outcome, since it was done using self-reported scales and thus, is was not possible to ensure that the outcomes were not likely to be influenced by lack of objectiveness, even assuming the difficulty of achieving it with assessments done by clinicians. As for the assessment of exposure only three were done by interviewing the participants and one used an objective measure with a

monitor, which means that, for the others, it was likely the data was not 100% accurate. Also the reviewers were no able to be sure of the who had or didn't have depression at the beginning of the studies, and although we asked the authors for such data, none was provided. As for measures of PND, the data provided was in magnitude of symptoms of depression and not its incidence.

Many other limitations were appointed by the authors of the studies:

The difficulty to generalize the study findings to more diverse populations[82,88,92] and a study just considering overweight and obese women and impossibility of determining the study variables for women with normal to low weight[85] . No study included explicitly pregnant women with multiple fetus and six of them excluded these women[83,84,88–90,92]. The population not being representative of the overall study[88,90,92]. The apparent low baseline risk for antenatal and post-partum depression[84]. Low level of adherence to the exercise program and assessment bias[86].

Selection bias was found in two studies[91,92] and there was one with homogenization of population due to lost to follow up that resulted in a higher socioeconomic status of the study's participants[83] . There was also the inherent bias of self-report measures of EB and PA (all studies, except for the Shakeel *et al.*[91] for PA), but in the Shakeel et al.[91] the monitor didn't measure bicycle activity or water sports and using the monitor might have had an influence in increasing PA behavior; they added the concern that culture and traditions might play a role in PA habits; in fact Ko *et al.*'s[87] participants were Taiwanese whose culture makes it expectable for women to stay indoors for a full month PP (4 weeks) and adopt the "doing the month" regimen of avoiding cold, possible making them more prone to go outside and adhere to the exercise program after this period.

Also, the assessment of PA just in the week before can cause bias because of the variability of behavior regarding it[88,90,92], and not accounting for the routine changes during pregnancy and in the PP period[92] can also cause bias. Regarding the inherent bias of self-report measures of DS (all of the eleven studies), one study emphasized the need of cross-cultural validity of the screening tools[91] and another study added that self-report screening tools also include DS that overlap with pregnancy[88], although a more recent study suggest those so called overlap symptoms should not be dismissed and, instead, the meaning of the changes of these symptoms over gestation should be carefully analyzed[93].

In the Demissie *et al.*[88] study, the assessment of DS and the end of the PA were too close together and they refer to it as a limitation because depression is not an acute condition and it is likely that it takes an extended period of time for PA to have an effect on depression.

There was no information about the groups in the PP, regarding PA, which may have decreased due to new life routine with the child[89].

4.3 Future directions

There is an enormous challenge to both clinicians and patients regarding the prevention of PND. It starts with awareness for this condition that includes both antenatal depression and PPD and goes to the recognition of its challenges both by the woman, by her partner, by her family and, very importantly, by her clinician.

Despite of PPD being a spread subject, antenatal depression isn't. And regarding PA or exercise, most studies didn't regard pre-pregnancy activities, which might have some protective effect on pregnancy and PPD since depression is not an acute condition and the effects of such activities are not seem from night to day. In the future more large-scale well-designed clinical trials are needed, focusing on the whole spectrum of PND and accounting for PA and exercise before pregnancy and for a large period of time (i.e. more assessment points during pregnancy and in the PP period). None of our included studies accounted for women with non-singleton pregnancies and the reasons pointed for this were that these women were subject to higher levels of PPD and anxiety symptoms, and higher levels of general psychiatric distress and parenting stress in the postpartum compared to singleton pregnant women[94].

Culture plays a vital role in every society and so this should always be kept in mind, as well as individual characteristics: every woman is unique (i.e. resistance to stress, reaction to stress, what is stressful or not, adaptability, mental status before pregnancy, exercise beliefs, physical condition, financial status, life conditions, social conditions), because this can influence cut-off points for depression and well as exercise and PA behavior.

Therefore, well-designed clinical trials are still needed, with larger sample sizes and including non-singleton pregnant women, adapting to the culture of a population, and trying to have in mind the individual characteristics of a given population, in order to achieve moderate-to-large clinical effect of interventions to a larger population of women. As for the assessment of outcomes (depression, PA and EB) more objective measures are needed, such as pedometers or monitors, having in mind that these objects might produce an increase in PA or exercise, and eliminate almost completely the need for women to recall their activity and the possible lack of truth of those statements; regarding depression, although its assessment by clinicians might be expensive, it would be the best way to measure DS and make PND definitive diagnosis, in order for us to understand effective disease incidence decrease.

5. CONCLUSIONS

Although some studies reported lower perinatal depressive symptoms associated with higher exercise practice behavior[82,85,87], according to current evidence synthesized and meta-nalysis performed in this review, there is no evidence of EB impact in the prevention of PND with large heterogeneity between studies population, design and outcome assessment.

As for PA, the majority of the studies associated PA with lower DS but the meta-analysis of physical activity performed with three studies[90–92] pointed to a nonexistence of impact of PA in depression. PA should be looked thoroughly, since some studies advocate that women should participate in specific MVPA in specific time periods and avoid others in specific time periods. In fact, we should encourage women to stay physically active, but always avoid activities that they feel as stressful, and we should educate women in the direction of mindfulness, to be aware of their body reactions and their state of mind regarding a specific activity done in a specific time.

More studies are needed to evidence these findings: more RCTs, with larger samples, including non-singleton pregnant women, overweight and obese women, that are in higher risk of PND, women in possible social risk (e.g. women that do not speak or understand the official language of the country), adapting the study to the population's culture. Studies should englobe pre-conception, as well as more assessment times, both for PND and EB/PA during pregnancy and in the PP period. As for the assessment PA and EB outcomes, more objective measures are needed, such as pedometers or monitors. About depression outcome, although its assessment by clinicians might be expensive, it would be the best way to measure DS and make PND definitive diagnosis, for us to understand effective disease incidence decrease.

There is an enormous challenge for clinicians regarding the prevention of PND. Clinicians should recommend exercise practice to pre-pregnant women, pregnant women and PP women, as a way of improving health condition in general, since the evidence for perinatal depression is still unclear.

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APPENDIX

APPENDIX I - PRISMA 2009 Checklist; *Physical activity and physical exercise in perinatal depression prevention: a Systematic review and Meta-analysis*

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	

Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency ($e.g., I^2$) for each meta-analysis.	

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	

Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

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