Preventive Factors of Postpartum Depression in Adult Mothers: A Systematic Review of Randomized Controlled Trials

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Research article

Keywords: postpartum depression, postnatal, prevention, systematic review

Posted Date: June 22nd, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-36611/v1>

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Abstract

Background: Postpartum Depression (PPD) is defined as major depressive disorder with peripartum onset. It is the most common mental illness that occurs after childbirth, affecting not only mother but also newborn. Considering the great impact PPD has, it is relevant to investigate the effectiveness of preventive interventions.

Objective: This review investigates published literature of the last decade (2009-2019) regarding the topic of preventive factors of PPD in adult mothers.

Methods: An electronic search was conducted by using PubMed, psycINFO and Google Scholar. The search term included a combination of postpartum depression, postnatal depression, predictor, prevention and risk factor. Inclusion criteria were: 1) randomized controlled trials (RCT) published in English or German language that deal with 2) adult pregnant or adult mothers (>18 years). Extraction of articles by two independent raters using predefined data fields, including study quality indicators.

Results: The electronic search resulted in a total of 905 articles, whereby only 22 articles were relevant for this synthesis. The interventions were divided into five major topics, these being psychological, psychosocial, nutritional, medical, and exercise interventions. Significant preventive effects concerning PPD in adult mothers were found in psychological and psychosocial interventions. Nutritional, medical and exercise interventions did not have a significant preventive impact.

Conclusion: Psychological and psychosocial interventions seem to be effective in the prevention of PPD. Consequently, preventive programs should include such components. Implications for future research might include the comparison of already existing prevention programs for PPD and the observation of their long-term effects.

Introduction

Postpartum depression (PPD) is the most common mental illness that occurs after childbirth [1]. The Diagnostic and Statistical Manual of Mental Disorders does not define it as an independent diagnosis, but rather as a major depressive disorder “with peripartum onset” [2]. A major depressive disorder may include the following diagnostic criteria: depressed mood, loss of pleasure, change of body weight, insomnia or hypersomnia, psychomotor agitation, fatigue, feelings of worthlessness, concentration difficulties, suicidal thoughts [2]. The time criterion refers to the time “during pregnancy or four weeks postpartum” [2].

The terms postnatal depression and postpartum depression are frequently used interchangeably, but they do not mean the same: postnatal describes the time after birth, related to the child, whereas postpartum refers to the period after giving birth, in relation to the mother [3]. The medically correct term is postpartum depression, accordingly we only refer to a major depressive disorder with peripartum onset as postpartum depression (PPD). However, we included studies in this review that used the term postnatal depression [4–8].

The most common differential diagnosis is the so called *Baby Blues* or *Postpartum Blues* [9]. It occurs around the 2nd and 5th day after delivery and is marked by a greater irritability of the mother and unexpected mood changes. The incidence of *Baby Blues* is very high, with approximately 17–80% of newly delivered mothers being affected by it [9].

Estimations of the prevalence of PPD vary strongly, mostly ranging from 10–15% regarding western developed countries [10] or from 13–19% as an overall prevalence [11]. In Germany, the prevalence for PDD was 3.6% in the year 2005 [12], newer studies have estimated a total of 70,000 mothers that are affected every year [10]. However, a meta-analysis showed a range from almost 0–60% in 40 countries. The authors state that the frequently cited rate of 10–15% is too low and is therefore not representative of the global prevalence rate of PPD [13].

PPD affects not only the mother but also the newborn. Researchers have found a negative correlation between depression and breastfeeding [14]. This implies that the numerous health benefits of breastfeeding for mother and child and the promoted bonding are at risk because of maternal depression [15]. Moreover, infants of depressed mothers are at risk for negative emotional development, e.g. disturbance in self-regulation [16].

In a study conducted with 360 pregnant women, Gotlib et al. [17] found out, that 25% of the sample had higher depressive outcomes, 10% depression during pregnancy and 6.8% were depressed postpartum. Yet out of these only 3.4% were new onset. It has been established that psychiatric history is the strongest predictor of PPD [18, 19]. Werner et al. [19] summarized 15 risk factors for PPD, supporting the hypothesis that a history of depression is decisive for the development of PPD:

(1) lower social class, (2) life stressors during pregnancy, (3) complicated pregnancy/birth, (4) difficult relationship with family or partner, (5) lack of support from family or friends, (6) prior history of psychopathology (depression, anxiety), (7) chronic stressors postpartum (this can include problems with child care and difficult infant temperament), (8) unemployment/instability, (9) unplanned pregnancy, (10) ambivalence over becoming a pregnant, (11) poor relationship with own mother, (12) history of sexual abuse, (13) lack of a confidante, (14) bottle feeding, and (15) depression during pregnancy, with the last generally acknowledged to be the strongest predictor of PPD [19].

These are only some of the reasons why an early approach to prevent PPD is so beneficial. PPD has extensive influencing factors. Given the relevance of PPD, there are already reviews addressing the topic of preventive interventions of PPD [19, 21]. Sangsawang et al [21] performed a systematic review regarding preventive interventions for PPD in adolescent mothers (10–19 years). They analyzed 13 published, English-language randomized controlled trials (RCT) with psychosocial and psychological intervention programs. They found that nearly half of the interventions had a significant effect in reducing PPD symptoms in adolescent mothers. Psychosocial interventions like home-visiting interventions, prenatal antenatal and postnatal education programs and infant massage training were effective; as well as psychological interventions including psycho-educational and cognitive behavioral therapy and group interpersonal therapy.

Werner et al. [19] conducted a literature review regarding biological, psychological, and psychosocial preventive interventions for PPD. They analyzed 45 published, English-language RCTs. Out of those, 20 showed clear positive effects of an intervention. Among biological studies, the intake of calcium, sertraline and selenium had successful effects. Out of the psychological interventions interpersonal therapy, individual cognitive behavioral therapy (rather than group-based interventions) and postnatal psychological debriefing found positive effects. Out of the psychosocial interventions only antenatal and postnatal classes were effective.

It is important to foster the research on the prevention of PPD, since it is a disease with serious impact on mother and child. The aim of this review is to provide a current overview on published RCTs investigating preventive factors for PPD. Different interventions designed to protect high risk as well as low risk pregnant and postpartum adult women in culturally diverse samples are investigated.

Methods

The systematic review was conducted in accordance with the *Prisma* guideline [22]. The search was applied to PubMed, psycINFO and Google Scholar. All articles published between the years 2009 to 2019 were considered. The following search term was used to search all databases:

((("postpartum depression" OR "postnatal depression") AND "predictor" [Title/Abstract]) OR ("postpartum depression" OR "postnatal depression") AND "prevention" [Title/Abstract]) OR ("postpartum depression" OR "postnatal depression") AND "risk factor" [Title/Abstract]).

Primary outcome measures were depressive symptoms and major or minor depression with peripartum onset. No restrictions regarding types of intervention were imposed. The inclusion criteria were as following: (1) already published studies in English or German language; (2) studies involving human subjects; and (3) adult pregnant or adult mothers (>18 years). At the second step research designs other than RCT, such as non-comparative studies, qualitative studies, literature reviews, systematic reviews and meta-analyses, were excluded. Including only randomized studies ensured a reduction of bias and the integration of studies of a high-quality design.

Eligibility assessment was performed in an unblinded standardized manner by two independent raters (NM, KF). Disagreements were resolved by consensus between the two review authors (NM, KF); if no agreement could be reached, a third author was consulted (TO). All titles and abstracts were reviewed by NM to assess their eligibility. The eligibility of the included studies was checked by KF. Afterwards, the full texts from the eligible studies which report on risk and preventive factors of PPD were analyzed by NM and checked by KF.

The quality assessment tool *Qualsyst* [23] was used to evaluate the quality of the included studies. It includes 14 items, for example "Question/objective sufficiently described?" and "Study design evident and appropriate?" [23] (the remaining items are detailed in Table 1). Each of the items is scored on a 3-point Likert scale ("yes" = 2, "partial" = 1, "no" = 0), not applicable criteria are marked "n/a" [23]. For each paper a *Qualsyst* sum score and a percentage score was calculated. Criteria marked with "n/a" were excluded from both calculations. The quality classification was based on the percentage score: poor quality (score<50%), fair quality (score=50-69%), good quality (score=70-79%) and strong quality (score>80%) [21].

The following information was extracted from the included studies: author(s), year of publication, study title, study design, sample characteristics (mean age, inclusion/exclusion criteria, sample size), type of intervention (including duration and frequency), control intervention, protective factors for PPD, outcome measures and findings. The structured approach commonly known by the acronym *PICOS* ("the patient population or the disease being addressed (P), the interventions or exposure (I), the comparator group (C), the outcome or endpoint (O), and the study design chosen (S)" [24]) was used for the evaluation of results.

Results

Search Results

A total of 905 records were identified in the databases. After removing duplicates, 884 records were screened for relevance in protective factors for PPD based on titles and abstracts. 751 records were excluded based on not fitting content and 11 records were not available in the English or German language. No unpublished relevant studies were obtained. The remaining 153 records were screened for full text of which 106 records had a different study design than RCT, 9 records included participants under the age of 18, 8 records were study protocols, therefore not yet completed, and 8 records were thematically unfitting. This resulted in 22 records that met the inclusion criteria and were included in the systematic review (see Figure 1).

Summary of quality assessment

The results of the quality assessment with *Qualsyst* are presented in Table 1. None of the studies were classified as of poor quality. One study [25] was rated with fair quality (score = 50-69%), two studies [26, 27] with good quality (score=70-79%) and 19 studies [4–8, 19, 28–40] with strong quality (score > 80%).

Methods

All studies finally selected for the review were RCTs published in English. The duration of the interventions varied strongly, with the shortest one being only one single session during which a drug was administered [39] and the longest being 12 months with a follow-up at 27 months [5].

Participants

The 22 included studies involved 10448 participants in total. Study sample sizes ranged from 27 to 2,241 participants. The main inclusion criteria were fulfilling certain age limits, if pregnant within determined weeks of gestation, having a history of depression/scoring a set baseline score on a depression

instrument or having no depression at all.

Setting

The majority of the studies (n=8) were conducted in the USA [27, 30, 31, 34, 35, 37, 40, 41], two in the UK [4, 28] and two in China [7, 39]. One study was conducted in each of the following countries: Canada [29], Mexico [33], Norway [8], Hungary [32], France [5], Iran [26], Australia [6], Denmark [36], South Africa [25], Brazil [38].

Interventions

In the reviewed studies, psychological (n=7642), psychosocial (n=1318), nutritional (n=185), medical (n=330) and exercise-based (n=849) interventions were investigated. Table 2 provides an overview about the interventions and their effect. Out of the 22 studies 15 turned out to have a significant impact on the prevention of postpartum depression. 7 studies had no overall significant impact. In the following section the reviewed studies are reported in detail.

Psychological interventions

Lara et al. [33] conducted the first randomized control depression prevention trial on high-risk pregnant Mexican women. 138 adult pregnant women with ≤ 26 weeks gestation and a baseline depression score on CES-D > 16 or a self-reported history of depression, took part in an 8-week prospective. The psycho-educational intervention included a manual that covered the following three components: educational (information on normal pregnancy and the postpartum period), psychological (aimed at reducing depression through e.g. increasing positive thinking) and group component (atmosphere of support of facilitator). The control group received usual postpartum care. Primary outcome were major depression and depressive symptoms, anxiety symptoms as well as perceived intervention impact. There were significantly fewer new depression cases in the intervention group ($p<0.05$). Repeated-measures analysis of variance found neither significant effects of treatment ($p=0.54$) nor significant effects within group (time effect) ($p=0.00$) and in the interaction of time by condition ($p=0.02$). Main effect for treatment and for initial CES-D level was significant ($p=0.54$), but interaction between initial level of symptoms and treatment was not significant. Within groups significant effects of time ($p=0.00$), interaction between time by initial level of depression ($p=0.00$), time by treatment ($p=0.02$), and time by treatment by initial level of depression ($p=0.04$) were found.

Brugha et al. [4] tested in a cluster RCT, whether receiving care from a specialized health visitor is effective in preventing depression in low-risk women. 2241 adult pregnant women at low risk (EPDS score < 12) received either psychologically orientated sessions based on cognitive behavioral therapy (CBT) or person-centered principles for 8 weeks or usual postpartum care. Primary outcome was depressive symptoms. At 6 months postpartum more women in the control group scored ≥ 12 on the EPDS than in the intervention group ($p=0.016$). The covariates living alone, having a history of postnatal depression, having experienced an adverse life event and the 6-week EPDS score were significant predictors of PPD at 6 months ($p=0.031$).

Mao et al. [7] studied the impact of an emotional self-management training program on postnatal depression symptomatology. 240 primiparous pregnant females enrolled in the RCT. The emotional self-management group training program, which is based on CBT with elements of Chinese culture of delivery included 4 weekly group sessions and 1 individual counseling session, whereas the control group received usual antenatal care (four 90-minute childbirth education sessions). Primary outcome was depressive symptoms. Results show significantly lower mean score of PHQ-9 at 36 weeks antenatal in the intervention group compared to the control group ($p<0.01$) and significantly lower mean score of EPDS at 6 weeks postnatal in the intervention group than in the control group ($p<0.05$). This resulted in more people having PPD within the control group ($p<0.05$).

In Kozinszky et al.'s [32] study the impact of a preventive group intervention for PPD was investigated. All pregnant women living in the catchment area were approached for the RCT, resulting in 1719 participants. Psychoeducation and psychotherapy for PPD were held in group sessions, including elements of interpersonal psychotherapy (IPT) and CBT. The control group received treatment as usual but in group meetings, also 4 times. Primary outcome was depressive symptoms. There were significant lower LQ scores ($p<0.001$) and PPD prevalences ($p<0.01$) 6 weeks postpartum in the intervention group than the control group.

Moshki et al. [26] assessed the effectiveness of application of health locus of control (HLC) for prevention of PPD. In a pre-post experimental design with a control group, 230 pregnant females with 28–30 weeks gestation took part. The intervention combined information on anatomical and physiological changes, nutrition, common complications during pregnancy, mental health and communication skills, familiarity with stages of pregnancy, delivery and pain reduction methods, postpartum health, emotions and attitudes of women. This was performed with particular emphasis on components of the HLC, including internal HLC, strong other HLC and random HLC, lasting in total 36 hours. The control group received usual postpartum care. Primary outcomes were health behaviors according to participants' beliefs and depressive symptoms. This led to a significantly reduced chance HLC ($p=0.003$) and a significantly increased internal HLC ($p=0.03$) immediately after the intervention. Moreover, a significant difference between the two groups in reduced PPD outcomes one month after intervention ($p=0.001$) and a significant correlation between internal belief ($p<0.05$) and chance belief ($p<0.01$) with EPDS was found.

Hiscock et al. [6] evaluated in a RCT a program for preventing infant sleep and cry problems and postnatal depression. 781 infants born at 32 weeks or later were recruited with their families to participate. The intervention supplied various informations on topics like infant sleep, cry behavior and settling techniques. Families in the control group received usual childcare. Primary outcome was depressive symptoms and sleep quality and quantity. Between the two caregiver groups there were no differences in depression symptoms at 4 months ($p=0.07$), but a significant greater reduction of depressive symptoms in the intervention caregivers at 6 months ($p=0.03$) was found.

Nugent et al. [27] tested the efficacy of the Newborn Behavioral Observations (NBO) in lowering postnatal depression. 104 primiparous mothers were eligible for the participation in this RCT. The inclusion criteria were raising the baby with the baby's father, having a vaginal delivery between 36 and 42 weeks of gestation and an Apgar score above 7. The intervention included routine care plus NBO within two days post-delivery (in hospital) and one-month postpartum

(during home visit), meaning 18 NBO of behavioral spectrum of infants along four dimensions (autonomic, motor, state organization and attentional-interactive). The control group received, next to the usual postpartum care, a short home visit to carry out the EPDS. Primary outcome was depressive symptoms. The intervention group had significantly fewer mothers with elevated depression scores compared to the control group ($p=0.05$).

Maimburg et al. [36] studied the influence of a structured general antenatal program on PPD. 1062 nulliparous adult pregnant females between 10 + 0 to 21 + 6 days of gestation with a singleton pregnancy took part in the parallel RCT. The antenatal education program was conducted between the 30th - 35th weeks of gestation. It provided material on the content of the birth module, the newborn module and the parent module with information about PPD, lasting 9 hours in total. The control group received usual antenatal care. Primary outcome were depressive symptoms and identifying risk factors for PPD. There were no significant differences in EPDS scores at 6 weeks postpartum between the two groups (OR= 0.89, 95% CI: 0.57-1.40).

Dimidjian et al. [30] evaluated treatment acceptability and efficacy of mindfulness-based cognitive therapy adapted for perinatal depression (MBCT-PD). 86 adult pregnant females with >32 weeks gestation that met criteria for prior major depressive disorder (but not in the last two months) participated in the pilot randomized clinical trial. The MBCT-PD consisted of eight sessions and additionally at-home practice for 6 days each week between Sessions 1 and 7. The intervention lasted 42 days in total. They were compared to the control group, which received usual antenatal care. Primary outcomes were baseline diagnostic status, treatment acceptability, women's satisfaction with study condition, depression relapse/recurrence and depression symptom severity. The intervention group had significantly improved depressive outcomes compared to the control group, including significantly lower rates of depressive relapse/recurrence ($p=0.005$) in the postpartum period and fewer depressive symptoms throughout the trial ($p=0.002$).

Werner et al. [41] examined the effectiveness of Practical Resources for Effective Postpartum Parenting (PREPP) to treat women at risk for PPD. In a RCT 54 pregnant females in 2nd or 3rd trimester of their pregnancy and at high-risk (score of > 24 on Predictive Index of Postnatal Depression), aged 18-45 years took part. The intervention included 3 PREPP sessions in which five specific infant behavioral (feeding, day-night rhythm, carrying duration, swaddling) and mindfulness techniques were covered. Moreover, the participants received supportive psychological interviewing (using motivational interviewing techniques) and psychoeducation conducted by a psychologist. Participants in the control group received enhanced treatment as usual, they met on two occasions with a psychologist and were provided with information about PPD and referred to treatment if necessary. Primary outcome were depressive symptoms, symptoms of anxiety and infant fuss/cry episodes. This showed significantly decreased depressive symptoms in the intervention group in contrast to the control group ($p=0.01$) at 36–38 weeks gestation and 6 weeks postpartum and significantly more depressive symptoms at 6 weeks postpartum in control group in contrast to intervention group ($p=0.02$).

Tsai et al. [25] evaluated the link between food shortages, depression and the role of social support. For this population-based, cluster-randomized trial all pregnant females living in the study catchment area who were willing to participate were recruited, resulting in 958 subjects. The home visiting intervention offered problem-solving and cognitive-behavioral techniques on topics like HIV, tuberculosis, malnutrition and alcohol use in 4 visits and a 36-month follow-up interview. The control group received standard clinic care which consisted of primary health care, tuberculosis and HIV testing, antiretroviral therapy, antenatal and postnatal care. Primary outcomes were depression symptom severity, number of days of hunger in the past week and emotional and instrumental support. This trial showed a strong significant association between lagged food insufficiency and depression symptom severity ($\beta=0.70$; 95% CI, 0.46-0.94), no statistically significant association with food insufficiency and depression symptom severity among women with a level of instrumental support greater than the median ($\beta=0.12$; 95% CI, -0.35 to 0.59), but a significant association between food insufficiency and depression among women with low levels of instrumental support ($\beta=0.79$; 95% CI, 0.51-1.07).

Duncan et al. [31] conducted a mindfulness-based childbirth preparation course. In the RCT 29 primiparous pregnant females in the last part of their singleton pregnancy with no extensive prior experience with meditation or yoga practice were suitable. The intervention group participated in the program called *Mind in Labor (MIL): Working with Pain in Childbirth* [31], which is a 2.5-day mindfulness-based childbirth preparation course based on Mindfulness-Based Childbirth and Parenting (MBCP). The control group received usual antenatal care and a list of approved, comparable childbirth courses, but with no mind-body focus. Primary outcomes were childbirth self-efficacy, maladaptive pain appraisal, perceived pain in labor, use of pain medication in labor, using medical record review, birth satisfaction and depression. Results for perinatal and PPD symptoms showed a significant interaction between group and time ($p=0.04$), the estimated treatment effect was -3.34 (80% CI [-5.22, -1.28]).

Psychosocial interventions

Barnes et al. [28] evaluated in a cluster-randomized study if a home-visiting support program is effective in preventing maternal depression. 250 adult mothers with social disadvantage (Social Disadvantage Screening Index score >9), infant birthweight ≥ 2500 g and infant being under 5 days in special care baby unit took part. The home visits included different activities like providing advice or assistance with childcare and varied individually in length and frequency. The matched control group receiving no support and those who declined home-start-support also receiving no support were compared to the intervention group. Primary outcomes were major or minor depression and depressive symptoms. Depression at 2 months was the only significant predictor for having depression at 12 months. Social support at 2 months led to significantly lower depression scores ($p<0.0001$).

In a cross-sectional RCT, Dennis [29] evaluated whether peer support is effective in the prevention of PPD. 701 adult mothers with a EPDS baseline score < 9 participated. In contrast to the control group, which just received usual postpartum care, the intervention group also received telephone-based peer support, which provided emotional, informational and appraisal support. Primary outcome was maternal perceptions of peer support, which was evaluated by using PSEI at 12 weeks postpartum. The items in *Maternal perceptions of perceived benefits* subscale the perspective *Stress and Coping* in the domain *Depression* showed moderate to strong correlations (*Life is more enjoyable* ($r=0.41$), *Less depressed* ($r=0.62$) [29]), resulting in significantly lower EPDS scores at 12 weeks in the intervention group ($p<0.001$).

Dugravier et al. [5] tested in a prospective RCT the impact of a home-visiting program conducted by psychologists on postnatal depression. 367 primiparous pregnant females with 12-27 weeks gestation who are under 26 years old and fulfill at least one of the following characteristics: "1) having less than twelve years of education, 2) planning to bring up their child without the child's father, 3) having low income" [5] took part. The CAPEDP (*Compétences parentales et Attachement dans la Petite Enfance: Diminution des risques liés aux troubles de santé mentale et Promotion de la résilience - Parental Skills and Attachment in Early Childhood: reducing mental health risks and promoting resilience*) [5] included 14 intensive multifocal home visits done by psychologists who promoted mental and physical health and provided support. It lasted for 12 months, with a 27-month follow-up. The control group received usual postpartum care. Primary outcome was depressive symptoms. The home-visiting program had no overall impact on postnatal depression symptomatology, however post-hoc analysis revealed that the intervention group had significantly lower EPDS scores in the following subgroups: women with lower depressive scores at inclusion ($p=0.05$), women who were planning on cohabiting with the child's father ($p=0.04$) and well-educated women ($p=0.05$).

Lewis et al. [35] examined the relation between employment status and PPD among high-risk women. This was a post hoc analysis from a previously conducted RCT, which was also included in this review and is described in more detail below (see [34]). 124 healthy women (six participants were lost to follow-up), who had a (maternal family) history of depression aged between 18–42 years have been examined. They filled out a demographic questionnaire, completed a telephone interview at the beginning of the study on race/ethnicity, age, body mass index and use of antidepressants, and a telephone interview after 7 months on employment and breastfeeding status and history of depression. Lewis et al. found evidence for a significant association between employment status and higher depression symptomatology ($p=0.010$), especially employed women at 7 months postpartum had significantly fewer depressive symptoms than non-employed women. However, there were no significant differences between women who worked full-time versus part-time on depression symptoms ($r=-0.022$, ns.). They also found a significant correlation between being single and higher depression symptomatology at 7 months postpartum ($p=0.001$).

Nutritional interventions

Mozurkewich et al. [37] conducted a double-blind RCT to investigate whether different types of fish oil supplementation lowers depressive symptoms during pregnancy or postpartum. 126 adult pregnant women with 12–20 weeks gestation and at risk for PPD took part. They either received 6 capsules of EPA-rich (1060 mg EPA plus 274 mg DHA) fish oil supplementation or DHA-rich (900 mg DHA plus 180 mg EPA) fish oil supplements or soy oil placebo twice daily for 3 months. No differences between the groups in any depression outcomes at any of the three time points after supplementation were found (significance=0.051). but DHA levels did predict BDI score at 34–36 weeks ($p<0.05$).

Vaz et al. [38] evaluated the efficacy of fish oil supplementation on the prevention of PPD. 32 pregnant females who were at risk for PPD (past history of depression or baseline EPDS score ≥ 9), between 5-13 weeks of gestation at the time of enrolment and aged 20-40 years were eligible to participate in the randomized, placebo-controlled, double blind trial. They either received 6 capsules per day of fish oil (1.08 g of EPA and 0.72 g of DHA) or soybean oil placebo starting at week 22–24 of gestation for 16 consecutive weeks. Primary outcomes were prevalence of EPDS, length of gestation and birth weight. There were no significant differences between intervention and control groups in EPDS scores (T0 $p=0.809$, T1 $p=0.299$, T2 $p=0.630$, T3 $p=1.000$), but women in the intervention group with a history of depression scored significantly lower on the EPDS from the second to the third trimester in the ITT analyses compared to the control group ($p=0.038$).

Young et al. [40] analyzed the maternal placentophagy's effect on postpartum mood, energy, and bonding. 27 adult pregnant females who had previously decided they would ingest their placenta after birth took part in the randomized, double-blind, placebo-controlled pilot study. Participants consumed their processed, encapsulated placenta: two 550 mg capsules 3 times daily for the first 4 days of supplementation, decreased the dosage of 2 capsules twice daily on days 5 through 12 of supplementation, and reduced the dosage to 2 capsules once daily through completion. The control group received a similarly prepared placebo with the same intake times. Both groups had 4 meetings with researchers. Primary outcomes were basic demographic information, various psychometric, social and lifestyle variables, depression symptoms, saliva sample, length and weight of the neonate. No significant main effects were found ($p=0.016$).

Medical interventions

Xu et al. [39] evaluated in a randomized, double-blind, placebo-controlled design the preventive effect of ketamine on PPD. 330 women who were scheduled to undergo caesarean section with spinal anesthesia received either intravenous low-dose ketamine (0.25 mg/kg diluted to 10 mL with 0.9% saline) or placebo (10 mL of 0.9% saline) within a short time after giving birth. Primary outcome was depression. There were no significant differences found between the two groups in the prevalence of PPD at 3 days ($p=0.965$) and 6 weeks ($p=0.900$) after delivery.

Exercise

Lewis et al. [34] examined in a RCT the effectiveness of a telephone-based exercise program in preventing PPD among high-risk women. 130 adult mothers with a (maternal family) history of depression who are currently not exercising were recruited for *The Healthy Mom Study*. The intervention group took part in a telephone-based exercise intervention including telephone counseling sessions, motivational print materials and completion of exercise logs. The wellness/support contact control condition provided a counselor who only gave support for general issues related to health and wellness and no information regarding exercise, also lasting 6 months. Primary outcome was depression. There were no significant differences in PHQ-9 ($p=0.09$), PSS ($p=0.87$), and PSQI ($p=0.995$) scores between participants in the two groups. The three baseline measures were all correlated with one another: PHQ-9 scores were significantly correlated with the PSS scores ($r=0.43$, $p<0.0001$) and PSQI scores ($r=0.41$, $p<0.0001$).

Songøygard et al. [8] investigated whether exercising during pregnancy is effective in preventing postnatal depression. They conducted a RCT with 719 adult pregnant women. The intervention consisted of a 12-week exercise program exercise groups once weekly and a 45-min home exercise program several times a

week, starting from week 20 of pregnancy. The control group received usual antenatal care. Primary outcome was depressive symptoms. There were no significant differences in depressive symptoms between the two groups ($p=0.35$), but women in the intervention group who did not engage in physical activity regularly before pregnancy had a reduced risk of postnatal depression ($p<0.05$).

Discussion

PPD is one of the most frequent mental diseases of the perinatal period [1] and the importance of prevention of PPD has been highlighted frequently [11, 19, 21]. Therefore, the aim of this current review was to provide an overview of current literature on preventive interventions for PPD in adult mothers. In our systematic review we have investigated 22 studies in total. Out of these, 12 studies included psychological interventions, four studies included psychosocial interventions, three studies included nutritional interventions, one study performed a medical intervention and two studies included exercise programs. 15 studies had a significant effect in preventing PPD. All psychological interventions investigated showed a significant preventive effect concerning PPD, except for one [36]. The psychological interventions which included psychoeducation, elements of CBT and IPT, prevention programs, home visits and a focus on mindfulness had a significant impact in the reduction of PPD. The study of Maimburg et al. [36] carried out an antenatal education program with information about birth and PPD. In comparison to the other studies investigated the intervention was carried out relatively late in pregnancy (30-35 weeks of gestation), which may be a possible explanation for lack of significant preventive effect.

All psychosocial interventions showed significant effects, they contained home-visiting and peer support. Nutritional interventions did not show any significant effects. In the studies of Mozurkewich et al. [37] and Vaz et al. [38] Omega 3 supplementation was given to pregnant women. Both studies did not show significant results regarding the prevention of PPD, which leads to the assumption that Omega 3 is not effective in that case. Young et al. [40] investigated the effects of placentophagy. No significant results were found, this might be due to the small sample size ($n=27$). The medical intervention showed no significant effect, this could be caused by the fact that in the study of Xu et al. [39] a relatively low dose of ketamine (0.25 mg/kg) was used. Exercise programs did not result in an overall lower prevalence of PPD, but only partially in one study [8]. One difference was, that Lewis et al. [34] examined women postpartum (on average 5.7 weeks postpartum), whereas the intervention of Songøygard et al. [8] took place during pregnancy. Songøygard et al. found that a subgroup of women in the intervention group who did not exercise regularly prior to pregnancy but then exercised during pregnancy had a reduced risk of PPD, indicating that exercise programs during pregnancy can be effective among certain participants for preventing PPD.

These results can be compared with the findings of previous reviews. Sangsawang et al. [21] found effective results for psychological and psychosocial interventions, whereas Werner et al. [19] found both significant and non-significant effects for psychological and psychosocial interventions. In line with those findings, we found psychological and psychosocial interventions to be effective in the prevention of PPD. Werner et al. showed that biological interventions, namely with anti-depressants and nutrients provided the most evidence, but interventions using thyroxine, Omega 3 and progestogen showed negative results. In our study no comparable intervention was successful. A factor that could be responsible for this is that these groups had the lowest total number of participants (nutritional $n=185$, medical $n=330$). Parallels can be drawn for Omega 3, since both studies in our review investigating the effect of Omega 3 on PPD in high risk women led to negative results, as well as the three negative results of Werner et al. investigating Omega 3 effect's on low risk women led to the assumption that Omega 3 is not effective in lowering PPD symptoms. In summary, significant effects were found for home visits, psychoeducation, preventative measures, CBT and IPT in both the review of Sangsawang et al. and ours. Nevertheless, their work focused on American adolescent mothers up to the age of 19 years and therefore cannot be generalized to mothers of all ages and ethnicities and should be interpreted with that in mind. There is accordance regarding the review by Werner et al. and our results in the following interventions: IPT, CBT and preventative measures.

The majority of the studies did not put any emphasis on reaching over or under certain cut-offs for baseline depression scores, nor was there a special focus on ethnic minority populations. Due to the fact, that the studies were conducted globally, a wide variability of various populations in different cultures and countries was ensured. The findings may be generalized and implemented in the general adult female population of childbearing age.

Most of the studies ($n=19$) classified as strong quality, none had poor quality. The items 5 (random allocation), 6 and 7 (blinding of investigator and subjects) and 9 (appropriate sample size) were the ones where reporting was most lacking. Therefore, more attention should be drawn to proper randomization techniques including the description of the method used, if applicable reporting of blinding of investigators and subjects, if not, clearly saying why not applicable and having a large enough sample size based on sample size calculations and mentioning of power/effect size.

It is important to foster the research regarding the topic of preventive interventions for PPD since there are ambivalent findings. Implications for future research might include the comparison of already existing prevention programs for PPD and the observation of their long-term effects.

Limitations

Our study has several limitations. The search term was strictly limited to a combination of postpartum or postnatal depression, predictor, prevention and risk factor. This excludes some studies that may be important for this work in advance. For example, studies that focus on the *Baby Blues* were neglected, which might be interesting since there is a link between *Baby Blues* and PPD [10]. Furthermore, only three databases were used to conduct the electronic search, meaning there was no greater variability in the outcome sources. Another limitation is that the screening of PPD symptoms varied widely between the different studies. Although at the beginning we determined the primary outcomes with depressive symptoms and major or minor depression with peripartum onset, it would have been more consistently and comparable if we had decided on a reliable screening instrument, like the EPDS, to measure PPD [42].

Conclusions

15 studies had a significant effect in preventing PPD. Of these 15 studies, 11 psychological interventions and four psychosocial interventions showed significant effects of lower depression scores. To conclude this systematic review, effective interventions should include the following: psychoeducation,

elements of CBT and IPT, preventative measures, home visits, peer support, and a focus on mindfulness.

Abbreviations

BDI-II=Beck Depression Inventory

CAPEDP=Promoting Parental Skills and Enhancing Attachment in Early Childhood

CBT=Cognitive behavioral therapy

CES-D=Center for Epidemiologic Studies-Depression Scale

CORE-OM=Clinical Outcomes in Routine Evaluation – Outcome Measure

DASS-21=Depression Anxiety Stress Scales

DHA=Docosapentaenoic

ESMGT=Emotional self-management group training

EPA=Eicosapentaenoic

EPDS=Edinburgh Postnatal Depression Scale

EPS=Edinburgh Postnatal Scale

FAS=Fatigue Assessment Scale

HFIAS=Household Food Insecurity Access Scale

HLC=Health locus of control

HRSD=Hamilton Rating Scale for Depression

ICQ=Infant Characteristics Questionnaire

ITT=Intention-to-treat

KBQ=Kennerley Blues Questionnaire

LIFE=Longitudinal Interval Follow-up Evaluation

LQ=Leverton Questionnaire

MBCP=Mindfulness-Based Childbirth and Parenting

MBCT-PD=Mindfulness-based cognitive therapy for perinatal depression

MHLCS=Multidimensional Health Locus of Control Scale

MIBS=Mother-to-Infant Bonding Scale

MIL=Mind in Labor: Working with Pain in Childbirth

MINI=Mini International Neuropsychiatric Interview

MSSI=Maternal Social Support Index

NBO=Newborn Behavioral Observations

PPD= Postpartum depression

PHQ-9=Patient Health Questionnaire

PREPP =Practical Resources for Effective Postpartum Parenting

PSEI=Peer Support Evaluation Inventory

PSI=Parenting Stress Index

PSI-SF =Parenting Stress Index Short Form

PSQI=Pittsburgh Sleep Quality Index

PSS=Perceived Stress Scale

RCT=Randomized controlled trial

SCID=Structured Clinical Interview for Diagnostic and Statistical Manual

SCID-I/P=Structured Clinical Interview for DSM-IV-TR Axis I Disorders

SCID-II=Structured Clinical Interview for DSM-IV Axis II Personality Disorders

SCL-90-R=Symptom Checklist-90-Revised

SF-12=12-item Short Form Health Survey

STAI=State–Trait Anxiety Inventory

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

All data generated or analyzed during this study are included in this published article and its supplementary information files.

Competing interests

The authors declare that they have no competing interests.

Funding

Not applicable.

Authors' contributions

NM undertook the literature search and analysis and wrote the first draft of the manuscript. KF contributed to the analysis and writing of the manuscript and took the lead in redrafting. TO reviewed the manuscript. All of the authors read and approved the final manuscript.

Acknowledgements

This research paper submitted in partial fulfillment of the requirements for the degree Bachelor of Science in the degree program Psychology and Psychotherapy at the University Witten/Herdecke.

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Tables

Table 1

Items									
Authors	1. Question / objective sufficiently described?	2. Study design evident and appropriate?	3. Method of subject/comparison group selection or source of information/input variables described and appropriate?	4. Subject (and comparison group, if applicable) characteristics sufficiently described?	5. Random allocation	6. Blinding of investigators	7. Blinding of subjects	8. Outcome and (if applicable) exposure measure(s) well defined and robust to measurement	9. Sample size appropriate?
Barnes et al. 2009	2	2	2	2	2	2	2	2	1
Dennis CL. 2010	2	2	2	2	1	2	0	2	1
Lara et al. 2010	2	2	2	2	2	0	0	2	1
Brugha et al. 2011	2	2	2	2	2	2	0	2	2
Lewis et al. 2012	2	2	2	2	2	2	0	2	2
Mao et al. 2012	2	2	2	2	2	2	0	2	1
Songøygard et al. 2012	2	2	2	2	2	n/a	n/a	2	2
Kozinszky et al. 2012	2	2	1	2	2	2	2	2	1
Mozurkewich et al. 2013	2	2	2	2	2	2	2	2	2
Dugravie et al. 2013	2	2	2	2	2	2	2	2	2
Moshki et al. 2014	2	2	2	2	1	0	0	2	1
Hiscock et al. 2014	2	2	2	2	2	n/a	n/a	2	2
Nugent et al. 2014	2	2	1	2	2	0	0	2	2
Maimburg et al. 2015	2	2	2	2	2	2	0	2	2
Dimidjian et al. 2016	2	2	2	2	1	2	0	2	1
Werner et al. 2016	2	2	2	2	1	2	0	2	1
Tsai et al. 2016	2	2	1	1	0	0	0	2	1
Lewis et al. 2017	2	2	2	2	1	n/a	n/a	2	2
Xu et al. 2017	2	2	2	2	2	2	2	2	2
Vaz et al. 2017	2	2	2	2	1	2	2	2	2
Duncan et al. 2017	2	2	2	1	2	2	0	2	1
Young et al. 2018	2	2	2	2	1	2	2	2	1

Table 2

Author(s)/year	Study title	Study design	Sample characteristics	Intervention	Control	Outcome	Findings
Barnes et al. 2009	The utility of volunteer home-visiting support to prevent maternal depression in the first year of life.	RCT	Adult mothers, mean age 29.0 years, infant birthweight $\geq 2500\text{g}$, ≤ 5 days in special care baby unit, baseline score on modified version of SDI > 9 , 250 subjects	Home-start-support, included different activities like providing company, assistance with childcare or other household tasks, going out on joint trips to local facilities or giving parenting advice, individual length and frequency, average number of visits 15.1, average months of support were 5.5	Matched control group receiving no support, those who declined home-start-support also receiving no support	Primary outcome: major or minor depression occurring between 2 and 12 months by using SCID and depressive symptoms at 12 months by using EPDS, Secondary outcome: ICQ, MSSSI, PSI	More social support at 2 months predictor of lower likelihood of depression, Significant predictor of more depression symptoms at 12 months was more at 2 months ($p < 0.0001$)
Dennis CL. 2010	Postpartum depression peer support: maternal perceptions from a randomized controlled trial.	RCT	Adult mothers, mean age 30.9 years, baseline score on EPDS < 9 , 701 subjects	Usual postpartum care plus telephone-based peer support, a minimum of four contacts and then interactions as deemed necessary (provision of emotional, informational, and appraisal support), mean of 8.8 contacts with their peer volunteers	Usual postpartum care	Maternal perceptions of peer support were evaluated at 12 weeks postpartum using PSEI (supportive interactions, relationship qualities, perceived benefits, satisfaction with support), EPDS	Significantly lower EPDS at 12 weeks in intervention group (no effect at 24 weeks) ($p < 0.001$) in the domains Life is more enjoyable ($r = 0.41$), Less depressed ($r = 0.62$)
Lara et al. 2010	Outcome results of a psycho-educational intervention in pregnancy to prevent PPD: a randomized control trial.	RCT	Adult pregnant with ≤ 26 weeks gestation, mean age 26.9 years, baseline depression score on CES-D > 16 or self-reported history of depression, 138 subjects	Psycho-educational manual with 3 components: educational, psychological, group component, 2-h, 8 weekly group counseling sessions	Usual postpartum care	Primary outcome: major depression by using SCID, depressive symptoms by using BDI-II, outcomes were collected at baseline, 6-weeks and 4-6 month postpartum	Significantly fewer new depression cases in the intervention group ($p < 0.05$) Main effect for treatment and for initial CES-D level was significant ($p = 0.54$), but interaction between initial level of symptoms and treatment was not significant Within groups significant effects of time ($p = 0.00$), interaction between time by initial level of depression ($p = 0.00$), time by treatment ($p = 0.02$), and time by treatment by initial level of depression ($p = 0.04$)

Author(s)/year	Study title	Study design	Sample characteristics	Intervention	Control	Outcome	Findings
Brugha et al. 2011	Universal prevention of depression in women postnatally: cluster randomized trial evidence in primary care	RCT	Adult pregnant, mean age 31.8 years, EPDS score <12 at 6 weeks postnatally, 2241 subjects	Psychologically orientated sessions based on CBT or person-centered principles, 1-h, maximum 8 weekly sessions	Usual postpartum care	Primary outcome: proportion of women scoring ≥ 12 on the EPDS at 6 months postnatally, Secondary outcomes: mean EPDS score, CORE-OM score, STAI, SF-12 and PSI-SF scores at 6, 12 and 18 months	Significantly less women in intervention group scoring ≥ 12 on the EPDS at 6 months postpartum compared to control group ($p=0.016$) Significant predictor of the EPDS at 6 months were the covariates living alone, previous postnatal depression, the presence of one or more adverse life events and the 6-week EPDS score ($p=0.031$)
Lewis et al. 2012	Examination of a Telephone-Based Exercise Intervention for the Prevention of Postpartum Depression: Design, Methodology, and Baseline Data from The Healthy Mom Study	RCT	Adult mothers with a history of depression or a maternal family history of depression, mean age 31.5 years, not exercising, 130 subjects	Telephone-based exercise intervention including telephone counseling sessions, motivational print materials, and completion of exercise logs, 6 months	Wellness/support contact control condition including counselor only providing support for general issues related to health and wellness and not information regarding exercise, print-based mailings on various topics related to wellness, 6 months	Primary outcome: depression by using SCID, Secondary outcome: scores on EPS, PHQ-9, PSQI, PSS	No significant differences between the PHQ-9 ($p=0.09$), PSS ($p=0.87$), and PSQI ($p=0.995$) between participants in the two groups Three baseline measures were all correlated with one another: PHQ-9 scores were significantly correlated with the PSS scores ($p<0.0001$) and PSQI scores, ($p<0.0001$)
Mao et al. 2012	Effectiveness of Antenatal Emotional Self-Management Training Program in Prevention of Postnatal Depression in Chinese Women	RCT	Primiparous pregnant females, mean age 28.6 years, 240 subjects	Emotional self-management group training (ESMGT) program, based on CBT with elements of Chinese culture of delivery, 90-min, 4 weekly group sessions and 1 individual counseling session	Usual antenatal care (childbirth education sessions), 90-min, 4 times	Depressive symptoms were assessed before and after the intervention and 6 weeks after delivery by using PHQ-9, EPDS, SCID	Significantly lower mean scores for PHQ-9 ($p<0.01$), EPDS ($p<0.05$) and SCID ($p<0.05$) in intervention group compared to control group
Songøygard et al. 2012	Does exercise during pregnancy prevent postnatal depression?: A randomized controlled trial.	RCT	Adult pregnant, mean age 30.5 years, 719 subjects	12-week exercise program (including aerobic and strengthening), exercise groups once weekly for 60-min, 45-min home exercise program at least twice a week (endurance training and strength/balance exercises), conducted between week 20 and 36 of pregnancy	Usual antenatal care	Primary outcome: depressive symptoms at 3 months postpartum by using EPDS	No significant difference in total EPDS scores between the intervention and the control group ($p=0.35$) A subgroup of women in the intervention group who did not exercise regularly prior to pregnancy had a reduced risk of postnatal depression ($p<0.05$)

Author(s)/year	Study title	Study design	Sample characteristics	Intervention	Control	Outcome	Findings
Kozinszky et al. 2012	Can a brief antepartum preventive group intervention help reduce postpartum depressive symptomatology?	RCT	All pregnant women living in catchment area were approached, mean age 27.3 years, 1719 subjects	Group sessions consisting of psychoeducation and psychotherapy for PPD utilizing group therapy, interpersonal psychotherapy, and CBT elements, 3-h, once weekly, 4 times	Treatment as usual but in group meetings, once weekly, 4 times	Primary outcome: depressive symptoms by using LQ, 4 times during pregnancy and 6 weeks postpartum	Significant lower LQ scores ($p < 0.001$) and PPD prevalences ($p < 0.01$) 6 weeks postpartum in the intervention group than the control group
Mozurkewich et al. 2013	The Mothers, Omega-3, and Mental Health Study: a double-blind, randomized controlled trial	RCT	Adult pregnant with 12–20 weeks gestation, mean age 30.3 years, baseline EPDS score 9–19, history of depression, currently not taking omega-3 fatty acid supplements or eating more than 2 fish meals per week, 126 subjects	EPA-rich (1060 mg EPA plus 274 mg DHA) fish oil supplementation or DHA-rich (900 mg DHA plus 180 mg EPA) fish oil supplement, 6 capsules twice daily, 3 months	Soy oil placebo, 6 capsules twice daily, 3 months	BDI and Mini-International Neuropsychiatric Interview at enrollment, 26–28 weeks, 34–36 weeks, and at 6–8 weeks' postpartum, serum fatty acids were analyzed at entry and at 34–36 weeks' gestation	No differences between groups in BDI scores or other depression endpoints at any of the 3 time points after supplementation (Significance=0.051) DHA levels did predict BDI score at 34–36 weeks ($p < 0.05$)
Dugravier et al. 2013	Impact of a Manualized Multifocal Perinatal Home-Visiting Program Using Psychologists on Postnatal Depression: The CAPEDP Randomized Controlled Trial	RCT	Primiparous pregnant females with 12 to 27 weeks gestation, less than 26 years old, at least one of the following criteria: 1) having less than twelve years of education, 2) planning to bring up their child without the child's father, 3) having low income; mean age 22.3 years, 367 subjects	CAPEDP: 14 intensive multifocal home visits done by psychologists who promoted perinatal mental and physical health, identified depressive symptoms, provided support and referred to care if necessary, 12 months, 27-month follow-up	Usual postpartum care	Primary outcome: depressive symptoms by using EPDS at baseline and 3 months postpartum	No overall impact on postnatal depression symptomatology Intervention was effective in reducing levels of PPD for subgroups: women who had few depressive symptoms at baseline ($p = 0.05$), women who were planning to raise the child with the child's father ($p = 0.04$) and women with a higher educational level ($p = 0.05$)

Author(s)/year	Study title	Study design	Sample characteristics	Intervention	Control	Outcome	Findings
Moshki et al. 2014	The effect of educational intervention on prevention of postpartum depression: An application of health locus of control	RCT	Pregnant females with 28–30 weeks gestation, mean age 27.9 years, 230 subjects	Participatory educational program: information about anatomic and physiological changes, nutrition, common complications during pregnancy, mental health and communication skills, familiarization with pregnancy stages, delivery and pain reduction methods, postpartum health, emotions and attitudes of women with special emphasis on components of HLC including internal HLC, powerful others HLC, chance HLC, 36 hours in total, 9 workshops	Usual postpartum care	Primary outcome: health behaviors according to participants' beliefs by using MHLCS immediately after the intervention sessions, depressive symptoms by using EPDS after four weeks postpartum	Significantly reduced chance HLC ($p=0.003$) and internal HLC ($p=0.03$) significantly increased immediately after intervention Significant difference between the two groups in reducing postpartum depression one month after intervention ($p=0.001$) Significant correlation between internal belief ($p<0.05$) and chance belief ($p<0.01$) with EPDS
Hiscock et al. 2014	Preventing Early Infant Sleep and Crying Problems and Postnatal Depression: A Randomized Trial	RCT	Families with infants >32 weeks gestation, mean age caregiver 33.15 years, 781 infants	Prevention program for infant sleep and cry problems and postnatal depression including supplying information about normal infant sleep and cry patterns, settling techniques, medical causes of crying and parent self-care, delivered via booklet and DVD (at infant age 4 weeks), telephone consultation (8 weeks), parent group sessions (13 weeks); follow-up at infant age 4- and 6-months	Usual childcare	EPDS, sleep quality and quantity, breastfeeding duration	No group differences in caregiver reports of depression symptoms at 4 months ($p=0.07$) Significant greater reduction of depressive symptoms in the intervention caregivers at 6 months ($p=0.03$)

Author(s)/year	Study title	Study design	Sample characteristics	Intervention	Control	Outcome	Findings
Nugent et al. 2014	Effects of an Infant-focused Relationship-based Hospital and Home Visiting Intervention on Reducing Symptoms of Postpartum Maternal Depression: A Pilot Study	RCT	First-time mothers cohabitating with the father of the baby, vaginal delivery of an infant between 36- and 42-weeks gestational age, Apgar scores not less than 7, mean age 28 years, 104 subjects	Routine care plus Newborn Behavioral Observations (NBO) within two days post-delivery (in hospital) and one-month postpartum (home visit), 18 NBO of the infant's behavioral repertoire along four dimensions (autonomic, motor, state organization and attentional-interactional), 12 to 25 minutes	Usual postpartum care and short attention-control home visit to administer the EPDS	Primary outcome: depressive symptoms at 1 month postpartum using EPDS	Significantly fewer mothers had elevated depression scores in the intervention group (p=0.05)
Maimburg et al. 2015	Postpartum depression among first-time mothers – results from a parallel randomised trial	RCT	Nulliparous adult pregnant females between 10 + 0 to 21 + 6 days of gestation, singleton pregnancy, mean age 29.3 years, 1062 subjects	"The Ready for Child" antenatal education program, between the 30th - 35th weeks of gestation: content of the birth module, the newborn module and the parent module with information about PPD (information on prevalence, prevention, symptoms (shared and different symptoms in men and women), and PPD treatment), 3 modules of 3 hours	Usual antenatal care	Primary outcomes: demographics, depressive symptoms using EPDS at 6 weeks postpartum and identifying risk factors for PPD	No significant difference in EPDS at 6 weeks postpartum between the two groups
Dimidjian et al. 2016	Staying Well during Pregnancy and the Postpartum: A Pilot Randomized Trial of Mindfulness Based Cognitive Therapy for the Prevention of Depressive Relapse/Recurrence	RCT	Adult pregnant females with >32 weeks gestation, meeting criteria for prior major depressive disorder (MDD), exclusion if diagnosis of MDD in the last two months, mean age 29.85 years, 86 subjects	MBCT-PD, at-home practice for 6 days each week, 42 days in total	Usual antenatal care	Primary outcome: baseline diagnostic status via SCID-I/P and SCID-II Depression relapse/recurrence using LIFE at 8-weeks, 1 month prior to delivery and 1 and 6 months postpartum; Depression symptom severity using EPDS	Significant difference in the rate of relapse/recurrence between intervention and control group (p=0.005) in the postpartum period Significantly lower levels of depressive severity in intervention than in control group (p=0.002)

Author(s)/year	Study title	Study design	Sample characteristics	Intervention	Control	Outcome	Findings
Werner et al. 2016	PREPP: Postpartum Depression Prevention through the Mother-Infant Dyad	RCT	Pregnant females in 2nd or 3rd trimester of pregnancy, Predictive Index of Postnatal Depression score > 24, aged 18-45 years, mean age 30.22 years, 54 subjects	3 PREPP sessions covering: five specific infant behavioral techniques (feeding, day-night rhythm, carrying duration, swaddling) Supportive psychological interviewing (using Motivational Interviewing techniques) Psychoeducation Mindfulness techniques	Enhanced treatment as usual and 2 meetings with psychologists (34–38 weeks gestation and 6 weeks postpartum): participants were provided with information about PPD and referral for treatment if warranted	Primary outcome: predictive index of PPD (PPD risk = >24), indexes depressive symptoms via HRSD and PHQ-9	Significantly decreased depressive symptoms in intervention group in contrast to control group (p=0.01) at 36–38 weeks gestation and 6 weeks postpartum Significantly more depressive symptoms at 6 weeks postpartum in control group in contrast to intervention group (p=0.02)
Tsai et al. 2016	Food Insufficiency, Depression, and the Modifying Role of Social Support: Evidence from a Population-Based, Prospective Cohort of Pregnant Women in Peri-Urban South Africa	RCT	All pregnant females living in study catchment area who were willing to participate, 958 subjects	Home visiting intervention: problem-solving and cognitive-behavioral techniques to address major community health challenges (HIV, tuberculosis, malnutrition, alcohol use), 4 visits and follow-up	Standard clinic care groups generally consisted of tuberculosis and HIV testing, partner HIV testing, antiretroviral therapy, antenatal and postnatal care, well-child clinics, and primary health care	Primary outcome: depression symptom severity measured at all time points using EPDS, surveys were conducted at baseline, 6, 18, and 36 months, number of days of hunger in the past week via single-item food insufficiency measure; 10 questions about emotional and instrumental support, 36-month follow-up interview using HFIAS	Strong significant association between lagged food insufficiency and depression symptom severity ($\beta=0.70$; 95% CI, 0.46-0.94) Significant association between food insufficiency and depression among women with low levels of instrumental support ($\beta=0.79$; 95% CI, 0.51-1.07)
Lewis et al. 2017	The relationship between employment status and depression symptomatology among women at risk for postpartum depression	RCT	Healthy women who had participated in a randomized trial (see Lewis et al. 2012) and had a personal or maternal family history of depression, aged 18–42 years, mean age 30.8 years, 124 subjects	Telephone-based exercise intervention, 6 months	Wellness/support contact, 6 months	Demographic questionnaire (income, marital status, education level) Telephone-based interview at baseline (approximately 6 weeks postpartum): race/ethnicity, age, body mass index, antidepressant use Telephone-based interview at 7 months: employment and breastfeeding statuses, EPDS	Significant association between employment status and higher depression symptomatology (p=0.010) Significant association between being single and higher depression symptomatology at 7 months postpartum (p=0.001) No significant differences between women who worked full-time versus part-time on depression symptomatology (r=-0.022, ns.)

Author(s)/year	Study title	Study design	Sample characteristics	Intervention	Control	Outcome	Findings
Xu et al. 2017	Single bolus low-dose of ketamine does not prevent postpartum depression: a randomized, double-blind, placebo-controlled, prospective clinical trial	RCT	Pregnant women who were scheduled to undergo caesarean section with spinal anaesthesia, mean age 31.5, 330 subjects	Ketamine group: subjects received intravenous ketamine (0.25 mg/kg diluted to 10 mL with 0.9% saline) within 5 min following clamping of the neonatal umbilical cord	Saline group: subjects received intravenous placebo (10 mL of 0.9% saline) within 5 min following clamping of the neonatal umbilical cord	Primary outcome: degree of depression by using the EPDS (a threshold of 9/10 was used) at 3 days and 6 weeks after delivery Secondary outcome: numeric rating scale score of pain at 3 day and 6 week postpartum	No significant differences in the prevalence of postpartum depression between the two groups at 3 days ($p=0.965$) and 6 weeks ($p=0.900$) after delivery
Vaz et al. 2017	Omega-3 supplementation from pregnancy to postpartum to prevent depressive symptoms: a randomized placebo-controlled trial	RCT	Pregnant females, past history of depression or baseline EPDS score ≥ 9 , between 5-13 weeks of gestation at the time of enrolment; aged 20-40 years, mean age 26.25 years, 32 subjects	6 fish oil capsules (1.08 g of EPA and 0.72 g of DHA) per day starting at week 22–24 of gestation for 16 consecutive weeks	Soybean oil placebo (6 capsules per day), 16 consecutive weeks	Primary outcome: Prevalence of EPDS ≥ 11 (EPDS was scored at 5–13 (baseline), 22–24, 30–32 weeks of gestation and 4–6 weeks' postpartum) Secondary outcome: mean and changes in EPDS score, Baseline: blood collection, psychiatric interview using the MINI, general questionnaire, mental health scales (including EPDS)	No significant difference between intervention and control groups in the prevalence of EPDS (T0 $p=0.809$, T1 $p=0.299$, T2 $p=0.630$, T3 $p=1.000$) Women in intervention group with previous history of depression presented a higher reduction on the EPDS score from the second to the third trimester in the fish oil comparing to the control group in the ITT analyses ($p=0.038$)
Duncan et al. 2017	Benefits of preparing for childbirth with mindfulness training: a randomized controlled trial with active comparison	RCT	First-time mothers in the late 3rd trimester of singleton pregnancy, no extensive prior experience with meditation or yoga practice, 29 subjects	Mind in Labor (MIL): Working with Pain in Childbirth (Preparation course based on Mindfulness-Based Childbirth and Parenting (MBCP) education, subjects completed self-report assessments pre-intervention, post-intervention, and post-birth, and medical record data were collected; 2.5-day weekend workshop	Usual antenatal care, participants received a list of childbirth courses of comparable length and quality to the MIL intervention, but without any mindfulness meditation, mindful movement/yoga, or other core mind/body component (e.g., hypnosis), they were strongly encouraged to participate in the control childbirth education with a support person, just as with MIL	Depression using CES-D at average gestational age 29.4 weeks, in the week immediately following intervention, within six weeks after birth	Perinatal and postpartum depression symptoms: significant interaction between group and time ($p=0.04$)

Author(s)/year	Study title	Study design	Sample characteristics	Intervention	Control	Outcome	Findings
Young et al. 2018	Placentophagy's effects on mood, bonding, and fatigue: A pilot trial, part 2	RCT	Adult pregnant females who had previously decided they would ingest their placenta after birth, mean age 29.9 years, 27 subjects	Participants consumed their processed, encapsulated placenta: two 550 mg capsules 3 times daily for the first 4 days of supplementation, decreased dosage of 2 capsules twice daily, on days 5 through 12 of supplementation, and reduced dosage to 2 capsules once daily through completion, 4 meetings with researcher	Similarly prepared placebo, same intake	Primary outcome: scored results of the EPDS, KBQ, DASS-21, FAS, MIBS, and SCL-90-R	No significant main effects ($p=0.016$)

Figures

Figure 1

Flow diagram of the selection process

Supplementary Files

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