EVIDENCE-BASED CLINICAL PRACTICE GUIDELINES

FOR PREVENTION, SCREENING AND TREATMENT OF PERIPARTUM DEPRESSION

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RISEUP-PPD
Research Network in PeriPartum Depression Disorder

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These guidelines were developed to support healthcare decisions, by guiding professionals on the evidence-based interventions to support shared decision-making between them and their patients. These are evidence-based guidelines, informed by a systematic review of the evidence and an assessment of the benefits and harms of different treatment and care options. Therefore, recommendations should be considered within the intervention protocols available in the literature, and to some extent described in the literature synthesis sections. However, recommendations, even when strong, might not apply to all circumstances and all patients. Also, some recommendations might reflect that there are difficulties in the accessibility and availability of psychological treatments or resistance of women to pharmacological or psychological treatments. Of note, clinical practice guidelines do not supersede clinical judgment in diagnosis and personalised care considering the specific circumstances of each patient.

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A. Development of the guidelines

A. // Development of the guidelines

Scope of the guidelines

These guidelines aim to synthesise the current evidence concerning interventions to prevent, screen, and treat peripartum unipolar depression (PPD). The guidelines are targeting at healthcare professionals who, in their clinical practice, care for women planning pregnancy, pregnant women or women within the first year postpartum, in relation to their risk for depression, or those that currently have depression. Throughout this work, the term "women" is used. We acknowledge that there could be individuals other than those identifying themselves as women planning pregnancy or being pregnant; however, because all the evidence that was extracted in this work concerns women, we opted for using women when referring to pregnant people. Additionally, there is increasing evidence that PPD also can affect fathers. However, the evidence is still too sparse to develop recommendations about treatment of paternal PPD.

Why were these guidelines developed?

In order to prevent PPD and offer timely screening followed by appropriate treatment, it is crucial to have clinical practice guidelines to instruct on all these steps, from prevention, to screening, and treatment with different options. A recent systematic review of the guidelines for PPD in European countries (Motrico et al., 2022) found 14 clinical practice recommendations in 11 countries (Belgium, Denmark, Finland, Germany, Italy, Malta, Netherlands, Norway, Serbia, Spain, and the United Kingdom). From these, only five recommendations were rated with adequate methodological quality, including recommendations from Finland, The Netherlands, and three from the United Kingdom and, in general, the information of prevention was scarce. In addition, only one of these recommendations (the one from Finland) was published within the last five years. Also, none of the existing guidelines, including the one published in 2023 by the American College of Obstetricians and Gynaecologists (ACOG)(«Screening and Diagnosis of Mental Health Conditions During Pregnancy and Postpartum», 2023; «Treatment and Management of Mental Health Conditions During Pregnancy and Postpartum», 2023), specifically focus on PPD. Considering that PPD is the most prevalent mental health disorder in the peripartum period, and given the large amount of new evidence in this field, up-to-

date evidence-based guidelines on preventing, screening and treatment of PPD are still needed.

The COST Action Research Innovation and Sustainable Pan-European Network in Peripartum Depression Disorder (Riseup-PPD) has pursued several lines of action (Fonseca et al., 2020) over the past four years. One of these lines was to identify clinical practice guidelines for the management of PPD and to tackle the remaining gaps in the field. The absence of specific guidelines for PPD management in European countries might lead to disparities in treating PPD across Europe and, consequently, to inequality for women with PPD. This is especially evident for recommendations on pharmacological treatment, given that recent synthesis of the European clinical practice guidelines (CPGs) for antidepressants and other psychotropic medication highlighted dissimilarities in the available recommendations and the need for evidence-based CPGs (Kittel-Schneider et al., 2022). As a result, we have developed this document by relying on the wealth of international evidence-based literature available. Additionally, we drew on the collective expertise of clinicians, researchers, ethicists, and women who have personally experienced PPD from various European countries.

Target users of the guidelines

These guidelines primarily target mental health professionals (MHP) (such as psychiatrists, psychologists, counsellors, psychosomatic medicine practitioners, and other MHPs), other healthcare professionals including midwives, obstetricians/gynaecologists, paediatricians, nurses, general practitioners, social workers, pharmacists, and others who play key roles in developing and implementing interventions for the prevention, screening, or treatment of PPD. Further targets for these guidelines also include politicians, economists, policy makers, and non-profit organisations, including patient organisations, who may be involved in decision-making about funding, developing and implementing interventions for preventing, screening, or treating PPD.

The interventions presented in these guidelines encompass a wide range of strategies, incorporating biological interventions such as pharmacotherapy and non-invasive brain stimulation, psychological and psychosocial interventions, and other non-conventional and complementary interventions in PPD.

Methodolowy used in these guidelines

The Riseup-PPD evidence-based guidelines for prevention, screening and treatment of PPD disorder were developed based

on the GRADE framework (Schünemann et al., 2013) and follow the recommendations for reporting evidence suggested by the AGREE II Checklist (Brouwers et al., 2010). Extra attention was paid to transparency, coherence and continuous dialogue in the process. In these discussions, the value judgements and ethical grounds inherent to the guidelines' development were identified and discussed.

The main stages for the development of these guidelines are depicted in **Table 1**.

Table 1. Main stages of the development of these Guidelines

Topic selection	The selection of the topic for the guidelines was proposed by the Core Group of the Riseup-PPD COST Action and approved by its Management Committee (MC). Peripartum depression and its management regarding prevention, screening and treatment was chosen as the main targets of the guideline.
Formation of the Guidelines Development Group	The Core Group of the Riseup-PPD COST Action established the criteria for the formation of the Riseup-PPD Guidelines Development Group (RU-GDG). The Core Group of the Riseup-PPD contacted the Working Groups (WGs) involved in the Action and requested each WG to invite 1) experts in the field of PPD prevention, screening and treatment; 2) experts in the methodology of evaluating evidence, mainly systematic reviews and meta-analysis; 3) experts in retrieving the evidence; 4) a patient representative; 5) an expert in research ethics and bioethics; and 6) an information specialist, expert in devising search strategies. The roles of the RU-GDG members and their conflicts of interest disclosure are presented in Appendix 1. Whenever a member of the RU-GDG reported conflicts of interest on a specific question, the evidence that sustained the recommendation was analysed by all authors, to assure that the conflicts of interest were not affecting the recommendation.
Scoping the guidelines	The RU-GDG met to define the scope of the guidelines and establish the main topics. The RU-GDG agreed that the guidelines will be dedicated to women, above 18 years old, namely in the following conditions: 1) Pregnant women diagnosed with PPD; 2) Women within the first year after birth diagnosed with PPD; 3) Pregnant women diagnosed with Major depression before pregnancy; 4) Pregnancy planners that were diagnosed with Major depression; 5) Pregnant and postpartum women at risk for depression; 6) women in reproductive age.

Formulating key questions	The RU-GDG met to formulate the key questions of the guidelines. These are available as an Appendix online at the RiseupPPD website. The search terms were also defined within the RU-GDG. Five subgroups were established based on the selected topics and were requested to elaborate the PICO questions on (1) prevention, (2) screening, (3), pharmacological treatment, (4) psychological treatment, (5) non-invasive brain stimulation, and (6) complementary and alternative therapies.
Search and synthesis of the evidence	The five subgroups of the RU-GDG performed the search, extraction and analysis of the evidence. The search strategy included systematic reviews and meta-analysis only. Considering that there is a significant number of RCT's on the topics of these guidelines, the RU-GDG considered that the level of evidence provided by SRs and MAs would be adequate. The specific search strategies that were used by each subgroup are avaiable as an Appendix online at the RiseupPPD website.
Developing the key recommendations	The development of the recommendations was based on the GRADE framework. Each of the five subgroups developed the key recommendations. All recommendations were discussed within the RU-GDG until consensus was achieved. Whenever consensus was not achieved, recommendations were reached by majority after voting within the RU-GDG.
Writing the guidelines draft	All RU-GDG members contributed to the writing of the guidelines. Each subgroup wrote the evidence synthesis of their topics and the guidelines' draft. The document was reviewed and approved by all members.
Stakeholder consultation	The draft of the guidelines was disseminated and open for consultation by other stakeholders. The document was published in the RiseUp-PPD COST Action website. Emails were sent to scientific societies, patient organisations and other institutions and associations working in the field of perinatal mental health. The document was open for comments from 15th August to 31st August 2023. Comments from the reviewers were addressed by the RU-GDG and are available online at the RiseupPPD website.
Approval	The final version of the document was approved by the Riseup-PPD Management Committee.

Search and analysis of the evidence

Where available, a recent umbrella review which included a member of the RU-GDG as an author was used as a basis for the studies to be evaluated for each PICO question. If it was felt the review required an update, either the original team or the RU-GDG information specialist performed a new search as appropriate. Where no relevant umbrella review by a project member was available, a new search was devised by the information specialist in consultation with the relevant members of the Group.

Results for each PICO question were then imported into the Covidence tool for screening, before data being extracted. A sample search for each strand, together with a detailed description of the screening process and a PRISMA diagram, is available as an online Appendix on the Riseup-PPD website (www.riseupppd18138.com). In addition, evidence tables showing the data extracted for each study as they relate to each strand are also available at the website. The quality assessment of the articles identified was performed using the AMSTAR2 tool (Shea et al., 2017), which is a measurement tool to assess systematic reviews for evidence-based healthcare.

Evidence for inclusion was limited to systematic reviews and meta-analyses. Although this helps assure the quality of the evidence, it is of ethical importance to acknowledge that this methodological choice may exclude relevant documents (namely randomised control trials, large population-based observational studies or qualitative studies) that were recently published and therefore were not included in the selected systematic reviews.

Development of the recommendations

The development of the recommendations was based on the GRADE framework (Schünemann et al., 2013). This framework offers a system for rating the quality of a body of evidence in systematic reviews and other evidence-synthesis documents, supporting the development of evidence-based recommendations. The evidence for each key question was synthesised and is presented in this document, in text and summary format.

To assess the quality of the evidence, the GRADE system's four levels (high, moderate, low and very low) were used. Two RU-GDG members for each study first rated the study up or down according to the factors that affect the quality of the evidence. According to the GRADE handbook, to rate the quality of the evidence downwards, five factors were considered: limitations in

the study design or execution (risk of bias), inconsistency of results, indirectness of evidence, imprecision, and publication bias. Conversely, large magnitude of effects, adjustment for confounders, and presence of dose response gradient, were considered for increasing the quality of the evidence, if applicable.

Following the GRADE framework, two types of recommendations were used: strong recommendations and weak recommendations.

A strong recommendation is suggested when the RU-GDG finds strong evidence that desirable effects greatly overweight the undesirable ones. A weak recommendation is suggested when the RU-GDG is not absolutely certain of the balance between desirable and undesirable effects and the factors that support it, and therefore, increased caution is warranted.

Additionally, a Good Practice Point (GPP) may be added when there is a recommendation for best practice based on the experience of the RU-GDG.

Table 2. Types of recommendations that can be suggested

Strong recommendation for the intervention	Benefits clearly outweigh harms/risks. The great majority of patients will benefit from this intervention and therefore should receive it.
Weak recommendation for the intervention	There is some uncertainty regarding the balance between the benefits and harms/risks, although it is expected that some patients will benefit from this intervention. The benefit may be uncertain and will vary depending on patient characteristics and their values, preferences and personal circumstances. Additionally, contextual resources that determine the unavailability/ inaccessibility of higher quality interventions are considered. When an intervention is weakly recommended, special attention is recommended and should be dedicated in assuring tailored and shared decision-making between the healthcare professional and the patient to best support the healthcare decision that is most suitable to each patient
No recommendation	There is not enough evidence to make a recommendation.
Strong recommendation against the intervention	Harms/risks and burdens clearly outweigh the benefits. Most patients will not benefit from this intervention and therefore should not receive it.
Weak recommendation against the intervention	There is some uncertainty regarding the balance between t he benefits and harms/risks, and it is expected that only a few patients will benefit from this intervention. The benefit may be uncertain and will vary depending on patient characteristics and their values, preferences and personal circumstances. When an intervention is weakly recommended, special attention is recommended and should be dedicated in assuring tailored and shared decision-making between the healthcare professional and the patient to best support the healthcare decision that is most suitable to each patient.
Recommended in research setting	There is insufficient evidence to recommend the use (or no use) of the intervention, but there is great potential of research to reducing the uncertainty about the effects of the intervention at a reasonable cost
GPP	Recommendation for best practice based on the experience of the RU-GDG members

The recommendations will be presented with the following display and symbols:

Table 3. Example of the table of recommendations.

Overall recommendation	Strength of ecommendation	Quality of evidence	Comment
Text of the recommendation.	Strong or Weak	High ⊕⊕⊕⊕ Moderate ⊕⊕⊕◯ Low ⊕⊕◯◯ Very Low ⊕◯◯◯	A comment providing additional information regarding the recommendation.

B. Introduction

B. // Introduction

Definition, prevalence, impact and cost of peripartum depression

Definition of peripartum depression

Peripartum depression (PPD) is formally defined as an episode of unipolar major depressive disorder (MDD) with onset during pregnancy or within four weeks after childbirth (American Psychiatric Association (APA)., 2013). However, several studies in this field show that it can occur up to one year postpartum (Gavin et al., 2005; Gelaye et al., 2016) so, for the purpose of this document, the RU- GDG adopted the broad definition of PPD including pregnancy and postpartum up to one year after childbirth. The symptoms of PPD are supposed to be similar to those in depression outside the peripartum period. As described in the DSM-5 classification system, these include the core symptoms of "depressed mood" and "loss of interest or pleasure in nearly all activities", and at least three other symptoms of the following: changes in weight, sleep, loss of energy, psychomotor changes (agitation or retardation), feelings of worthlessness or inappropriate guilt, impaired concentration, thought of death, or suicidal ideation. These symptoms should last at least two weeks and should give significant distress or impairment in important areas of functioning (American Psychiatric Association (APA)., 2013).

Although PPD is not yet considered as an entity separate from MDD, increasing evidence makes a strong case for symptoms that are typical for PPD when compared to MDD. These symptoms include increased anxiety, psychomotor symptoms, obsessive thoughts, impaired concentration/decision-making, fatigue and loss of energy, and specific guilt about not being a good mother, but less sad mood and suicidal ideation, compared to MDD (Beck & Indman, 2005; Hoertel et al., 2015; Kettunen et al., 2014). Whether depression during pregnancy is distinct from postpartum depression is still understudied, but there is some evidence that they present with different symptoms (Batt et al., 2020; Di Florio & Meltzer-Brody, 2015). In addition, the literature suggests that the manifestation of PPD symptoms may differ across different cultures (Di Florio et al., 2017).

It is noteworthy to differentiate PPD from baby blues, which occurs in up to 50% of postpartum women during the first ten days postpartum (Chechko et al., 2023). Baby blues is not considered a mental disorder due to its transient

state, a non-debilitating condition, which therefore does not need additional professional interventions.

Prevalence and incidence

The prevalence of postpartum depression varies across countries and regions, and there are several factors that influence its occurrence. According to a comprehensive meta-analysis of postpartum depression conducted by Wang et al. (Z. Wang et al., 2021), including 565 studies from 80 different countries, the overall global prevalence rate is approximately 17.4%. In Europe the prevalence of moderate-to-severe depressive symptoms by region is diverse. During pregnancy, this rate ranges from 3.5% in Northern Europe, to 4.9% in Western Europe, and 5.9% in Eastern Europe. During postpartum, it ranges from 3.3% in Northern Europe to 5.8% in Eastern and 6.1% in Western Europe.

The use of different assessment instruments might have influenced the prevalence rates of postpartum depression found. The Postpartum Depression Screening Scale (PDSS) resulted in the highest prevalence rate of 37.2%, while the Structured Clinical Interview for DSM Disorders (SCID) had the lowest prevalence rate of 10.1%. The Edinburgh Postnatal Depression Scale (EPDS) was the most used diagnostic tool, with a prevalence rate of 16.9%.

Sample size of the pooled studies may also influence the reported prevalence rates of postpartum depression. Overall, studies with more than 1,000 participants had lower prevalence rates (13.0%) compared to studies with fewer than 1,000 participants (19.4%).

The global prevalence of postpartum depression also varied across different time periods after childbirth, being higher in the first 1-3 months (17.7%), followed by 3-6 months (15.3%), 6-12 months (18.2%), and greater than 12 months (18.0%).

Another influential predictor found by Z. Wang et al. (2021), was country development level. Interestingly, developed countries or high-income areas displayed lower rates of postpartum depression. Furthermore, the prevalence of postpartum depression was influenced by cultural variations, diverse reporting practices, different viewpoints on mental health issues, the stigma surrounding mental health, socioeconomic class, poverty, limited access to social services, deficient nutrition, elevated stress levels, and biological factors.

Prevalence of depression during pregnancy has been also extensively studied. According to recent systematic review and meta-analysis (Yin et al., 2021), the pooled prevalence of any type of depression during pregnancy across 173 studies was found

to be 20.7%, with a pooled prevalence of major depression being 15.0%. Globally, high-income countries showed a prevalence rate of depression during pregnancy of 8.1%, and in the European region it was 17.9%. When analysing different stages of pregnancy, the prevalence of depression was found to be 21.2% during the first trimester, 15.8% during the second trimester, and 18.9% during the third trimester.

Risk factors for PPD

The risk factors for PPD are often considered from the biological, psychosocial, and environmental domains («Screening and Diagnosis of Mental Health Conditions During Pregnancy and Postpartum», 2023). The major risk factors for antenatal depression are low socioeconomic status, unplanned pregnancy, history of mental disorders, and experience of violence (Míguez & Vázquez, 2021; Yin et al., 2021). Some of the above factors, but also history of premenstrual syndrome, variations of the 5-HTTLPR polymorphism, gestational diabetes, anaemia during pregnancy, preterm birth and operative delivery mode constitute risk factors for postpartum depression (Gastaldon et al., 2022; Hutchens & Kearney, 2020) While, on the other hand, a very sharp drop in hormones after birth is held partly responsible for postpartum depression, the hormonal changes during pregnancy are more gradual. An inverse relationship between oestradiol levels and monoamine oxidase A gene expression has been demonstrated in animal models, as well as MAO-A activity in a human PET study in the immediate postpartum period. These are the first indications of how the sharp drop in hormone levels after birth could contribute to the development of depression via increased degradation of monoamine neurotransmitters such as serotonin. There are still far fewer findings on pregnancy, as human studies during this period are even more challenging from an ethical perspective than in the postpartum period. The progesterone level, which rises 20-fold during pregnancy, also drops back to the level of the menstrual cycle a few days after birth (for an overview see Sacher et al., 2020). This too could possibly trigger fluctuations in the neurotransmitter balance and thus contribute to depressive symptoms, but there is no evidence on this yet.

The first studies that looked at structural changes in the brain during and after pregnancy focused on the pituitary gland as a control organ of the stress axis and performed regional analyses that showed an increase in volume during late

pregnancy and the first days after birth compared to early pregnancy and the later postpartum period. Whole-brain analyses demonstrated plasticity of grey matter volume after pregnancy. Comparison of structural data before delivery and before conception showed a significant decrease in brain size and an increase in ventricular size, while comparison of pre-birth images with those six months postpartum indicated an increase in brain and ventricular size. These dynamic and initially physiological changes could also contribute to the triggering of depressive symptoms in vulnerable women, but there are no data on this yet regarding pregnancy depression. There are several more potential biological risk mechanisms that have been shown to be associated with maternal postpartum depression, lower BDNF levels in the blood (Y. Lee et al., 2021), higher sensitivity to periportal progesterone/ allopregnanolone fluctuations (Rathi et al., 2022), history of premenstrual syndrome (PMS) (Hahn et al., 2021) and (hair) cortisol alterations (Stickel et al., 2021). Recent studies show a large genetic overlap with unipolar depression in general, but also differentially associated genes in PPD such as genes expressed in ovarian tissue. Identification of the neurobiological mechanisms of PPD would contribute to developing predictive biomarkers and revealing new prevention and treatment targets in the future (Kiewa et al., 2022).

Impact of PPD

Impact on mothers, children and the family

The literature has documented the negative impact of PPD on mothers and families (Rodriguez- Muñoz, et al. 2023). PPD affects the mother and her well-being with symptoms such as guilt, loss of interest in doing things, shame, irritability, or even suicidal ideation (Fonseca et al., 2020; Legazpi et al., 2022). In addition, the literature has identified how PPD is associated with adverse peripartum outcomes among which are smoking, substance abuse, and increased poor adherence to medical care routines (Marcos-Nájera et al., 2020; Slomian et al., 2019).

The literature has specified that children of mothers with symptoms of depression were more likely to have shorter gestation, a lower birth weight, lower Apgar score, or more time at the nursery (Aoyagi & Tsuchiya, 2019; Dowse et al., 2020; Slomian et al., 2019). Additionally, problems in mother-child interactions, including difficulties in bonding or breastfeeding, or problems associated with the maternal role, seem

to be more frequent in women presenting depressive symptoms (Höflich et al., 2022; Nakić Radoš et al., 2023; Slomian et al., 2019). In studies of older children, the consequences of maternal PPD to the offspring are emotional., behavioural, cognitive and language problems or special educational needs (Bauer et al., 2015; Slomian et al., 2019). Fathers also suffer from the effects of maternal postpartum depression. The impacts of maternal PPD on fathers have been linked especially to a higher risk of relational problems including low marital satisfaction, difficulties in coping with maternal emotions (D. Wang et al., 2021), and paternal depression (Thiel et al., 2020). In summary, there is a bulk of evidence showing the detrimental effects of maternal PPD for the mother, the infant, the partner, and the family as a whole.

Impact on the wider context/society

In addition to the consequences of PPD for the mother, the children and their family, it is important to note that PPD has significant economic costs to the society. In an economic report about the lifetime costs of PPD and anxiety, Bauer et al. (2016) examined the consequences and costs of anxiety and depression in women during pregnancy and 12 months after giving birth. The authors used a decision-modelling approach and adopted a lifetime perspective, meaning that the costs included expenses related to the mother and the child across life. Results highlight the elevated cost of the peripartum depression, with an estimated total cost of more than £75,000 (about €88,000 in 2023) per woman diagnosed. The authors identified that the majority of the costs were related not to the mother but to the adverse impacts on the child. Costs related to the mother are linked with health and social care expenses (which are especially borne by the public sector), loss of productivity, and health-related quality of life losses. Costs related to the child are linked with healthcare, developmental difficulties, and mental health and educational issues. This study highlighted the high cost of peripartum mental illness, and it is suggested that the actions undertaken to prevent depression during the peripartum are likely to be cost effective, especially for the public sector (Bauer et al., 2015).

C. Clinical practice recommendations: Summary list of recommendations

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#	Recommendation	Strength of the recommendation	Quality of the evidence	Comments
Prevention of PPD				
Psychological and psychosocial preventive interventions				
1	Psychological and psychosocial interventions are strongly recommended for preventing PPD among pregnant and postpartum women at-risk for developing PPD, as well as among pregnant and postpartum women with no symptoms and no known risk factors.	Strong	Moderate ⊕⊕⊕◯	While there is moderate evidence on psychological and psychosocial interventions, there is no information about cost-effectiveness of these interventions, so this should be taken into account when deciding on preventive implementations.
2	Psychological interventions are weakly recommended to prevent PPD among women with sub-clinical depressive symptoms.	Weak	Low ⊕⊕◯◯	The recommendation is weak, based on the lack of evidence on the effectiveness of preventive interventions in women with subclinical symptoms. Although offering preventive interventions may have positive effects, it is uncertain whether it is efficient in preventing PPD in women with subclinical symptoms. Only one systematic review and meta-analysis examined the effectiveness of PPD preventive interventions for women with sub-clinical depressive symptoms and their findings were inconclusive.

#	Recommendation	Strength of the recommendation	Quality of the evidence	Comments
Psychopharmacological preventive interventions				
3	It is not recommended to use antidepressant medication for prevention of postpartum depression in women with previous depression.	Strong	Low ⊕⊕◯◯	There is limited evidence available to support initiating antidepressants after delivery for prevention of postpartum depression.
4	It is not recommended to use antidepressants for prevention of depression during pregnancy.	Strong	Very Low ⊕◯◯◯	There is no evidence available to support the efficacy of antidepressants for prevention of antenatal depression.
Dietary supplements preventive interventions				
5	We have no recommendation on use of dietary supplements to prevent PPD.	No recommendation		There is no evidence supporting the effect of dietary supplements in preventing PPD.
Physical activity based preventive interventions				
6	Physical activity is weakly recommended to prevent PPD among pregnant and postpartum women from the general population.	Weak	Moderate ⊕⊕⊕◯	The participants in the literature that was examined were not assessed for risk factors. There are populations that may have medical conditions to which physical activity may be harmful
Interventions for screening for PPD				
Screening programmes for the general population				
7	Screening programmes for depression during pregnancy and in the postpartum period are strongly recommended.	Strong	Moderate ⊕⊕⊕◯	Due to ethical considerations, screening should be implemented as long as appropriate diagnosis, treatment and follow-up can be ensured.

#	Recommendation	Strength of the recommendation	Quality of the evidence	Comments
Screening programmes for high-risk women				
8	Screening programmes for the presence of risk factors for vulnerability to PPD are weakly recommended.	Weak	Very low ⊕◯◯◯	Screening women is important after receiving information on how to interpret the screening results and which preventive interventions can be offered.
Interventions for treating PPD				
Psychological treatment				
9	Cognitive-behavioural therapy (CBT) is strongly recommended for the treatment of depressive symptoms during pregnancy and postpartum.	Strong	High ⊕⊕⊕⊕	Most women find psychological treatment acceptable and were satisfied. The major advantage is that for most women, any undesirable effects will probably be trivial, and no adverse effects for pregnant women, mothers and foetus/ infants are expected.
10	Third wave CBT therapies, including behavioural activation and mindfulness techniques, are weakly recommended for the treatment of depressive symptoms during pregnancy and postpartum.	Weak	Low ⊕⊕◯◯	There is a lack of information about acceptability and satisfaction with third-wave CBT therapies. However, undesirable and adverse effects for pregnant women, mothers and foetus/ infants are not expected.
11	Interpersonal therapy (IPT) is weakly recommended for the treatment of depressive symptoms during pregnancy and postpartum.	Weak	Low ⊕⊕◯◯	There is a lack of information about acceptability and satisfaction with IPT However, undesirable and adverse effects for pregnant women, mothers and foetus/ infants are not expected.

#	Recommendation	Strength of the recommendation	Quality of the evidence	Comments
Pharmacological treatment				
Pregnancy				
12	Antidepressant medication in pregnancy is strongly recommended, after careful consideration of individual risk-benefit ratio for each woman and her unborn child. The decision-making about antidepressant intervention should consider the history of depression recurrence and severity of symptoms, previous response to the intervention, and individual preference.	Strong	Low ⊕⊕◯◯	There is no evidence available from systematic reviews and meta-analyses on the efficacy of antidepressant intervention in pregnancy. There is moderate evidence on the reproductive safety of antidepressants in pregnancy on maternal and offspring outcomes. Individual risk-benefit assessment of the intervention is needed for each woman, but antidepressant medication should be considered in women with moderate to severe depressive symptoms or after non-response to non-pharmacological interventions.
13	Women with severe and/or recurrent depression are strongly recommended not to discontinue the antidepressant medication during pregnancy due to the increased risk of relapse.	Strong	Low ⊕⊕◯◯	Evidence supports the elevated risk of relapse of the depression with discontinuation of the intervention, particularly in cases of severe or recurrent depression.

#	Recommendation	Strength of the recommendation	Quality of the evidence	Comments
18	It is strongly recommended that clinicians provide information to women about the possible risks of antidepressant exposure in pregnancy on maternal-child health versus the potential risks posed by maternal depression.	Strong	Moderate ⊕⊕⊕◯	Both maternal depression and the antidepressant intervention in pregnancy can increase the risk of multiple negative health outcomes in mother-child pairs. Women must be informed about both sets of risks in order to make informed clinical decisions about their antidepressant treatment. However, there are no data about interventions informing or not informing women about potential risks and benefits of medication vs untreated PPD.

#	Recommendation	Strength of the recommendation	Quality of the evidence	Comments
19	It is strongly recommended that all women under antidepressant interventions and their offspring should be closely monitored during pregnancy, as well as delivery being in a specialised obstetric centre with neonatal intensive care unit.	Strong	Moderate ⊕⊕⊕◯	There is an elevated risk of poor neonatal adaptation at birth in infants prenatally exposed to antidepressant intervention as well as in mothers with depressive disorders in general, which supports the recommendation to deliver in a specialised obstetric centre.
Postpartum				
20	It is strongly recommended to treat depression during the postpartum period with antidepressant medication, after careful consideration of individual risk-benefit ratio for each woman and her child if breastfed. The decision-making about antidepressant intervention should consider the history of depression recurrence and severity in the woman, previous response to the intervention, and individual preference as well as the health condition of the breastfed child.	Strong	Low ⊕⊕◯◯	Few data are available about the efficacy of antidepressant intervention in postpartum. However, as opposed to reproductive safety data about antidepressants in pregnancy, there is substantially less data about the short- and long-term safety of children exposed to antidepressant while breastfed. However, the risk of untreated depression and the benefits of breastfeeding on those negative outcomes needs to be weighed in each woman and child individually. In case a woman does not breastfeed, there is weak evidence of the effectiveness of antidepressant treatment for postpartum depression, however, there is also no risk to the child to be considered.

#	Recommendation	Strength of the recommendation	Quality of the evidence	Comments
21	It is strongly recommended to use brexanolone for moderate to severe postpartum depression treatment if available and if accepted as a treatment option by the woman.	Strong	Moderate ⊕⊕⊕◯	The strong recommendation is based on the clinical effectiveness of this intervention. However, it must be considered that few aspects may affect its use : (i) need of inpatient care, which may be less acceptable for women, due to the possibility of separation of the newborn; (ii) breastfeeding cessation for 3 days, which also may affect women's acceptability of the intervention; (iii) the very high cost, making the intervention less accessible than others; (iv) there is scarcity of evidence on the safety of brexanolone exposure via breast milk on the infant. Brexanolone is currently not licensed In Europe. Therefore, although brexanolone is strongly recommended for moderate to severe cases of depression, its use requires careful discussion between the woman and her HCP.

#	Recommendation	Strength of the recommendation	Quality of the evidence	Comments
Non-invasive Brain Stimulation interventions				
Repetitive transcranial magnetic stimulation (rTMS)				
Pregnancy				
22	rTMS is weakly recommended for the treatment of mild to moderate depressive symptoms.	Weak	Very Low ⊕◯◯◯	rTMS might be beneficial and risks of adverse effects for the woman or the foetus are unlikely. The evidence on its effectiveness is very low. Our recommendation considers that in clinical settings where it might be difficult to access psychological treatments or there is resistance of women to pharmacological or psychological interventions, rTMS could be an alternative treatment, if accessible and available, for women with mild to moderate depressive symptoms.

#	Recommendation	Strength of the recommendation	Quality of the evidence	Comments
Postpartum				
23	rTMS is weakly recommended for the treatment of mild to moderate depressive symptoms in the postpartum period.	Weak	Low ⊕⊕◯◯	rTMS might be beneficial and risks of adverse effects for the mother or the breastfed child are unlikely. The evidence on its effectiveness is low. Our recommendation considers that in clinical settings where it might be difficult to access psychological treatments or there is resistance of women to pharmacological or psychological interventions, rTMS could be an alternative treatment, if accessible and available, for women with mild to moderate depressive symptoms in postpartum.

#	Recommendation	Strength of the recommendation	Quality of the evidence	Comments
Transcranial direct current stimulation (tDCS)				
Pregnancy				
24	Transcranial direct current stimulation (tDCS) is weakly recommended for the treatment of mild to moderate depressive symptoms in pregnant women.	Weak	Low ⊕⊕◯◯	tDCS might be beneficial and risks of adverse effects for the mother or the foetus are unlikely. The evidence on its effectiveness is low. Our recommendation considers that in clinical settings where it might be difficult to access psychological treatments or there is resistance of women to pharmacological or psychological interventions, tDCS could be an alternative treatment, if accessible and available, for women with mild to moderate depressive symptoms during pregnancy.

#	Recommendation	Strength of the recommendation	Quality of the evidence	Comments
Postpartum				
25	There is not enough evidence to make a recommendation regarding the use of tDCS in the treatment of depression for women in the postpartum.	No recommendation		There is one single case study reported in a systematic review showing the efficacy of tDCS in reducing depressive symptoms in a postpartum woman. For this reason, although no harmful effects are expected to occur in the postpartum, the RU-GDG considered that there is not enough evidence on the efficacy of tDCS in women in the postpartum. Therefore, we cannot yet make a recommendation.

#	Recommendation	Strength of the recommendation	Quality of the evidence	Comments
Q3.3.3 Electroconvulsive therapy (ECT)				
Pregnancy				
26	ECT is strongly recommended for the treatment of therapy-resistant or life-threatening severe depression in pregnant women. The treatment should take place under strict obstetrical monitoring.	Strong	Very Low ⊕◯◯◯	ECT is a relatively fast-acting option in severe cases of depression during pregnancy and despite the moderate risks of adverse effects (for the mother and the foetus) and pregnancy/ delivery complications, the benefits seem to outweigh the adverse effects if women did not respond to previous regular treatment or in need of urgent treatment due to life-threatening situations. Therefore, ECT is strongly recommended and should be offered within specialised hospitals to women presenting severe depression (with or without psychotic features) which did not respond to previous regular treatment or in need of urgent treatment due to life-threatening situations.

#	Recommendation	Strength of the recommendation	Quality of the evidence	Comments
Postpartum				
27	ECT is strongly recommended for the treatment of therapy resistant or life-threatening severe depression in the postpartum period.	Strong	Very Low ⊕◯◯◯	ECT is a relatively fast-acting treatment that seems to be beneficial in severe cases of postpartum depression. Risks of adverse effects (prolonged seizures due to co-administered medication and transient memory loss particularly after the first ECT sessions) are small. ECT should be offered within specialised hospitals to women presenting severe depression (with or without psychotic features) which did not respond to previous regular treatment or in need of urgent treatment due to life-threatening situations.
Bright light therapy (BLT)				
Pregnancy				
28	There is no evidence on the efficacy of BLT in pregnancy, therefore we cannot make a recommendation.	No recommendation		There are no systematic reviews and meta-analyses available supporting the efficacy of BLT in reducing depressive symptoms in pregnant women.

#	Recommendation	Strength of the recommendation	Quality of the evidence	Comments
Postpartum				
29	There is no evidence on the efficacy of BLT in postpartum, therefore we cannot make a recommendation.	No recommendation		There are no systematic reviews and meta-analysis available supporting the efficacy of BLT in reducing depressive symptoms in postpartum women.
Complementary and alternative treatment interventions				
Physical activity				
Pregnancy				
30	Physical activity is weakly recommended for the treatment of mild to moderate depressive symptoms in otherwise healthy pregnant women.	Weak	Very Low ⊕◯◯◯	Physical activity might be beneficial for otherwise healthy women and risk for the foetus is unlikely. Our recommendations are based on very low quality of evidence available for women with uncertain severity of depressive symptoms and assuming good physical health.
Postpartum				
31	Low-to-moderate intensity physical activity is weakly recommended for the treatment of mild to moderate depressive symptoms in postpartum as it might be beneficial, and no risks of adverse effects are reported.	Weak	Low ⊕⊕◯◯	Physical activity might be beneficial for otherwise healthy women and risks for newborn is unlikely. Our recommendations are based on low to moderate quality of the evidence available for women with uncertain severity of depressive symptoms. In these conditions, supervised and specialised physical activity could be an accessible alternative treatment for women with mild to moderate depressive symptoms during the postpartum.

#	Recommendation	Strength of the recommendation	Quality of the evidence	Comments
Yoga				
Pregnancy				
32	Yoga is weakly recommended for the treatment of mild to moderate depressive symptoms as it might be beneficial, and no risks of adverse effects are reported.	Weak	Low ⊕⊕◯◯	Yoga might be beneficial for otherwise healthy women and risk for the foetus is unlikely. Our recommendations are based on low quality of the evidence available for women with uncertain severity of depressive symptoms.
Postpartum				
33	There is no evidence on the efficacy of yoga in postpartum, therefore we cannot make a recommendation.	No recommendation		There are no systematic reviews available supporting the efficacy of yoga in reducing depressive symptoms in postpartum women.
Massage				
Pregnancy				
34	Massage is weakly recommended for the treatment of mild to moderate depressive symptoms during pregnancy.	Weak	Low ⊕⊕◯◯	This recommendation is based on low quality evidence that showed positive effects in the reduction of depressive symptoms in pregnant women. Effects found were of moderate size and risk for the foetus is unlikely.
Postpartum				
35	There is no evidence on the efficacy of massage in postpartum, therefore we cannot make a recommendation.	No recommendation		There are no systematic reviews and meta-analysis supporting the efficacy of massage in reducing depressive symptoms in postpartum women.

#	Recommendation	Strength of the recommendation	Quality of the evidence	Comments
Music therapy				
Pregnancy				
36	There is no evidence on the efficacy of music therapy during pregnancy, therefore we cannot make a recommendation.	No recommendation		There are no studies supporting the efficacy of music therapy in reducing depressive symptoms in pregnant women.
Postpartum				
37	There is no information on the effectiveness of music therapy as a stand-alone treatment. Music therapy is weakly recommended as an additive intervention when combined with other interventions (such as psychological treatment, Chinese medicine or pharmacotherapy) for the treatment of mild to moderate depressive symptoms as it might be beneficial, and no risks of adverse effects are reported.	Weak	Low ⊕⊕◯◯	Music therapy might be beneficial in addition to other treatments. Our recommendations are based on low quality of the evidence available for women with uncertain severity of depressive symptoms.
Peer support				
Pregnancy				
38	There is no evidence on the efficacy of peer support in pregnancy, therefore we cannot make a recommendation.	No recommendation		There is only one single study supporting the efficacy of peer support in reducing depressive symptoms in pregnant women.

#	Recommendation	Strength of the recommendation	Quality of the evidence	Comments
Postpartum				
39	There is no evidence to support a recommendation regarding traditional face-to-face peer support. Technology-based peer support is weakly recommended for the treatment of mild to moderate depressive symptoms in the postpartum period.	Weak	Very Low ⊕◯◯◯	Peer support that was assessed in the literature refers to peers which are women with lived experience of PPD. Technology-based peer support might be beneficial and risks of adverse effects are unlikely.
Chinese herbs				
Pregnancy				
40	There is no evidence on the efficacy of the use of Chinese herbs in pregnancy, therefore we cannot make a recommendation.	No recommendation		There are no studies available supporting the efficacy and reproductive risks of Chinese herbs in reducing depressive symptoms in pregnant women.

#	Recommendation	Strength of the recommendation	Quality of the evidence	Comments
Postpartum				
41	Chinese herbs alone and in combination are weakly recommended for the treatment of mild to moderate depressive symptoms in the postpartum period.	Weak	Low ⊕⊕◯◯	There is evidence that specific Chinese herbs might be beneficial as a stand-alone treatment and also in combination treatment (with antidepressants) and have low risks of acute adverse effects, in women who are not breastfeeding. A special caution is made for the specific Chinese herbs that also contain of St John's wort, because in combination with other antidepressants, it might cause serotonine syndrome.
Acupuncture				
Pregnancy				
42	There is no evidence on the efficacy of the use of acupuncture in pregnancy, therefore we cannot make a recommendation	No recommendation		Evidence about the efficacy of acupuncture during pregnancy is inconsistent.
Postpartum				
43	There is no evidence on the efficacy of the use of acupuncture in the postpartum, therefore we cannot make a recommendation	No recommendation		Evidence about the efficacy of acupuncture in the postpartum is inconsistent.

#	Recommendation	Strength of the recommendation	Quality of the evidence	Comments
Fatty acids				
44	Fatty acids are weakly recommended for the treatment of mild to moderate depressive symptoms in pregnancy and in the postpartum period.	Weak	Low ⊕⊕◯◯	Fatty acids might be beneficial and low risks of adverse effects are reported.

D. Overview of the clinical recommendations

D. // Overview of the clinical recommendations

Below, we present three figures offering a schematic overview of the clinical recommendations for preventing, screening and treating PPD during pregnancy (Figure 1) and in the postpartum period (Figure 2).

Below, we provide a decision flowchart

Figure 1. Overview of the clinical recommendations for interventions during pregnancy

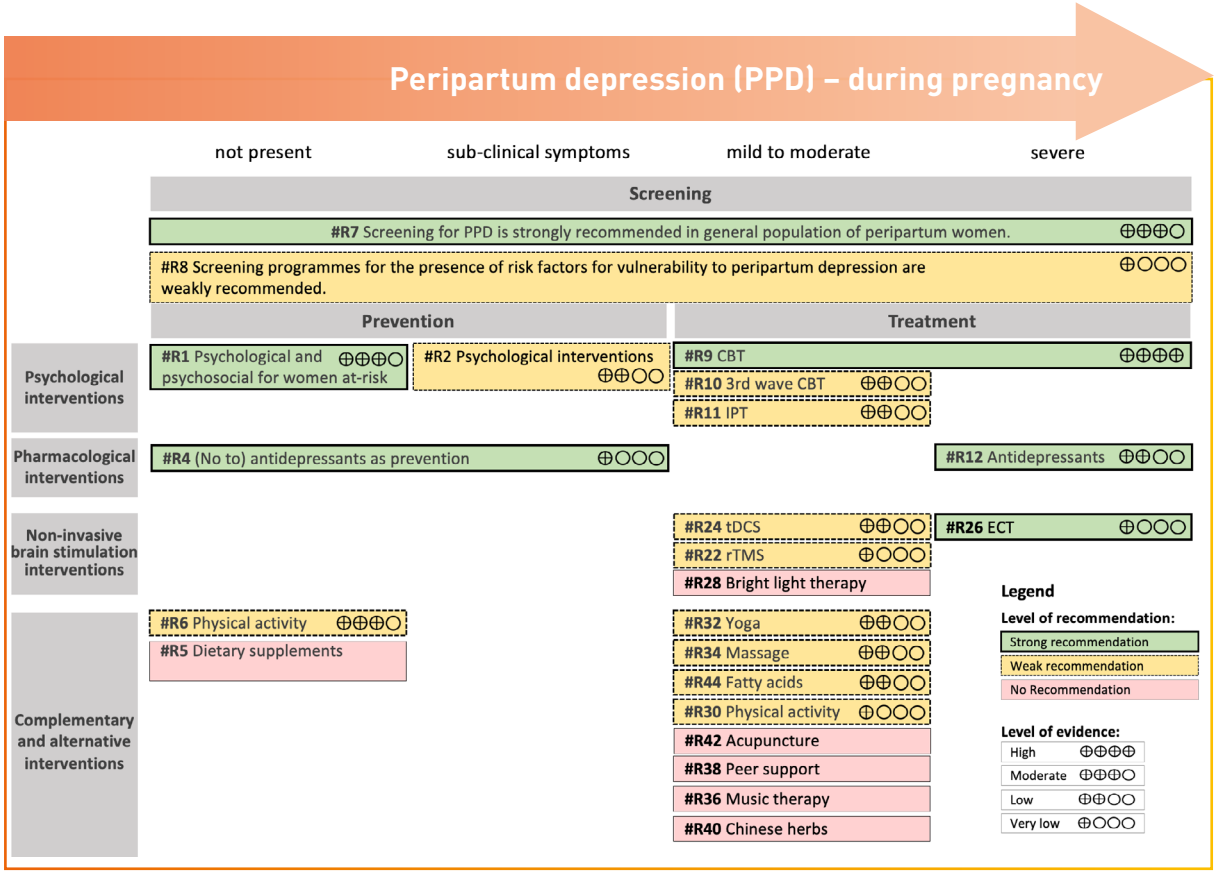
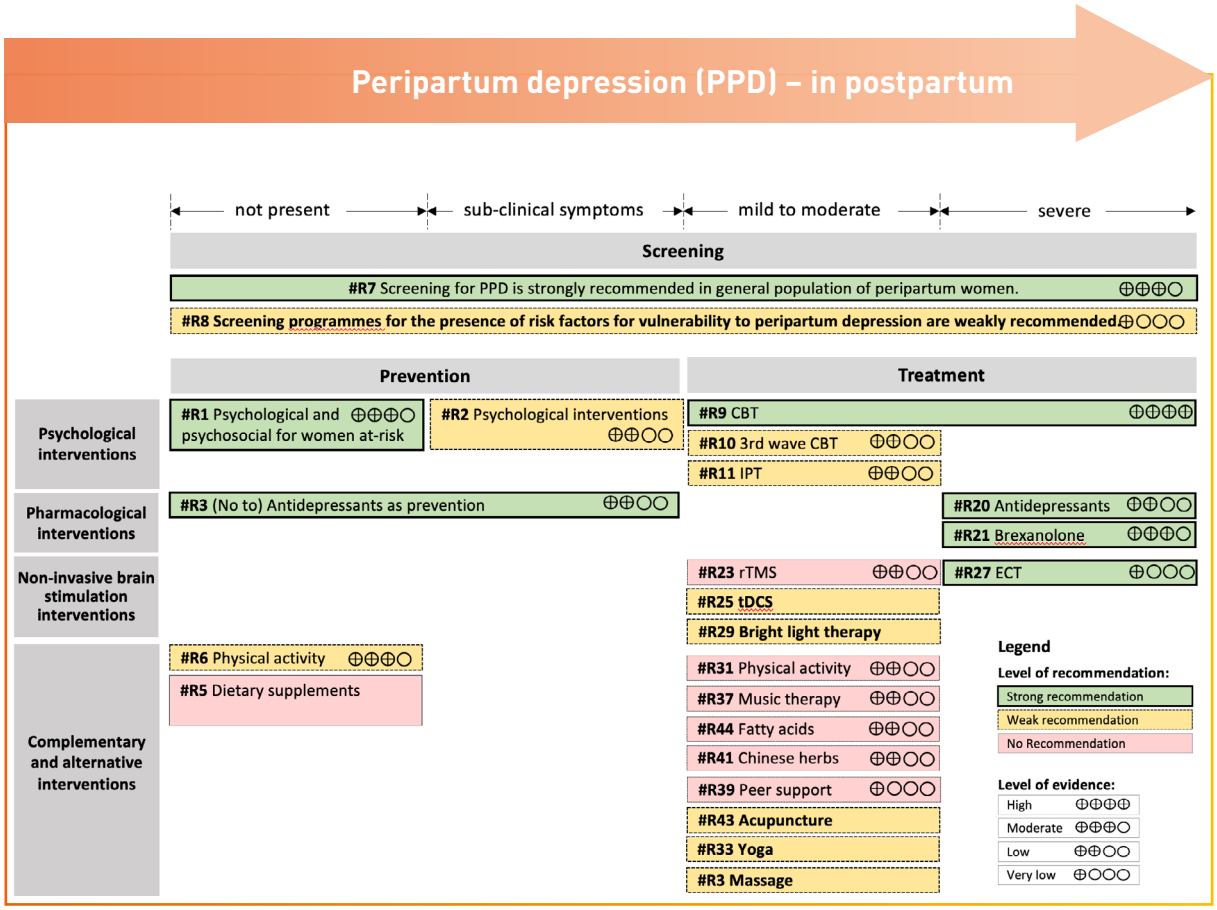
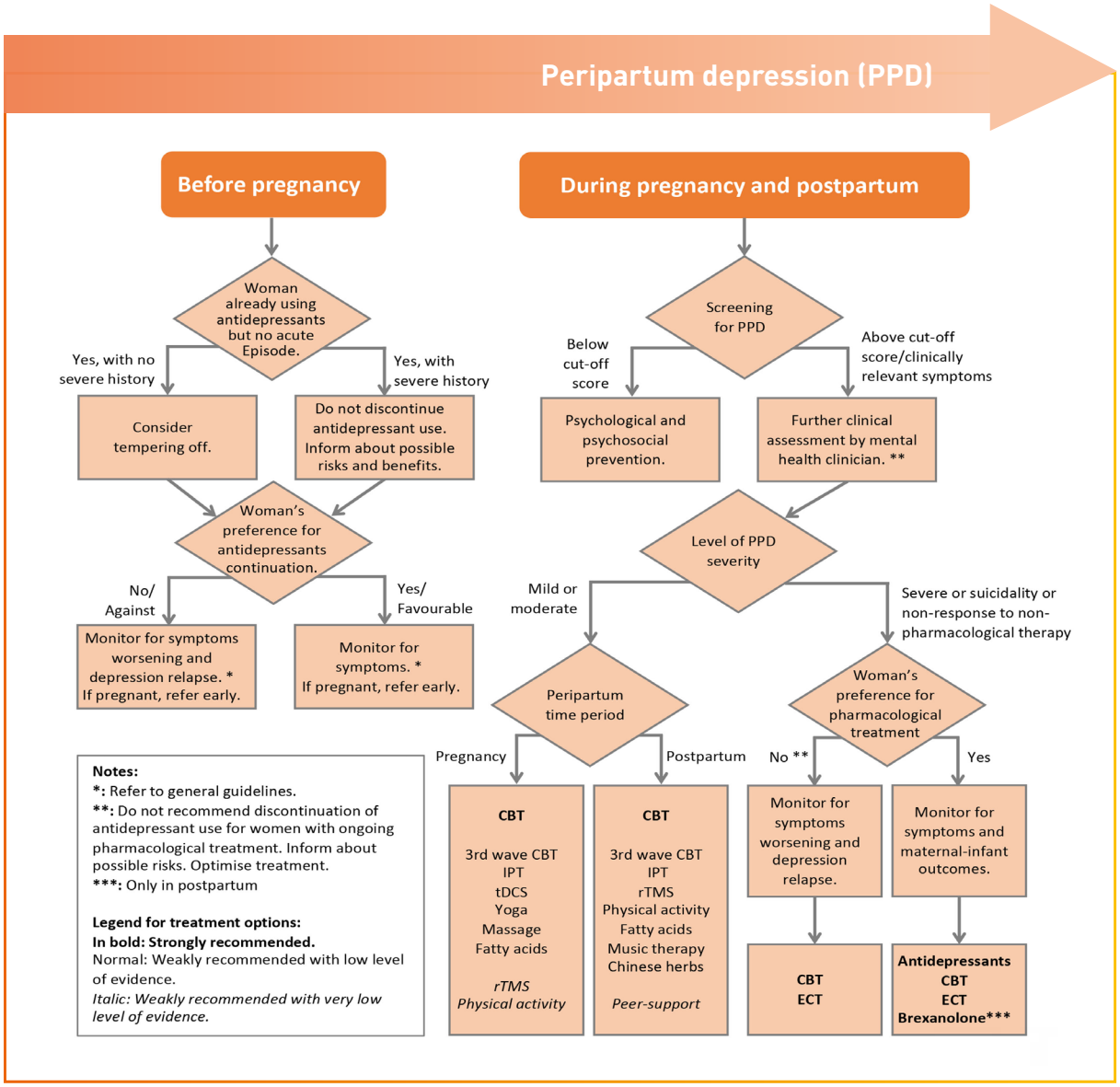


Figure 2. Overview of the clinical recommendations for interventions in the postpartum period



for the management of PPD for women with or without previous depression who either plan pregnancy or are pregnant or in the postpartum period. Proposed interventions are based on the previously outlined recommendations. This flowchart provides a rationale for the management of PPD, but requires careful consideration of the specific country, context and setting where the interventions will take place.

Figure 3. Clinical pathway for managing PPD in clinical settings



E. Synthesis of the evidence and recommedations

E. // Synthesis of the evidence

Prevention for PPD

Are interventions in the form of psychological and psychosocial interventions effective in preventing PPD among women from the general population, non-depressed, with no known risks or not identified as at-risk for developing PPD?

Ten papers focused on psychological interventions as preventing PPD. Out of them, four were of high quality (Dennis & Dowswell, 2013b; Martín-Gómez et al., 2022; Morrell et al., 2016; O'Connor et al., 2019) (Dennis & Dowswell, 2013b; Martín-Gómez et al., 2022; Morrell et al., 2016; O'Connor et al., 2019)four low quality, one low-medium quality, and one critically low (which was an outdated paper and therefore was not included in the summary of evidence). Overall, all studies concluded that psychosocial and psychological interventions are effective in preventing postpartum depression.

In a high-quality systematic review and meta-analysis of 28 RCTs, Dennis and Dowswell (2013b) examined the effectiveness of psychosocial and psychological interventions compared to treatment as usual as preventing postpartum depression among pregnant and up to one month postpartum women with no known risks and women identified as at-risk for developing PPD (involving 32,421 women (17,000 women in the intervention groups) from 7 countries and 4 continents). Women who received a psychosocial or psychological intervention were significantly less likely to experience postpartum depression than those who received standard care (psychosocial: 12 trials; n=11,322; RR 0.83, 95% CI 0.70 to 0.99, I2=57%, T2 0.04; psychological: eight trials; n=3405, RR 0.61, 95% CI 0.39 to 0.96, I2=75%, T2 0.27). Looking at variations of psychosocial interventions, a beneficial effect was found when the intervention involved postpartum professional-based home visits (two trials, n=1262; RR 0.56, 95% CI 0.43 to 0.73, I2=0%,T2 0.0) and for postpartum lay-based telephone support (one trial., n=612; RR 0.54, 95% CI 0.38 to 0.77). There were not enough data in studies to examine differences in effects of different psychological interventions.

In another systematic review and meta-analysis including 17 RCTs involving 4,958 women (around 2,800 women in the intervention groups) from six countries and four continents, Martín-Gomez et al. (2022) examined the effectiveness of psychological interventions (CBT, person-centred approach, IPT, Metacognitive therapy, Positive psychology and Couple therapy) in preventing postpartum depression among

pregnant and postpartum non-depressed women. Psychological interventions had a very small effect on preventing PPD in non-depressed women. When only RCTs with a low risk of bias from qualitative criteria were included, the pooled SMD decreased substantially (SMD: -0.101; 95% CI -0.241 to 0.038), indicating a more significant effect. Moreover, interventions focused on primiparous women are more effective than those focused on primiparous and multiparous women.

In another high-quality systematic review, (2019) assessed the effectiveness of psychological interventions in preventing perinatal depression among pregnant and up to 1 year postpartum non-depressed or at-risk women in 20 studies (n=4107). Overall, psychological interventions were effective in preventing perinatal depression (RR=0.6, 95% CI, 0.47 to 0.78; I2 = 39.0%). When limited to trials that only included women at increased risk of perinatal depression, the pooled RR was 0.55 (95%CI 0.44 to 0.68; I2 = 0%). Moreover, effects were larger for CBT (RR= 0.51, 95%CI 0.33-0.79)) and IPT-based (RR= 0.71, 95% CI 0.50-1.00).

In another high-quality systematic review and meta-analysis, Morrel et al. (2016) assessed nine universal (all pregnant or up to six-weeks postpartum women) and selective (pregnant or up to six-weeks postpartum women at risk of developing PPD because of social factors) interventions (CBT, IPT, person-centred approach, promoting parent-child interaction, psychoeducation, empowerment, mindfulness) to prevent postpartum depression.

Universal preventive psychological interventions (three studies) most effective at three months postpartum were midwifery-redesigned postpartum care, at six months postpartum CBT-based intervention and PCA-based intervention, and at 12 months postpartum, midwifery-redesigned postpartum care, CBT-based interventions, and PCA-based interventions.

The effectiveness of selective preventive interventions (six studies) was inconclusive. The most beneficial treatments appeared to be CBT-based interventions, IPT-based interventions and education on preparing for parenting (most cost-effective among educational interventions).

Also, other meta-analyses and systematic reviews with lower quality found the same conclusions, e.g., that psychological interventions, i.e., IPT, CBT, mindfulness, psychoeducation, CB-based approach, solution-focused approach are effective (compared to treatment as usual) for preventing perinatal depression among the universal population of pregnant and postpartum women (Corbally

& Wilkinson, 2021; Missler et al., 2021; Sockol, 2015, 2018; Yasuma et al., 2020) as well as among women at-risk (Sockol, 2015, 2018) and women with sub-clinical symptoms (Sockol, 2015).

Regarding partner inclusive psychological interventions, findings are inconclusive. Some studies found lower depressive symptoms among women in the intervention group (Milgrom et al., 2011; Thomas et al., 2014) while others did not find differences between the intervention and control groups (e.g. Hayes & Muller, 2004; Matthey et al., 2004) as reported by (Alves et al., 2018).

Overall recommendation	Strength of the recommendation	Quality of the evidence	Comments
Psychological and psychosocial interventions are strongly recommended for preventing PPD among pregnant and postpartum women at-risk for developing PPD as well as among pregnant and postpartum women with no symptoms and no known risk factors	Strong	Moderate ⊕⊕⊕◯	While there is moderate evidence on psychological and psychosocial interventions, there is no information about cost-effectiveness of these interventions, so this should be taken into account when deciding on preventive implementations

There is not enough information to conclude which types of psychological and psychosocial interventions are most effective in preventing PPD. However, extra visits from a midwife, person-centred approaches (PCAs) or CBT-based approaches showed promising positive effects in preventing PPD among the general population of pregnant and postpartum women. Additionally, education on preparing for parenting or IPT-based interventions seemed useful for women at-risk for developing PPD.

The interventions that appear to be most cost-effective are midwifery-redesigned postpartum care (universal) and education on preparing for parenting (selective). Interventions focused on primiparous women seem to be more effective than those focusing on both primiparous and multiparous women.

Are interventions in the form of psychological and psychosocial interventions effective in preventing PPD among women with sub-clinical depressive symptoms?

One paper focused on psychological interventions as preventing postpartum depression among women with sub-clinical depressive symptoms (Morrell et al., 2016). This high-quality systematic review and meta-analysis assessed 19 indicated (pregnant women or up to six weeks postpartum at risk of developing PPD because of psychological risk factors) interventions (CBT, IPT, person-centred approach, promoting parent-child interaction, psychoeducation, empowerment, mindfulness) to prevent postpartum depression. The effectiveness of indicated preventive interventions (19: seven CBT, one CBT and PCA, one empowerment training, five IPT, one mindfulness, three promoting parent-infant interaction, and one psychoeducation) was inconclusive and the CIs were wide. The most beneficial interventions appeared to be those promoting parent-infant interaction when depressive symptoms were assessed at six weeks and three months postpartum, those providing peer support when depressive symptoms were assessed at three months postpartum or educational information when depressive symptoms were assessed at three months postpartum, CBT-based intervention when depressive symptoms were assessed at three to four months postpartum, IPT-based intervention when depressive symptoms were assessed at seven months postpartum, PCA-based intervention when depressive symptoms were assessed at six and 12 months postpartum and CBT-based intervention when depressive symptoms were assessed at six and 12 months postpartum.

Overall recommendation	Strength of the recommendation	Quality of the evidence	Comments
Psychological interventions are weakly recommended to prevent PPD among women with sub-clinical depressive symptoms	Weak	Low ⊕⊕◯◯	The recommendation is weak, based on the lack of evidence on the effectiveness of preventive interventions in women with subclinical symptoms. Although offering preventive interventions may have positive effects, it is uncertain whether it is efficient in preventing PPD in women with subclinical symptoms. Only one systematic review and meta-analysis examined the effectiveness of PPD preventive interventions for women with sub-clinical depressive symptoms and their findings were inconclusive

Are interventions in the form of psychopharmacological preventive interventions effective in preventing PPD?

There is one Cochrane review (Molyneaux et al., 2018) that investigated if antidepressant initiation after delivery prevents postpartum depression. The review includes two RCT studies with 73 women (n=26 in the nortriptyline arm, n=14 in the sertraline arm, and n=33 in the placebo arm) with history of postpartum depression, not depressed or using antidepressants at the beginning of the studies. The relative risk for postpartum depression was 0.14 (95% CI: 0.02 to 1.07) in the sertraline arm versus placebo, but there was no significant difference between nortriptyline and the placebo group (Molyneaux et al., 2018). Due to low statistical power and scarce evidence, there cannot be drawn a conclusion about the effectiveness of antidepressants in the prevention of PPD.

Loss of follow-up rate from each treat-

ment group was used as an indirect measure of acceptability. In the nortriptyline-placebo RCT, one woman in the nortriptyline arm was lost to follow-up after developing mania in the first postpartum week, while three women withdrew from the placebo arm owing to side effects, personal reasons and pregnancy. No difference in loss of follow-up was found in the sertraline-placebo RCT.

There is no available evidence about the efficacy of antidepressant initiation during pregnancy for prevention of depression during pregnancy.

Overall recommendation	Strength of the recommendation	Quality of the evidence	Comments
It is not recommended to use antidepressant medication for prevention of postpartum depression in women with previous depression.	Strong	Low ⊕⊕◯◯	There is limited evidence available to support initiating antidepressants after delivery for prevention of postpartum depression.
It is not recommended to use antidepressants for prevention of depression in pregnancy.	Strong	Very Low ⊕◯◯◯	There is no evidence available to support the efficacy of antidepressants for prevention of antenatal depression.

Are interventions in the form of dietary supplements effective in preventing PPD?

Three papers focused on dietary supplements as preventing PPD. Out of them, one paper was of high quality (O'Connor et al., 2019) and two papers of low quality (Sparling et al., 2017; Suradom et al., 2021)

In a high-quality systematic review assessing the effect of dietary supplements on prevention of PPD (included 2 studies with a total of 1824 women at increased risk for perinatal depression or with no risk) omega-3 fatty acid supplementation showed no benefit (study RRs ranged from 0.99 [95% CI, 0.87 to 1.11] [n=1745] to 2.70 [95% ci, 0.56 to 13.09] [n=79] (O'Connor et al., 2019). One more low-quality paper supported these findings- a systematic review and meta-analysis of 779 pregnant women without depression or with sub-threshold symptoms indicated that the pooled standardized mean obtained from eight comparisons showed no statistically significant superiority of n-3 polyunsaturated

fatty acids (PUFA) supplement over placebo (n=779, smd = 0.03, 95% ci 0.20 to 0.13, i2= 24%) (Suradom et al., 2021). in another low-quality systematic review, which included 88,051 women (35 studies) with no previous diagnose of depressive symptoms and with no underlying health conditions findings were inconsistent. Overall, there is limited evidence that dietary intake influences the risk of PPD. While 13 studies, including three PUFA supplementation trials, found no evidence of an association, 22 studies showed some weak protective effects from healthy dietary patterns, multivitamin Supplementation, fish and PUFA intake, calcium, zinc and possibly selenium. Note that the studies included in this systematic review had methodological limitations (such as small sample sizes or cross-sectional studies with limitation of showing causality) (Sparling et al., 2017).

Are interventions in the form of physical activity effective in preventing PPD?

Two high-quality papers focused on physical activity (PA) as a preventive intervention for PPD. In a high-quality meta-analysis investigating the effect of physical activity on prevention of postpartum depression, including 186,412 pregnant and up to one-year postpartum women from 30 studies (one study included women from age 16) of which 55,867 participated in intervention groups. The main finding of this meta-analysis was that PA was positively associated with a reduced risk of PPD. According to analysis of PA type (e.g., stretching, Pilates, aerobics, work and household activities), sports activities were associated with relieving PPD symptoms (adjusted OR = 0.89, 95% CI: 0.78–1.00, p < 0.001). However, work (adjusted OR = 1.05, 95% CI: 0.37–2.97, p = 0.065) and household activities (all kinds of housework and childcare) (adjusted OR = 1.16, 95% CI: 0.89–1.52, p = 0.986) were identified as risk factors of PPD. Moreover, the dose-response analysis showed a reduced risk of PPD with a longer PA duration and that at least 90 minutes of

Overall recommendation	Strength of the recommendation	Quality of the evidence	Comments
We have no recommendation on use of dietary supplements to prevent PPD	No recommendation		There is no evidence supporting the effect of dietary supplements in preventing PPD.

PA per week could efficiently prevent PPD (adjusted OR = 0.92, 95% CI: 0.85–1.00). According to PA timing, PA during pregnancy (adjusted OR = 0.99, 95% CI: 0.91–1.06, p = 0.689) or after pregnancy (adjusted OR = 0.94, 95% CI: 0.80–1.10, p = 0.435) demonstrated a downward trend for PPD risk (Yuan et al., 2022).

In a high-quality systematic review (O'Connor et al., 2019) assessing the effect of physical activity in preventing PPD, 1021 women from the general population (no risk for developing perinatal depression) (from three studies), the physical activity interventions consistently reported point estimates in the direction of benefit (Adjusted Risk Differences ranged from −1.3% to −12.5%), but only 1 trial found statistically significant group differences (RR=0.49 95%CI- 0.25-0.97).

Overall recommendation	Strength of the recommendation	Quality of the evidence	Comments
Physical activity is weakly recommended to prevent PPD among pregnant and postpartum women from the general population	Weak	Moderate ⊕⊕⊕◯	The participants in the literature that was examined were not assessed for risk factors. There are populations that may have medical conditions to which physical activity may be harmful.

Screening for PPD

Are screening programmes effective in detecting and/or reducing peripartum depressive symptoms?

We identified nine systematic reviews. The one by Thombs et al. (2014) was already included in other reviews and was thus excluded. The other eight SRs had different criteria for inclusion, such as type of studies included, period of screening (during pregnancy and/or postpartum period), type of setting for screening, delivery agents, provision of dedicated training for the involved professionals, enhanced care combined to screening and therefore they were all used to assess the evidence.

Referrals and later depression rates

According to the SR by Bhat et al. (2022), with 49 studies of mixed methodology on screening for depression during pregnancy

and/or postpartum in community-based settings, EPDS was most frequently used as the screening instrument. Screening was performed mainly at home, by health visitors or nurses. Interventions provided for women who screened positive, and types of training and technical assistance provided to the screening delivery agents varied widely. Referral and referral tracking for those who screened positive for symptoms were inadequately described by the included studies. The review did not provide information on depression rates later in the postpartum period or good description of the risk of bias in the included studies. The authors pointed out that despite screening for PPD has been implemented in several community-based settings around the world, frequency of screening, timing of screening, or training required in these non-healthcare settings should be further investigated.

In the Byatt et al. (2015) systematic review including both RCTs and observations studies (of moderate risk of bias) conducted in outpatient perinatal care settings - screening with EPDS and/or other screening tools (PHQ, CES-D, PRIME-MD BHQ) during pregnancy or postpartum was associated with an average of 22% (13.8–33.0%) higher mental healthcare use among women who screened positive for depression, compared to usual care or pre-screening groups. However, implementation - alongside screening - of additional interventions such as patient engagement strategies, on-site assessments, and perinatal care provider training were associated with a two to four-fold increased use of mental healthcare (81%, 72.0–90.0%). The authors conclude that the benefits of screening outweigh the risks when the provision of appropriate mental health assessment and treatment can be ensured.

In the systematic review by Hansotte et al. (2017) two RCTs among 18 studies involving low-income women in western countries found lower depression scores (CES-D) at follow-up in the intervention group underwent to postpartum depression screening by master-prepared psychiatric mental health nurse or paraprofessional home visitor followed by face-to-face interaction and/or phone calls from intervention staff, compared to the control group.

Interventions for healthcare professionals (through education, Electronic Medical Record change or standardised patients for training) to improve screening and referral for perinatal mood and anxiety disorders demonstrated moderate positive impacts on screening completion rates, referral rates for peripartum mood and anxiety disorders (Long et al., 2019). All 11 of the pre-post design studies reported that

detection of depression and referral for treatment increased after the educational programme.

The systematic review by O'Connor et al. (2016) included six RCTs (one of good and five of moderate quality). In pregnant and postpartum women screened in healthcare settings, there were relative reductions of 18% to 59% in the risk of depression at follow-up compared with usual care, which translated to 2.1% to 9.1% absolute reductions in depression prevalence, according to a variety of EPDS cut-off definitions. In 3 studies that reported outcomes similar to remission (i.e., no longer screened positive) or treatment response (i.e., showed a predetermined level of improvement on a scale score) in postpartum women, there was a 21% to 33% increase in the likelihood of remission or response at 4.5 to 12 months (6-14 months postpartum), ranging from 10.0% to 33.8% absolute increases in the likelihood or remission or response. When looking at the pregnancy study only, no significant results on postpartum depression were evident. These are in general bigger effects than other SRs including also observational studies and women screened outside healthcare settings.

In the latest high-quality systematic review by Waqas et al. (2022), including nine RCTs addressing depression screening both in pregnancy and in the postpartum period in a meta-analysis, the relative effect on rates of depression in the intervention group (screening) was 0.55 (OR; 95%CI: 0.41-0.66; n=9,009) compared to usual care, while the Odds Ratio of treatment seeking among women exposed to screening was 3.74 (95%CI: 2.14 to 6.52; n=1,082). Settings included primary care centres (i.e., GP practices, antenatal care or maternal and child healthcare centres, child wellness centres, hospitals and home visits), while delivery agents for screening programmes varied from nurses, nurses specialising in public health, midwives, health visitors, psychology students, and physicians. Six of the studies reported screening in the postpartum period and three during pregnancy; EPDS was the tool adopted by the majority of the studies. Non-directive counselling, psychoeducation and pharmacological therapy were the most frequently cited post-screening treatment strategies utilised in these trials.

The overall pooled uptake rate for women with positive screening results was 43% (95% CI:35–50%) in the systematic review and meta-analysis by (2020), which included 39 observational studies and one quasi-experimental study (total n=9,380 women with positive screening results) and one RCT

(n=555 women with positive screening results). The RCT showed significant improvement in uptake rates after the implementation of referral interventions. Among the different methods of referral after screening, on-site assessment or treatment appeared to be more effective.

Van der Zee – Van den Berg et al. (2017) study included six pre-post, quasi or RCTs on screening for postpartum depression in well-baby care settings. Four of the six studies (Gerrard et al., 1993; Glavin et al., 2010; S. S. L. Leung et al., 2011; Yawn et al., 2012) (including the two studies of better quality) in which screening and enhanced care were combined in the intervention, showed significant improvement of depression scores later in the postpartum year in the intervention arms (OR around 0.5 for not screening positive later in the postpartum period).

Conclusion

A series of systematic reviews and two meta-analyses reveal a reduction in PPD and uptake rates of referral interventions among peripartum women undergoing screening programmes in healthcare setting. The direct evidence suggested that screening pregnant and postpartum women for depression may reduce depressive symptoms and reduce the prevalence of depression in a given population, particularly in the presence of additional interventions combined to screening (e.g., treatment protocols, care management, availability of personnel trained on screening and on providing PPD counselling and/or treatment) provided on-site. The indirect evidence showed that screening instruments can identify pregnant and postpartum women who need further evaluation and may need treatment.

Anxiety, quality of life, parental distress

There is a lack of information regarding peripartum anxiety screening and a lack of uniformity in training regarding screening in community-based settings (Bhat et al., 2022).

Screening programmes for common maternal mental health disorders were favourable for the outcomes such as quality of life, symptoms of anxiety (SMD = – 0.18, 95% CI:–0.25 to–0.12, n=3654) and parental distress in the systematic review by Waqas et al. (2022).

Feasibility/acceptability/ barriers

It is feasible and acceptable to screen for PPD in community settings, but there is a need for systematic research examining which screening tools to use, the ideal frequency of screening, and referral completion rates (Bhat et al., 2022).

Themes that emerged as treatment ob-

stacles after screening among low-income women in western countries included financial barriers, cultural barriers, physical barriers, systemic healthcare barriers, and social barriers; home health visitors could overcome some of these (Hansotte et al., 2017).

Studies that implemented an educational intervention for healthcare professionals involved in the screening procedures reported screening completion rates ranging from 39 to 100% and increased patient-provider communication (Long et al., 2019). Studies suggested positive receptivity to screening protocols by mothers and providers. Of the two studies that implemented a change in Electronic Medical Record as the intervention, results indicated that providers administered the EPDS 98% of the time and referred mothers with positive screens 100% of the time. Of the two studies that implemented a standardised patient exercise, the percent of women screened for perinatal mood and anxiety disorders ranged from 39 to 100%.

Patient satisfaction toward screening programmes ranged from 73.4 to 100% in five studies included in the SR by Waqas et al. (2022). An important factor for the high acceptability of these programmes was that the screening providers had not labelled, stigmatised, or distressed the mothers (reported by two studies). Openness to emotional issues and ability to validate mother's feelings rather than concentrating on the baby were major barriers to woman's perception of health professionals in one study (Morrell et al., 2009).

Cost-effectiveness

Two studies (Morrell et al., 2009; Wilkinson et al., 2017) included in the systematic review by Waqas et al. (2022) evaluated cost-effectiveness and found screening interventions to be cost-effective. Compared to usual care, the intervention cost $296,919 more, but resulted in an additional 21.43 quality adjusted life years (QALYs) and 29 remissions achieved; accounting for an incremental cost-effectiveness ratio of $13,857/QALY gained and $10,182/remission achieved. Using the commonly accepted U.S. willingness to pay a threshold of $50,000 per QALY gained, screening and treating women for postpartum depression was found to be cost-effective. There is a 70% possibility that screening is cost-effective.

Ethical aspects in screening

Peripartum depression screening should only be offered with adequate systems in place (i.e., having systems and clinical staff to ensure that women, if they screen positive, are appropriately diagnosed and treated with evidence-based care or referred to a setting that can provide the necessary care).

Overall recommendation	Strength of the recommendation	Quality of the evidence	Comments
Screening programmes for depression during pregnancy and in the postpartum period are strongly recommended	Strong	Moderate ⊕⊕⊕◯	Due to ethical considerations, screening should be implemented as long as appropriate diagnosis, treatment and follow-up can be ensured.

Are screening programmes effective in detecting the presence of risk factors for vulnerability to depression?

In the systematic review by Felice et al. (2018), the authors focused on four RCTs on pregnant populations screened by a psychosocial assessment tool, e.g., the Antenatal Psychosocial Health Assessment tool (ALPHA), or the Antenatal Risk Questionnaire (ANRQ), including some among a list of factors such as unplanned pregnancy, history of domestic violence, history of depression, being single, having no social support, anxiety symptoms, low education, smoking, poor relationship quality, low socio-economic status and history of childhood trauma or recent stressful life events, personality traits, etc. When compared to routine care, psychosocial assessments were found to be sensitive to detect risk factors associated with postpartum depression. Results from three of the included studies reported no statistically significant differences in postpartum depression. One study did not report on depression outcomes. One study found higher referral rates to social worker in the intervention group, while another one showed higher social support postpartum. Two of the studies were deemed as offering weak, one moderate and one high level of evidence.

In the systematic review on screening for intimate partner violence (IPV) by Feltner et al. (2018), five studies focusing on IPV screening among pregnant/postpartum women showed lower IPV rates postpartum in the screening group. Two RCTs reported on depressive symptoms postpartum measured with EPDS after a brief IPV counselling intervention provided during pregnancy and after delivery to screen-detected women; one found a trend towards less postpartum depressive symptoms in the intervention group [SMD (95% CI)=- 0.32 (-0.91 to 0.26)] (Zlotnick et al., 2011), while the second one reported lower postpartum depression scores [SMD (95% CI) =- 0.72 (-1.24 to 0.26)] (Tiwari et al., 2005).

Acceptability

Women find it beneficial to disclose sensitive information and the tools were found acceptable and non-invasive by participants and midwives in the systematic review by Felice et al. (2018).

Ethical aspects

It is very important to have an effective preventive intervention to offer and other necessary resources available before implementing screening programmes to identify high-risk individuals. Also, it is necessary to properly inform women about possible negative effects and consider women's needs and preferences regarding such an assessment.

Overall recommendation	Strength of the recommendation	Quality of the evidence	Comments
Screening programmes for the presence of risk factors for vulnerability to PPD are weakly recommended.	Weak	Very Low ⊕◯◯◯	Screening women is important after receiving information on how to interpret the screening results and which preventive interventions can be offered.

Additional comments

There is very low evidence available regarding this topic, based on systematic reviews only. Nevertheless, it should be considered that there are individual studies that, due to the methodological criteria for extracting data, were not considered in this work, as well as significant theoretical benefits, from a risk assessment point of view, for later depression development.

Further research for assessing efficacy, feasibility, acceptability, preferences and cost-effectiveness of such high-risk assessment programmes is needed.

Treatment of PPD

Psychological Interventions

Are psychological interventions effective in treating PPD?

We identified 15 systematic reviews, out of which 12 were also meta-analyses. These studies include 3 to 35 original studies, with sample sizes from 10 to 463 in the intervention group. In respect to the language used, 12 SRs included studies only in English, two SRs included both studies in English and Chinese, and one did not report a language. In respect to the timing of the intervention, three systematic reviews evaluated interventions during pregnancy, five in the postpartum, and nine at both time points.

Out of 15 systematic reviews, 14 were consistent showing that psychological interventions were effective in treating depressive symptoms during pregnancy and postpartum compared to no treatment. One study showed inconsistent findings, but it was on a specific sample including only pregnant Black and Latina women (Ponting et al., 2020). In respect to different psychological approaches, Cognitive behavioural therapy (CBT) was included in all 15 systematic reviews, so it is the most tested psychotherapeutic approach. The next most prevalent is CBT's third wave techniques with nine SRs, out of which all nine included behavioural activation (BA), four included mindfulness-based techniques, and one included acceptance-commitment therapy (ACT). Furthermore, interpersonal therapy (IPT) was included in four systematic reviews.

In respect of the intervention delivery format, seven systematic reviews included studies with individually delivered therapy (most of them online) and eight had mixed delivered therapy including individual and group (most including face-to-face and online).

Cognitive behavioural therapy

One meta-analysis (X. Li et al., 2022) showed that CBT-only delivered during pregnancy, postpartum, or both, was effective in the reduction of the depression levels compared to control groups both in short (SMD 0.69, 95% CI: 0.85-0.52) and long term (SMD 0.55, 95% CI: 0.77-0.33). However, four original studies included minors so we conducted our analysis excluding studies with minors and the results showed that CBT-only delivered during pregnancy, postpartum or both, was effective in the reduction of the depression levels compared to control groups both in short (SMD -0.67, 95% CI: -0.91, -0.43, $p<0.0001$, $I2=86.15\%$) and long term (SMD -0.59, 95%CI: -0.81,

-0.38, p<0.001, I2=84.55%) with a medium effect size.

Another meta-analysis (Z. Li et al., 2020) showed that CBT is effective in pregnancy (SMD=-0.52, 95%CI: -0.77, -0.28, p<0.001, I2=67.0%) and postpartum less than 4 months postpartum (SMD=-0.41, 95%CI: -0.74, -0.08, p=0.02, I2=69.0%). However, some original studies included minors, so we conducted our analysis excluding studies with minors and the results showed that in pregnancy (SMD=-0.61, 95%CI: -0.94, -0.29, p<0.001, I2=74.04%) and postpartum less than 4 months postpartum (SMD=-0.57, 95%CI: -1.03, -0.13, p<0.05, I2=68.98%), with medium effect size.

Four other SRs were consistent in showing CBT is effective in reducing depressive symptoms compared to control group (L. Huang et al., 2018; Mendelson et al., 2017; Nillni et al., 2018; Shortis et al., 2020). However, there was some overlap between the studies, e.g., all original papers included in the study by Shortis et al. (2020) was also included in the more recent one by (X. Li et al., 2022).

One meta-analysis Li, X. et al (2022) showed that CBT accompanied by other co-interventions (e.g., mindfulness, social support) was effective in depressive symptoms reduction compared to controls both in short (SMD -0.79, 95% CI: -1.16, -0.43, p< 0.001, I2=87.08%) and long term (SMD -0.76, 95%CI: -1.20, -0.32, p< 0.001, I2=89.43%). In line with that, Lau et al. (2022) showed that CBT with other interventions has a greater effect size than behavioural activation-only or CBT-only.

Third-wave CBT approach

Out of 15 systematic reviews on psychological interventions, there were nine SRs on the CBT's third wave techniques, out of which all nine included behavioural activation (BA), four included mindfulness-based techniques, and one included acceptance-commitment therapy (ACT).

Behavioural activation was included in nine SRs, with six original studies including behavioural activation separately. All six original studies were in favour of BA on depressive symptoms in comparison with the control group (Bagnall, 2014; Dimidjian et al., 2017; Forsell et al., 2017; Kieffer et al., 2013; O'Mahen et al., 2013, 2014). However, the effect size is not known, and the SR by Liu et al. (2022) for two out of these seven studies showed no significant effect.

Mindfulness-based techniques were included in four SRs, with three original studies. Out of these, one showed no effect (H. Zhang & Emory, 2015) and three in favour of mindfulness-based technique on depressive symptoms in comparison with the con-

trol group (Sun et al., 2021; M. Yang et al., 2019). However, the effect size is not known.

Finally, there was no original study providing ACT only.

Interpersonal therapy

Out of 15 systematic reviews on psychological interventions, four of them included IPT, and one systematic review showed that both CBT and IPT are effective in depressive symptoms reduction compared to control groups (Nillni et al., 2018).

Other non-specific-therapy interventions

Psychoeducation was included also in five SRs, but almost always as a co-intervention to some other therapy (e.g., CBT, IPT), so the SRs did not provide any specific conclusion about effectiveness of the psychoeducation as a stand-alone intervention. Support-based interventions were included in five SRs, with 10 original studies including intervention only based on support. Out of these, two studies showed no difference between support-based intervention group and control group (Carvalho et al., 2009; Gjerdingen et al., 2013), one study favoured control group (Letourneau et al., 2011), and seven studies showed at least some improvement in depressive symptoms in groups with support-based intervention (Chen et al., 2000; Dennis, 2003; Dennis et al., 2009; Field et al., 2013; Mohammad-Alizadeh-Charandabi et al., 2013; Shamshiri Milani et al., 2015; Shorey et al., 2019)

Delivery format: Online/internet/telehealth psychological interventions

More recent systematic reviews and meta-analysis are focused on online delivery formats including mobile applications, web pages, telephone, WhatsApp, or text messages. We identified seven systematic reviews on online psychological interventions, and they were all consistently showing that they were effective in reducing the depressive symptoms levels. (2022) showed that internet-based psychological interventions reduced depressive symptoms size (SMD=−0.72, 95% CI: −1.02, −0.42, p< .01). Liu et al. (2022) showed that the risk of PPD was significantly lower in the on-line interventions group than in the control group (OR=0.50, 95% CI: 0.29, 0.87, p<.0001). The other three systematic reviews (E. W. Lee et al., 2016) and meta-analyses (Loughnan et al., 2019; L. Zhao et al., 2021) were consistent with the effectiveness of online psychological interventions. Additionally, two meta-analyses pointed out that of all the interventions, online-delivered CBT was the most effective in depression reduction

compared to control groups, with medium effect sizes (Roman et al.,(2020): d=–0.54, 95%CI: −0.716, −0.423); Lau et al. (2022): SMD=0.7896, 95% CI: -1.29, -0.29, p<0.01).

Adverse effects

None of the systematic reviews provided information on adverse effects of the psychological interventions.

Acceptability

In terms of acceptability, there are quite wide range of attrition rate (2.6% to 61%) (Lau et al., 2022; E. W. Lee et al., 2016; L. Li et al., 2023), but with a high rate of satisfaction (L. Li et al., 2023; Loughnan et al., 2019).

Feasibility

Regarding feasibility of the psychological treatment intervention, no systematic review included information about this topic.

Values and preferences

None of the systematic reviews provided information on patients' preferences and values, except the systematic review by Ponting et al. (2020) on pregnant Latina and Black women. The study pointed out that some of the included studies made cultural adaptations to the treatment protocols.

Cost-effectiveness

None of the 15 indicated systematic reviews offered information about cost-effectiveness of the psychological treatment.

Secondary outcomes

Out of 15 systematic reviews, 13 examined maternal anxiety and three examined stress as the secondary outcome. Most of them showed effectiveness of the psychological treatment in the reduction of maternal anxiety compared to the control groups. On the other hand, infant outcomes were rarely examined as the outcome of psychological interventions for PPD.

Specific samples

Out of 15 systematic reviews, only two reviews included specific samples. The study by Ponting et al. (2020), on Black and Latina women in the US, showed inconsistent findings about the effectiveness of psychological interventions during pregnancy, although for CBT there was good rate of evidence of the effectiveness in depressive symptoms reduction. The other study, by Mendelson et al. (2017), was on mothers with newborns at the neonatal intensive care unit. They showed effectiveness of psychological interventions on depressive symptoms compared to controls, with CBT having the most evidence for its effectiveness.

Overall recommendation	Strength of the recommendation	Quality of the evidence	Comments
Cognitive-behavioural therapy (CBT) is strongly recommended for the treatment of depressive symptoms during pregnancy and postpartum	Strong	High ⊕⊕⊕⊕	Most women find psychological treatment acceptable and were satisfied. The major advantage is that for most women, any undesirable effects will probably be trivial, and no adverse effects for pregnant women, mothers and foetus/infants are expected.
Third wave CBT therapies, including Behavioural Activation and Mindfulness techniques, are weakly recommended for the treatment of depressive symptoms during pregnancy and postpartum.	Weak	Low ⊕⊕◯◯	There is a lack of information about acceptability and satisfaction with third-wave CBT therapies. However, undesirable and adverse effects for pregnant women, mothers and foetus/infants are not expected.
Interpersonal therapy (IPT) is weakly recommended for the treatment of depressive symptoms during pregnancy and postpartum	Weak	Low ⊕⊕◯◯	There is a lack of information about acceptability and satisfaction with IPT However, undesirable and adverse effects for pregnant women, mothers and foetus/infants are not expected.

Pharmacological Interventions

Are pharmacological interventions effective in treating PPD?

Effectiveness of antidepressant medication in the peripartum period

There is a scarcity of randomised controlled trials (RCT) investigating the efficacy of antidepressant medication for treatment of PPD. There are only a few studies for the postpartum period, but not for the pregnancy period.

A Cochrane meta-analysis from Brown et al. (2021) showed limited evidence regarding the effectiveness of antidepressants in the management of postpartum depression, particularly for those women with more severe depression. There is low-certainty evidence that selective serotonin reuptake inhibitors (SSRI) antidepressants are more effective in treating postpartum depression than placebo as measured by response and remission rates (pooled risk ratio (RR) 1.27, 95% confidence interval (CI) 0.97 to 1.66 for response; RR 1.54, 95% CI 0.99 to 2.41 for remission); and reduced depressive symptoms (SMD −0.30, 95% CI −0.55 to −0.05; 4 studies, n=251 women). The magnitude of the effect by the SSRI antidepressant is moderate relative to placebo; given the low number of women included in the available RCTs, the evidence remains low (Brown et al., 2021).

There was a higher remission rate (EPDS score less than 13) in the antidepressant group compared with treatment as usual after four weeks treatment (RR 2.31, 95% CI 1.50 to 3.54; n=218 women). There was no statistically significant difference between antidepressant and psychological treatment (n=49 in quantitative synthesis) in response and remission rates. However, in one study the remission rate (EPDS score less than 13) was greater in the sertraline group at 18 weeks (RR 1.20, 95% CI 0.95 to 1.53; n=206 women) compared with the listening visits group (Brown et al., 2021).

There is one systematic review (Komori et al., 2018) investigating the effectiveness of acupuncture compared with antidepressant medication for the treatment of postpartum depression, showing similar effectiveness as fluoxetine (SMD -2.22, 95% CI -7.02 to 2.58, n=56 women); however, the quality was rather low and the confidence interval very wide (Komori et al., 2018).

Two systematic reviews and meta-analyses (Sun et al., 2018; L. Wang et al., 2022) investigating herbal substances from traditional Chinese medicine, Chai Hu Shu Gan San and Shuganjieyu. Shuganjieyu consists of St John's wort herb and Acanthopanax

senticosus. Shu Gan San consists of Chai Hu (Bupleurum Chinese), Xiangfu (Cyperus rotundus) and Chuanxiong (Ligusticum chuanxiong). The results showed that Shuganjieyu (n=1409 women, Shuganjieyu capsule alone versus any antidepressant (sertraline/citalopram/paroxetine/fluoxetine), is not more effective for treatment of postpartum depression than antidepressant (odds ratio (OR) for response rate: 1.51, 95% CI: 0.87 to 2.63). The combination Shuganjieyu capsule + antidepressant showed greater response rate than antidepressant alone (OR: 4.00, 95% CI: 2.72 to 5.28) (L. Wang et al., 2022).

Chai Hu Shu Gan San in combination with fluoxetine compared to fluoxetine alone, MD = −4.10, 95% CI −7.48 to −0.72, n=170 women) may have an increased antidepressant effect compared with the substance alone or regular antidepressant alone (Sun et al., 2018). However, quality of the studies was weak.

Taken together, there is weak evidence that antidepressant medication is more effective than placebo in treating postpartum depression. Traditional Chinese herbal medicine and acupuncture are not superior to antidepressant medication, but these show less acute adverse effects. There were studies reporting a higher efficacy when treating depression with a combination of TCM substances in combination with antidepressants, however, the quality of studies is very low.

Additionally, (2017) reported higher response rates of a fluoxetine-treated group compared with a saffron-treated group after six weeks (RR 1.23, 95% CI 0.71 to 2.12; n=64 women) (Brown et al., 2021).

There were only two studies undertaking head-to-head comparison of different antidepressant substances, sertraline vs nortriptyline and sertraline vs transdermal oestradiol; here, no significant differences between treatments were reported (at week 8, RR 0.98, 95% CI 0.76 to 1.27) (Brown et al., 2021).

Discontinuation of existing antidepressant medication

One meta-analysis (Bayrampour et al., 2020) of four observational cohort studies (n=206 with discontinued antidepressant before pregnancy versus n=312 with maintained antidepressant in pregnancy) shows a higher risk of relapse of the depression during pregnancy after discontinuation of antidepressants, relative to maintained antidepressant during pregnancy (RR: 1.74, 95% CI: 0.97-3.10). In the subanalysis among the population suggestive of severe or recurrent depression, the risk of relapse was significantly higher with antidepressant discontinuation relative to

maintained antidepressant (RR: 2.30, 95% CI: 1.58-3.35). There was no evidence for this effect for the population with mild to moderate depression severity, however the confidence intervals were very wide here (RR: 1.59, 95% CI: 0.83-3.04) (Bayrampour et al., 2020)

Augmentation or combination psychopharmacotherapy

There is no data about the effectiveness of antidepressant augmentation with other psychotropics (mood stabilisers, antipsychotics, or anxiolytics) in reducing depressive symptoms during pregnancy or in the postpartum period, compared to antidepressant alone.

Hormonal treatment

There are two systematic reviews about the neuroactive steroid allopregnanolone, also known as brexanolone. The first systematic review and meta-analysis on brexanolone by Zheng et al. (2019) investigated the efficacy of brexanolone in treating postpartum depression compared with placebo (2 studies). Compared with placebo, patients with brexanolone infusion had a significantly better response that started at 24 h (brexanolone infusion=52.9% vs placebo=39.3%; RR=1.34, 95% CI 1.03–1.73) and peaked at 36 h (brexanolone infusion=65% vs placebo=44.7%; RR=1.50, 95% CI 1.06–2.13) and lasted until day 7 (brexanolone infusion=63.5% vs placebo=47.3%; RR=1.32, 95% CI 1.01–1.73; the number needed to treat (NNT) was 5). Also, the remission rates for brexanolone infusion were significantly higher in short-term at 24 h (brexanolone infusion=24.3% vs placebo= 12.7%; RR=1.86, 95% CI 1.03–3.34; NNT=8), peaked at 60 h (brexanolone infusion=50.7% vs placebo=24.0%; RR= 2.20, 95%CI 1.31–3.70; NNT=3;) and lasted until 72 h (3 brexanolone infusion=48.6% vs placebo= 24.0%; RR=1.96, 95% CI 1.41–2.72; NNT=4).

Cooper et al. (2019) (six studies) investigated the efficacy of brexanolone injections compared with SSRI in postpartum depression. Brexanolone-treated patients showed lower mean score of depressive symptoms, as follows: 2.79 (95% CI 8.04–17.53) on day three, 5.87 (95% CI −1.62 to 13.37) after week four, and 0.97 (95% CI −6.35 to 8.30) at the last visit for the Hamilton Depression Rating Scale (HAM-D). For the EPDS, the differences were 7.98 (95% CI 5.32–10.64) on day three, 6.35 (95% CI 3.13–9.57) after week four and 4.05 (95% CI 0.79–7.31) for the last follow up in the studies. In

conclusion, after three days brexanolone performed better than SSRIs and about equally after four weeks and the last follow-up visits.

Acute adverse effects in women as reported in randomised clinical trials

In the antidepressant treatment groups, overall, there were nominally or slightly significant more side effects reported with SSRIs and nortriptyline; these included nausea, decreased appetite, dizziness, headache, dry mouth, somnolence, diarrhoea, and drowsiness. In rare cases, there occurred hypomanic and psychotic episodes in the women; this was rather due to an initial misdiagnosis of unipolar depression and underlying diagnosis of bipolar or psychosis spectrum disorder (Brown et al., 2021).

Brexanolone did not lead to significantly different adverse effects compared with placebo in the meta-analysis of Zheng et al. (2019). No deaths or other unexpected adverse effects were reported. Reported adverse drug reaction were cited as: rash, fatigue, dizziness, dry mouth, abnormal dreams, headache, infusion site pain, somnolence, abdominal pain, anxiety, postural dizziness, hot flush, infusion site extravasation, localised oedema, pain in extremity, pyrexia, sedation, sinus tachycardia, vertigo, nausea and vomiting, back pain, alanine aminotransferase increased, aspartate aminotransferase increased, loss of consciousness, device infusion, issue, oropharyngeal pain, infusion site erythema, syncope, infusion site pruritus. There is no data on adverse drug reactions under brexanolone treatment compared with other antidepressant medication.

Short-term reproductive safety of antidepressants for the infant

Major congenital anomalies

A substantial number of observational studies have investigated the risk of any major congenital anomaly in the offspring following in-utero exposure to antidepressants during the first trimester, by class (SSRI or SNRI) and individual substance level. Based on most recent data from seven systematic reviews and meta-analyses, there is moderate certainty that antidepressants are not teratogenic. The accumulated evidence suggests a generally small risk for major congenital anomalies when antidepressant exposed infants are compared to unexposed infants born to women who may or may not have a mental illness (RR for SSRIs: 1.11, 95% CI 1.03-1.19) (Gao et al., 2018) RR for SNRIs: 1.07, 95% CI 0.95-

1.13) (Lou et al., 2022). This small risk is no longer evident when SSRI-exposed infants are compared to unexposed children born to women with a psychiatric diagnosis (RR: 1.04, 95% CI 0.95 to 1.13) (Gao et al., 2018), and similarly for SNRI-exposed infants (RR: 1.04, 95% CI 0.9–1.2) (Lou et al., 2022). The risk for any major congenital anomaly is slightly higher after SNRI exposure in the first trimester (RR = 1.12, 95% CI 0.97-1.31) relative to SSRI exposure, but the magnitude of risk remains small (Lou et al., 2022). Tricyclic antidepressants in the first trimester are not linked to an increased risk of congenital anomalies (OR: 1.02, 95% CI 0.82-1.25) (De Vries et al., 2021).

For the individual antidepressants, there is moderate evidence for the SSRI citalopram, fluoxetine, paroxetine, and sertraline. The evidence is very limited for bupropion and the individual SNRIs. Compared to unexposed infants born to women who may or may not have a mental illness, there is a small increased risk of any major anomaly after exposure in the first trimester to the SSRIs citalopram (RR: 1.20, 5% CI 1.09 to 1.31), fluoxetine (RR: 1.17, 95% CI 1.07-1.28), paroxetine (RR: 1.18, 95% CI 1.05-1.32), or sertraline (RR: 1.10, 95% CI 0.99-1.22); this risk is no longer evident when the comparison group is constituted by unexposed infants born to women with a psychiatric diagnosis for these substances (RR for citalopram: 1.17, 95% CI 0.84-1.62; RR for fluoxetine: 1.17, 95% CI: 0.67-1.05; RR for paroxetine: 1.17, 95% CI 0.97-1.41; RR for sertraline: 1.12, 95% CI 0.87-1.44) (Gao et al., 2017, 2018). There is no evidence for an association between first-trimester exposure to fluvoxamine and major congenital anomalies (RR: 0.77, 95% CI 0.49-1.21).

There is limited evidence, based on a single meta-analysis (Grigoriadis et al., 2019) that concurrent use of benzodiazepines with antidepressant in the first trimester increases the risk of congenital malformations (OR: 1.40, 95% CI: 1.09-1.80) compared to no use. In the studies included in this meta-analysis, confounding by indication and severity of the maternal psychiatric illness remains uncontrolled for, as the comparison group included healthy controls rather than unexposed children born to women with a psychiatric diagnosis.

Cardiac anomalies

The accumulated evidence suggests a generally moderate risk for major cardiac anomalies when SSRI exposed infants are compared to unexposed infants born to women who may or may not have a mental illness (RR for SSRI exposure: 1.24, 95%

CI 1.11 to 1.37; RR for SNRI exposure: 1.33, 95% CI 1.15–1.53). For SSRIs, the small risk was observed for the specific cardiac malformations of septal defects (RR 1.38, 95% CI 1.00- 1.91), atrial septal defects (RR 1.83, 95% CI 1.22-2.73), and right ventricular outflow tract defects (RVOTD) (RR 1.38, 95% CI 1.09 to 1.75).

The risk for any cardiac anomaly is no longer evident when SSRI antidepressant exposed infants are compared to unexposed children born to women with a psychiatric diagnosis (1.06, 95% CI 0.90 to 1.26), and similarly for SNRI antidepressant exposure (RR: 1.17, 95% CI 0.95–1.42) (Lou et al., 2022).

For the individual antidepressants, there is moderate evidence for the SSRI citalopram, fluoxetine, paroxetine, and sertraline. The evidence is more limited for the individual SNRIs, and very limited for bupropion. Compared to unexposed infants born to women who may or may not have a mental illness, there is a moderate increased risk of any cardiac anomaly after exposure in the first trimester to the SSRIs citalopram (RR: 1.24, 5% CI 1.02-1.51), fluoxetine (RR: 1.30, 95% CI 1.12-1.53), sertraline (RR: 1.42, 95% CI 1.12- 1.80) and paroxetine (RR: 1.35, 95% CI 1.19-1.53); this risk is no longer evident when the comparison group is constituted by unexposed infants born to women with a psychiatric diagnosis (RR for citalopram: 1.08, 95% CI 0.75-1.56; RR for fluoxetine: 0.94, 95% CI 0.65-1.37; RR for sertraline: 1.12, 95% CI 0.92-1.35; RR for paroxetine: 1.27, 95% CI 0.89-1.80) (Gao et al., 2018). The risk of cardiac anomaly following sertraline exposure in the first trimester is 1.20 (95% CI 0.94-1.53), and this risk emerged mainly in studies among the North American population (RR: 1.26, 1.06-1.49) in the meta-regression analysis by Shen et al. (2017).

The increased risk for septal defects and RVOTD is in the range 59-81% for citalopram and fluoxetine, and 36% for sertraline in first trimester (Shen et al., 2017), relative to unexposed infants born to women who may or may not have a mental illness. In another meta-analysis (Gao et al., 2018) the effect size for sertraline for septal defects and ASD was greater (about two-fold increased risk) than in Shen et al. (2017).

The risk of RVOTD is greater following use of paroxetine in the first trimester (RR 2.15, 95% CI 1.04-4.44), albeit confounding by indication and severity of the maternal psychiatric illness remains uncontrolled for. In one additional meta-analysis (Bérard et al., 2016), exposure to paroxetine was associated with an increased risk of bulbus cordis anomalies and anomalies of cardiac septal closure (OR 1.42: 95% CI 1.07-1.89), atrial

septal defects (OR: 2.38, 95% CI 1.14-4.97) and right ventricular outflow tract obstruction defects (OR: 2.29, 95% CI 1.06-4.93). Yet, albeit confounding by indication and severity of the maternal psychiatric illness remains uncontrolled for, as the comparison group included healthy controls rather than unexposed children born to women with a psychiatric diagnosis.

Other major anomalies

There is limited evidence about the risk for other major anomalies, and the available studies did not account for severe confounding by maternal psychiatric illness. Compared to unexposed infants born to women who may or may not have a mental illness, SSRI exposure in the first trimester is associated with an increased risk for neural tube defects (RR: 1.49, 95% CI 1.05-2.10), cystic kidney disease (RR: 2.96, 95% CI 1.87-4.70), clubfoot (RR: 1.30, 95% CI 1.06-1.61), abdominal wall defects (RR: 1.81, 95% CI 1.22-2.68), omphalocele (RR 1.73, 95% CI 1.03-2.89), and gastroschisis (RR: 1.89, 95% CI-1.19) (Gao et al., 2018).

There is limited evidence regarding the risk for other major anomalies after exposure to individual antidepressants in the first trimester. For citalopram, an elevated risk for eye defects (RR: 2.00, 95% CI 1.13-3.54), urinary system defects (RR: 1.72, 95% CI 1.27-2.33), and hypospadias (RR: 1.87, 95% CI 1.23-2.83) is observed using unexposed infants born to women who may or may not have a mental illness as comparator (Gao et al., 2018). For escitalopram however, there is an increased risk of clubfoot (RR: 2.18, 95% CI 1.16-4.08), abdominal wall defects (RR: 3.52, 95% CI 1.56-7.93), and gastroschisis (RR: 3.95, 95% CI 1.46-10.68). Despite escitalopram and citalopram being very similar drugs, the risk for other congenital anomalies is not coherent, which posits against true drug effects. For fluoxetine, the evidence remains mixed in relation to neural tube defects, as well as for ear, face, and neck defects; in one systematic review the risk for these major anomalies was elevated (Gao et al., 2018) but there was no association in the meta-analysis conducted by Gao and colleagues in 2017. Sertraline use during the first trimester was associated with an increased risk of respiratory system defects (RR 2.65, 95% CI 1.32-5.32), limb defects (RR 1.42, 95% CI 1.03-1.95), and clubfoot (RR 1.72, 95% CI 1.11-2.65) in one meta-analysis (Shen et al., 2017). Yet, confounding by indication and severity of the maternal psychiatric illness remains uncontrolled for, as the comparison group included healthy controls rather than unexposed children born to women with a psychiatric diagnosis.

Immediate pregnancy and birth outcomes

Pregnancy loss (spontaneous abortion, stillbirth)

Based on most recent data from two systematic reviews and meta-analyses, there is moderate certainty that antidepressants do not increase the risk of spontaneous abortion or stillbirth beyond the risk posed by maternal mental illness. One review (Mitchell & Goodman, 2018) found no consistent differences in risk level for spontaneous abortion when antidepressant-exposed were compared to women with a registry-recorded diagnosis of depression (RR: 1.00, 95% CI 0.80–1.24). A slightly higher rate of spontaneous abortion was observed when compared to unexposed pregnancies within women who may or may not have a mental illness (RR =1.49, 95% CI: 1.29, 1.73; n=14 studies), and similarly for stillbirths (RR = 1.16, 95% CI: 1.02, 1.32; n=9) (Xing et al., 2020). Yet, confounding by indication and severity of the maternal psychiatric illness remains uncontrolled for in Xing et al. (2020), as the comparison group included healthy controls rather than unexposed children born to women with a psychiatric diagnosis.

Prematurity, low birth weight, small or large for gestational age

A substantial number of observational studies have investigated the risk of prematurity, low birth weight and small-for-gestational age (SGA) infants following in-utero exposure to antidepressants during pregnancy, by class (SSRI or SNRI) and individual substance level. Based on most recent data from six systematic reviews and meta-analyses, there is no consistent difference in risk level for birth weight outcomes, percent small for gestational age, or preterm birth, and most studies indicated statistically significant but very small differences in average length of gestation.

The accumulated evidence is mixed in relation to the rate of preterm delivery (Mitchell & Goodman, 2018). In some studies, antidepressant exposure has been associated with a greater moderate risk of prematurity (adjusted OR: 1.4, 95% CI 1.1–1.8), particularly the use of SSRIs (aOR 1.9, 95% CI 1.2–2.8), compared to unexposed infants born to women who may or may not have a mental illness (Chang et al., 2020; Kautzky et al., 2022; Vlenterie et al., 2021). This risk reduced slightly when unexposed children born to women with depressive symptoms or a clinical diagnosis of depression acted as comparators (adjusted OR: 1.6, 95% CI 1.0–2.5; RR: 1.62, 95%

CI: 1.37, 1.93) (Vlenterie et al., 2021; Xing et al., 2020). When examining the studies that assessed length of gestation, the absolute difference in gestational length following prenatal antidepressant was found to be less than a week, with the averages all within the full-term range. Because having depressive symptoms during pregnancy (adjusted OR 1.2, 95% CI 1.1–1.4) or a clinical diagnosis of depression (adjusted OR 1.6, 95% CI 1.2–2.1) are also associated with preterm birth (Vlenterie et al., 2021), it is unlikely that pharmacologic treatment alone drives these associations.

Fluoxetine (adjusted OR: 1.9, 95% CI 1.1–3.3) and sertraline (adjusted OR: 2.2,95% CI 1.2–4.3) were associated with greater risk of prematurity, also when the cohort was restricted to women with depressive symptoms or a clinical diagnosis of depression (Vlenterie et al., 2021).

For the outcome of low birth weight and SGA, the risk with prenatal antidepressant exposure was 1.45 (95%CI = 1.18–1.76) with a high heterogeneity (X. Zhao et al., 2018), and reduced slightly when women with children born to women with untreated depression acted as control (RR = 1.27, 95% CI: 1.10, 1.46; n=15 studies) (Xing et al., 2020). Residual and unmeasured confounding by maternal psychiatric illness severity remains a concern and that is uncontrolled in the evaluated studies.

Seizures and neonatal convulsions

Most recent data from two systematic reviews and meta-analyses indicate an increased risk for neonatal convulsions when infants prenatally exposed to antidepressants are compared to infants born to women (RR: 1.97, 95% CI: 1.56-2.48; n=4 studies) who may or may not have a mental illness (Xing et al., 2020). This risk was moderate for early antidepressant exposure in pregnancy (43% increased risk) and of greater magnitude for antidepressant late exposure (140% increased risk), and it emerged for SSRI and TCA antidepressants. (RR for SSRI: 2.47, 95% CI: 1.37-4.44; RR for TCA exposure: 3.22, 95% CI: 1.36-7.67) (M. T. Y. Leung et al., 2021). Yet, confounding by indication and severity of the maternal mental illness remains uncontrolled for in the evaluated studies, as the comparison group included healthy controls rather than unexposed children born to women with a psychiatric diagnosis.

Hypoglycemia, feeding problems, low Apgar score, and NICU admission

Recent data from four systematic reviews and meta-analyses indicate an association between exposure to antidepressants prenatally and the adverse neonatal outcomes of low Apgar score,

hypoglycaemia, feeding problems neonatal intensive care unit (NICU) admission. Prenatal exposure to antidepressants, especially fluoxetine and sertraline use, was associated with increased risks of low Apgar score (RR: 1.91, 95% CI: 1.42, 2.56; n=7), also when the comparator group consisted of women with depressive symptoms or a clinical diagnosis of depression, at least partly ruling out confounding-by-indication (Vlenterie et al., 2021; Xing et al., 2020). In relation to NICU admission, children whose mothers received antidepressants during pregnancy had increased risks of this outcome compared with children born by depressed but untreated pregnant women (RR: 1.60, 95% CI: 1.38, 1.85; n=4) (Xing et al., 2020). However, admission to NICU showed high heterogeneity between studies and may require a stricter definition in terms of duration and applied treatment to draw definitive conclusions (Kautzky et al., 2022).

There is limited and low-quality evidence about the association of prenatal antidepressant exposure with neonatal hypoglycaemia (Kautzky et al., 2022; Uguz, 2021). Compared to children unexposed born to women who may or may not have a psychiatric illness, the relative risk for neonatal hypoglycaemia was in the range of 1.33-1.73 for any antidepressant, 1.30-1.35 for SSRI, 1.42-2.11 for SNRIs, and 2.07 for TCAs. Yet, none of the available studies included any adjusted analyses for maternal psychiatric disorders such as depression and anxiety disorders. Hence, confounding by indication and severity of the maternal mental illness remains uncontrolled in the evaluated studies on neonatal hypoglycaemia.

Persistent pulmonary hypertension of the newborn

A substantial number of observational studies, with a total of 156,978 infants prenatally exposed to antidepressants, have investigated the risk of persistent pulmonary hypertension of the newborn (PPHN) (Masarwa et al., 2019). Based on most recent data from the systematic review and meta-analysis by Masarwa et al. (2019), there is moderate certainty of an increased risk for PPHN after prenatal antidepressant exposure (OR: 1.82; 95% CI, 1.31-2.54; adjusted ORs for eight studies: 2.42; 95% CI, 1.68- 3.48). The magnitude of risk was slightly higher for late pregnancy antidepressant exposure (OR: 2.08). Yet, in absolute terms, the risk of PPHN remains small. Sertraline ranked as most likely to have the lowest risk for PPHN compared to other SSRIs (sertraline versus fluoxetine: OR, 0.34; 95% CI, 0.11-0.96), suggesting it may have the best safety profile for use in

pregnancy. Confounding by indication and severity of the maternal mental illness remains an issue, and the studies evaluated have high heterogeneity.

Neonatal withdrawal symptoms

A substantial number of observational studies have investigated the risk of neonatal withdrawal symptoms with prenatal antidepressant exposure, especially at the end of gestation. Based on most recent data from one systematic review and meta-analysis (Kautzky et al., 2022), there is certainty that prenatal antidepressant exposure is associated with symptoms of convulsions (OR: 3.25, $p = 0.0002$), respiratory problems (OR: 1.96, $p < 0.0001$), temperature dysregulation (OR: 1.75, $p = 0.004$) (n=1058), and feeding problems (OR 2.25, $p = 0.031$), but not for jaundice. The symptoms are usually transient and rarely life threatening.

Long-term safety of antidepressants for the infant

We included six systematic reviews that investigated long-term outcomes in children exposed to antidepressant medication during pregnancy (Al-Fadel & Alrwisan, 2021; Andalib et al., 2017; Halvorsen et al., 2019; Leshem et al., 2021; Man et al., 2018; Rommel et al., 2020). Among these studies, there was one each that dealt with the topic of Attention-Deficit/Hyperactivity Disorder (ADHD), Autism Spectrum Disorder (ASD), mental disorders in general, the broad outcome of physical, developmental and mental outcomes, and motor and intellectual disability outcomes.

The systematic review from Rommel et al. (2020) investigated a very broad range of long-term outcomes in the exposed children up to 19 years after birth. They concluded that there were associations between some neurodevelopmental and mental disorders and in-utero antidepressant exposure, however, this association seems to be mainly driven by the maternal disorder rather than the antidepressant medication. When comparing antidepressant-exposed children with children not exposed born to women with a mental illness, the increased risk for internalising and externalising behaviour in children was no longer significantly different; similarly, it was for the risk for lower intelligence quotient, special education needs or delayed school start. The risk of speech and language disorders was significantly higher in antidepressant-exposed children relative to unexposed. No significant association was found between antenatal antidepressant exposure and cognitive performance.

The results for the risk of ASD are incon-

clusive: two studies indicating an increased risk for ASD after controlling for confounding factors, while 5 studies did not find any significant association. Andalib et al. (2017) examined the risk of ASD risk after SSRI exposure and reported an OR of 1.83 (95% CI 1.59-2.10), however these were poorly adjusted estimates, and the role of confounders was poorly addressed. In relation to ADHD, controlling for confounding by indication resulted in loss of the significant association between antidepressant exposure and this outcome in all studies that conducted such analysis. Lehsem et al. (2021) analysed prenatal SSRI and SNRI exposure and the risk of ADHD and ASD. They came to similar conclusions as Rommel et al (2020)., i.e., that there was a significant association of SSRI and SNRI prenatal exposure with an increased small risk of ADHD and ASD in the offspring; however, this risk was equally present for pre-pregnancy antidepressant exposure, indicating that the elevated risk posed by the antidepressant is attributable to confounding by indication and other unmeasured factors. Man et al. (2018) concluded that the increased ADHD risk reported after antidepressant exposure is more likely caused by unmeasured familial and genetic factors, as sibling-design studies did not show an increased risk with antidepressant exposure. The systematic review and meta-analysis by Halvorsen et al. (2019) examined offspring risk of mental disorders in general., and the results were consistent with Rommel et al. The reported associations of prenatal antidepressant exposure with ASD, ADHD, mental retardation, mood disorders, anxiety disorders and speech disorder, were considered to be largely driven by confounding by indication.

The risk of altered BMI and the increased risk of affective disorders in the children remained significantly associated with prenatal antidepressant exposure after adjustment for confounding by indication (Rommel et al., 2020). However, the severity of the mental illness of the mothers was not taken into account in any of those studies, which challenges to infer whether these associations may be causal. Child motor and neurocognitive development was investigated up to 14 years after birth by Al-Fadel and Alrwirsan (2021); the study concluded that there was only a minimal impairment in exposed children and the results of the studies were rather inconclusive. Several methodological limitations existed so that confounding by indication and other potential confounders could not be ruled out.

In conclusion, the increased risk of long-term outcomes in children following

prenatal antidepressant exposure are of small-moderate effect size and these associations are thought to be largely explained by the mental illness of the mother, genetic, and familial factors.

Maternal outcomes in pregnancy and early postpartum

We included one systematic review each investigating the risk of preeclampsia, postpartum haemorrhage and weight gain/gestational diabetes mellitus in mothers taking antidepressants during pregnancy. Gumusuglu et al. (2022) reported a pooled RR of 1.43 (95% CI 1.15-1.78) with regards to preeclampsia following prenatal exposure to SSRI; however, the study had high heterogeneity and high risk of confounding in the included studies. A systematic review and meta-analysis (H. Jiang et al., 2016) examined the risk of postpartum haemorrhage after antidepressant use in pregnancy and reported an overall slightly increased risk (RR 1.32, 95% CI 1.17-1.48) in antidepressant users relative to non-users. The risk was moderately elevated following prenatal exposure to the specific antidepressant subgroups (non-SRI: RR=1.31, 95% CI=1.1-1.56); SRI: RR=1.23, 95% CI=1.06-1.44; SSRIs: RR=1.2, 95% CI:1.04-1.38; SNRIs: RR=1.62, 95% CI=1.41-1.85). There was an increased risk of postpartum haemorrhage among current (RR=1.37, 95% CI=1.09-1.71) and recent users (RR=1.32, 95% CI=1.15-1.51) of the antidepressant, but not past users (RR=1.08, 95% CI=0.88-1.31). However, the definition of blood loss varied from 500 ml to 1000 ml in the studies and potentially confounding factors were not consistently included, limiting any causal inference of these associations.

Lopez-Yarto et al. (2012) (n=2 studies) investigated metabolic adverse effects of antidepressant exposure in pregnant women, specifically the risk of weight gain and gestational diabetes mellitus. Pregnant women with major depressive disorder receiving treatment with an SSRI had a non-significantly higher weight gain than depressed pregnant women not receiving SSRIs (mean difference 4.9 kg, 95% CI −3.4 kg to 13.2 kg). Gestational weight gain was similar in depressed women receiving SSRIs compared to women without depression (mean difference −1.2 kg, 95% CI −3.1 kg to 0.8 kg). There was no significant risk of gestational diabetes mellitus in pregnant women with one SSRI prescription dispensed in the 1-year period prior to delivery, compared to women not prescribed SSRIs during the same period (adjusted OR 1.31; 95% CI 0.86–2.01).

Safety of antidepressants while breastfeeding

We included one systematic review (Or-

solini & Bellantuono, 2015) investigating infant outcomes after exposure to antidepressants via breastmilk. The evidence is limited and based mainly on small studies and case reports. The available data indicate that when the use of SSRIs is clearly indicated in a nursing woman, the preferred antidepressants are paroxetine and sertraline because of their best safety profiles as reported in exposed infants. The least preferred antidepressant while breastfeeding is fluoxetine. However, the passage of antidepressants into the breastmilk is limited, thereby the actual drug exposure of the child is considered to be minimal.

Patient decision aid

There is very limited data on the effect of patients' decision aid (PDA) in women with PPD considering pharmacological treatment. We included one systematic review about PDA concerning the clinical dilemma on whether to take or not to take antidepressant medication in pregnancy (Broughton et al., 2021), where a summary of the findings of three pilot studies on this topic can be found. Overall, 82-100% of the women found the PDA useful to decide if they should take antidepressants or not. No conclusion can be made due to lack of data.

Overall recommendations

Pregnancy

Overall recommendation	Strength of the recommendation	Quality of the evidence	Comments
Antidepressant medication in pregnancy is strongly recommended, after careful consideration of individual risk-benefit ratio for each woman and her unborn child. The decision-making about antidepressant intervention should consider the history of depression recurrence and severity of symptoms, previous response to the intervention, and individual preference	Strong	Low ⊕⊕◯◯	There is no evidence available from systematic reviews and meta-analysis on the efficacy of antidepressant intervention in pregnancy. There is moderate evidence on the reproductive safety of antidepressants in pregnancy on maternal and offspring outcomes. Individual risk-benefit assessment of the intervention is needed for each woman, but antidepressant medication should be considered in women with moderate to severe depressive symptoms or after non-response to non-pharmacological interventions.
Women with severe and/or recurrent depression are strongly recommended not to discontinue the antidepressant medication during pregnancy due to the increased risk of relapse.	Strong	Low ⊕⊕◯◯	Evidence supports the elevated risk of relapse of the depression with discontinuation of the intervention, particularly in cases of severe or recurrent depression.

Overall recommendation	Strength of the recommendation	Quality of the evidence	Comments
It is strongly recommended that pregnant women should be treated with antidepressants at the lowest effective dose and possibly as monotherapy.	GPP		
It is recommended to carry on regular monitoring of drug levels and to aim for low effective drug level during gestation.	GPP		
It is recommended to avoid abrupt discontinuation of the antidepressant upon recognition of the pregnancy.	GPP		
It is strongly recommended that clinicians provide information to women about the possible risks of antidepressant exposure in pregnancy on maternal-child health versus the potential risks posed by maternal depression.	Strong	Moderate ⊕⊕⊕◯	Both maternal depression and the antidepressant intervention in pregnancy can increase the risk of multiple health outcomes in mother-child pairs. Women must be informed about both sets of risks in order to take informed clinical decisions about their antidepressant treatment. However, there are no data about interventions informing or not informing women about potential risks and benefits of medication vs untreated PPD.

Overall recommendation	Strength of the recommendation	Quality of the evidence	Comments
It is strongly recommended that all women under antidepressant interventions and their offspring should be closely monitored during pregnancy, as well as delivery being in a specialised obstetric centre with neonatal intensive care unit.	Strong	Low ⊕⊕◯◯	Few data are available about the efficacy of antidepressant intervention in postpartum. However, as opposed to reproductive safety data about antidepressants in pregnancy, there is substantially less data about the short- and long-term safety of children exposed to antidepressant while breastfed. However, the risk of untreated depression and the benefits of breastfeeding on those negative outcomes needs to be weighed in each woman and child individually. In case a woman does not breastfeed, there is weak evidence of the effectiveness of antidepressant treatment for postpartum depression, however, there is also no risk to the child to be considered.

Additional comments

Based on a substantial number of observational studies, there is moderate certainty that antidepressants do not increase the risk of multiple adverse perinatal and long-term outcomes in the child beyond the risk posed by maternal mental illness, and similarly for maternal adverse outcomes. Antidepressants may pose a small increased risk of shorter gestation and lower birth weight beyond that posed by maternal depression, but the absolute difference in these measures is low.

There is moderate certainty of an increased risk for PPHN and neonatal abstinence symptoms after prenatal antidepressant exposure, especially in late pregnancy. The absolute risk for PPHN remains low due to the rarity of the outcome. Sertraline ranked as most likely to have the lowest risk for PPHN compared to other SSRIs. Neonatal abstinence symptoms are usually transitory and can develop in one out of five infants prenatally exposed to antidepressants.

Paroxetine and fluoxetine were initially considered as not medication of first choice in pregnancy due to possible increased risk of cardiac malformation. However, more recent methodologically sound evidence indicates that antidepressants are generally not causally associated with increased risk of malformation.

No recommendation can be given regarding the effectiveness of antidepressant augmentation with other psychotropics for treatment of depression in pregnancy, as there are no available data.

Postpartum

Overall recommendation	Strength of the recommendation	Quality of the evidence	Comments
It is strongly recommended to use brexanolone for moderate to severe postpartum depression treatment if available and if accepted as a treatment option by the woman.	Strong	Moderate ⊕⊕◯◯	The strong recommendation is based on the clinical effectiveness of this intervention. However, it must be considered that few aspects may affect its use : (i) need of inpatient care, which may be less acceptable for women, due to the possibility of separation of the newborn; (ii) breastfeeding cessation for 3 days, which also may affect women's acceptability of the intervention; (iii) the very high cost, making the intervention less accessible than others; (iv) there is scarcity of evidence on the safety of brexanolone exposure via breast milk on the infant. Brexanolone is currently not licensed In Europe. Therefore, although brexanolone is strongly recommended for moderate to severe cases of depression, its use requires careful discussion between the woman and her HCP.

The evidence about possible risks to the infant following breastmilk exposure to antidepressants is low and based on case reports and small studies. However, we recommend that women can continue breastfeeding while using antidepressants as the medication transfer into breast milk is low. No recommendation can be given regarding the effectiveness of antidepressant augmentation with other psychotropics for treatment of depression in postpartum, as there are no available data.

Non-invasive brain stimulation interventions

Repetitive transcranial magnetic stimulation (rTMS)

rTMS in pregnancy

To date, five systematic reviews have been published discussing the efficacy of repetitive transcranial magnetic stimulation (rTMS) in the perinatal period (Cole et al., 2019; Ganho-Ávila et al., 2019; Konstantinou et al., 2020; Pacheco et al., 2021; Z. Peng et al., 2018) and presenting data from somewhat overlapping studies. Pacheco et al. (2021) found 16 studies conducted in pregnant women for a total of 76 participants who started treatment at the first, second or third trimesters. Approximately half of the studies observed the effect of rTMS as an adjunctive treatment to medication (citalopram, bupropion, duloxetine, escitalopram, fluoxetine, sertraline, clonazepam, quetiapine, venlafaxine, pregabaline, lamotrigine, and aripiprazole).

Stimulation protocols were heterogeneous, with stimulation frequencies ranging between 1-25 Hz, number of pulses between 50-4000, and stimulation intensity between 80-120% of the individual motor threshold. Inter-train intervals also varied. Most treatments applied stimulation over the dorsolateral prefrontal cortex (DLPFC), either bilaterally or only over one of the hemispheres.

According to Pacheco et al. (2021), the available evidence from the single RCT (Kim et al., 2019) testing a four-week protocol of 20 daily sessions (right DLPFC, at 1 Hz and 100% MT intensity, 900 pulses per session), comparing active rTMS (n=11) with sham rTMS (n=11), showed that active rTMS resulted in a significant decrease in depressive symptoms as assessed by the Hamilton Rating Scale for Depression (HDRS-17) (mean value at baseline = 23.2; mean value at the end of treatment = 9.3). The authors did not specify effect sizes.

Overall, bilateral, left High Frequency (left-HF), right-Low Frequency (right-LF) and left-

LF protocols were so far tested with the left-HF being the most common protocol, followed by right-LF, and both alternatives showing encouraging results. However, response and remission rates were not significantly different between active rTMS and sham groups. Additionally, across RCTs and single-arm studies, the rate of response to treatment of the participants in rTMS treatment ranged from 38.8%-81.8%, and remission rates ranged between 18.8%-61.1%.

In what concerns secondary measures, these authors report improvement of cognitive functions in several studies observing the impact of rTMS. Pacheco et al. (2021) resente data from the study by Kim et al. (2019) with pregnant women, using the Mini-Mental State Examination (MMSE), the Trail Making Test A&B (TMT-A; TMT-B), the Stroop Interference Test, the Wechsler Memory Scale 3rd Edition, the Letter-Number Sequencing (LNS), and the Wechsler Memory Scale 3rd Edition and Digit Span that shows significant differences in LNS in the control group with a worse performance from pre-to-post treatment.

Concerning adverse effects, two preterm births were described in case reports and three in RCTs. In one case series, an APGAR < 7 was also reported. However, the association between the reported adverse effects and the treatment was not established. Otherwise, pregnancies progressed with no complications, and no complications were reported at birth, resulting in healthy babies. Across studies, transient side effects commonly reported were headache, contraction of facial muscles, supine hypotension, and pain/discomfort at the application site.

As for acceptability, the RCT showed that 84.6% of women completed the intervention (Kim et al., 2019). Across single-arm studies, treatment completers corresponded to 93.8%; Across case reports, all women completed treatment (100%). Highly demanding daily schedules were appointed as the reason for withdrawal. In this scenario, intermittent Theta Burst Stimulation (iTBS) protocols could be a good alternative as these reduce treatment sessions duration to approximately 3 minutes.

Regarding feasibility, the survey by Kim and colleagues (2011) evaluating patient acceptability to rTMS, found that the likelihood of women considering rTMS during pregnancy increased after an informational video, suggesting that lack of knowledge and stigma may be an obstacle to choosing rTMS as a treatment alternative in the peripartum period

Overall, evidence of the efficacy of rTMS as a stand-alone or coadjuvant treatment in improving depressive symptoms during pregnancy (including iTBS in one case re-

port) is favourable to the treatment. The recommended acute treatment protocol involves a four-weeks course for 20 daily sessions, of right-LF over the rDLPFC, at 1 Hz and 100% MT intensity, 900 pulses per session. A maintenance phase of one to two sessions per week might be discussed for the following weeks, as needed.

However, the synthesised data come from studies with heterogeneous protocol treatments, most of them uncontrolled trials, case series, and case studies with an intrinsically higher risk of bias, due to potential selection of data reported, and incomplete information obtained. Additionally, the clinically meaningful benefit is yet to be established in pregnancy as most studies report estimated differences between baseline and end-of-treatment across a disorder that is already expected to spontaneously decrease along the course of the disease.

Overall recommendation	Strength of the recommendation	Quality of the evidence	Comments
rTMS is weakly recommended for the treatment of mild to moderate depressive symptoms in the postpartum period.	Weak	VeryLow ⊕◯◯◯	rTMS might be beneficial and risks of adverse effects for the woman or the foetus are unlikely. The evidence on its effectiveness is very low. Our recommendation considers that in clinical settings where it might be difficult to access psychological treatments or there is resistance of women to pharmacological or psychological interventions, rTMS could be an alternative treatment, if accessible and available, for women with mild to moderate depressive symptoms.

rTMS in the postpartum period

Five systematic reviews were published discussing the efficacy of repetitive transcranial magnetic stimulation (rTMS) in the postpartum period (Cole et al., 2019; Ganho-Ávila et al., 2019; Konstantinou et al., 2020; Pacheco et al., 2021; L. Peng et al., 2020) with overlapping studies. Pacheco et al. (2021), report one RCT, three single-arm studies, and one case report), including 45 women diagnosed with postpartum depression.

The study by Peng et al. (2020) identified 14 studies in rTMS delivered to women in the postpartum, combined with or without other PPD routine treatment (e.g., drug therapy) for a total of 448 women. As comparator, the authors found routine treatment only or routine treatment combined with sham rTMS. The direct difference identified between Peng et al. (2020) and a later systematic review by Pacheco et al. (2021) concerns language and the databases used. Whereas Pacheco searched the literature in English, French, Spanish, or Portuguese, Peng's study included the literature in English and Chinese. Moreover, whereas Pacheco's study searched on PubMed/MEDLINE, PsycINFO, Web of Science, and LILACS for peer-reviewed studies and for unpublished studies in the Networked Digital Thesis and Dissertations, Peng's study included literature in Chinese and English and searched in China National Knowledge Infrastructure, WanFang, VIP Information, Embase, PubMed, CENTRAL, Web of Science, and Physiotherapy Evidence Database.

Across these two systematic reviews, stimulation protocols were heterogeneous, with stimulation frequencies ranging between 1-25 Hz, number of pulses between 50-4000, and stimulation intensity between 80-120% of the individual motor threshold. Inter-train intervals also varied. Most treatments applied stimulation over the dorsolateral prefrontal cortex, either bilaterally or only over one of the hemispheres.

According to Pacheco et al. (2021), the available evidence from the RCT testing a four-week protocol of 20 daily sessions (lD-LPFC, at 5 Hz and 120% MT intensity, with 20s ITI, leading to 1250 pulses per session), and comparing active rTMS with sham rTMS, showed that active rTMS resulted in a significant decrease in depressive symptoms.

Overall, studies in the postpartum period followed the principles of rTMS use in MDD, with the left-HF in the DLPFC being the single protocol under study.

According to Peng et al. (2020), rTMS shows a large and significant reduction of depressive symptoms as measured by Hamilton Depression rating Scale (SMD = -1.02 (95% CI [-1.37 to-0.66], I2=83%) using a random-effects model analysis. Similarly, a meta-analysis pooling the two studies using EPDS scores showed also promising large and significant

effects of rTMS, compared with sham (MD =-8.27, 95% CI [-9.96 to -6.58], I^2 = 0%).

The authors further conducted meta-regression analysis to test treatment duration (3-4 weeks or 7-10 weeks) and found that the duration of intervention impacts the heterogeneity of the results, with treatment protocols between 7-10 weeks showing better results. On the contrary, stimulation methods (HF of left DLPFC or LF of right DLPFC) are not related to treatment efficacy heterogeneity. Furthermore, the authors report both improvement of cognitive functions after treatment as measured by the Mini-Mental State Examination (MMSE; MD= 3.64, 95% CI [0.19 to 7.09], I^2=89%) or no statistically significant differences from pre to post treatment.

Across studies, transient side effects concern only the mother and the ones commonly reported were headache, contraction of facial muscles, supine hypotension, and pain/discomfort at the application site.

In the postpartum, the RCT and the single-arm studies reported an adherence between 76%-100% and in case reports, all patients completed the treatment protocol. Highly demanding daily schedules were appointed as the reason for withdrawal. In this scenario, iTBS protocols could be a good alternative as these reduce treatment sessions duration to approximately 3 minutes.

Overall, evidence of the efficacy of rTMS as a stand-alone or coadjuvant treatment in improving depressive symptoms in the postpartum is favourable to the treatment. Recommended acute treatment protocol includes a7-10 weeks (HF of left DLPFC or LF of right DLPFC) course of treatment, number of pulses between 50-4000, and stimulation intensity between 80-120% of the individual motor threshold. A maintenance phase of 1-2 sessions/week might be discussed for the following weeks, as needed.

However, data from this synthesis come from studies with heterogeneous protocol treatments, most of them uncontrolled trials, with an intrinsically higher risk of bias, due to potential selection of data reported, and incomplete information obtained. In the postpartum the data seems to be of higher quality with optimal information size (448 for a minimum of 63) and large effect sizes.

Overall recommendation	Strength of the recommendation	Quality of the evidence	Comments
rTMS is weakly recommended for the treatment of mild to moderate depressive symptoms in the postpartum period.	Weak	Low ⊕⊕◯◯	rTMS might be beneficial and risks of adverse effects for the mother or the breastfed child are unlikely. The evidence on its effectiveness is low. Our recommendation considers that in clinical settings where it might be difficult to access psychological treatments or there is resistance of women to pharmacological or psychological interventions, rTMS could be an alternative treatment, if accessible and available, for women with mild to moderate depressive symptoms in postpartum.

Transcranial electrical stimulation (tES)

tES in pregnancy

So far, four systematic reviews have been published discussing the efficacy of transcranial electric stimulation [tES] in the perinatal period (Konstantinou et al., 2020; Kurzeck et al., 2018; Laurin et al., 2022; Pacheco et al., 2021), presenting data from overlapping studies. To date, five studies were conducted including 16 pregnant women diagnosed with PPD. Of these, three studies tested the efficacy of transcranial direct current stimulation [tDCS], one the efficacy of transcranial alternating current stimulation [tACS], and one the efficacy of transcranial Vagus Nerve Stimulation [TNS]). Overall, the available data rely on one RCT, one single-arm study and three case reports in pregnancy. Although the quality of the systematic review is considered moderate to high, none presents a meta-analysis.

Currently, the available evidence suggests

the benefit of tES as a stand-alone or coadjuvant with psychotherapy in improving depressive symptoms during pregnancy, regardless of the trimester. Recommended acute treatment protocol is 4-12 weeks of daily or (by-daily) sessions of 30-min, over the F3 and F4, current intensity of 2mA. A maintenance phase of one to two sessions per week might be discussed for the following weeks, as needed. In particular, early treatment response is seen after two weeks of treatment and remission after one month, with remission rates between 33% and 75%. The tDCS protocol is quite consistent across studies (by-daily or daily sessions of 30 min duration over the F3, F4 at a current intensity of 2 mA, for 4 to 6 weeks). The single RCT available showed that tDCS treatment was beneficial with a moderate effect size (d = 0.61).

Adverse effects

tES is well tolerated with minor transient adverse effects (mild burning sensations, buzzing or tingling at the electrode site; and fleeting experience of phosphenes) being reported associated with the fade-in phases. tES seems to be not associated with fetal and maternal health complications during prenatal and neonatal periods.

Acceptability and feasibility

As for acceptability data, retention, and satisfaction rates reported are high (e.g. Vigod et al., 2019) reported 88% retention rate and 87.5% of satisfaction rates with global satisfaction and acceptance by patients who refused medication).

Regarding feasibility, the portability and low cost of tDCS devices allow the realisation of tDCS sessions at home, addressing the limitations of the daily visits to the hospital required when the treatment is home-based.

Overall, evidence of efficacy of tES in depressive symptoms during pregnancy comes from tDCS studies showing a moderate to high/critical risk of bias and the quality of the current evidence is low (due to its limitedness, and association with risk of bias). Adverse effects seem to be trivial.

Data on other secondary outcomes (e.g., anxiety, stress, foetus/newborn outcomes) are not available.

Overall recommendation	Strength of the recommendation	Quality of the evidence	Comments
Transcranial direct current stimulation (tDCS) is weakly recommended for the treatment of mild to moderate depressive symptoms in pregnant women	Weak	Low ⊕⊕◯◯	tDCS might be beneficial and risks of adverse effects for the woman or the foetus are unlikely. The evidence on its effectiveness is low. Our recommendation considers that in clinical settings where it might be difficult to access psychological treatments or there is resistance of women to pharmacological or psychological interventions, tDCS could be an alternative treatment, if accessible and available, for women with mild to moderate depressive symptoms during pregnancy

tES in the postpartum period

So far, only one case report in the postpartum period was presented in the latest systematic review (Laurin et al., 2022), describing a three months postpartum patient who received 15 daily 30-minute tDCS sessions followed by four weekly 30-minute sessions (F3-F4, at 2 mA intensity, 15s fade-in/fade-out) and presented a partial response to treatment, according to MADRS scores from baseline (36/60) to after treatment (25/60) for a 6.6% reduction. While in treatment, the woman was breastfeeding and reported improved mood and attention. One month after treatment, the woman presented symptom relapse. Minor transient effects were reported and included mild fatigue, paresthesia of the scalp, and a transient low-intensity headache. Although we only have one case report published on the effect of tES in the postpartum, its safety profile and beneficial effects in pregnant women and on the general population, suggests that tDCS might be a promising alternative for treating depressive symptoms in

postpartum women as well.

Data on other secondary outcomes (e.g., anxiety, stress, foetus/newborn outcomes) are not available.

Overall recommendation	Strength of the recommendation	Quality of the evidence	Comments
There is not enough evidence to make a recommendation regarding the use of tDCS in the treatment of depression for women in the postpartum.	No recommendation		There is one single case study reported in a systematic review showing the efficacy of tDCS in reducing depressive symptoms in a postpartum woman. For this reason, although no harmful effects are expected to occur in the postpartum, the RU--GDG considered that there is not enough evidence on the efficacy of tDCS in women in the postpartum. Therefore, we cannot yet make a recommendation.

Electroconvulsive therapy (ECT)

Pregnancy

Currently, three systematic reviews have been published discussing the efficacy of electroconvulsive therapy (ECT) in women diagnosed with PPD; three during pregnancy (Calaway et al., 2016; Leiknes et al., 2015; Pompili et al., 2014) and one focusing on the whole peripartum period (Pacheco et al., 2021). The systematic reviews report only case series and case studies (no RCTs were included). All articles report patients with severe PPD, from both inpatient and outpatient units. None conducted a meta-analysis. Therefore, the overall quality of the evidence is low.

Depending on the systematic review, we may find studies describing from three to up to 192 cases suggesting the antidepressant effect of ECT treatments during pregnancy, when the treatment is started from the first trimester to the third (eg. Calaway et al., 2016; Leiknes et al., 2015; Pacheco et al., 2021; Pompili et al., 2014)

According to Pacheco et al. (2021), ECT parameters used in the first and second trimesters placed the electrodes bilaterally, used seizure durations between 17-186s, across 9–10 sessions. Alternatively, a few studies reported unilateral right and bifrontal montages, with seizure durations between 20-201s, for 7–15 sessions. For ECT treatments delivered in the third trimester the bilateral montages over the temporal., frontal, or frontotemporal regions, or unilaterally at the right hemisphere were adopted, with seizure durations between 37s-90s for 5-9 sessions.

Pacheco et al. (2021) showed that remission and response rates during pregnancy are largely unknown with only 6/24 cases reporting symptoms' remission and 11/24 not reporting this information.

Obstetrical complications are referred across the systematic reviews. For example, Leiknes et al. (2015) case series reports rates of obstetrical complications of up to 27%, including vaginal bleeding (12%), uterine contractions (24%), abdominal pain (9%), miscarriage (7%), preeclampsia (3%) and premature birth (28%). However, this article mixed MDD diagnosis with other diagnoses. Pompili et al. (2014), report 27.7% of obstetrical complications among MDD pregnant patients and these included spontaneous abortion and pelvic pain when the treatment was delivered during the 1st trimester. These data were further supported by Calaway et al. (2016) reporting the adverse effects after ECT treatments delivered in the first trimester which included vaginal bleeding and miscarriage at an unknown

rate. For ECT treatments delivered in later semesters, caesarean, premature labour, and uterine contractions associated with the treatment are the most common obstetric complications, occurring in three out of five cases. Likewise, Pacheco et al. (2021) report a rate of 52.4% of obstetric complications associated with ECT treatments. Moreover, neurocognitive assessment after ECT extracted from one single study (Salzbrenner et al., 2011) suggests that the maximum number of ECT sessions before achieving cognitive decline should be nine.

As for adverse outcomes to the foetus and the child, Leiknes et al. (2015) study observing a mixed population of pregnant patients, report 43% of foetal cardiac arrhythmia and bradycardia, 3% of neonatal respiratory distress, 5% of general mental impairment, 20% of malformations, 8.9% of foetal death and 6.0% of child death (miscarriages/abortion and foetal death not included). Likewise, Pompili et al. (2014) report 27.7% of complications for the foetus in a sample of MDD patients, namely heart rate decelerations associated with the mother's contractions, transient arrhythmia, and spontaneous abortion. Pacheco et al. (2021), confirm these data presenting a ratio of 57.1% of adverse events to the foetus and the child after ECT treatments. The most used anaesthetic agents were thiopental, methohexital or, propofol. Of note, reduced foetal heart rate was reported after propofol, and severe foetal bradycardia was reported by methohexital. To avoid pulmonary aspiration, several authors suggest tracheal intubation of pregnant women beyond the 1st trimester.

Data on the foetus/baby/child status associated with anaesthetics were also inconsistent, both in earlier reports and the later ones. When reported, information was limited to the APGAR score, weight, and classifications such as "healthy baby" or "normal/abnormal". Information about the monitorisation of the foetus during the ECT treatment varies, from none to obstetric consultations and ultrasounds between ECT sessions and before and after foetal heart rate and doppler monitoring. Follow-ups on the child development were diverse, from no follow-up to follow-ups up to six years.

These figures warrant strict supervision of the pregnancy, preferably in the hospital setting.

Pacheco et al. (2021) report treatment stoppage or discontinuation by pregnant women due to obstetric complications, observation of cognitive decline, issues related to transportation to access to treatment and other unknown reasons with na overall acceptability of 83.2% (acceptability according to dropout rates in case series

and case reports is naturally biased).

When looking over case reports and case series, acceptability according to dropout rates is naturally biased to 100%. As for retrospective studies, no data are available.

Overall recommendation	Strength of the recommendation	Quality of the evidence	Comments
ECT is strongly recommended for the treatment of therapy resistant or life-threatening severe depression in pregnant women. The treatment should take place under strict obstetrical monitoring	Strong	Very Low ⊕◯◯◯	ECT is a relatively fast-acting option in severe cases of depression during pregnancy and, despite the moderate risks of adverse effects (for the mother and the foetus) and pregnancy/ delivery complications, the benefits seem to outweigh the adverse effects if women did not respond to previous regular treatment or in need of urgent treatment due to life-threatening situations. Therefore, ECT is strongly recommended and should be offered within specialised hospitals to women presenting severe depression (with or without psychotic features) which did not respond to previous regular treatment or in need of urgent treatment due to life-threatening situations.

Recommended treatment protocol for the first and second trimesters consists of bilateral montage, seizure durations between 17-186 s, for 9–10 sessions, or unilateral right and bifrontal montages, with seizure duration between 20-201 s, for 7–15 sessions.

Recommended treatment protocol for the third trimester consists of bilateral montages over the temporal., frontal or frontotemporal regions, or unilateral at the right hemisphere, with seizure durations between 37-90 s for five to nine sessions.

Postpartum period

One systematic review was published discussing the efficacy of electroconvulsive therapy (ECT) in women diagnosed with postpartum depression (Gressier et al., 2015) and one focusing on the whole peripartum period (Pacheco et al., 2021). The SRs report case series/case studies and retrospective and observational studies (no RCTs were included).

All studies report patients with severe PPD, from both inpatient and outpatient units. Gressiers et al. (Gressier et al., 2015) included 14 studies ranging from 1-192 women. The Pacheco et al. (2021) study data do not completely overlap Gressiers', but they further extend the search to 2020 and included seven case reports/case series for a total of 21 women. Both studies observed women from the first days and up to 11 months postpartum and the majority was in the context of severe psychiatric disorder not responding to previous pharmacotherapy, or pharmacotherapy combined with rTMS.

None of the indicated systematic reviews conducted a meta-analysis. Therefore, despite the satisfactory results, the overall quality of the evidence regarding the efficacy of ECT in pregnancy and the postpartum is low.

Regarding stimulation protocols, Pacheco et al. (2021) mostly describes ECT treatment with bilateral, bifrontal with suprathreshold intensities between 17.5-32.1 J, from five to nine sessions and the seizure duration established between 37s and 90s. Reports are unclear regarding concomitant pharmacologic treatment but those that report, refer to stoppage of lorazepam, fluvoxamine and alprazolam before ECT.

Overall, the authors report a ratio of 28.6% adverse events including prolonged seizures due to co-administered medication and transient memory loss particularly after the first ECT sessions.

When looking over case reports and case series, acceptability according to dropout rates is naturally biased to 100%. As for retrospective studies, no data are available.

Remission rates in the postpartum were between 76.9% and 92% with faster and improved efficacy compared with other treatments in resistant depression.

Data on anaesthetic agents combined with muscle relaxants were referred to inconsistently. The most used anaesthetic agents were thiopental, methohexitalal, and propofol.

Overall recommendation	Strength of the recommendation	Quality of the evidence	Comments
ECT is strongly recommended for the treatment of therapy resistant or life-threatening severe depression in pregnant women. The treatment should take place under strict obstetrical monitoring	Strong	Very Low ⊕◯◯◯	ECT is a relatively ast-acting option in severe cases of depression during pregnancy and, despite the moderate risks of adverse effects (for the mother and the foetus) and pregnancy/delivery complications, the benefits seem to outweigh the adverse effects if women did not respond to previous regular treatment or in need of urgent reatment due to life-threatening situations. Therefore, ECT is strongly recommended and should be offered within specialised hospitals to women presenting severe depression (with or without psychotic features) which did not respond to previous regular treatment or in need of urgent treatment due to life-threatening situations.

Bright light therapy

BLT in pregnancy

To date, one systematic review (Nillni et al., 2018) and four meta-analyses have been published (Al-Karawi & Jubair, 2016; Dennis & Dowswell, 2013a; Ravesteyn et al., 2017; Smith et al., 2019) discussing the efficacy of bright light therapy (BLT) during pregnancy period. These studies were performed between 2002-2011 and included in total two RCTs in which 38 pregnant women received either the intervention (7,000 or 20,000 lux) or placebo (70 or 500 lux) for 5 weeks. One single-arm trial was discussed with 16 women being exposed to 10,000 lux for 3-5 weeks. In all these studies women were diagnosed with a depressive disorder and the Structured Interview Guide for the Hamilton Depression Rating Scale-Seasonal Affective Disorders (SIGH-SAD) was used as a validated measure for depressive symptoms as an outcome.

Overall, in all three studies (active BLT and sham) a reduction of depressive symptoms occurred. In the meta-analysis of Ravesteyn et al., (2017), the two RCTs were meta-analysed. This meta-analysis revealed no significant difference in depressive symptoms (SMD= -0.59, 95% CI -1.25 to 0.06, I2= 0, p= 0.362).

Concerning adverse effects, one study (Wirz-Justice et al., 2011) performed during pregnancy reported no clinically meaningful side effects, and all women gave birth with no complications. As for acceptability, no data were available. Regarding feasibility no data were reported.

Currently, no data were reported on the acceptability, feasibility, patient preferences and values, and costs of BLT as a treatment for PPD in pregnancy.

Data on secondary outcomes (e.g., anxiety, stress, foetus/newborn outcomes) are not available.

Overall, the quality of the current evidence of efficacy of BLT compared to control in depressive symptoms during pregnancy is very low, given that only two RCTs with a low number of women are published and different intensity of BLT in the intervention and control were applied. The risk of bias was considered moderate.

BLT in the postpartum period

Overall recommendation	Strength of the recommendation	Quality of the evidence	Comments
There is no evidence on the efficacy of BLT in pregnancy, therefore we cannot make a recommendation	No recommendation		There are no systematic reviews and meta-analyses available supporting the efficacy of BLT in reducing depressive symptoms in pregnant women.

To date, only one meta-analysis was published discussing the efficacy of bright light therapy (BLT) in non-seasonal depression, including the postpartum period (Al-Karawi & Jubair, 2016). This meta-analysis included one study performed in 2007 in which 10 women exposed to 10,000 lux for 6 weeks were compared to 5 women who were exposed to 600 lux. Both groups significantly improved with no significant difference between groups (MD= 0.37, 95% CI: -0.72 to 1.45). In this same meta-analysis, a significant moderate effect was found in decreasing depressive symptoms in MDD including postpartum period (SMD=-0.62, P<0.001, I2=37%).

Currently, there are no studies available about the acceptability, feasibility, patient preferences and values, and costs of BLT as a treatment for PPD in pregnancy.

Data on secondary outcomes (e.g., anxiety, stress, foetus/newborn outcomes) are not available.

Overall, the quality of the current evidence of efficacy of BLT compared to control in depressive symptoms during pregnancy is very low, given that there is only evidence from one RCT with a low number of women.

Complementary and alternative treatments

Are complementary and alternative treatment interventions effective in treating PPD?

Physical exercise

Physical exercise in pregnancy

A few reviews focusing on physical activity in pregnant women have been published. However, most of these include mixed interventions combining exercise with yoga, massage and tai-chi (e.g. He et al., 2023; Jarbou & Newell, 2022; Nillni et al., 2018) which we aim to discuss in a distinctive section. Only Zhu et al. (2021) present data on the effect of exercise alone (10-60 minutes exercise, three sessions a week, 4-31 weeks) for women with established or suspected PPD diagnosis. The studies pooled by the authors included moderate to vigorous intensity dancing, walking, aerobic exercise, stretching, and relaxation. The results of this meta-analysis show a significant large effect of exercise on antenatal depression [SMD = -0.66, 95%CI -1.00 to -0.31, p = 0.0002, I2 = 69%, Chi2 = 9.79, p = 0.02]. Adverse effects for the foetus and other secondary outcomes (e.g., anxiety) regarding exercise during pregnancy were not reported. Despite the promising results of Zhou et al. (2021) and the high quality of their review, the authors warrant attention to the unclear risk of bias in the included original studies.

An older study by Shivakumar et al. (2011) systematically reviewed randomised controlled studies, case–control studies, case series, and expert opinions or commentaries. According to this review, exercise is highly encouraged in all pregnant women (regardless of existing MDD diagnosis or depressive symptoms), both by the American College of Obstetricians and Gynaecologists (ACOG) and Society of Obstetricians and Gynaecologists of Canada (SOGC). The recommendation foresees 20–30 minutes of moderate-intensity exercise per day or exercise intensity defined according to the maximal heart rate target zones determined by age (< 20 years: 140-155 beats/min; 20-29 years:135-150 beats/min; 30-39 years: 130-145 beats/min; ≥40 years: 125-140 beats/min).

The review by Shivakumar et al. (2011) reports the clinical consensus for sub-populations of pregnant women who are willing to initiate exercise to treat depressive symptoms. According to the authors, the beneficial effect of exercise on gestational diabetes and the high correlation between gestational diabetes and the risk of PPD could justify the up taking of exercise to address both illnesses simultaneously. Additionally, the American College of Obstetricians and Gynaecologists (ACOG) considered that aerobic

exercise should be contraindicated in pregnant women with the following conditions: hemodynamically significant heart disease, restrictive lung disease, incompetent cervix/cerclage, multiple gestations at risk for premature labour, persistent second or third trimester bleeding, placenta praevia, premature labour, ruptured membranes, and pregnancy-induced hypertension. Hence, aerobic exercise is relatively contraindicated in pregnant women with severe anaemia, unevaluated maternal cardiac arrhythmia, chronic bronchitis, extreme morbid obesity, extreme underweight (body mass index <12), a historically sedentary lifestyle, intrauterine growth restriction, poorly controlled hypertension/preeclampsia, orthopaedic limitation, poorly controlled type II diabetes, seizure disorder, thyroid disease, and history of heavy cigarette smoking. Warning signs and symptoms that prompt immediate termination of exercise are vaginal bleeding, dyspnoea before exertion, dizziness, headache, chest pain, muscle weakness, calf pain or swelling that raises suspicion of thrombophlebitis, preterm labour, decreased foetal movement, and amniotic fluid leakage. (Ongoing monitoring is highly recommended (Shivakumar et al., 2011 p. 238)

To date, after the review by Shivakumar (2011), no other study offered detailed data on the optimal parameters for exercise interventions in pregnancy.

In sum, adverse effects of exercise interventions in pregnancy are absent for healthy perinatal women, showing the safety profile during this period. However, a thorough assessment of previous training and close monitoring during pregnancy should be secured according to women's health conditions and previous exercise history.

The quality of the evidence is very low, given the reduced number of trials conducted with pregnant women examining the effects of exercise interventions (that do not include yoga, massage, and tai-chi), and the high risk of bias presented by the trials conducted so far. Thus, evidence about the efficacy of exercise for treating PPD during pregnancy is limited.

Data on other secondary outcomes (e.g., anxiety, stress, foetus/newborn outcomes) are not available.

Overall recommendation	Strength of the recommendation	Quality of the evidence	Comments
Physical activity is weakly recommended for the treatment of mild to moderate depressive symptoms in otherwise healthy pregnant women.	Weak	Very Low ⊕◯◯◯	Physical activity might be beneficial for otherwise healthy women and risk for the foetus is unlikely. Our recommendations are based on very low quality of evidence available for women with uncertain severity of depressive symptoms and assuming good physical health.

Recommended treatment protocols: low-to-moderate or moderate to vigorous dancing, walking, aerobic exercise, stretching, and relaxation intensity, for 10-60 minutes sessions, three sessions a week, for 4-31 .

Physical exercise in the postpartum period

The most recent meta-analysis estimating the effect of exercise in postpartum women, included 196 women from birth to 12 months postpartum diagnosed with PPD (He et al., 2023). Exercise embraced diverse types, from fitness combined with web/app-guided and online forms; mild to medium levels of exercise complemented with intense exercise; group or individual interventions; at the hospital setting combined with exercise at the homebound; pram walking alone, and pram walking combined with social support. The included eight studies were conducted between 2003-2021. The meta-analysis showed a statistically significant moderate effect of low to moderate intensity exercise in postpartum depression severity when compared with placebo (WMD = -3.38, 95%CI [-5.15 to -1.61], P = 0.001), measured using the EPDS. Moreover, either moderate (WMD: -4.57, 95%CI: 8.25 to 0.90, P = 0.015) or low (WMD: -2.50, 95%CI: 4.36 to 0.64, P = 0.008) physical activity intensity were effective, regardless the duration of the intervention (<12 weeks; WMD: -5.25, 95%CI: 6.34 to 4.16, P < 0.001; ≥ 12 weeks; WMD: -2.82, 95%CI: 4.52 to 1.12).

In 2018, Lin and colleagues systematic review and meta-analysis (2018) focused only on the effectiveness of self-help tools based on physical activity to treat postpartum depression and found that self-guided exercise based on e-health tools effectively reduced levels of depressive symptoms (ES = -1.08, 95%CI [-1.61, -0.55) with a moderate effect].

Likewise, one year before, an extensive meta-analysis conducted by McCurdy et al. (2017) included 10 trials for a total of 258 postpartum women observing the efficacy of exercise in perinatal depressive symptoms. The authors considered trials that were excluded in later reviews because these enrolled a mixed population, including women without clinically meaningful depressive symptoms (e.g. Robichaud, 2008), studies in Farsi (Saeedi, 2013) and studies not included in the reviews published afterwards due to the type of intervention or unclear reasons (e.g. Boath, E., 2015; Buttner et al., 2015; Da Costa et al., 2009) Nine of these trials assessed depressive symptoms using the EPDS, and showed that at postintervention, exercise was superior to the control groups (WMD = -2.57, 95% CI [-4.15, -1.00]) with a moderate effect. The authors further note that all studies that included women presenting depressive symptoms at baseline (with or without formal diagnosis) described only supervised exercise (in group or individually, e.g., aerobic, walking and pram walking, whole-body gentle stretching, resistance training, 30-90 minutes duration, one to five times a week, for 4-48 weeks).

Other systematic reviews available in the literature present results of exercise-based interventions without meta-analysis (A.-M. Brown et al., 2017; Saligheh et al., 2016, 2017), that in general included the same studies comprised in the above-mentioned reviews.

In what concerns adverse effects in the postpartum, Liu et al. (2022) stated that no adverse effects induced by exercise interventions were reported by the included studies, whereas Poyatos-Léon and García-Hermoso (2017) and Saligheh et al. (2017) stated that the included studies did not examine for side effects. Otherwise, available systematic reviews and meta-analyses did not report adverse effects associated with the interventions.

As for acceptability data, a few studies offer data on adherence, attrition and/or dropout rates (A.-M. Brown et al., 2017; P. Z. Lin et al., 2018; McCurdy et al., 2017; Poyatos/León & García/Hermoso, 2017). Overall, adherence to exercise interventions was high, from 100% for 12-week walking intervention with various support

strategies; 99% for aerobic exercise complemented with physical activity coaching, 98.6% for self-chosen physical activity and 91% for group-based, supervised aerobic strengthening (A.-M. Brown et al., 2017). The lower adherence rates were reported by studies observing the effect of self-help exercise-based interventions (P. Z. Lin et al., 2018), walking and group walking in sedentary and overweight/obese postpartum women (54,9%; A.-M. Brown et al., 2017).

Most studies do not report women's preferences. Exception goes to Saligheh et al. (2017), that reports that participants' choice of exercise is often solitary exercise (in the postpartum), which might be the most feasible option due to the logistics associated with caregiving in the first months. This is well aligned with the examples of reasons for dropout presented in previous studies (Saligheh et al., 2016), such as not having enough time, a new pregnancy, changes in residency and mother or newborn health problems.

Overall, the quality of the current evidence about the effectiveness of exercise in the postpartum is low to moderate given that several systematic reviews and meta-analyses published in the last 10 years confirm its benefits when compared with placebo or treatment as usual. However, exercise interventions included are heterogeneous in what concerns the setting, modality (group vs individual; supervised vs unsupervised/self-help/self-guided), intensiveness, duration, and type of exercise, leading to uncertainty about the parameters for optimal results. Also of note, the latest and more robust review (He et al., 2023) presents a high risk of bias, given that the tool used to assess the risk of bias in individual studies (the Quality Assessment Tool for Quantitative Studies, EPHPP, 1988) does not include allocation concealment. Hence, the original studies across reviews are generally of low to medium quality, further increasing the risk of bias.

Data on other secondary outcomes (e.g., anxiety, stress, foetus/newborn outcomes) are not available.

Overall recommendation	Strength of the recommendation	Quality of the evidence	Comments
Low-to-moderate intensity physical activity is weakly recommended for the treatment of mild to moderate depressive symptoms in postpartum as it might be beneficial, and no risks of adverse effects are reported.	Weak	Low ⊕⊕◯◯	Physical activity might be beneficial for otherwise healthy women and risks for newborn is unlikely. Our recommendations are based on low to moderate quality of the evidence available for women with uncertain severity of depressive symptoms. In these conditions, supervised and specialised physical activity could be an accessible alternative treatment for women with mild to moderate depressive symptoms during the postpartum.

Recommended treatment protocols are group or individual aerobic, walking and pram walking, whole-body stretching sessions with 30-90 minutes duration, one to five times a week, for 4-48 weeks, either in group or individual; in-person or through e-health systems; supervised programmes might increase efficacy and adherence.

Yoga

Yoga in pregnancy

In total, ten individual studies on the effectiveness of yoga in women with depression during pregnancy compared to treatment as usual or other were analysed in seven different meta-analyses (Gong et al., 2015; X. Jiang et al., 2022; I. H. Lin et al., 2022; Liu, Wang, et al., 2022; Vollbehr et al., 2018; G. Wang et al., 2022; Zhu et al., 2021).

Considering tai-chi, no meta-analyses or systematic reviews are available on its effect during pregnancy.

The meta-analysis of Zhu et al. (2021) included seven studies focusing on women with depression during pregnancy performed between 2012-2019 for a total of 189 women from China and USA with unknown age, diagnosed with either validat-

ed self-rating scales or diagnosis. Yoga varied from 20-75 minutes, weekly or twice a week for 6 to 12 weeks. Control groups were treatment as usual, perinatal health education, standard antenatal exercises and social support. The primary outcome was the change in depressive symptoms according to evidence-based instruments (CES-D or EPDS). In the meta-analysis of these studies also healthy women were included, so we performed separate meta-analysis including only women with depression. The results showed a significant and moderate effect in favour of yoga (SMD= -0.46, 95% CI: -0.77 to -0.15, I2= 49%, p = 0.0036).

The meta-analysis of Lin et al. (2022), including five studies of which four overlapped with Zhu et al. (2021) and one unique, showed a large and significant effect in favour of yoga (SMD = -1.93, 95% CI -3.08 to -0.77, I2= 91%). This meta-analysis included studies conducted between 2012-2016, and a total of 103 pregnant women from USA and Iran, with partly unknown age, diagnosed with depression although without mentioning the assessment criteria. The primary outcome was the change in depressive symptoms according to evidence-based instruments (CES-D, HADs and HDRS). The meta-analysis included only RCTs and did not report on risk of bias.

The meta-analysis of Jiang et al. (2022) included five studies performed in peripartum period of which three during pregnancy. Of these three studies one overlapped with both Zhu et al. (2021) and Lin et al. (2022) and one with Zhu et al. (2021) and another one with Lin et al. (2022) studies. These studies were performed between 2013 and 2015, including in total 81 women from the USA, with a mean age of 24.4-29.74 years, having yoga with varying protocols for up to 16 weeks. The primary outcome was EPDS. We meta-analysed these three studies in pregnancy and found no significant effect (SMD= -0.10, 95% CI -1.41 to 0.21, I2= 0%, p= 0.71).

The meta-analysis of Wang et al. (2022) included five studies performed during pregnancy which totally overlapped with Zhu et al. (2021), Lin et al. (2022), Jiang et al. (2022). The meta-analysis of Liu, Wang et al. (2022) included one study performed which overlapped with Jiang et al., (2022). The meta-analysis of Gong et al. (2015) included four studies of which three overlapped with the meta-analysis of I. H. Lin et al. (2022) and one with Zhu et al. (2021). A meta-analysis of Vollbehr et al (2018) focusing on hatha yoga included four studies which were also included in previous studies(I. H. Lin et al., 2022; Zhu et al., 2021).

Considering adverse effects and dropout rates, none of the studies reported adverse

effects associated with yoga in the postpartum period. Exception goes to a systematic review on exercise that also included yoga during pregnancy, which reported no side effects in three studies all of which were also included in Jarbou and Newell (2022) study previously discussed. Otherwise, no information about adverse effects and dropout rates, patient preferences and values, and cost-effectiveness of yoga in peripartum period is available.

Considering anxiety as a secondary outcome, the meta-analysis of Wang et al. (2022), included four studies with depressed women in which there was no significant reduction of anxiety symptoms measured with the State-Trait Anxiety Inventory (STAI) compared to controls (SMD= -2.3, 95% CI: -4.83 to 0.23, I2= 12,2%). The meta-analysis of I. H. Lin et al. (2022) included two studies in which anxiety as measured with the STAI, was used as a secondary outcome measure. These studies were included in the meta-analysis of Wang et al. (2022). The meta-analysis of Zhu et al. (2021) included six studies, restricted to pregnant women, in which anxiety as measured by the STAI or Self-rating Anxiety Scale (SAS), were used as a secondary outcome measure, next to depressive symptoms. In the meta-analysis, also healthy women were included, so we separately meta-analysed the reports performed in depressed women. The results did not show a significant difference (SMD= -.076, 95% CI: -1.72 to 0.19, I2= 92,1%, p= 0,01).

Data on other secondary outcomes (e.g., stress, foetus/newborn outcomes) are not available.

Overall recommendation	Strength of the recommendation	Quality of the evidence	Comments
Yoga is weakly recommended for the treatment of mild to moderate depressive symptoms as it might be beneficial, and no risks of adverse effects are reported.	No recommendation		Yoga might be beneficial for otherwise healthy women and risk for the foetus is unlikely. Our recommendations are based on low quality of the evidence available for women with uncertain severity of depressive symptoms.

Recommended treatment protocols vary from 20-75 minutes once or twice a week for 6-12 weeks.

Yoga in the postpartum period

In total three meta-analyses focussed on the effectiveness of yoga in patients with postpartum depression compared to treatment as usual (X. Jiang et al., 2022; Liu, Wang, et al., 2022; G. Wang et al., 2022).

Considering tai chi, no meta-analyses or systematic reviews are available on its effect in the postpartum period.

The meta-analysis of X. Jiang et al. (2022) included five studies of which two studies performed in postpartum period (2013 and 2015), including in total 79 women from the USA and India, with a mean age of 26.4-29.8 years, having 1-2 hours, 2 to 3 times a week for between 8 and 36 weeks. The primary outcome was HADS. We meta-analysed these two studies because in this meta-analysis they were mixed with the studies performed during pregnancy. Our results showed no significant effect (SMD= 0.09, 95% CI -1.43 to 1.62, I2= 95%, p= 0.90). The meta-analysis of Wang et al (2022), included six studies of which one study was performed in postpartum period, which overlapped with Jiang et al., 2022. The meta-analysis of Liu, Wang et al. (2022) included three studies of which one performed in postpartum depressed women, which overlapped with Jiang et al. (2022).

Considering adverse effects and dropout rates, no studies reported about adverse ef-

fects associated with yoga in the postpartum period. A systematic review on exercise that also included yoga during pregnancy, reported no side effects in three studies which were also included in the before discussed meta-analyses (Jarbou & Newell, 2022). No information about adverse effects and dropout rates in postpartum yoga is available. No information about patient preferences and value is available and no information about cost-effectiveness of yoga in postpartum period is available.

Overall, the quality of the current evidence about the effectiveness of yoga on depression compared to treatment as usual in the postpartum period is very low because only two RCTs were performed which did not show a significant effect.

Data on other secondary outcomes (e.g., anxiety, stress, foetus/newborn outcomes) are not available.

Overall recommendation	Strength of the recommendation	Quality of the evidence	Comments
There is no evidence on the efficacy of the use of Chinese herbs in pregnancy, therefore we cannot make a recommendation	No Recommendation		There are no studies available reporting the efficacy and reproductive risks of Chinese herbs in reducing depressive symptoms in pregnant women.

Massage

Massage in pregnancy

One meta-analysis (Zhu et al., 2021) reported on the effect of massage in patients with depression during pregnancy compared to treatment as usual or other, which showed a moderate significant effect (SMD= -0.26, 95% CI -0.49 to -0.02, I2= 55%). In this meta-analysis five RCTs (2008-2012) were included, consisting of in total 208 women from Australia and the US with unknown age and self-reported or diagnosed depression. The intervention consisted of 5-12 weeks, weekly (n=3) or twice/week (n=2) and 20 minutes for each intervention. The massage was either applied by partners (n=3) or therapists (n=2). The control groups consisted of treatment as usual, self-directed stress management training programme or an interpersonal psychotherapy group. The primary outcome was the change in depressive symptoms according to self-report instruments. The meta-analysis included only RCTs. The quality of evidence was rated very low with a high risk of bias.

In addition, two reviews were published (Jarbou & Newell, 2022; Nillni et al., 2018), which among other interventions reported about the effect of massage in the perinatal period. The studies included in this review were also included in the meta-analysis, so they will not be separately discussed.

A systematic review on exercise that also included massage during pregnancy, reported no adverse effects (Jarbou & Newell, 2022). No information about dropout rates, patient preferences and values, and no information about cost-effectiveness of massage in perinatal period is available.

Considering secondary outcomes, the study of Zhu et al. (2021) included four studies, restricted to pregnant women, in which anxiety as measured by the STAI, was used as a secondary outcome measure, next to depressive symptoms. This meta-analysis showed a small significant reduction of anxiety compared to controls (SMD= -0.26, 95% CI: -0.49 to -0.02, I2= 0%)

Overall recommendation	Strength of the recommendation	Quality of the evidence	Comments
Massage is weakly recommended for the treatment of mild to moderate depressive symptoms during pregnancy.	Weak	Low ⊕⊕◯◯	This recommendation is based on low quality evidence that showed positive effects in the reduction of depressive symptoms in pregnant women. Effects found were of moderate size and risk for the foetus is unlikely.

Massage in the postpartum period

To our knowledge no systematic reviews or meta-analyses were published on the effect of massage in reducing depressive symptoms in the postpartum period. Therefore, we consider having not enough information available concerning the efficacy of massage for postpartum women presenting depressive symptoms.

Overall recommendation	Strength of the recommendation	Quality of the evidence	Comments
There is no evidence on the efficacy of massage in postpartum, therefore we cannot make a recommendation.	No recommendation		There are no systematic reviews and meta-analysis reporting the efficacy of massage in reducing depressive symptoms in postpartum women.

Music therapy

Music therapy in pregnancy

One meta-analysis reported on the effect of music therapy in women with depressive symptoms during pregnancy (Zhu et al., 2021). This meta-analysis included six studies which all included women from the general population. Therefore, we do not have enough information available concerning the efficacy of music therapy for pregnant women presenting depressive symptoms to make a recommendation.

Overall recommendation	Strength of the recommendation	Quality of the evidence	Comments
There is no evidence on the efficacy of music therapy during pregnancy, therefore we cannot make a recommendation.	No Recommendation		There are no studies supporting on the efficacy of music therapy in reducing depressive symptoms in pregnant women.

Music therapy in the postpartum

One meta-analysis reported on the effect of music therapy in women with postpartum depression (W. J. Yang et al., 2019).

This meta-analysis included five studies, consisting of in total 461 women from China, Korea, Iran and the US with unknown age and unclear clinical assessment procedures/instruments at baseline. In addition to receiving traditional treatment, the women in the experimental group listened to different types of music: light music, pure music, lullaby or according to their own preference. The frequency and duration of listening ranged from: 30-120 minutes, one or two times a day for two days to six weeks.

In four studies the outcomes were measured continuously by self-report scales and showed that music therapy had a significant and large effect on depression compared to the control group consisting of psychological treatment, drug treatment, traditional treatment, health education or kangaroo care (SMD= −0.87, 95% CI: −1.23 to -0.51, I2= 79%, p= 0.003). In one study the outcome was measured on a binary level and showed that music therapy had a significant moderate to large effect compared to the control

group consisting of psychological treatment and traditional Chinese medicine (RR: 0.73, 95% CI: 0.63 to 0.86, p= 0.0001).

The meta-analysis included only RCTs. The risk of bias was largely unknown. No significant impact on heterogeneity was found. Due to the small number of studies included in this meta-analysis, it was not possible to assess publication bias.

Considering secondary outcomes, the meta-analysis of W. J. Yang et al. (2019) additionally investigated the effect of music on anxiety, insight, pain, sleep, satisfaction and maternal attachment. Regarding anxiety, a meta-analysis of three studies with in total 301 women receiving music therapy and focusing on anxiety as a continuous outcome measured with the STAI and the SAS, showed a non-significant effect (SMD= -1.26, 95% CI: -2.81 to 0.29, I2= 98%). A meta-analysis of two studies with 230 women receiving music therapy and focusing on anxiety as a binary outcome measured with the STAI and the SAS, did also show a non-significant effect (RR= 0.38, 95% CI: 0.09 to 1.63, I2= 0%). Regarding self-knowledge measured with the Insight and Treatment Attitude Questionnaire, one study in which 80 women received music therapy showed a large and significant effect (MD= 5.18, 95% CI: 4.49 to.5.87). Regarding pain as measured with a visual analogue scale, one study in which 71 women received music therapy showed a large significant effect (MD= -1.13, 95%: -1.25 to -1.01). Regarding sleep as measured with the Pittsburgh Sleep Quality Index, one study in which 41 women received music therapy showed a large and significant effect (MD= -2.30, 95%: -2.75 to -1.85). Regarding satisfaction as an outcome of music therapy and as measured with a visual analogue scale, one study in which 71 women received music therapy showed a large and significant effect (MD= 2.92, 95%: 2.67 to 3.17). Regarding maternal attachment as measured with the maternal attachment tool, one study in which 30 women received music therapy showed a large and significant effect (MD= 3.30, 95%: 1.72 to 4.88).

The authors stated that the studies did not mention side effects or adverse reactions to music therapy. No information about dropout rates, patient preferences and values, and no information about cost-effectiveness of music in postpartum period is available.

Overall recommendation	Strength of the recommendation	Quality of the evidence	Comments
There is no information on the effectiveness of music therapy as a stand-alone treatment. Music therapy is weakly recommended as an additive intervention when combined with other interventions (such as psychological treatment, Chinese medicine, or pharmacotherapy) for the treatment of mild to moderate depressive symptoms as it might be beneficial, and no risks of adverse effects are reported.	Weak	Low ⊕⊕◯◯	Music therapy might be beneficial in addition to other treatments. Our recommendations are based on low quality of the evidence available for women with uncertain severity of depressive symptoms.

Recommended treatment protocols: different or preferred types of music with a duration 30-120 minutes, one or two times a day for two days to six weeks.

Peer support

Peer support in pregnancy

To our knowledge only one systematic review reported so far one single study observing the effect of peer support in reducing depressive symptoms in pregnancy (Fang et al., 2022).

Therefore, we do not have enough information available concerning the efficacy of peer support for pregnant women presenting depressive symptoms to make a recommendation.

Overall recommendation	Strength of the recommendation	Quality of the evidence	Comments
There is only one single study reporting the efficacy of peer support in reducing depressive symptoms in pregnant women.	No recommendation		There is only one single study reporting the efficacy of peer support in reducing depressive symptoms in pregnant women.

Peer support in the postpartum period

The latest systematic review with meta-analysis (Fang et al., 2022) looking at the effect of peer support in reducing depressive symptoms in the peripartum period defined peer support as a type of intervention where providers were peers who had similarities with pregnant women (e.g., health concern, stressor, other similar characteristics) and had specific knowledge resulting from personal experience. Fang et al. (2022) combined studies that included both pregnant and postpartum women with a diagnosis of PPD or presenting depressive symptoms above the clinical cut-off score (e.g., according to EPDS) and women at risk to develop PPD (this systematic review included all studies previously reported by R. Huang et al. (2020)). Although the authors conducted several sensitivity analyses they did not conduct subgroup analysis separately for depressed vs at-risk women. Therefore, we reanalysed the data to include only those studies focusing on postpartum women over 18 years old (mean age across studies is unclear) presenting depressive symptoms and excluding women at-risk during the peripartum period. We have pooled three original studies with postpartum women and one with pregnant women for a total of 62 participants. The studies included diverse types of interventions (weekly group face-to-face sessions with 20-120 minutes duration for four to 12 weeks; individual telephone-based peer support according to women's needs and preferences across three months; individual home-based face-to-face peer support complemented by telephone contacts across 12 weeks. The results of our sensitivity analysis using the random effects model do not favour the intervention (SDM = -0.372, 95% CI [-0.87, 0.13], p = 0.144).

A prior systematic review with meta-analysis (Zhou et al., 2020) focused on the efficacy of technology-based peer-support interventions in the postpartum and included 10 RCTs on peer-support programmes delivered through mHealth. This study pooled diverse sub-populations (e.g., women presenting PPD symptoms, and women with previous history of PPD or at risk for PPD) but did not present a subgroup analysis on peripartum women presenting depressive symptoms. Therefore, we have conducted this analysis ourselves, pooling the data from four RCTs for a total of 545 postpartum women. These studies observed the efficacy of heterogeneous interventions, from correspondence with a trained peer volunteer (e.g., phone call or mobile apps such as WhatsApp for four weeks), a nurse-led mobile app-based group; proactive individualised telephone-based peer support, provided by a trained peer with previous

lived experienced one to three times a week or whenever needed by the mother. Interventions started within the first 48 hours after birth and up to 12 weeks postpartum. The random effects model favours intervention (g = -0.325, 95% CI [-0.536, -0.114] with a small to medium effect size.

Previously, Pfeiffer et al. (2011) and Goodman and Santangelo (2011) had likewise conducted systematic reviews observing the effect of peer support on depressive symptoms in postpartum women with diagnosed PPD or presenting depressive symptoms above the clinical cut-off score. Together, these systematic reviews show overlapping original reports. In Pfeiffer's study, two original reports out of 10 are of interest of which one was reported by Goodman and Santangelo (2011). These original studies included group peer-support programmes lasting for four to five weeks (Chen et al., 2000) and telephone-based individualised peer support for 10 weeks (Dennis et al., 2009). Both studies' results were promising but data are not available for subgroup analysis.

Currently, the available evidence varies regarding the benefit of peer support for postpartum women presenting above clinical cut-off depressive symptoms/women diagnosed with PPD. Therefore, the direction of the benefit and what are the characteristics of the programmes that would most benefit women (individual vs group, telephone-based vs app-based, intensity and duration) is still unclear.

Adverse effects are not reported across studies nor other secondary outcomes concerning the mother or the newborn health.

As for acceptability data, the four SRs reported adherence rates between 59.1%-100%. Regarding women's satisfaction, Huang et al. (2020) found that between 81-87.5% of women were satisfied with the intervention. For these authors, the total number of peer-contacts, number of conversations and number of messages were weakly related with the overall satisfaction (r = .29-.35) whereas emotional support and practical assistance were the core factors associated with satisfaction. On the other hand, Huang et al. (2020) also reports that peer volunteers were available to repeat the experience and on cost-analysis. However, these data were not extracted from the interventions targeting depressed women with established diagnose of PPD. Therefore, economic studies of peer-support interventions in PPD are still lacking.

Overall, the quality of the current evidence about the efficacy of peer support in the postpartum is inconsistent, being more favourable for technology-based peer-support interventions. A note must be added to acknowledge that technology-based interventions are a

double-edged sword – they allow ease of access to those who have the resources and are willing to use technology, but the digital divide will increase inequality with those who do not have the resources or willingness to go digital for some other reason.

Overall recommendation	Strength of the recommendation	Quality of the evidence	Comments
There is no evidence to support a recommendation regarding traditional face-to-face peer support. Technology-based peer support is weakly recommended for the treatment of mild to moderate depressive symptoms in the postpartum period.	Weak	Very Low ⊕◯◯◯	Peer support that was assessed in the literature refers to peers which are women with lived e xperience of PPD. Technology-based peer support might be beneficial and risks of adverse effects are unlikely.

Chinese herbs

Chinese herbs in pregnancy

To our knowledge no systematic reviews or meta-analyses have been published on the effect of Chinese herbs in reducing depressive symptoms in pregnancy.

Therefore, we consider we do not have enough information available concerning the efficacy of Chinese herbs for pregnant women presenting depressive symptoms to make a recommendation.

Overall recommendation	Strength of the recommendation	Quality of the evidence	Comments
There is no evidence on the efficacy of the use of Chinese herbs in pregnancy, therefore we cannot make a r ecommendation	No Recommendation		There are no studies available reporting the efficacy and reproductive risks of Chinese herbs in reducing depressive symptoms in pregnant women.

Chinese herbs in the postpartum

Four meta-analyses reported on the effect of Chinese herbs in patients with postpartum depression compared to regular antidepressants (Y. Li et al., 2016; Sun et al., 2018; L. Wang et al., 2022; Zeng et al., 2022).

In the meta-analysis of L. Wang et al.c(2022), 16 RCTs were included in which Shuganjieyu capsules (3-4 capsules/day) were compared to antidepressant medication (11 citalopram 20-40mg; three paroxetine 10-50 mg; one fluoxetine 20 mg; one sertraline 50-150 mg). Shuganjieyu capsule is a Chinese Patent Medicine (CPM) prepared from Hypericum perforatum L. (St John's wort) and Radix Acanthopanacis Senticosi. In view of traditional Chinese medicine, it has the function of "soothing liver and relieving depression, clearing away heat and dampness, detumescence and soothing breast". In this meta-analysis, a total of 1,409 women of whom 707 receiving the intervention, all from China, were included with a mean age between 25.7-31.0 years and who developed depression within six weeks after delivery according to DSM-IV diagnosis. Outcome measures were reduction in depressive symptoms according to HAMD and response rate. In this meta-analysis two separate groups of studies were investigated: 1) Shuganjieyu capsules alone versus regular antidepressant medication and 2) Shuganjieyu capsules plus regular antidepressant versus regular antidepressant medication. In group 1) in six studies with a total of 245 treated women, a moderate to large significant effect was found in symptom reduction after six weeks of treatment (SMD= 0.71, 95% CI: 0.10 to 1.31, I2= 0%). In six studies with a total of 227 treated women the response rate was not significant (OR= 1.51, 95% CI: 0.87 to 2.63, I2= 0%). In 10 studies with a total of 337 treated women a small to moderate significant lower effect of adverse events in favour of Shuganjieyu was found (OR = 0.22, 95% CI: 0.15 to 0.32, I2= 0%). In group 2) in three studies with in total 118 treated women a large significant effect was found in HAMD reduction after six weeks of treatment (SMD= 4.00, 95% CI: 2.72 to 5.28, I2= 0%). In five studies with a total of 200 treated women a moderate to strong significant response rate was found (OR= 4.69, 95% CI: 2.27 to 9.68; I2= 0%). In four studies with a total of 180 treated women no significant effect of adverse events between Shuganjieyu capsules plus regular antidepressant versus regular antidepressant was found (OR= 1.26, 95% CI: 0.73 to 2.17, I2= 0%). The quality of the included studies was low. The risk of bias was low regarding attrition bias, unknown regar-

ding selection bias, detection bias reporting bias, and high for blinding of participants and personnel. The heterogeneity between studies within sub-group analysis was low.

The meta-analysis of Zeng et al. (2022) focused on interventions based on paroxetine combined with traditional Chinese medicine prescriptions versus paroxetine. For this meta-analysis 11 RCTs were included with a total of 955 Chinese women, of whom 491 receiving the intervention, with a postpartum depression determined by clinical manifestations, HAMD and EPDS scores. The age of women varied between 20-46 years. The duration of the therapy varied between two weeks and three months of which six weeks was most common. Seven Chinese prescriptions were used: Xiaoyaosan (two studies), Xiaochaihu Decoction (two studies), Chaihu plus Longgumuli Decoction (one study), Shugan Jieyu Decoction (two studies), Yangxue Tiaogan Decoction (two studies), Anshen Shengua Decoction (one study), Shengui Yangxue Decoction (one study). In all trials the clinical efficacy rate was calculated. In seven trials the effect was evaluated by HAMD and in three trials by EPDS. The clinical effectiveness of paroxetine combined with traditional Chinese medicine prescriptions was significantly better than that of paroxetine alone (RR= 1.22, 95% CI 1.16 to 1.30, I2= 0%). In seven studies with in total 308 treated women a large significant effect was found in HAMD reduction compared to control (WMD= -7.35, 95% CI: -10.84 to -3.87, I2= 99%). In three studies with in total 153 treated women a large significant effect was found in EPDS reduction compared to control (WMD= -3.24, 95% CI: -5.96 to -0.53, I2= 98%). The quality of the included studies was low. The risk of bias in included studies was low regarding random sequence generation, incomplete outcome data and selective reporting. Allocation concealment, blinding of participants and personnel, blinding of outcome of assessment and other bias was unknown. In the analyses with continuous outcomes of depressive symptoms there was a considerable amount of unexplained heterogeneity. There was no report of adverse events.

The meta-analysis of Sun et al. (2018), focused on the treatment of depression with Chai Hu Shu Gan San in general. The primary constituent of this formula is Chai Hu (Bupleurum Chinese) and two other constituents: Xiangfu (Cyperus rotundus) and Chuanxiong (ligusticum chuanxiong). In this meta-analysis two RCTs were included consisting of in total 170 definite postpartum depressed Chinese women of whom 86 were treated with Chai Hu Shu Gan in combination with fluoxetine compared to

84 women treated with fluoxetine alone. The duration of treatment was four weeks in one study and eight weeks in the other. The dose of fluoxetine was not reported. The main outcome was the mean difference of HAMD. The meta-analyses of these two studies showed a large and significant effect of Chai Hu Shu Gan San and fluoxetine compared to fluoxetine alone (MD= -4.10, 95% CI: -7.48 to -0.72; I2= 86%). The quality of the included studies was low. The risk of bias was low regarding selective reporting. The risk of bias in allocation concealment, blinding of participants and personnel, blinding of outcome of assessment and other bias was high. The risk of random sequence generation and incomplete outcome data was unknown. The heterogeneity in the studies was considerable. Considering adverse effects, nausea, appetite descent, somnipathy, quiver, dry mouth, dizziness, and tiredness were reported.

The meta-analysis of Li et al. (2016) focused on Chinese herbs in general for the treatment of postpartum depression. This study included 34 RCTs from 2006-2015 covering 1,499 women in the intervention arm, with an age ranging from 18-43 years. In these studies, 20 different types of herbs were studied. Of these studies, four studies showed overlap with the meta-analysis of Wang et al., 2022, four showed overlap with Zeng et al. (2022) and one study showed overlap with Sun et al. (2018).

One trial evaluated Chinese herbs versus placebo, seven trials versus routine treatment and 27 trials evaluated Chinese herbs plus routine treatment versus routine treatment alone. The routine treatment mainly consisted of (combinations of) antidepressant medication, psychotherapeutic and psychosocial interventions. In 30 trials the effect was evaluated by HAMD and in six trials by EPDS. In seven studies using the HAMD, there were statistically significant differences between Chinese herbs and routine treatments (MD = −2.60, 95% CI −4.55 to −0.64; I2= 95%) in reducing depressive symptoms. In 23 studies comparing Chinese herbs plus routine treatment and routine treatments alone, there was a statistically significant difference (MD = −3.00, 95% CI −3.73 to −2.26; I2= 85%) in reducing HAMD scores. For studies using the EPDS, in one trial comparing Chinese herbs with placebo, a significant effect was seen (MD = −2.67, 95% CI −3.88 to −1.46) in reducing depressive symptoms. Two trials which compared Chinese herbs with routine treatments showed significant beneficial effects of Chinese herbs as compared to routine treatments (MD = −3.36, 95% CI −6.05 to −0.66; I2= 90%). Three trials showed that Chinese herbs alone combined with routine treatment showed significant effectiveness when compared to routine treatments alone (MD = −3.80, 95% CI −5.27 to −2.34; I2= 75%) in reducing EPDS score.

The quality of the Iled studies was low. All trials provided limited information about design and methodology, and all trials had a high risk of bias.

Separate meta-analyses were performed on the incidence of adverse effects. No significant difference was found between Chinese herbs compared to placebo. Chinese herbs had a significantly lower incidence of adverse events compared to routine treatment alone (RR= 0.18, 95% CI 0.09 to 0.38; I2 = 57%) and Chinese herbs combined with routine treatments also had a significantly lower incidence of adverse events compared to routine treatment alone (RR 0,45, 95% CI 0.32 to 0.64; I2= 56%). However, whether Chinese herbs could affect breastfeeding or have adverse effects on newborns was not reported. Therefore, the safety of Chinese herbs for the newborn is unknown.

No information about dropout rates, patient preferences and values, and no information about cost-effectiveness of Chinese herbs in peripartum period is available. Data on secondary outcomes (e.g., anxiety, stress, foetus/newborn outcomes) are not available.

Overall recommendation	Strength of the recommendation	Quality of the evidence	Comments
Chinese herbs alone and in combination are weakly recommended for the treatment of mild to moderate depressive symptoms in the postpartum period.	Weak	Low ⊕⊕◯◯	There is evidence that specific Chinese herbs might be beneficial as a stand-alone treatment and also in combination treatment (with antidepressants) and have low risks of acute adverse effects, in women who are not breastfeeding. A special caution is made for the specific Chinese herbs that also contain of St John's wort, because in combination with other antidepressants this might cause serotonine syndrome.

Acupuncture

Acupuncture in pregnancy

Dennis and Dowswell (2013a) work is an update of a previous review by the same authors, focused on PPD during pregnancy. The authors concluded that evidence was still insufficient to allow recommendations for the treatment of depression during pregnancy using acupuncture as only two studies were available. One compared depression-specific acupuncture with maternal massage (Manber et al., 2004) and another compared depression-specific acupuncture with depression non-specific acupuncture (Manber et al., 2010), but samples were either small or estimations were statistically non-significant.

Five systematic reviews were published afterward synthesising the efficacy of acupuncture in pregnant women with depressive symptoms (W. Li et al., 2019; Nillni et al., 2018; Ravesteyn et al., 2017; Tong et al., 2019; L. Yang et al., 2018). Of particular interest are the publications from Ravesteyn et al. (2017) and Tong et al. (2019), as these additionally present meta-analyses estimates associated with the intervention.

Nillni et al. (2018) and Ravesteyn et al. (2017) summarise the literature between 2002 and 2013 published in English, on the efficacy of acupuncture as a treatment of MDD during pregnancy, presenting data from two overlapping studies comparing depression-specific acupuncture with depression non-specific acupuncture to massage therapy, overall showing inconsistent results. That is, whereas, in the first study with 61 pregnant women, there were no differences between groups after treatment or at 10 weeks postpartum, in the second study (with 150 pregnant women) the treatment group showed greater improvement, compared with the control groups after eight weeks of treatment. The meta-analytical estimates show a small effect size of acupuncture (Edges g = -0.43, 95% CI [-0.80, -0.06], p = 0.857, I2 = 0%, using a random effects model and an adequate optimal information size (OIS)). However, considering the p-value above the typical threshold ($p<0.05$), we cannot exclude that the observed effect is not due to chance.

Across the literature, adverse effects of regular acupuncture are not reported, suggesting it is safe during pregnancy. However, the quality of the evidence is low and the evidence concerning publication bias is inconsistent.

Currently, there are no data available about the acceptability, feasibility, patient preferences and values, and costs of acupuncture as a treatment for PPD in pregnancy.

Overall recommendation	Strength of the recommendation	Quality of the evidence	Comments
There is no evidence on the efficacy of the use of acupuncture in pregnancy, therefore we cannot make a recommendation.	No recommendation		Evidence about the efficacy of acupuncture during pregnancy is inconsistent.

Acupuncture in the postpartum period

Five systematic reviews were published synthesising the efficacy of acupuncture in postpartum depression (S. Li et al., 2018; W. Li et al., 2019; Nillni et al., 2018; Tong et al., 2019; L. Yang et al., 2018).

Nillni et al. (2018) present one small RCT involving 20 postpartum women, which compared electroacupuncture to sham acupuncture, showing no significant differences between groups post-treatment. Hence, L. Yang et al. (2018), S. Li et al. (2018), W. Li et al. (2019), and Tong et al. (2019) summarise the literature published between 2004 and 2015 in English and Chinese, on the efficacy of acupuncture (including electro-acupuncture) in postpartum, with overlapping studies. Tong et al. (2019) study is the most exhaustive one, presenting data from 450 women across 14 RCTs. Pooling the effects of six of these RCTs, the authors show close to significant clinical improvement in the acupuncture group compared with controls when assessed with the HDRS with a small effect size (MD = −1.27, 95% CI [−2.55, 0.01], p = 0.05, I2 = 83%) and using a random-effect model. The effective rate of acupuncture (rate of improvement in the outcome of interest) was reported by Li et al. (2018), from a pool of seven trials with low heterogeneity (I2 = 24%, p = 0.25), which included a total of 576 women. The authors show a significant difference between acupuncture and control groups (RR = 1.15, 95% CI [1.06, 1.24], p < 0.001) favouring acupuncture with a moderate effect size. All other studies observing the effect of acupuncture alone that were included in Li et al. (2018) and Li et al. (2019) were also included in Tong et al. (2019).

Except for the effective rate reported by S. Li et al. (2018), the overall total sample of the trials pooled for the meta-analyses is unknown (halting the calculation of the optimal information size (OIS)). Hence, although the confidence interval of the meta-analysis shows a potentially significant effect of acupuncture in the postpartum period, the p-value is above the typical threshold (p <0.05), and we cannot exclude

that the observed effect is due to chance.

The meta-analysis by L. Yang et al. (2018) offers comparative data on acupuncture vs fluoxetine from two studies for a total of 112 women. The authors report that acupuncture is not superior to fluoxetine according to the HDRS (SMD = -0.36, 95% CI [-1.03, 0.31]; I2 = 68.2%).

Furthermore, L. Yang et al. (2018) reported one study comparing acupuncture with electro-acupuncture and listed the electro-acupuncture's possible adverse effects (discomfort at the needle site, headache, needle site pain, bruising at the needle site, and dizziness) which seem to be present as well in sham-acupuncture.

Across the literature, adverse effects of regular acupuncture are not reported, suggesting it is safe in the postpartum. However, the authors recognise the low quality of the evidence and the inconsistent evidence concerning publication bias.

Overall recommendation	Strength of the recommendation	Quality of the evidence	Comments
There is no evidence on the efficacy of the use of acupuncture in the postpartum, therefore we cannot make a recommendation	No recommendation		Evidence about the efficacy of acupuncture in the postpartum is inconsistent

Fatty acids

A high-quality systematic review was conducted by Dennis and Dowswell (2013a) which presented inconclusive results regarding the effect of fatty acids (FA) in pregnancy. However, two meta-analyses conducted later showed the beneficial effects of omega-3 FA. Wei-Hong et al. (2017) found omega-3 fatty acids to be of benefit in pregnant women with PPD (SMD = 0.75, 95% CI [0.47, 1.04], p = 0.352) for treatment durations of 6-8 weeks and FA daily doses ranging between 0.42-2.2g/day for Eicosapentaenoic Acid (EPA) and 0.8-1.64g/day for Docosahexaenoic Acid (DHA). This meta-analysis was later updated by M. M. Zhang et al. (2020), that included eight studies, used a broader number of databases, and also did not impose language restrictions, finding a beneficial effect of FA on moderate depression both during pregnancy (SMD =

0.46, 95% CI [0.01, 0.91], p = 0.05) and in the postpartum (SMD = 1.59, 95% CI [0.65, 2.53], p < 0.001) compared with placebo for FA ratios ≥ 1.5. ≥1.5 or <1.5. In Zhang et al. (2020) FA ratio ≥1.5 approached statistical significance compared with placebo (SMD = 0.52, 95% CI [0.00, 1.04], p = 0.05), whereas no significant effects were seen when the FA ratio was <1.5 group (SMD = −0.09, p = 0.76) (Fig. 3). Additionally, FA effects are shown in mild-to-moderate depressive symptoms but not in severe symptoms (SMD = 0.28, p = 0.48). As for the treatment duration, there seems to be no advantage on treatment protocols longer than eight weeks (SMD = 0.58, p = 0.17). M. M. Zhang et al. (2020) overall quality evidence of the included studies was moderate, although the authors recognise that information about blinding and allocation concealment was insufficient across studies. Similarly to Suradom et al. (2021), the statistical analyses conducted in the original studies were based on intention-to-treat or modified intention-to-treat methods.

The most recent meta-analysis examining the effectiveness of omega-3 fatty acids (n-3 polyunsaturated fatty acids (PUFA), [DHA] and EPA]) in patients with postpartum depression compared with placebo, revealed no statistically significant superiority of n-3 PUFA supplement compared with placebo (SMDs = -0.14, 95% CI [-0.55, 0.27]; Suradom et al., 2021). This meta-analysis included four studies conducted between 2008-2020, and a total of 73 women meeting either the diagnosis of PPD defined by the DSM systems or according to the clinical threshold, between 18-45 years of age. The primary outcome was the change in depressive symptoms according to self-report instruments (e.g., EPDS, BDI-II, HAMD). The meta-analysis included only RCTs of which one showed a high risk of bias. Also, the authors extracted the data based on intent-to-treat (ITT) analysis or modified ITT data. This result is consistent with four other reviews (Grosso et al., 2014; Jans et al., 2010; Mocking et al., 2020; Ravesteyn et al., 2017). Mocking et al. (2020) meta-analysis found non-significant effects of fatty acids both when pooling the effects of studies conducted across the peripartum period (random effects: SDM = −0.545, 95% CI [−1.182, 0.093]; Z = −1.673; p =.094) and when pooling the effects of studies conducted only in the postpartum period (SDM = −0.886, 95% CI [−2.088 to 0.316]; Z = −1.444; p = .149). In their study, Mocking et al. (2020) did not present language restrictions and adopted a dimensional perspective on PPD symptoms, leading the authors to include studies on the complete spectrum of depressive symptoms in the peripartum period even if women did not fulfil major depressive episode criteria.

All studies included were RCTs with moderate to low-quality of evidence due to the lack of pre-published protocol and heterogeneity of the population.

The above inconsistencies between the most informative studies could be led by the primary outcome chosen by the authors (e.g., M. M. Zhang et al. (2020) converted outcome measures' scores into EPDS, whereas Mocking et al. (2020) reported mixed data across different outcome measures (e.g., EPDS, BDI-II)). Additionally, according to M. M. Zhang et al. (2020), increasing FA dosage only led to near-significant benefits, meaning that no significant effect is yet proven.

In what concerns adverse effects, the review by Dennis and Dowswell (2013a) reported no differences between FA and placebo. Similarly, M. M. Zhang et al. (2020) reported no significant difference in the incidence of gastrointestinal and neurological events for FA and control groups and Suradom et al. (2021) reported no adverse effects associated with FA. Dropout rates across studies ranged between 0-33% across intervention and control groups (Jans et al., 2010; Wei-Hong et al., 2017; M. M. Zhang et al., 2020).

Overall, the quality of the current evidence about the effectiveness of FA in reducing depressive symptoms is low to moderate, given that when compared with placebo, FA efficacy for treating PPD is limited, inconsistent, and associated with risk of bias to some extent. Additionally, adverse effects are likely to be trivial.

Data on other secondary outcomes (e.g., anxiety, stress, foetus/newborn outcomes) are not available.

Overall recommendation	Strength of the recommendation	Quality of the evidence	Comments
Fatty acids are weakly recommended for the treatment of mild to moderate depressive symptoms in pregnancy and in the postpartum period.	Weak	Low ⊕⊕◯◯	Fatty acids might be beneficial and low risks of adverse effects are reported.

Recommended protocol should be set within the following parameters: EPA and DHA, > 1,9 g/d, for six to eight weeks duration.

F. Recommendations for future research on prevention, screening and treatment of PPD

F. // Recommendations for future research on prevention, screening and treatment of PPD

As this work shows, there are many areas that require further research. While strides have been made, there is a pressing need for comprehensive investigations that consider the unique challenges of this period. This, naturally, should be done in an ethically sustainable way. Obstacles such as the stigma surrounding mental health issues in pregnancy and after childbirth, limited awareness among healthcare providers, and variations in screening practices across healthcare settings must be elucidated to devise effective strategies. Ethical considerations are paramount, as research in this realm involves vulnerable populations, necessitating sensitive protocols, informed consent procedures, and safeguards for maternal, foetal and the newborn well-being. From an ethical perspective, gaining new knowledge on PPD, its prevention, screening and effective treatment is important for all stakeholders. For instance, the women diagnosed with PPD need to be able to make informed decisions whether to consent to different interventions. Healthcare professionals need to be trained and to have a set of distinctive intervention alternatives according to women's singular conditions, preferences and values. Health managers need to be informed about the direct and indirect costs associated with each intervention to decide for the allocation of limited budget to the most cost-effective interventions for the largest number of individuals. This effect bears not only on women's and the (future) children's health, but on their families and the wider society. Information may also unravel stigma and negative feelings such as guilt.

Without robust research, the potential for identifying effective screening tools, preventive measures, and evidence-based treatments remains untapped, perpetuating the intergenerational transmission of mental health issues. Supporting further research on PPD interventions will ensure the well-being of mothers and future generations.

Pregnant and postpartum women are typically considered a vulnerable population in research which may result in not conducting enough research as a form of protecting them. However, without such research, there is no information on whether the interventions work. The in-

terventions themselves need to be safe, timely and effective. They also need to be cost effective to ensure the resources of healthcare are directed to the ones who need them.

Therefore, the authors of these guidelines strongly endorse further research and investment to address the following needs in the development of high-quality perinatal mental healthcare across Europe.

Prevention of PPD

– Further studies should compare various psychological and psychosocial interventions in order to discover if there is a specific intervention that is more effective than others.

– Further studies should differentiate between targeted (women at risk as opposed to women with no known risk factors) populations in examining the effectiveness of preventive interventions.

– More high-quality research needs to be done to examine the effect of dietary supplements on preventing perinatal depression with differentiation between targeted (women at risk as opposed to women with no known risk factors and with sub-clinical symptoms) populations in examining the effectiveness of preventive interventions.

– Future studies should focus on exercise as a preventive intervention among women with risk factors and women with sub-clinical symptoms.

Screening of PPD

– Further research should focus on assessing efficacy, feasibility, acceptability, preferences and cost-effectiveness of screening programmes for the early identification of women at high-risk for perinatal depression.

– Research is still needed among the general population of pregnant and postpartum women regarding acceptability, feasibility, preferences and cost-effectiveness of screening for depression.

Treatment of PPD

Psychological Interventions

– Future studies should have larger sample sizes and pay more attention to the setting of inclusion of the participants in the studies.

– Future studies should provide better insight of the dosage of the intervention or the therapy sessions, necessary to produce the effect on depressive symptoms.

– Future studies should include active comparator between therapies (psychological treatment vs psychopharmacological treatment) and within type of therapies (CBT vs 3rd wave CBT). Also, it would be necessary to compare CBT face-to-face interventions with CBT delivered online. Furthermore, enough data are not available on long-term effects, so future studies should include follow-up assessments of the interventions.

– Future studies should evaluate the effectiveness of (psychological) treatment in women with depression established with the clinical interview.

Pharmacological interventions

– Further research should assess the efficacy and safety of antidepressants in pregnancy and postpartum in larger populations and possibly in RCT settings, as well as the efficacy and safety of antidepressant augmentation with other psychotropics on maternal-child health.
– Systematic studies should be conducted to assess the safety of antidepressants and brexanolone in breastfed infants. More research is needed regarding the necessity and frequency of monitoring of drug levels during gestation.
– Methodologically sound research should assess the effect of discontinuing or reducing the dose of the antidepressant (or the add-on medication) proximal to childbirth in reducing poor neonatal adaptation in newborns compared with stable medication intake.

– Because the elevated risk of negative developmental outcomes in the children is largely explained by the maternal mental illness, genetic and familial environment, more longitudinal research assessing support and early intervention in women with perinatal depression with or without antidepressant treatment is needed.

– There is a crucial need for more research determining the epidemiology of difficult-to-treat-depression and psychotic depression in the peripartum period, as well as what therapeutic strategy (medication) is effective in their treatment.

Non-invasive Brain stimulation Interventions

– **rTMS in pregnancy:** Future research should replicate existing findings in high-quality study designs, and larger groups of pregnant women with clinically relevant depressive symptoms and per TMS modality. Treatment protocols ranging from 13 to 20 sessions (once daily), bi-

lateral, left-HF, right-LF and left-LF were so far tested with promising results. Stimulation intensities between 80% and 120% of the MT, delivering 1200 to 3000 pulses per session are suggested and should be further tested and compared. Moreover, accelerated rTMS (arTMS; several sessions/day) and iTBS (50Hz bursts, repeated at 5Hz [2s on and 8s off], with a total of 600 pulses [3min, 9s] per session during 20 sessions, using 120% of the motor threshold) as it potentially shortens treatment courses, and the time per session from 30 to 3 mins, respectively. Both alternatives could potentially alleviate the burden of long daily schedules. Personalised maintenance treatment schedules should be tested as well. Moreover, research should consider testing the effect of rTMS/iTBS/arTMS on other secondary outcomes of interest, such as anxiety, stress, and foetus and newborn outcomes. Finally, research should focus on adverse effects, cost-effectiveness, patient acceptability and feasibility and patient values and preferences.

– **rTMS in the postpartum:** Future research should replicate existing findings in high-quality study designs, and larger groups of women with clinically relevant depressive symptoms in postpartum period and per TMS modality. Treatment protocols of 7-10 weeks over the left and right DLPFC, number of pulses between 50-4000, and stimulation intensity between 80-120% of the individual motor threshold should be tested and compared back-to-back. Moreover, arTMS and iTBS protocols, and personalised maintenance protocols should be tested, similarly to recommendations for pregnancy. Personalised maintenance phases of one to two sessions per week should be considered in future studies. Likewise, research should consider testing the effect of rTMS/iTBS/arTMS on other secondary outcomes of interest, on adverse effects, cost-effectiveness, patient acceptability and feasibility and patient values and preferences.

– **tES in pregnancy and the postpartum:** Future research should replicate existing findings in high-quality study designs, among larger groups of pregnant women in the peripartum period with clinically relevant depressive symptoms and per tES modality, given that further research has a large potential for reducing uncertainty about the effects of different types of tES in depressive symptoms in the perinatal period. Research should fo-

cus on optimal dosage, intensity, duration, adverse events, feasibility and patient´s acceptability, values and preferences. tES interventions (especially those accelerated and home-based) are thought to be of good value for the anticipated costs, therefore, economic studies are required. Current modelling informed protocols should be considered towards increased personalisation of treatment. Moreover, research should consider testing the effect of tES on other secondary outcomes of interest, such as anxiety, and stress.

– **ECT in pregnancy and postpartum:** Future research is needed, offering updated data, although ethically mainly observational studies should be considered (due to known adverse effects for women and foetus), either retrospective or prospective. More details about the protocols, and comparative studies with other treatments should be conducted to inform treatment algorithms based on updated knowledge. Additionally, data on adverse effects associated with ECT and ECT vs other treatments, cost-effectiveness, feasibility and patient's acceptability, values and preferences are warranted.

– **BLT in pregnancy and postpartum:** Future research should replicate existing findings in high-quality study designs and larger groups of women in the peripartum period with clinically relevant depressive symptoms. In addition, research should focus on the optimal dosage, adverse events, cost-effectiveness, patient acceptability and feasibility. Moreover, research should consider testing the effect of BLT on other secondary outcomes of interest, such as anxiety, stress, and foetus/newborn outcomes.

Complementary and alternative treatments

– **Physical exercise and yoga in pregnancy:** Given the specificities of distinctive physical conditions, commonly presented during pregnancy, further research should consider larger sub-groups of women with clinically relevant depressive symptoms and most common concomitant health issues in pregnancy in high-quality study designs. In addition, research should focus on the efficacy of distinctive physical exercise strategies, define the best protocols, adverse effects, cost-effectiveness, feasibility and patient´s acceptability, values and preferences.

– **Physical exercise and yoga in postpartum:** Further research should consider high-quality study designs and larger groups with clinically relevant depressive

symptoms. In addition, research should focus on the efficacy of distinctive stand-alone physical exercise and yoga strategies, define the best protocols, adverse effects, cost, and feasibility and patient's values and preferences.

– **Massage in pregnancy and postpartum:** Further research should consider high-quality study designs and larger groups with clinically relevant depressive symptoms. In addition, research should focus on the efficacy of treatments, define the best protocols, adverse effects, cost-effectiveness, and feasibility and patient's values and preferences.

– **Music therapy in pregnancy and postpartum:** High-quality research focusing exclusively in the peripartum period is warranted to test the efficacy of music therapy in reducing depressive symptoms in pregnancy and the postpartum periods.

– **Peer support in pregnancy and postpartum:** Future research should replicate existing findings in high-quality study designs and larger groups of pregnant women with clinically relevant depressive symptoms. In addition, research should focus on technology-based and non-technology-based peer-support programmes' protocols, women and newborn secondary outcomes, adverse effects, cost-effectiveness, and feasibility.

– **Chinese herbs in pregnancy and postpartum:** Future research conducted outside of China should replicate existing findings in high-quality study designs, including studies on the effect of Chinese herbs compared to placebo and on the interactions with prescribed antidepressants. Ethically, given the current inconsistency of findings, future research in pregnant women and postpartum breastfeeding women should rely on data from observational and retrospective studies. Variables of interest include optimal dosage/combination of components, intensity, and duration. Outcomes of interest should include adverse effects for woman, the foetus and the newborn, newborn outcomes, mother's anxiety and stress, cost-effectiveness, patient acceptability and feasibility and patient's values and preferences.

– **Acupuncture in pregnancy and postpartum:** The use of acupuncture in pregnant women with PPD symptoms warrants particular attention as adverse effects are unknown and the quality of the evidence of

efficacy is very low. Future research should test the efficacy of acupuncture against placebo, and conduct comparative studies between depression-specific acupuncture vs depression non-specific acupuncture, traditional acupuncture vs electro-acupuncture, and acupuncture against other active treatments in high-quality study designs and larger groups of pregnant women with clinically relevant depressive symptoms. In addition, research should focus on the optimal dosage, adverse events, cost-effectiveness, patient acceptability, and feasibility. Moreover, research should consider testing the effect of acupuncture on other secondary outcomes of interest, such as anxiety, stress, and newborn outcomes.

Fatty acids: Future research should replicate existing findings on the effect of EPA and DHA in high-quality study designs and larger groups of women in the peripartum period with clinically relevant depressive symptoms. In addition, research should focus on the optimal dosage, adverse events, cost-effectiveness, patient acceptability and feasibility. Moreover, research should consider testing the effect of FA on other secondary outcomes of interest, such as anxiety, stress, and foetus/newborn outcomes.

Focus on other individuals affected by PPD

– There is increasing evidence that fathers can also be affected by PPD. However, evidence about prevention and treatment of PPD in fathers is still very scarce. Therefore, interventional studies are urgently needed including fathers with PPD.

– There are increasing "non-traditional" and diverse family constellations, including same-sex parents, transgender parents, and co-parenting without being in a sexual relationship. To date there is a scarcity of evidence about prevalence, risk factors, prevention and treatment of PPD in those diverse family constellations; research is needed here.

– In high-income countries, there is an increasing number of fertility treatments available. However, we could not identify systematic reviews about the prevention and treatment of PPD in this subgroup of women. More research is needed here if this subgroup requires special attention and differing treatment.

G. Final remarks

G. // Final remarks

Our Evidence-based Clinical Practice Guidelines for the Prevention, Screening, and Treatment of PPD represent a subs—tantial advancement toward improved and high-quality peripartum mental health care. Nevertheless, their effectiveness per se is limited due to three overarching factors:

1) disparities in existing knowledge and available data across countries and regions;

2) disparities in the availability of local resources for peripartum mental health care;

3) disparities of women contextual/social conditions.

Disparities in existing knowledge and available data are not restricted to global variations but also manifest within regions and individual countries, even inside Europe. These disparities add to the complex nature of addressing peripartum depression comprehensively. Despite our best efforts during the development of these Evidence-based Guidelines, we acknowledge that the landscape of peripartum mental health research and data availability is biased toward the accessible data, falling short to depict those not easily represented across studies (e.g., minorities, immigrants, people living in conflict areas). Recognising such intra-regional and intra-national disparities is essential for understanding the limitations of the current work and being sensitive to fully accommodating the unique features, circumstances and needs of specific populations, into improved effective strategies for prevention, screening, and treatment of peripartum depression.

Additionally, disparities in the availability of local resources for peripartum mental health care further add to the challenge of addressing peripartum depression. Access to adequate healthcare services, trained and updated mental health professionals, and strong support networks can vary significantly from one community to another. These resource disparities create uneven opportunities in what concerns prevention, early detection, and adequate intervention and care for individuals experiencing peripartum depression. To ensure that every woman receives the care and support she needs during this critical period, policy-makers and health managers need to work toward minimising these resource gaps, aiming for equitable access to mental health services for all, regardless geographic location or socioeconomic status.

Furthermore, it is essential to acknowledge the disparities in contextual and social conditions experienced by women, which significantly influence their vulnerability to peripartum depression. Women's experiences and challenges during pregnancy and the postpartum period can vary greatly based on factors such as socioeconomic status, access to education, employment opportunities, and social support networks. Additionally, cultural norms and societal expectations exert considerable pressure, affecting women's mental well-being. Such contextual and social disparities underscore the need for a comprehensive approach to mental health in pregnancy and postpartum that not only addresses clinical aspects but also takes into account these societal and cultural factors that contribute to the increased risk of peripartum depression.

Recognising and addressing these three overarching factors and the disparities each entail, is fundamental to ensure that all women receive the comprehensive care and support they need during this critical phase of their lives, ultimately impacting at least two generations at once.

H. References

H. // References

Al-Fadel, N., & Alrwisan, A. (2021). Antidepressant use during pregnancy and the potential risks of motor outcomes and intellectual disabilities in offspring: A systematic review. *Drugs - Real World Outcomes, 8*(2), 105–123. https://doi.org/10.1007/s40801-021-00232-z

Al-Karawi, D., & Jubair, L. (2016). Bright light therapy for nonseasonal depression: Meta-analysis of clinical trials. *Journal of Affective Disorders, 198*, 64–71. https://doi.org/10.1016/j.jad.2016.03.016

Alves, S., Martins, A., Fonseca, A., Canavarro, M. C., & Pereira, M. (2018). Preventing and treating women's postpartum depression: A qualitative systematic review on partner-inclusive interventions. *Journal of Child and Family Studies, 27*(1), 1–25. https://doi.org/10.1007/s10826-017-0889-z

American Psychiatric Association (APA). (2013). *Diagnostic and Statistical Manual of Mental Disorders, 5th Edition.* (5th ed.). American Psychiatric Association.

Andalib, S., Emamhadi, M. R., Yousefzadeh-Chabok, S., Shakouri, S. K., Høilund-Carlsen, P. F., Vafaee, M. S., & Michel, T. M. (2017). Maternal SSRI exposure increases the risk of autistic offspring: A meta-analysis and systematic review. *European Psychiatry: The Journal of the Association of European Psychiatrists, 45*, 161–166. https://doi.org/10.1016/j.eurpsy.2017.06.001

Aoyagi, S.-S., & Tsuchiya, K. J. (2019). Does maternal postpartum depression affect children's developmental outcomes? *Journal of Obstetrics and Gynaecology Research, 45*(9), 1809–1820. https://doi.org/10.1111/jog.14064

Bagnall, K. M. (2014). *Long-term follow-up of NetmumsHWD: A feasibility randomised controlled trial of telephone supported online behavioural activation for postnatal depression at 16 months post-randomisation.* https://ore.exeter.ac.uk/repository/handle/10871/15289

Batt, M. M., Duffy, K. A., Novick, A. M., Metcalf, C. A., & Epperson, C. N. (2020). Is postpartum depression different from depression occurring outside of the perinatal period? A review of the evidence. *FOCUS, 18*(2), 106–119. https://doi.org/10.1176/appi.focus.20190045

Bauer, A., Knapp, M., & Parsonage, M. (2016). Lifetime costs of perinatal anxiety and depression. *Journal of Affective Disorders, 192,* 83–90. https://doi.org/10.1016/j.jad.2015.12.005

Bauer, A., Pawlby, S., Plant, D. T., King, D., Pari-

ante, C. M., & Knapp, M. (2015). Perinatal depression and child development:

Exploring the economic consequences from a South London cohort. *Psychological Medicine, 45*(1), 51–61. https://doi.org/10.1017/S0033291714001044

Bayrampour, H., Kapoor, A., Bunka, M., & Ryan, D. (2020). The risk of relapse of depression during pregnancy after discontinuation of antidepressants: A systematic review and meta-analysis. *The Journal of Clinical Psychiatry, 81(*4), 19r13134. https://doi.org/10.4088/JCP.19r13134

Beck, C. T., & Indman, P. (2005). The many faces of postpartum depression. *Journal of Obstetric, Gynecologic, and Neonatal Nursing: JOGNN, 34*(5), 569–576. https://doi.org/10.1177/0884217505279995

Bérard, A., Iessa, N., Chaabane, S., Muanda, F. T., Boukhris, T., & Zhao, J.-P. (2016). The risk of major cardiac malformations associated with paroxetine use during the first trimester of pregnancy: A systematic review and meta-analysis. *British Journal of Clinical Pharmacology, 81*(4), 589–604. https://doi.org/10.1111/bcp.12849

Bhat, A., Nanda, A., Murphy, L., Ball, A. L., Fortney, J., & Katon, J. (2022). A systematic review of screening for perinatal depression and anxiety in community-based settings. *Archives of Women's Mental Health, 25*(1), 33–49. https://doi.org/10.1007/s00737-021-01151-2

Boath, E. (2015). Exercise as an adjunct therapy for postnatal depression. *Archives of Women's Mental Health, 18*(2), 269–408. https://doi.org/10.1007/s00737-014-0488-6

Broughton, L. C., Medlicott, N. J., & Smith, A. J. (2021). Effectiveness of patient decision aids in women considering psychotropic medication use during pregnancy: A literature review. *Archives of Women's Mental Health, 24*(4), 569–578. https://doi.org/10.1007/s00737-021-01118-3

Brouwers, M. C., Kho, M. E., Browman, G. P., Burgers, J. S., Cluzeau, F., Feder, G., Fervers, B., Graham, I. D., Grimshaw, J., Hanna, S. E., Littlejohns, P., Makarski, J., & Zitzelsberger, L. (2010). AGREE II: Advancing guideline development, reporting and evaluation in health care. *CMAJ: Canadian Medical Association Journal, 182*(18), E839–E842. https://doi.org/10.1503/cmaj.090449

Brown, A.-M., Robinson, A., Jones, F., Smith, A., Williams, P., & Hanley, J. (2017). The effectiveness of prescription exercises for women diagnosed with postnatal depression: A systematic review. *MIDIRS Midwifery Digest, 27*(4), 488–495. https://search.ebscohost.com/login.aspx?direct=true&db=jlh&AN=127264734&site=ehost-live

Brown, J. V. E., Wilson, C. A., Ayre, K., Robertson, L., South, E., Molyneaux, E., Trevillion, K., Howard, L. M., & Khalifeh, H. (2021). Antidepressant treatment for postnatal depression. *Cochrane Database of Systematic Reviews, 2*. https://doi.org/10.1002/14651858.CD013560.pub2

Buttner, M. M., Brock, R. L., O'Hara, M. W., & Stuart, S. (2015). Efficacy of yoga for depressed postpartum women: A randomized controlled trial. *Complementary Therapies in Clinical Practice, 21*(2), 94–100. https://doi.org/10.1016/j.ctcp.2015.03.003

Byatt, N., Levin, L. L., Ziedonis, D., Moore Simas, T. A., & Allison, J. (2015). Enhancing participation in depression care in outpatient perinatal care settings: A systematic review. *Obstetrics and Gynecology, 126*(5), 1048–1058. https://doi.org/10.1097/AOG.0000000000001067

Calaway, K., Coshal, S., Jones, K., Coverdale, J., & Livingston, R. (2016). A systematic review of the safety of electroconvulsive therapy use during the first trimester of pregnancy. *Journal of ECT, 32*(4), 230–235. https://doi.org/10.1097/YCT.0000000000000330

Carvalho, A. E. V., Linhares, M. B. M., Padovani, F. H. P., & Martinez, F. E. (2009). Anxiety and depression in mothers of preterm infants and psychological intervention during hospitalization in neonatal ICU. *The Spanish Journal of Psychology, 12*(1), 161–170. https://doi.org/10.1017/s1138741600001578

Chang, Q., Ma, X.-Y., Xu, X.-R., Su, H., Wu, Q.-J., & Zhao, Y.-H. (2020). Antidepressant use in depressed women during pregnancy and the risk of preterm birth: A systematic review and meta-analysis of 23 cohort studies. *Frontiers in Pharmacology, 11*, 659. https://doi.org/10.3389/fphar.2020.00659

Chechko, N., Stickel, S., & Votinov, M. (2023). Neural responses to monetary incentives in postpartum women affected by baby blues. *Psychoneuroendocrinology, 148*, 105991. https://doi.org/10.1016/j.psyneuen.2022.105991

Chen, C.-H., Tseng, Y.-F., Chou, F.-H., & Wang, S.-Y. (2000). Effects of support group intervention in postnatally distressed women: A controlled study in Taiwan. *Journal of Psychosomatic Research, 49*(6), 395–399. https://doi.org/10.1016/S0022-3999(00)00180-X

Cole, J., Bright, K., Gagnon, L., & McGirr, A. (2019). A systematic review of the safety and effectiveness of repetitive transcranial magnetic stimulation in the treatment of peripartum depression. *Journal of Psychiatric Research, 115,* 142–150. https://doi.org/10.1016/j.jpsychires.2019.05.015

Cooper, M. C., Kilvert, H. S., Hodgkins, P., Roskell, N.

S., & Eldar-Lissai, A. (2019). Using matching-adjusted indirect comparisons and network meta-analyses to compare efficacy of brexanolone injection with Selective Serotonin Reuptake Inhibitors for treating Postpartum Depression. *CNS Drugs, 33*(10), 1039–1052. https://doi.org/10.1007/s40263-019-00672-w

Corbally, L., & Wilkinson, M. (2021). The effect of mindfulness-based interventions on stress, depression and anxiety during the perinatal period in women without pre-existing stress, depressive or anxiety disorders: A systematic review and meta-analysis of controlled trials. *Mindfulness, 12*(10), 2357–2370. https://doi.org/10.1007/s12671-021-01697-3

Da Costa, D., Lowensteyn, I., Abrahamowicz, M., Ionescu-Ittu, R., Dritsa, M., Rippen, N., Cervantes, P., & Khalifé, S. (2009). A randomized clinical trial of exercise to alleviate postpartum depressed mood. *Journal of Psychosomatic Obstetrics and Gynaecology, 30*(3), 191–200. https://doi.org/10.1080/01674820903212136

De Vries, C., Gadzhanova, S., Sykes, M. J., Ward, M., & Roughead, E. (2021). A systematic review and meta-analysis considering the risk for congenital heart defects of antidepressant classes and individual antidepressants. *Drug Safety, 44*(3), 291–312. https://doi.org/10.1007/s40264-020-01027-x

Dennis, C.-L. (2003). The effect of peer support on postpartum depression: A pilot randomized controlled trial. *The Canadian Journal of Psychiatry, 48*(2), 115–124. https://doi.org/10.1177/070674370304800209

Dennis, C.-L., & Dowswell, T. (2013a). Interventions (other than pharmacological, psychosocial or psychological) for treating antenatal depression. *Cochrane Database of Systematic Reviews, 7*, CD006795. https://www.embase.com/search/results?subaction=viewrecord&id=L563012509&from=export

Dennis, C.-L., & Dowswell, T. (2013b). Psychosocial and psychological interventions for preventing postpartum depression. *The Cochrane Database of Systematic Reviews, 2*, CD001134. https://doi.org/10.1002/14651858.CD001134.pub3

Dennis, C.-L., Hodnett, E., Kenton, L., Weston, J., Zupancic, J., Stewart, D. E., & Kiss, A. (2009). Effect of peer support on prevention of postnatal depression among high risk women: Multisite randomised controlled trial. *British Medical Journal, 338*, a3064. https://doi.org/10.1136/bmj.a3064

Di Florio, A., & Meltzer-Brody, S. (2015). Is postpartum depression a distinct disorder? *Current Psychiatry Reports*. 10.1007/s11920-015-0617-6

Di Florio, A., Putnam, K., Altemus, M., Apter, G., Bergink, V., Bilszta, J., Brock, R., Buist, A., Deligiannidis, K. M., Devouche, E., Epperson, C. N., Guille, C., Kim, D., Lichtenstein, P., Magnusson, P.

K., Martinez, P., Munk-Olsen, T., Newport, J., Payne, J., ... Meltzer-Brody, S. (2017). The impact of education, country, race and ethnicity on the self-report of postpartum depression using the Edinburgh Postnatal Depression Scale. *Psychological Medicine, 47*(5), Artigo 5. https://doi.org/10.1017/S0033291716002087

Dimidjian, S., Goodman, S. H., Sherwood, N. E., Simon, G. E., Ludman, E., Gallop, R., Welch, S. S., Boggs, J. M., Metcalf, C. A., Hubley, S., Powers, J. D., & Beck, A. (2017). A pragmatic randomized clinical trial of behavioral activation for depressed pregnant women. *Journal of Consulting and Clinical Psychology, 85*(1), 26–36. https://doi.org/10.1037/ccp0000151

Dowse, E., Chan, S., Ebert, L., Wynne, O., Thomas, S., Jones, D., Fealy, S., Evans, T.-J., & Oldmeadow, C. (2020). Impact of perinatal depression and anxiety on birth outcomes: A retrospective data analysis. *Maternal and Child Health Journal, 24*(6), 718–726. https://doi.org/10.1007/s10995-020-02906-6

Fang, Q., Lin, L., Chen, Q., Yuan, Y., Wang, S., Zhang, Y., Liu, T., Cheng, H., & Tian, L. (2022). Effect of peer support intervention on perinatal depression: A meta-analysis. *General Hospital Psychiatry, 74*, 78–87. https://doi.org/10.1016/j.genhosppsych.2021.12.001

Felice, E., Agius, A., Sultana, R., Felice, E. M., & Calleja-Agius, J. (2018). The effectiveness of psychosocial assessment in the detection and management of postpartum depression: A systematic review. *Minerva Ginecologica, 70*(3), 323–345. https://doi.org/10.23736/S0026-4784.17.04080-1

Feltner, C., Wallace, I., Berkman, N., Kistler, C. E., Middleton, J. C., Barclay, C., Higginbotham, L., Green, J. T., & Jonas, D. E. (2018). Screening for intimate partner violence, elder abuse, and abuse of vulnerable adults: Evidence report and systematic review for the US Preventive Services Task Force. *JAMA, 320*(16), 1688–1701. https://doi.org/10.1001/jama.2018.13212

Field, T., Diego, M., Delgado, J., & Medina, L. (2013). Peer support and interpersonal psychotherapy groups experienced decreased prenatal depression, anxiety and cortisol. *Early Human Development, 89*(9), 621–624. https://doi.org/10.1016/j.earlhumdev.2013.04.006

Fonseca, A., Ganho-Ávila, A., Lambregtse-van den Berg, M., Lupattelli, A., Rodriguez-Muñoz, M. de la F., Ferreira, P., Radoš, S. N., & Bina, R. (2020). Emerging issues and questions on peripartum depression prevention, diagnosis and treatment: A consensus report from the cost action riseup-PPD. *Journal of Affective Disorders, 274,* 167–173. https://doi.org/10.1016/j.jad.2020.05.112

Forsell, E., Bendix, M., Holländare, F., Szymanska von Schultz, B., Nasiell, J., Blomdahl-Wetterholm, M., Eriksson, C., Kvarned, S., Lindau van der

Linden, J., Söderberg, E., Jokinen, J., Wide, K., & Kaldo, V. (2017). Internet delivered cognitive behavior therapy for antenatal depression: A randomised controlled trial. *Journal of Affective Disorders, 221*, 56–64. https://doi.org/10.1016/j.jad.2017.06.013

Ganho-Ávila, A., Poleszczyk, A., Mohamed, M. M. A., & Osório, A. (2019). Efficacy of rTMS in decreasing postnatal depression symptoms: A systematic review. *Psychiatry Research, 279*, 315–322. https://doi.org/10.1016/j.psychres.2019.05.042

Gao, S.-Y., Wu, Q.-J., Sun, C., Zhang, T.-N., Shen, Z.-Q., Liu, C.-X., Gong, T.-T., Xu, X., Ji, C., Huang, D.-H., Chang, Q., & Zhao, Y.-H. (2018). Selective serotonin reuptake inhibitor use during early pregnancy and congenital malformations: A systematic review and meta-analysis of cohort studies of more than 9 million births. *BMC Medicine, 16*(1), 205. https://doi.org/10.1186/s12916-018-1193-5

Gao, S.-Y., Wu, Q.-J., Zhang, T.-N., Shen, Z.-Q., Liu, C.-X., Xu, X., Ji, C., & Zhao, Y.-H. (2017). Fluoxetine and congenital malformations: A systematic review and meta-analysis of cohort studies. *British Journal of Clinical Pharmacology, 83*(10), 2134–2147. https://doi.org/10.1111/bcp.13321

Gastaldon, C., Solmi, M., Correll, C. U., Barbui, C., & Schoretsanitis, G. (2022). Risk factors of postpartum depression and depressive symptoms: Umbrella review of current evidence from systematic reviews and meta-analyses of observational studies. *The British Journal of Psychiatry: The Journal of Mental Science, 221*(4), 591–602. https://doi.org/10.1192/bjp.2021.222

Gavin, N. I., Gaynes, B. N., Lohr, K. N., Meltzer-Brody, S., Gartlehner, G., & Swinson, T. (2005). Perinatal Depression: A systematic review of prevalence and incidence. *Obstetrics & Gynecology, 106*(5 Part 1), 1071. https://doi.org/10.1097/01.AOG.0000183597.31630.db

Gelaye, B., Rondon, M. B., Araya, R., & Williams, M. A. (2016). Epidemiology of maternal depression, risk factors, and child outcomes in low-income and middle-income countries. *The Lancet. Psychiatry, 3*(10), 973–982. https://doi.org/10.1016/S2215-0366(16)30284-X

Gerrard, J., Holden, J. M., Elliott, S. A., McKenzie, P., McKenzie, J., & Cox, J. L. (1993). A trainer's perspective of an innovative programme teaching health visitors about the detection, treatment and prevention of postnatal depression. *Journal of Advanced Nursing, 18*(11), 1825–1832. https://doi.org/10.1046/j.1365-2648.1993.18111825.x

Gjerdingen, D. K., McGovern, P., Pratt, R., Johnson, L., & Crow, S. (2013). Postpartum doula and peer telephone support for postpartum depression: A pilot randomized controlled trial. *Journal of Primary Care & Community Health, 4*(1), 36–43. https://doi.org/10.1177/2150131912451598

Glavin, K., Smith, L., Sørum, R., & Ellefsen, B. (2010). Redesigned community postpartum care to prevent and treat postpartum depression in women—A one-year follow-up study. *Journal of Clinical Nursing, 19*(21–22), 3051–3062. https://doi.org/10.1111/j.1365-2702.2010.03332.x

Gong, H., Ni, C., Shen, X., Wu, T., & Jiang, C. (2015). Yoga for prenatal depression: A systematic review and meta-analysis. *BMC Psychiatry, 15*(1). https://doi.org/10.1186/s12888-015-0393-1

Goodman, J. H., & Santangelo, G. (2011). Group treatment for postpartum depression: A systematic review. *Archives of Women's Mental Health, 14*(4), 277–293. https://doi.org/10.1007/s00737-011-0225-3

Gressier, F., Rotenberg, S., Cazas, O., & Hardy, P. (2015). Postpartum electroconvulsive therapy: A systematic review and case report. *General Hospital Psychiatry, 37*(4), 310–314. https://doi.org/10.1016/j.genhosppsych.2015.04.009

Grigoriadis, S., Graves, L., Peer, M., Mamisashvili, L., Dennis, C.-L., Vigod, S. N., Steiner, M., Brown, C., Cheung, A., Dawson, H., Rector, N., Guenette, M., & Richter, M. (2019). Benzodiazepine use during pregnancy alone or in combination with an antidepressant and congenital malformations: Systematic review and meta-analysis. *The Journal of Clinical Psychiatry, 80*(4), 18r12412. https://doi.org/10.4088/JCP.18r12412

Grosso, G., Pajak, A., Marventano, S., Castellano, S., Galvano, F., Bucolo, C., Drago, F., & Caraci, F. (2014). Role of omega-3 fatty acids in the treatment of depressive disorders: A comprehensive meta-analysis of randomized clinical trials. *PLoS ONE, 9*(5). https://doi.org/10.1371/journal.pone.0096905

Gumusoglu, S. B., Schickling, B. M., Vignato, J. A., Santillan, D. A., & Santillan, M. K. (2022). Selective serotonin reuptake inhibitors and preeclampsia: A quality assessment and meta-analysis. *Pregnancy Hypertension, 30*, 36–43. https://doi.org/10.1016/j.preghy.2022.08.001

Hahn, L., Eickhoff, S. B., Habel, U., Stickeler, E., Schnakenberg, P., Goecke, T. W., Stickel, S., Franz, M., Dukart, J., & Chechko, N. (2021). Early identification of postpartum depression using demographic, clinical, and digital phenotyping. *Translational Psychiatry, 11*(1), 121. https://doi.org/10.1038/s41398-021-01245-6

Halvorsen, A., Hesel, B., Østergaard, S. D., & Danielsen, A. A. (2019). In utero exposure to selective serotonin reuptake inhibitors and development of mental disorders: A systematic review and meta-analysis. *Acta Psychiatrica Scandinavica, 139*(6), 493–507. https://doi.org/10.1111/acps.13030

Hansotte, E., Payne, S. I., & Babich, S. M. (2017). Positive postpartum depression screening practices and subsequent mental health treatment for

low-income women in Western countries: A systematic literature review. *Public Health Reviews, 38*(1), 3. https://doi.org/10.1186/s40985-017-0050-y

Hayes, B., & Muller, R. (2004). Prenatal Depression: A Randomized Controlled Trial in the Emotional Health of Primiparous Women. *Research and theory for nursing practice, 18,* 165–183. https://doi.org/10.1891/088971804780957072

He, L., Soh, K. L., Huang, F., Khaza'ai, H., Geok, S. K., Vorasiha, P., Chen, A., & Ma, J. (2023). The impact of physical activity intervention on perinatal depression: A systematic review and meta-analysis. *Journal of Affective Disorders, 321*, 304–319. https://doi.org/10.1016/j.jad.2022.10.026

Hoertel, N., López, S., Peyre, H., Wall, M. M., González-Pinto, A., Limosin, F., & Blanco, C. (2015). Are symptom features of depression during pregnancy, the postpartum period and outside the peripartum period distinct? Results from a nationally representative sample using Item Response Theory (IRT). *Depression and Anxiety, 32*(2), 129–140. https://doi.org/10.1002/da.22334

Höflich, A., Kautzky, A., Slamanig, R., Kampshoff, J., & Unger, A. (2022). Depressive symptoms as a transdiagnostic mediator of mother-to-infant bonding: Results from a psychiatric mother-baby unit. *Journal of Psychiatric Research, 149*, 37–43. https://doi.org/10.1016/j.jpsychires.2022.02.005

Huang, L., Zhao, Y., Qiang, C., & Fan, B. (2018). Is cognitive behavioral therapy a better choice for women with postnatal depression? A systematic review and meta-analysis. *PloS One, 13*(10), e0205243. https://doi.org/10.1371/journal.pone.0205243

Huang, R., Yan, C., Tian, Y., Lei, B., Yang, D., Liu, D., & Lei, J. (2020). Effectiveness of peer support intervention on perinatal depression: A systematic review and meta-analysis. *Journal of Affective Disorders, 276*, 788–796. https://doi.org/10.1016/j.jad.2020.06.048

Hutchens, B. F., & Kearney, J. (2020). Risk factors for postpartum depression: An umbrella review. *Journal of Midwifery & Women's Health, 65*(1), 96–108. https://doi.org/10.1111/jmwh.13067

Jans, L. A. W., Giltay, E. J., & Willem Van Der Does, A. J. (2010). The efficacy of n-3 fatty acids DHA and EPA (fish oil) for perinatal depression. *British Journal of Nutrition, 104*(11), 1577–1585. https://doi.org/10.1017/s0007114510004125

Jarbou, N. S., & Newell, K. A. (2022). Exercise and yoga during pregnancy and their impact on depression: A systematic literature review. *Archives of Women's Mental Health, 25*(3), 539–559. https://doi.org/10.1007/s00737-021-01189-2

Jiang, H., Xu, L., Li, Y., Deng, M., Peng, C., & Ruan, B. (2016). Antidepressant use during pregnancy

and risk of postpartum hemorrhage: A systematic review and meta-analysis. *Journal of Psychiatric Research, 83*, 160–167. https://doi.org/10.1016/j.jpsychires.2016.09.001

Jiang, X., Li, H., Wang, D., Shan, L., Kang, Y., & Wang, F. (2022). Efficacy of nondrug interventions in perinatal depression: A meta-analysis. *Psychiatry Research, 317*. https://doi.org/10.1016/j.psychres.2022.114916

Kashani, L., Eslatmanesh, S., Saedi, N., Niroomand, N., Ebrahimi, M., Hosseinian, M., Foroughifar, T., Salimi, S., & Akhondzadeh, S. (2017). Comparison of saffron versus fluoxetine in treatment of mild to moderate postpartum depression: A double-blind, randomized clinical trial. *Pharmacopsychiatry, 50*(2), 64–68. https://doi.org/10.1055/s-0042-115306

Kautzky, A., Slamanig, R., Unger, A., & Höflich, A. (2022). Neonatal outcome and adaption after in utero exposure to antidepressants: A systematic review and meta-analysis. *Acta Psychiatrica Scandinavica, 145*(1), 6–28. https://doi.org/10.1111/acps.13367

Kettunen, P., Koistinen, E., & Hintikka, J. (2014). Is postpartum depression a homogenous disorder: Time of onset, severity, symptoms and hopelessness in relation to the course of depression. *BMC Pregnancy and Childbirth, 14*, 402. https://doi.org/10.1186/s12884-014-0402-2

Kieffer, E. C., Caldwell, C. H., Welmerink, D. B., Welch, K. B., Sinco, B. R., & Guzmán, J. R. (2013). Effect of the healthy MOMs lifestyle intervention on reducing depressive symptoms among pregnant Latinas. *American Journal of Community Psychology, 51*(1–2), 76–89. https://doi.org/10.1007/s10464-012-9523-9

Kiewa, J., Meltzer-Brody, S., Milgrom, J., Guintivano, J., Hickie, I. B., Whiteman, D. C., Olsen, C. M., Colodro-Conde, L., Medland, S. E., Martin, N. G., Wray, N. R., & Byrne, E. M. (2022). Perinatal depression is associated with a higher polygenic risk for major depressive disorder than non-perinatal depression. *Depression and Anxiety, 39*(3), 182–191. https://doi.org/10.1002/da.23232

Kim, D. R., Sockol, L., Barber, J. P., Moseley, M., Lamprou, L., Rickels, K., O'Reardon, J. P., & Epperson, C. N. (2011). A survey of patient acceptability of repetitive transcranial magnetic stimulation (TMS) during pregnancy. *Journal of Affective Disorders, 129*(1–3), 385–390. https://doi.org/10.1016/j.jad.2010.08.027

Kim, D. R., Wang, E., McGeehan, B., Snell, J., Ewing, G., Iannelli, C., O'Reardon, J. P., Sammel, M. D., & Epperson, C. N. (2019). Randomized controlled trial of transcranial magnetic stimulation in pregnant women with major depressive disorder. *Brain Stimulation, 12*(1), 96–102. https://doi.org/10.1016/j.brs.2018.09.005

Kittel-Schneider, S., Felice, E., Buhagiar, R., Lam-

bregtse-van den Berg, M., Wilson, C. A., Banjac Baljak, V., Vujovic, K. S., Medic, B., Opankovic, A., Fonseca, A., & Lupattelli, A. (2022). Treatment of peripartum depression with antidepressants and other psychotropic medications: A synthesis of clinical practice guidelines in Europe. *International Journal of Environmental Research and Public Health, 19*(4), Artigo 4. https://doi.org/10.3390/ijerph19041973

Komori, A., Arthur, A., Radford, S., Tan, H. Y., Zheng, L., An, M., Umeda, R., & Zheng, Z. (2018). Acupuncture versus antidepressants in the management of postpartum depression: A systematic review. *British Journal Of Midwifery*. https://www.britishjournalofmidwifery.com/content/research/acupuncture-versus-antidepressants-in-the-management-of-postpartum-depression-a-systematic-review/

Konstantinou, G., Vigod, S., Mehta, S., Daskalakis, Z., & Blumberger, D. (2020). A systematic review of non-invasive neurostimulation for the treatment of depression during pregnancy. *Journal of Affective Disorders, 272*, 259–268. https://doi.org/10.1016/j.jad.2020.03.151

Kurzeck, A., Kirsch, B., Weidinger, E., Padberg, F., & Palm, U. (2018). Transcranial Direct Current Stimulation (tDCS) for depression during pregnancy: Scientific evidence and what is being said in the media-A systematic review. *Brain Sciences, 8*(8). https://doi.org/10.3390/brainsci8080155

Lau, Y., Yen, K. Y., Wong, S. H., Cheng, J. Y., & Cheng, L. J. (2022). Effect of digital cognitive behavioral therapy on psychological symptoms among perinatal women in high income-countries: A systematic review and meta-regression. *Journal of Psychiatric Research, 146*, 234–248. https://doi.org/10.1016/j.jpsychires.2021.11.012

Laurin, A., Nard, N., Dalmont, M., Bulteau, S., Benard, C., Bonnot, O., Winer, N., Dupont, F., Apter, G., Terranova-Commessie, F., Guillin, O., El-Hage, W., Sauvaget, A., & Rotharmel, M. (2022). Efficacy and safety of Transcranial Electric Stimulation during the perinatal period: A systematic literature review and three case reports. *Journal of Clinical Medicine, 11*(14). https://doi.org/10.3390/jcm11144048

Lee, E. W., Denison, F. C., Hor, K., & Reynolds, R. M. (2016). Web-based interventions for prevention and treatment of perinatal mood disorders: A systematic review. *BMC Pregnancy and Childbirth, 16,* 38. https://doi.org/10.1186/s12884-016-0831-1

Lee, Y., Kim, K.-H., Lee, B.-H., & Kim, Y.-K. (2021). Plasma level of brain-derived neurotrophic factor (BDNF) in patients with postpartum depression. *Progress in Neuro-Psychopharmacology & Biological Psychiatry, 109,* 110245. https://doi.org/10.1016/j.pnpbp.2021.110245

Legazpi, P. C. C., Rodríguez-Muñoz, M. F., Le,

H.-N., Balbuena, C. S., Olivares, M. E., & Méndez, N. I. (2022). Suicidal ideation: Prevalence and risk factors during pregnancy. *Midwifery, 106*, 103226. https://doi.org/10.1016/j.midw.2021.103226

Leiknes, K., Cooke, M., Jarosch-von Schweder, L., Harboe, I., & Hoie, B. (2015). Electroconvulsive therapy during pregnancy: A systematic review of case studies. *Archives of Women's Mental Health, 18*(1), 1–39. https://doi.org/10.1007/s00737-013-0389-0

Leshem, R., Bar-Oz, B., Diav-Citrin, O., Gbaly, S., Soliman, J., Renoux, C., & Matok, I. (2021). Selective Serotonin Reuptake Inhibitors (SSRIs) and Serotonin Norepinephrine Reuptake Inhibitors (SNRIs) during pregnancy and the risk for Autism Spectrum Disorder (ASD) and Attention deficit hyperactivity disorder (ADHD) in the offspring: A true effect or a bias? A systematic review & meta-analysis. *Current Neuropharmacology*, *19*(6), 896–906. https://doi.org/10.2174/1570159X19666210303121059

Letourneau, N., Stewart, M., Dennis, C.-L., Hegadoren, K., Duffett-Leger, L., & Watson, B. (2011). Effect of home-based peer support on maternal-infant interactions among women with postpartum depression: A randomized, controlled trial. *International Journal of Mental Health Nursing, 20*(5), 345–357. https://doi.org/10.1111/J.1447-0349.2010.00736.x

Leung, M. T. Y., Wong, K. H., Ho, P. W. H., Ip, P., Wei, L., Wong, I. C. K., & Man, K. K. C. (2021). Gestational exposure to antidepressants and risk of seizure in offspring: A systematic review and meta-analysis. *Neuroscience and Biobehavioral Reviews, 131*, 345–359. https://doi.org/10.1016/j.neubiorev.2021.09.040

Leung, S. S. L., Leung, C., Lam, T. H., Hung, S. F., Chan, R., Yeung, T., Miao, M., Cheng, S., Leung, S. H., Lau, A., & Lee, D. T. S. (2011). Outcome of a postnatal depression screening programme using the Edinburgh Postnatal Depression Scale: A randomized controlled trial. *Journal of Public Health (Oxford, England), 33*(2), 292–301. https://doi.org/10.1093/pubmed/fdq075

Li, L., Yue, S.-W., Xu, J., Qiao, J., Redding, S. R., & Ouyang, Y.-Q. (2023). Effectiveness of Internet-based psychological interventions for treating perinatal depression: A systematic review and meta-analysis. *Journal of Clinical Nursing, 32*(13–14), 3087–3101. https://doi.org/10.1111/jocn.16399

Li, S., Zhong, W., Peng, W., & Jiang, G. (2018). Effectiveness of acupuncture in postpartum depression: A systematic review and meta-analysis. *Acupuncture in Medicine, 36*(5), 295–301. https://doi.org/10.1136/acupmed-2017-011530

Li, W., Yin, P., Lao, L., & Xu, S. (2019). Effectiveness of acupuncture used for the management of Postpartum Depression: A systematic review and meta-analysis. *BioMed Research International,*

2019. https://doi.org/10.1155/2019/6597503

Li, X., Laplante, D. P., Paquin, V., Lafortune, S., Elgbeili, G., & King, S. (2022). Effectiveness of cognitive behavioral therapy for perinatal maternal depression, anxiety and stress: A systematic review and meta-analysis of randomized controlled trials. *Clinical Psychology Review, 92*, 102129. https://doi.org/10.1016/j.cpr.2022.102129

Li, Y., Chen, Z., Yu, N., Yao, K., Che, Y., Xi, Y., & Zhai, S. (2016). Chinese herbal medicine for Postpartum Depression: A systematic review of randomized controlled trials. *Evidence-Based Complementary and Alternative Medicine, 2016*, 5284234. https://doi.org/10.1155/2016/5284234

Li, Z., Liu, Y., Wang, J., Liu, J., Zhang, C., & Liu, Y. (2020). Effectiveness of cognitive behavioural therapy for perinatal depression: A systematic review and meta-analysis. *Journal of Clinical Nursing, 29*(17–18), 3170–3182. https://doi.org/10.1111/jocn.15378

Lin, I. H., Huang, C. Y., Chou, S. H., & Shih, C. L. (2022). Efficacy of prenatal yoga in the treatment of depression and anxiety during pregnancy: A systematic review and meta-analysis. *International Journal of Environmental Research and Public Health, 19*(9). https://doi.org/10.3390/ijerph19095368

Lin, P. Z., Xue, J. M., Yang, B., Li, M., & Cao, F. L. (2018). Effectiveness of self-help psychological interventions for treating and preventing postpartum depression: A meta-analysis. *Archives of women's mental health*. https://link.springer.com/article/10.1007/s00737-018-0835-0

Liu, X., Huang, S., Hu, Y., & Wang, G. (2022). The effectiveness of telemedicine interventions on women with postpartum depression: A systematic review and meta-analysis. *Worldviews on Evidence-Based Nursing, 19*(3), 175–190. https://doi.org/10.1111/wvn.12576

Liu, X., Wang, G., & Cao, Y. (2022). Physical exercise interventions for perinatal depression symptoms in women: A systematic review and meta-analysis. *Frontiers of Psychology, 13*, 1022402. https://doi.org/10.3389/fpsyg.2022.1022402

Long, M. M., Cramer, R. J., Jenkins, J., Bennington, L., & Paulson, J. F. (2019). A systematic review of interventions for healthcare professionals to improve screening and referral for perinatal mood and anxiety disorders. *Archives of Women's Mental Health, 22*(1), 25–36. https://doi.org/10.1007/s00737-018-0876-4

Lopez-Yarto, M., Ruiz-Mirazo, E., Holloway, A. C., Taylor, V. H., & McDonald, S. D. (2012). Do psychiatric medications, especially antidepressants, adversely impact maternal metabolic outcomes? *Journal of Affective Disorders, 141*(2–3), 120–129. https://doi.org/10.1016/j.jad.2012.01.043

Lou, Z.-Q., Zhou, Y.-Y., Zhang, X., & Jiang, H.-Y. (2022). Exposure to selective noradrenalin reuptake inhibitors during the first trimester of pregnancy and risk of congenital malformations: A meta-analysis of cohort studies. *Psychiatry Research, 316,* 114756. https://doi.org/10.1016/j.psychres.2022.114756

Loughnan, S. A., Joubert, A. E., Grierson, A., Andrews, G., & Newby, J. M. (2019). Internet-delivered psychological interventions for clinical anxiety and depression in perinatal women: A systematic review and meta-analysis. *Archives of Women's Mental Health, 22*(6), 737–750. https://doi.org/10.1007/s00737-019-00961-9

Man, K. K. C., Chan, E. W., Ip, P., Coghill, D., Simonoff, E., Chan, P. K. L., Lau, W. C. Y., Schuemie, M. J., Sturkenboom, M. C. J. M., & Wong, I. C. K. (2018). Prenatal antidepressant exposure and the risk of attention-deficit hyperactivity disorder in children: A systematic review and meta-analysis. *Neuroscience and Biobehavioral Reviews, 86*, 1–11. https://doi.org/10.1016/j.neubiorev.2017.12.007

Manber, R., Schnyer, R. N., Allen, J. J. B., Rush, A. J., & Blasey, C. M. (2004). Acupuncture: A promising treatment for depression during pregnancy. *Journal of Affective Disorders, 83*(1), 89–95. https://doi.org/10.1016/j.jad.2004.05.009

Manber, R., Schnyer, R. N., Lyell, D., Chambers, A. S., Caughey, A. B., Druzin, M., Carlyle, E., Celio, C., Gress, J. L., Huang, M. I., Kalista, T., Martin-Okada, R., & Allen, J. J. B. (2010). Acupuncture for depression during pregnancy: A randomized controlled trial. *Obstetrics and Gynecology, 115*(3), 511–520. https://doi.org/10.1097/AOG.0b013e3181cc0816

Marcos-Nájera, R., Rodríguez-Muñoz, M. de la F., Soto Balbuena, C., Olivares Crespo, M. E., Izquierdo Méndez, N., Le, H.-N., & Escudero Gomis, A. (2020). The prevalence and risk Factors for antenatal depression among pregnant immigrant and native women in Spain. *Journal of Transcultural Nursing, 31*(6), 564–575. https://doi.org/10.1177/1043659619891234

Martín-Gómez, C., Moreno-Peral, P., Bellón, J. A., Conejo-Cerón, S., Campos-Paino, H., Gómez-Gómez, I., Rigabert, A., Benítez, I., & Motrico, E. (2022). Effectiveness of psychological interventions in preventing postpartum depression in non-depressed women: A systematic review and meta-analysis of randomized controlled trials. *Psychological Medicine, 52*(6), 1001–1013. https://doi.org/10.1017/S0033291722000071

Masarwa, R., Bar-Oz, B., Gorelik, E., Reif, S., Perlman, A., & Matok, I. (2019). Prenatal exposure to selective serotonin reuptake inhibitors and serotonin norepinephrine reuptake inhibitors and risk for persistent pulmonary hypertension of the newborn: A systematic review, meta-analysis, and network meta-analysis. *American Journal of Obstetrics and Gynecology, 220*(1), 57.e1-57.e13. https://doi.

org/10.1016/j.ajog.2018.08.030

Matthey, S., Kavanagh, D. J., Howie, P., Barnett, B., & Charles, M. (2004). Prevention of postnatal distress or depression: An evaluation of an intervention at preparation for parenthood classes. *Journal of Affective Disorders, 79*(1–3), 113–126. https://doi.org/10.1016/S0165-0327(02)00362-2

McCurdy, A. P., Boulé, N. G., Sivak, A., & Davenport, M. H. (2017). Effects of exercise on mild-to-moderate depressive symptoms in the postpartum period: A meta-analysis. *Obstetrics & Gynecology, 129*(6), 1087–1097. https://doi.org/10.1097/aog.0000000000002053

Mendelson, T., Cluxton-Keller, F., Vullo, G. C., Tandon, S. D., & Noazin, S. (2017). NICU-based Interventions to reduce maternal depressive and anxiety symptoms: A meta-analysis. *Pediatrics, 139*(3), e20161870. https://doi.org/10.1542/peds.2016-1870

Míguez, M. C., & Vázquez, M. B. (2021). Risk factors for antenatal depression: A review. *World Journal of Psychiatry, 11*(7), 325. https://doi.org/10.5498/wjp.v11.i7.325

Milgrom, J., Schembri, C., Ericksen, J., Ross, J., & Gemmill, A. W. (2011). Towards parenthood: An antenatal intervention to reduce depression, anxiety and parenting difficulties. *Journal of Affective Disorders, 130*(3), 385–394. https://doi.org/10.1016/j.jad.2010.10.045

Missler, M., Donker, T., Beijers, R., Ciharova, M., Moyse, C., de Vries, R., Denissen, J., & van Straten, A. (2021). Universal prevention of distress aimed at pregnant women: A systematic review and meta-analysis of psychological interventions. *BMC Pregnancy and Childbirth, 21*(1), 276. https://doi.org/10.1186/s12884-021-03752-2

Mitchell, J., & Goodman, J. (2018). Comparative effects of antidepressant medications and untreated major depression on pregnancy outcomes: A systematic review. *Archives of Women's Mental Health, 21*(5), 505–516. https://doi.org/10.1007/s00737-018-0844-z

Mocking, R. J. T., Steijn, K., Roos, C., Assies, J., Bergink, V., Ruhé, H. G., & Schene, A. H. (2020). Omega-3 fatty acid supplementation for Perinatal Depression: A meta-analysis. *Journal of Clinical Psychiatry, 81*(5). https://doi.org/10.4088/JCP.19r13106

Mohammad-Alizadeh-Charandabi, S., Malakoti, J., Sohrabi, F., & Shokranian, N. (2013). The effect of telephone support on postpartum depression: A randomized controlled trial. *Journal of Caring Sciences, 2*(2), 147–155. https://doi.org/10.5681/jcs.2013.018

Molyneaux, E., Telesia, L. A., Henshaw, C., Boath, E., Bradley, E., & Howard, L. M. (2018). Antidepressants for preventing postnatal depression. *The Cochrane Database of Systematic Reviews, 2018*(4).

https://doi.org/10.1002/14651858.CD004363.pub3

Morrell, C. J., Sutcliffe, P., Booth, A., Stevens, J., Scope, A., Stevenson, M., Harvey, R., Bessey, A., Cantrell, A., Dennis, C.-L., Ren, S., Ragonesi, M., Barkham, M., Churchill, D., Henshaw, C., Newstead, J., Slade, P., Spiby, H., & Stewart-Brown, S. (2016). A systematic review, evidence synthesis and meta-analysis of quantitative and qualitative studies evaluating the clinical effectiveness, the cost-effectiveness, safety and acceptability of interventions to prevent postnatal depression. *Health Technology Assessment (Winchester, England), 20*(37), 1–414. https://doi.org/10.3310/hta20370

Morrell, C. J., Warner, R., Slade, P., Dixon, S., Walters, S., Paley, G., & Brugha, T. (2009). Psychological interventions for postnatal depression: Cluster randomised trial and economic evaluation. The PoNDER trial. *Health Technology Assessment (Winchester, England), 13*(30), iii–iv, xi–xiii, 1–153. https://doi.org/10.3310/hta13300

Motrico, E., Moreno-Peral, P., Uriko, K., Hancheva, C., Brekalo, M., Ajaz, E., Apter, G., Bramante, A., Conejo-Cerón, S., Christoforou, A., Dikmen-Yildiz, P., Evagorou, O., Fonseca, A., Lupattelli, A., Radoš, S. N., al Maach, N., Rodriguez-Muñoz, M. F., Žutić, M., & Lambregtse - van den Berg, M. P. (2022). Clinical practice guidelines with recommendations for perinatal depression: A European systematic review. *Acta Psychiatrica Scandinavica, 146*(4), 325–339. https://doi.org/10.1111/acps.13478

Nakić Radoš, S., Hairston, I., & Handelzalts, J. E. (2023). The concept analysis of parent-infant bonding during pregnancy and infancy: A systematic review and meta-synthesis. *Journal of Reproductive and Infant Psychology, 0*(0), 1–24. https://doi.org/10.1080/02646838.2022.2162487

Nillni, Y. I., Mehralizade, A., Mayer, L., & Milanovic, S. (2018). Treatment of depression, anxiety, and trauma-related disorders during the perinatal period: A systematic review. *Clinical Psychology Review, 66*, 136–148. https://doi.org/10.1016/j.cpr.2018.06.004

O'Connor, E., Rossom, R. C., Henninger, M., Groom, H. C., & Burda, B. U. (2016). Primary care screening for and treatment of depression in pregnant and postpartum women: Evidence report and systematic review for the US P4rreventive Services Task Force. *JAMA, 315*(4), 388–406. https://doi.org/10.1001/jama.2015.18948

O'Connor, E., Senger, C. A., Henninger, M. L., Coppola, E., & Gaynes, B. N. (2019). Interventions to prevent perinatal depression: Evidence report and systematic review for the US Preventive Services Task Force. *JAMA, 321*(6), 588–601. https://doi.org/10.1001/jama.2018.20865

O'Mahen, H. A., Richards, D. A., Woodford, J., Wilkinson, E., McGinley, J., Taylor, R. S., & Warren, F. C. (2014). Netmums: A phase II randomized con-

trolled trial of a guided Internet behavioural activation treatment for postpartum depression. *Psychological Medicine, 44*(8), 1675–1689. https://doi.org/10.1017/S0033291713002092

O'Mahen, H. A., Woodford, J., McGinley, J., Warren, F. C., Richards, D. A., Lynch, T. R., & Taylor, R. S. (2013). Internet-based behavioral activation--treatment for postnatal depression (Netmums): A randomized controlled trial. *Journal of Affective Disorders, 150*(3), 814–822. https://doi.org/10.1016/j.jad.2013.03.005

Orsolini, L., & Bellantuono, C. (2015). Serotonin reuptake inhibitors and breastfeeding: A systematic review. *Human Psychopharmacology, 30*(1), 4–20. https://doi.org/10.1002/hup.2451

Pacheco, F., Guiomar, R., Brunoni, A., Buhagiar, R., Evagorou, O., Roca-Lecumberri, A., Poleszczyk, A., Berg, M., Caparros-Gonzalez, R., Fonseca, A., Osorio, A., Soliman, M., & Ganho-Avila, A. (2021). Efficacy of non-invasive brain stimulation in decreasing depression symptoms during the peripartum period: A systematic review. *Journal of Psychiatric Research, 140*, 443–460. https://doi.org/10.1016/j.jpsychires.2021.06.005

Peng, L., Fu, C., Xiong, F., Zhang, Q., Liang, Z., Chen, L., He, C., & Wei, Q. (2020). Effects of repetitive transcranial magnetic stimulation on depression symptoms and cognitive function in treating patients with postpartum depression: A systematic review and meta-analysis of randomized controlled trials. *Psychiatry Research, 290.* https://doi.org/10.1016/j.psychres.2020.113124

Peng, Z., Zhou, C., Xue, S., Bai, J., Yu, S., LI, X., WANG, H., & TAN, Q. (2018). Mechanism of Repetitive Transcranial Magnetic Stimulation for Depression. *Shanghai Archives of Psychiatry, 30*(2), 84–92. https://doi.org/10.11919/j.issn.1002-0829.217047

Pfeiffer, P. N., Heisler, M., Piette, J. D., & Rogers, M. A. M. (2011). Efficacy of peer support interventions for depression: A meta-analysis. *General Hospital Psychiatry*. https://www.sciencedirect.com/science/article/pii/S0163834310001982

Pompili, M., Dominici, G., Giordano, G., Longo, L., Serafini, G., Lester, D., Amore, M., & Girardi, P. (2014). Electroconvulsive treatment during pregnancy: A systematic review. *Expert Review of Neurotherapeutics, 14*(12), 1377–1390. https://doi.org/10.1586/14737175.2014.972373

Ponting, C., Mahrer, N. E., Zelcer, H., Schetter, C. D., & Chavira, D. A. (2020). Psychological interventions for depression and anxiety in pregnant latina and black women in the United States: A systematic review. *Clinical Psychology & Psychotherapy, 27*(2), 249–265. https://doi.org/10.1002/cpp.2424

Poyatos-León, R., & García-Hermoso, A. (2017). Effects of exercise-based interventions on postpar-

tum depression: A meta-analysis of randomized controlled trials. *Birth.* https://onlinelibrary.wiley.com/doi/abs/10.1111/birt.12294

Rathi, A., Khapre, S., Chavada, J., Gupta, S., & Singla, T. (2022). Postpartum depression and Its biological biomarkers. *Cureus, 14*(11), e31124. https://doi.org/10.7759/cureus.31124

Ravesteyn, L. M. V., Berg, M. P. L. V. D., Hoogendijk, W. J. G., & Kamperman, A. M. (2017). Interventions to treat mental disorders during pregnancy: A systematic review and multiple treatment meta-Analysis. *PLoS ONE, 12*(3). https://doi.org/10.1371/journal.pone.0173397

Robichaud, K. (2008). *The effects of an exercise intervention on the psychological well-being of postpartum women /*. http://jewlscholar.mtsu.edu/handle/mtsu/4064

Roman, M., Constantin, T., & Bostan, C. M. (2020). The efficiency of online cognitive-behavioral therapy for postpartum depressive symptomatology: A systematic review and meta-analysis. *Women & Health, 60*(1), 99–112. https://doi.org/10.1080/03630242.2019.1610824

Rommel, A.-S., Bergink, V., Liu, X., Munk-Olsen, T., & Molenaar, N. M. (2020). Long-term effects of intrauterine exposure to antidepressants on physical, neurodevelopmental, and psychiatric outcomes: A Systematic review. *The Journal of Clinical Psychiatry, 81*(3), 19r12965. https://doi.org/10.4088/JCP.19r12965

Sacher, J., Chechko, N., Dannlowski, U., Walter, M., & Derntl, B. (2020). The peripartum human brain: Current understanding and future perspectives. *Frontiers in Neuroendocrinology, 59*, 100859. https://doi.org/10.1016/j.yfrne.2020.100859

Saeedi, S. (2013). Effect of exercise program on symptoms of postpartum depression. *Iranian Journal of Obstetrics, Gynecology and Infertility, 15*, 26–31.

Saligheh, M., Hackett, D., Boyce, P., & Cobley, S. (2016). The effectiveness of exercise on weight loss and postnatal depression: A systematic review. *European Psychiatry*. https://www.infona.pl/resource/bwmeta1.element.elsevier-a792c8e2-9211-323f-84c4-6f303ae4843c

Saligheh, M., Hackett, D., Boyce, P., & Cobley, S. (2017). Can exercise or physical activity help improve postnatal depression and weight loss? A systematic review. *Archives of Women's Mental Health, 20*(5), 595–611. https://doi.org/10.1007/s00737-017-0750-9

Salzbrenner, S., Breeden, A., Jarvis, S., & Rodriguez, W. (2011). A 48-year-old woman primigravid via in vitro fertilizattion with severe bipolar depression and preeclampsia treated successfully eith electroconvulsive herapy. *The Journal of ECT, 27*(1), e1. https://doi.org/10.1097/YCT.0b013e3181ca4d22

Schünemann, H., Brozec, J., Guyatt, G., & Oxman,

A. (Eds.). (2013). *The GRADE handbook for grading quality of evidence and strength of recommendations. Updated October 2013.* The GRADE Working Group.

Screening and Diagnosis of Mental Health Conditions During Pregnancy and Postpartum: ACOG Clinical Practice Guideline No. 4. (2023). *Obstetrics and Gynecology, 141*(6), 1232–1261. https://doi.org/10.1097/AOG.0000000000005200

Shamshiri Milani, H., Azargashb, E., Beyraghi, N., Defaie, S., & Asbaghi, T. (2015). Effect of telephone-based support on postpartum depression: A randomized controlled trial. *International Journal of Fertility and Sterility, 9*(2), 247–253. https://doi.org/10.22074/ijfs.2015.4246

Shea, B. J., Reeves, B. C., Wells, G., Thuku, M., Hamel, C., Moran, J., Moher, D., Tugwell, P., Welch, V., Kristjansson, E., & Henry, D. A. (2017). AMSTAR 2: A critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. *British Medical Journal, 358*, j4008. https://doi.org/10.1136/bmj.j4008

Shen, Z.-Q., Gao, S.-Y., Li, S. X., Zhang, T.-N., Liu, C.-X., Lv, H.-C., Zhang, Y., Gong, T.-T., Xu, X., Ji, C., Wu, Q.-J., & Li, D. (2017). Sertraline use in the first trimester and risk of congenital anomalies: A systemic review and meta-analysis of cohort studies. *British Journal of Clinical Pharmacology, 83*(4), 909–922. https://doi.org/10.1111/bcp.13161

Shivakumar, G., Brandon, A. R., Snell, P. G., Santiago-Muñoz, P., Johnson, N. L., Trivedi, M. H., & Freeman, M. P. (2011). Antenatal depression: A rationale for studying exercise. *Depression & Anxiety, 28*(3), 234–242. https://doi.org/10.1002/da.20777

Shorey, S., Chee, C. Y. I., Ng, E. D., Lau, Y., Dennis, C.-L., & Chan, Y. H. (2019). Evaluation of a technology-based peer-support intervention program for preventing Postnatal Depression (Part 1): Randomized controlled trial. *Journal of Medical Internet Research, 21*(8), e12410. https://doi.org/10.2196/12410

Shortis, E., Warrington, D., & Whittaker, P. (2020). The efficacy of cognitive behavioral therapy for the treatment of antenatal depression: A systematic review. *Journal of Affective Disorders, 272*, 485–495. https://doi.org/10.1016/j.jad.2020.03.067

Slomian, J., Honvo, G., Emonts, P., Reginster, J.-Y., & Bruyère, O. (2019). Consequences of maternal postpartum depression: A systematic review of maternal and infant outcomes. *Women's Health, 15*, 1–55. https://doi.org/10.1177/1745506519844044

Smith, C., Shewamene, Z., Galbally, M., Schmied, V., & Dahlen, H. (2019). The effect of complementary medicines and therapies on maternal anxiety and depression in pregnancy: A systematic review and meta-analysis. *Journal of Affective Disorders, 245*, 428–439. https://doi.org/10.1016/j.jad.2018.11.054

Sockol, L. E. (2015). A systematic review of the efficacy of cognitive behavioral therapy for treating and preventing perinatal depression. *Journal of Affective Disorders, 177*, 7–21. https://doi.org/10.1016/j.jad.2015.01.052

Sockol, L. E. (2018). A systematic review and meta-analysis of interpersonal psychotherapy for perinatal women. *Journal of Affective Disorders, 232*, 316–328. https://doi.org/10.1016/j.jad.2018.01.018

Sparling, T. M., Henschke, N., Nesbitt, R. C., & Gabrysch, S. (2017). The role of diet and nutritional supplementation in perinatal depression: A systematic review. *Maternal & Child Nutrition, 13*(1). https://doi.org/10.1111/mcn.12235

Stickel, S., Eickhoff, S. B., Habel, U., Stickeler, E., Goecke, T. W., Lang, J., & Chechko, N. (2021). Endocrine stress response in pregnancy and 12 weeks postpartum—Exploring risk factors for postpartum depression. *Psychoneuroendocrinology, 125*, 105122. https://doi.org/10.1016/j.psyneuen.2020.105122

Sun, Y., Li, Y., Wang, J., Chen, Q., Bazzano, A. N., & Cao, F. (2021). Effectiveness of ssmartphone-based mindfulness training on maternal perinatal depression: A randomized controlled trial. *Journal of Medical Internet Research, 23*(1), e23410. https://doi.org/10.2196/23410

Sun, Y., Xu, X., Zhang, J., & Chen, Y. (2018). Treatment of depression with Chai Hu Shu Gan San: A systematic review and meta-analysis of 42 randomized controlled trials. *BMC Complementary and Alternative Medicine, 18*(1), 66. https://doi.org/10.1186/s12906-018-2130-z

Suradom, C., Suttajit, S., Oon-arom, A., Maneeton, B., & Srisurapanont, M. (2021). Omega-3 polyunsaturated fatty acid (n-3 PUFA) supplementation for prevention and treatment of perinatal depression: A systematic review and meta-analysis of randomized-controlled trials. *Nordic Journal of Psychiatry, 75*(4), 239–246. https://doi.org/10.1080/08039488.2020.1843710

Thiel, F., Pittelkow, M.-M., Wittchen, H.-U., & Garthus-Niegel, S. (2020). The relationship between paternal and maternal depression during the perinatal period: A systematic review and meta-analysis. *Frontiers in Psychiatry, 11*. https://www.frontiersin.org/articles/10.3389/fpsyt.2020.563287

Thomas, N., Komiti, A., & Judd, F. (2014). Pilot early intervention antenatal group program for pregnant women with anxiety and depression. *Archives of Women's Mental Health, 17*(6), 503–509. https://doi.org/10.1007/s00737-014-0447-2

Thombs, B. D., Arthurs, E., Coronado-Montoya, S., Roseman, M., Delisle, V. C., Leavens, A., Levis, B., Azoulay, L., Smith, C., Ciofani, L., Coyne, J. C., Feeley, N., Gilbody, S., Schinazi, J., Stewart, D. E., & Zelkowitz, P.

(2014). Depression screening and patient outcomes in pregnancy or postpartum: A systematic review. *Journal of Psychosomatic Research, 76*(6), 433–446. https://doi.org/10.1016/j.jpsychores.2014.01.006

Tiwari, A., Leung, W. C., Leung, T. W., Humphreys, J., Parker, B., & Ho, P. C. (2005). A randomised controlled trial of empowerment training for Chinese abused pregnant women in Hong Kong. *BJOG: An International Journal of Obstetrics and Gynaecology, 112*(9), 1249–1256. https://doi.org/10.1111/j.1471-0528.2005.00709.x

Tong, P., Dong, L. P., Yang, Y., Shi, Y. H., Sun, T., & Bo, P. (2019). Traditional Chinese acupuncture and postpartum depression: A systematic review and meta-analysis. *Journal of the Chinese Medical Association, 82*(9), 719–726. https://doi.org/10.1097/jcma.0000000000000140

Treatment and Management of Mental Health Conditions During Pregnancy and Postpartum: ACOG Clinical Practice Guideline No. 5. (2023). *Obstetrics and Gynecology, 141*(6), 1262–1288. https://doi.org/10.1097/AOG.0000000000005202

Uguz, F. (2021). The relationship between maternal antidepressants and neonatal hypoglycemia: A systematic review. *Alpha Psychiatry, 22*(5), 224–229. https://doi.org/10.1530/alphapsychiatry.2021.21143

van der Zee-van den Berg, A. I., Boere-Boonekamp, M. M., IJzerman, M. J., Haasnoot-Smallegange, R. M. E., & Reijneveld, S. A. (2017). Screening for Postpartum Depression in well-baby care settings: A systematic review. *Maternal and Child Health Journal, 21*(1), 9–20. https://doi.org/10.1007/s10995-016-2088-8

Vigod, S. N., Murphy, K. E., Dennis, C.-L., Oberlander, T. F., Ray, J. G., Daskalakis, Z. J., & Blumberger, D. M. (2019). Transcranial direct current stimulation (tDCS) for depression in pregnancy: A pilot randomized controlled trial. *Brain Stimulation: Basic, Translational, and Clinical Research in Neuromodulation, 12*(6), 1475–1483. https://doi.org/10.1016/j.brs.2019.06.019

Vlenterie, R., van Gelder, M. M. H. J., Anderson, H. R., Andersson, L., Broekman, B. F. P., Dubnov-Raz, G., El Marroun, H., Ferreira, E., Fransson, E., van der Heijden, F. M. M. A., Holzman, C. B., Kim, J. J., Khashan, A. S., Kirkwood, B. R., Kuijpers, H. J. H., Lahti-Pulkkinen, M., Mason, D., Misra, D., Niemi, M., … Roeleveld, N. (2021). Associations between maternal depression, antidepressant use during pregnancy, and adverse pregnancy outcomes: An Individual participant data meta-analysis. *Obstetrics & Gynecology, 138*(4), 633–646. https://doi.org/10.1097/AOG.0000000000004538

Vollbehr, N. K., Bartels-Velthuis, A. A., & Nauta, M. H. (2018). Hatha yoga for acute, chronic and/or treatment-resistant mood and anxiety disorders: A systematic review and meta-analysis. *PLoS ONE.*

Wang, D., Li, Y.-L., Qiu, D., & Xiao, S.-Y. (2021). Fac-

tors influencing paternal postpartum depression: A systematic review and meta-analysis. *Journal of Affective Disorders, 293*, 51–63. https://doi.org/10.1016/j.jad.2021.05.088

Wang, G., Liang, C., & Sun, G. (2022). Yoga's therapeutic effect on perinatal depression: A systematic review and meta-analysis. *Psychiatric Danubio, 34*(2), 195–204. https://doi.org/10.24869/psyd.2022.195

Wang, L., Fan, Y., He, J., Liu, H., Chen, F., Dan, H., Zhao, J., Zhang, J., Wang, T., & Liu, X. (2022). Efficacy and safety of Shuganjieyu Capsule alone or in combination with other antidepressants in the treatment of Postpartum Depression: A meta-analysis. *Evidence-based Complementary and Alternative Medicine : eCAM, 2022*, 5260235. https://doi.org/10.1155/2022/5260235

Wang, Z., Liu, J., Shuai, H., Cai, Z., Fu, X., Liu, Y., Xiao, X., Zhang, W., Krabbendam, E., Liu, S., Liu, Z., Li, Z., & Yang, B. X. (2021). Mapping global prevalence of depression among postpartum women. *Translational Psychiatry, 11*(1), Artigo 1. https://doi.org/10.1038/s41398-021-01663-6

Waqas, A., Koukab, A., Meraj, H., Dua, T., Chowdhary, N., Fatima, B., & Rahman, A. (2022). Screening programs for common maternal mental health disorders among perinatal women: Report of the systematic review of evidence. *BMC Psychiatry, 22*(1), 54. https://doi.org/10.1186/s12888-022-03694-9

Wei-Hong, L., Cheng-Gui, Z., Peng-Fei, G., Heng, L., & Jian-Fang, Y. (2017). Omega-3 fatty acids as monotherapy in treating depression in pregnant women: A Meta-Analysis of randomized controlled trials. *Iran Journal of Pharmacy Research, 16(4)*, 1593–1599. https://www.embase.com/search/results?subaction=viewrecord&id=L619223794&from=export

Wilkinson, A., Anderson, S., & Wheeler, S. B. (2017). Screening for and treating postpartum depression and psychosis: A cost-effectiveness analysis. *Maternal and Child Health Journal, 21*(4), 903–914. https://doi.org/10.1007/s10995-016-2192-9

Wirz-Justice, A., Bader, A., Frisch, U., Stieglitz, R.-D., Alder, J., Bitzer, J., Hösli, I., Jazbec, S., Benedetti, F., Terman, M., Wisner, K. L., & Riecher-Rössler, A. (2011). A randomized, double-blind, placebo-controlled study of light therapy for antepartum depression. *The Journal of Clinical Psychiatry, 72*(7), 986–993. https://doi.org/10.4088/JCP.10m06188blu

Xing, D., Wu, R., Chen, L., & Wang, T. (2020). Maternal use of antidepressants during pregnancy and risks for adverse perinatal outcomes: A meta-analysis. *Journal of Psychosomatic Research, 137*, 110231. https://doi.org/10.1016/j.jpsychores.2020.110231

Xue, W., Cheng, K., Xu, D., Jin, X., & Gong, W. (2020). Uptake of referrals for women with positive perinatal depression screening results and the effectiveness of interventions to increase uptake: A systematic review and meta-analysis. *Epidemiology and Psychiatric Sciences, 29*, e143. https://doi.org/10.1017/S2045796020000554

Yang, L., Di, Y. M., Shergis, J. L., Li, Y., Zhang, A. L., Lu, C., Guo, X., & Xue, C. C. (2018). A systematic review of acupuncture and Chinese herbal medicine for postpartum depression. *Complementary Therapies in Clinical Practice, 33*, 85–92. https://doi.org/10.1016/j.ctcp.2018.08.006

Yang, M., Jia, G., Sun, S., Ye, C., Zhang, R., & Yu, X. (2019). Effects of an online mindfulness intervention focusing on attention monitoring and acceptance in pregnant women: A randomized controlled trial. *Journal of Midwifery & Women's Health, 64*(1), 68–77. https://doi.org/10.1111/jmwh.12944

Yang, W. J., Bai, Y. M., Qin, L., Xu, X. L., Bao, K. F., Xiao, J. L., & Ding, G. W. (2019). The effectiveness of music therapy for postpartum depression: A systematic review and meta-analysis. *Complementary Therapies in Clinical Practice, 37*, 93–101. https://doi.org/10.1016/j.ctcp.2019.09.002

Yasuma, N., Narita, Z., Sasaki, N., Obikane, E., Sekiya, J., Inagawa, T., Nakajima, A., Yamada, Y., Yamazaki, R., Matsunaga, A., Saito, T., Watanabe, K., Imamura, K., Kawakami, N., & Nishi, D. (2020). Antenatal psychological intervention for universal prevention of antenatal and postnatal depression: A systematic review and meta-analysis. *Journal of Affective Disorders, 273*, 231–239. https://doi.org/10.1016/j.jad.2020.04.063

Yawn, B. P., Olson, A. L., Bertram, S., Pace, W., Wollan, P., & Dietrich, A. J. (2012). Postpartum Depression: Screening, diagnosis, and management Programs 2000 through 2010. *Depression Research & Treatment, 2012*, 363964. https://doi.org/10.1155/2012/363964

Yin, X., Sun, N., Jiang, N., Xu, X., Gan, Y., Zhang, J., Qiu, L., Yang, C., Shi, X., Chang, J., & Gong, Y. (2021). Prevalence and associated factors of antenatal depression: Systematic reviews and meta-analyses. *Clinical Psychology Review, 83*, 101932. https://doi.org/10.1016/j.cpr.2020.101932

Yuan, M., Chen, H., Chen, D., Wan, D., Luo, F., Zhang, C., Nan, Y., Bi, X., & Liang, J. (2022). Effect of physical activity on prevention of postpartum depression: A dose-response meta-analysis of 186,412 women. *Frontiers in Psychiatry, 13*. https://www.frontiersin.org/articles/10.3389/fpsyt.2022.984677

Zeng, M., Gong, A., & Wu, Z. (2022). Paroxetine combined with traditional chinese medicine pre-

scriptions in the treatment of postpartum depression: A systematic review of randomized controlled trials. *Frontiers of Neuroendocrinology, 67*. https://doi.org/10.1016/j.yfrne.2022.101019

Zhang, H., & Emory, E. K. (2015). A mindfulness-based intervention for pregnant African-American women. *Mindfulness, 6*(3), 663–674. https://doi.org/10.1007/s12671-014-0304-4

Zhang, M. M., Zou, Y., Li, S. M., Wang, L., Sun, Y. H., Shi, L., Lu, L., Bao, Y. P., & Li, S. X. (2020). The efficacy and safety of omega-3 fatty acids on depressive symptoms in perinatal women: A meta-analysis of randomized placebo-controlled trials. *Translational Psychiatry, 10*(1). https://doi.org/10.1038/s41398-020-00886-3

Zhao, L., Chen, J., Lan, L., Deng, N., Liao, Y., Yue, L., Chen, I., Wen, S. W., & Xie, R.-H. (2021). Effectiveness of telehealth interventions for women with postpartum depression: Systematic review and meta-analysis. *JMIR mHealth and uHealth, 9*(10), e32544. https://doi.org/10.2196/32544

Zhao, X., Liu, Q., Cao, S., Pang, J., Zhang, H., Feng, T., Deng, Y., Yao, J., & Li, H. (2018). A meta-analysis of Selective Serotonin Reuptake Inhibitors (SSRIs) use during prenatal depression and risk of low birth weight and small for gestational age. *Journal of Affective Disorders, 241*, 563–570. https://doi.org/10.1016/j.jad.2018.08.061

Zheng, W., Cai, D.-B., Zheng, W., Sim, K., Ungvari, G. S., Peng, X.-J., Ning, Y.-P., Wang, G., & Xiang, Y.-T. (2019). Brexanolone for postpartum depression: A meta-analysis of randomized controlled studies. *Psychiatry Research, 279*, 83–89. https://doi.org/10.1016/j.psychres.2019.07.006

Zhou, C., Hu, H., Wang, C., Zhu, Z., Feng, G., Xue, J., & Yang, Z. (2020). The effectiveness of mHealth interventions on postpartum depression: A systematic review and meta-analysis. *Journal of Telemedicine Telecare*, 1357633X20917816. https://doi.org/10.1177/1357633x20917816

Zhu, Y., Wang, R., Tang, X., Li, Q., Xu, G., & Zhang, A. (2021). The effect of music, massage, yoga and exercise on antenatal depression: A meta-analysis. *Journal of Affective Disorders, 292*, 592–602. https://doi.org/10.1016/j.jad.2021.05.122

I. Appendices

I. // Appendices

Appendix 1. The Guidelines Development Group

Table i. GDG members' professional roles and affiliations

Name	Roles	Affiliation
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Ilaria LEGA	Psychiatrist, Researcher	Istituto Superiore di Sanità, Rome, Italy

Name	Roles	Affiliation
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Greg SHEAF	**Information Specialist**	**The Library of Trinity College Dublin, Ireland**
Alkistis SKALKIDOU	**Professor of Obstetrics and Gynaecology; Senior Consultant in Obstetrics and Gynaecology**	**Department of Women's and Children's Health, Uppsala University, Uppsala, Sweden; Outpatient Gynaecological Department, Akademiska University Hospital, Uppsala**
Ana UKA	**Counselling Psychologist, Researcher**	**Research Centre for Sustainable Development and Innovation, University College "Beder", Tirana, Albania**

Name	Roles	Affiliation
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Laurence VAN DEN ABEELE	Patient Representative	Make Mothers Matter, EU Delegation, Brussels, Belgium

Declaration of conflict of interest

All members of the Guidelines Development Group were asked to declare their possible conflicts of interest by filling out a conflict-of-interest disclosure form.

Table ii. Conflict of interest disclosure

Name	Roles
Rena BINA	No conflict of interest to declare
Ana GANHO ÁVILA	The following conflicts of interest are declared: Research support from companies (tDCS assessories and rTMS certification course registration by Soterix Medical Inc.) Compensation in the form of free home-based medical devices (tDCS) for consulting services on the advisory board from Flow NeuroscienceTM, Malmö, Sweden).
Sarah KITTEL-SCHNEIDER	No conflict of interest to declare
Mijke P. LAMBREGTSE-VAN DEN BERG	No conflict of interest to declare
Ilaria LEGA	No conflict of interest to declare
Angela LUPATTELLI	No conflict of interest to declare
Mariana MOURA RAMOS	No conflict of interest to declare
Sandra NAKIĆ RADOŠ	No conflict of interest to declare
Maria F. RODRIGUEZ-MUÑOZ	No conflict of interest to declare

Greg SHEAF	**The following conflicts of interest are declared:**
Alkistis SKALKIDOU	**No conflict of interest to declare**
Ana UKA	**No conflict of interest to declare**
Susanne UUSITALO	**No conflict of interest to declare**
Laurence VAN DEN ABEELE	**No conflict of interest to declare**

Appendix 2. The Guidelines Development Group

ACOG	American College of Obstetricians and Gynecologists
ACT	Acceptance Commitment Therapy
AD	Antidepressant
ADHD	Attention Deficit/Hyperactivity Disorder
APA	American Psychiatric Association
arTMS	accelerated transcranial magnetic stimulation
ASD	Autism Spectrum Disorder
BA	Behavioural activation
BLT	Bright light therapy
CBT	Cognitive Behavioural Therapy
CES -D	Center for Epidemiologic Studies Depression Scale
CI	Confidence Interval
COST	European Cooperation in Science and Technology
CPGs	Clinical Practice Guidelines
DHA	Docosahexaenoic Acid
ECT	Electroconvulsive therapy
EPA	Eicosapentaenoic Acid
EPDS	Edinburgh Postnatal Depression Scale
FA	Fatty acids
GPP	Good Practice Point
HAM-D	Hamilton Depression Rating Scale
HDRS-17	Hamilton Rating Scale for Depression
HCP	Health Care Professional
HF	High Frequency
IPT	Interpersonal Therapy
IPV	Intimate partner violence
IQ	Intelligence Quotient
ITBS	Intermittent theta burst stimulation

LF	Low Frequency
LNS	Letter Number sequencing
MC	Management Committee of the Riseup PPD
MDD	Major Depressive Disorder
MHCP	Mental Health Professionals
NICU	Neonatal intensive care unit
NNT	Number needed to treat
PA	Physical activity
PCA	Person Centered Approach
PDA	Patients' decision aid
PDSS	Postpartum Depression Screening Scale
PHQ	Patient Health Questionnaire
PPHN	Persistent pulmonary hypertension of the newborn
PPD	Peripartum Depression
OR	Odds ratio
PUFA	Polyunsaturated fatty acids
QALY	Quality adjusted life years
RCT	Randomised Controlled Trial
RiseUp PPD	COST Action Research Innovation and Sustainable Pan European Network in Peripartum Depression Disorder
rDLPFC	right dorsolateral prefrontal cortex
RR	Ratio risk effect size
rTMS	Repetitive Transcranial Magnetic Stimulation
RVOTD	Right ventricular outflow tract defects
RU-GDG	Riseup PPD Guidelines Development Group
SAS	Self-rating Anxiety Scale
SCID	Structured Clinical Interview for DSM Disorders
SGA	Small for gestational age
SIGH-SAD	Structured Interview Guide for the Hamilton Depression Rating Scale - Seasonal Affective Disorders
SMD	Standardised Mean Difference

SR	**Systematic review**
SNRI	**Serotonin and norepinephrine reuptake inhibitors**
SSRI	**Selective serotonin reuptake inhibitors**
STAI	**State Trait Anxiety Inventory**
tACS	**Transcranial alternating current stimulation**
TAU	**Treatment as usual**
TCA	**Tricyclic antidepressants**
tDCS	**Transcranial direct current stimulation**
TES	**Transcranial Electrical Stimulation**
TMT	**Trail Making Test**
TNS	**Transcranial Vagus Nerve Stimulation**
WMD	**Weighted mean difference**

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