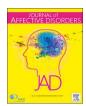
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Review article

Emerging issues and questions on peripartum depression prevention, diagnosis and treatment: a consensus report from the cost action riseup-PPD



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ABSTRACT

Background: Peripartum depression [PPD] is a public health problem which has been widely studied. Nonetheless, study findings and clinical guidelines for PPD treatment differ among countries and the condition is still underdiagnosed and undertreated, suggesting the importance of a global understanding of PPD. The Riseup-PPD Cost Action aims to establish a Pan-European and multidisciplinary network of researchers dedicated to the global understanding of PPD.

Methods: A literature search was performed in different databases (e.g., Medline, PsychInfo) including a combination of terms related with PPD diagnosis, prevention, treatment and cost-effectiveness of its management. A narrative synthesis of the literature, together with a critical overview of the current issues/questions to be addressed within the topic of PPD were performed.

Results: Emerging issues include challenges regarding definition and timing of PPD; heterogeneity in severity, timing of onset and assessment tools; comparative effectiveness of preventive and treatment interventions; help seeking for PPD; improving health professional's awareness of PPD; and cost-effectiveness of PPD management. Limitations: The main limitation is the non-systematic nature of the literature search.

Conclusions: The Riseup-PPD network will deal with these challenges through four lines of action: (1)provide an updated and comprehensive synthesis of existing knowledge that can contribute to inform clinical recommendations and guidelines for PPD management; (2) clarify inconsistent findings concerning diagnosis, prevention and treatment of PPD; (3) develop new lines of research in the field of PPD; and (4) develop international recommendations for PPD diagnosis, prevention and treatment, ultimately influencing maternal mental health policymaking at global and local levels.

1. Introduction

Peripartum depression [PPD] may be broadly defined as a non-psychotic depressive episode of mild to major severity that may occur during pregnancy or in the first year after childbirth (Gavin et al., 2005; Gelaye et al., 2016). PPD has been recognized as a public health problem that should be tackled to boost the overall health of populations (Muñoz, 2019), with the World Health Organization [WHO] positioning

maternal depression as an issue of global significance (Meaney, 2018; Miranda and Patel, 2005; WHO, 2013). Despite decades of inter-disciplinary research that focused on its characteristics, risk factors, consequences, prevention and treatment, a global understanding of PPD is still lacking. Three reasons seem to justify this need.

First, PPD is a prevalent condition worldwide, although existing studies report a wide range of prevalence estimates across countries (Halbreich and Karkun, 2006; Norhayati et al., 2015). A deeper look at

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these findings indicates that existing estimates suffer from methodological heterogeneity (e.g., diversity of instruments and sampling methods), lack of global coverage, and primarily focus on the postpartum period (Gavin et al., 2005; Gelaye et al., 2016; Woody et al., 2017). A recent systematic review showed an overall PPD prevalence of 11.9%, with women in low-and-middle-income countries (LMIC) showing a higher prevalence of depression compared to women in high-income countries (HIC), both in the prepartum (LMIC: 19.2% vs. HIC: 9.2%) and in the postpartum (LMIC: 18.7% vs. HIC: 9.5%) periods (Woody et al., 2017). A global understanding of cross-national variations in PPD prevalence may help identify global and national economic, health and policy factors that should be considered in prevention and treatment efforts of this clinical condition (Hahn-Holbrook et al., 2018).

Second, the broad-reaching effects of PPD on mothers, children and families, seem to be universal across different cultures and countries (Field, 2010). When left untreated, PPD may negatively impact the mother's physical and psychological health (Slomian et al., 2019) and be associated with higher rates of suicidality (Orsolini et al., 2016). Indeed, perinatal suicidality, including completed suicides, suicide attempts, suicidal ideation and thoughts of self-harm, has been acknowledged as one of the leading causes of maternal mortality in the first twelve months postpartum (Lindahl et al., 2005). Additionally, it can effect the mother-child interaction (Raine et al., 2019; Slomian et al., 2019; Tronick and Reck, 2009), caregiving activities (Field, 2010) and child attachment (Sliwerski et al., 2020). Ultimately, PPD can result in detrimental effects on the fetus (Field et al., 2006) and on the child's development, e.g., socioemotional and cognitive development (Kingston et al., 2012; Slomian et al., 2019; Stein et al., 2014). The strong societal and economic burden of PPD (e.g., Bauer et al., 2014) across countries and societies suggests the relevance of global approaches to reduce its impact.

Third, despite the prevalence and pervasive consequences of PPD, this clinical condition is still underdiagnosed and undertreated or treated below evidence-based standards (Alhusen and Alvarez, 2016; Vesga-Lopez et al., 2008). Although different treatment options (e.g., psychotherapy, psychopharmacotherapy) are available for PPD, the decision-making process to select the best option for each case may be complex. Therefore, distinctive profiles of the condition (genetic, endocrinal, symptoms clusters, the onset of symptoms, comorbidity, associated psychosocial risk factors) should be considered along with the safeness and effectiveness of therapies and women's preferences (Patel and Wisner, 2011), highlighting the need for a personalized approach to treatment. Although the existence of clinical practice guidelines (CPGs) for PPD management may facilitate this decision-making process, a recent review of these guidelines (Molenaar et al., 2018) identified that only 12 countries (the USA, Canada, Denmark, Germany, Norway, Spain, United Kingdom and the Netherlands, China, Australia, New Zealand, Singapore) have published CPGs considering the use of an antidepressant in the peripartum period. While some countries report the existence of common clinical practice guidelines (e.g., Israel, Malta), several countries, including European countries (e.g., Austria, Belgium, France, Luxembourg, Portugal, Sweden, Switzerland) report the absence of national guidelines for managing this condition (Molenaar et al., 2018). Moreover, most of the existing clinical guidelines were not specifically developed for the peripartum period, and there are discordant guidelines concerning some topics (e.g., the continuation of antidepressant use during pregnancy; Molenaar et al., 2018). These concerns may lead to disparities and inequalities in PPD management, not only between different countries (e.g., countries with vs. without CPGs), but also within the same country, if these clinical guidelines are absent. A global consensus on clinical recommendations and guidelines for PPD management, while taking into account national variations and a structured approach to implementation, may increase the number of women worldwide who gain access to evidence-based standard management care for PPD; ultimately enhancing the proportion of women effectively diagnosed and treated.

Taking into account these reasons for adopting a global approach to PPD, the Riseup-PPD COST Action "Research Innovation and Sustainable Pan-European Network in Peripartum Depression Disorder" (CA18138) aims to establish a Pan-European and multidisciplinary network of researchers dedicated to the global understanding of PPD, from prevention and diagnosis, to treatment and global impact; considering women, newborns and the wider family and social systems. The network currently includes researchers and clinicians from 28 COST countries (including Israel) plus the USA, Brazil, Canada and Monaco, with various backgrounds and expertise (e.g., Psychology, Psychiatry, Midwifery, Obstetrics/Gynecology, Infant Mental Health, Social Work, Pharmacoepidemiology, Anthropology, Health Economics, Statistics, Ethics), as well as representatives of end-users' associations. One of the main contributions of the Riseup-PPD network will be to provide the community of researchers and health professionals working in the field of PPD with a synthesis of the state-of-the-art knowledge concerning diagnosis criteria, prevention and treatment of PPD. In this narrative review, we aim to present a critical overview of the current emerging issues and questions concerning PPD diagnosis, prevention, treatment and cost-effectiveness of its management. Based on this narrative review, we aim to present a consensus about the main lines of action that should be taken within the scope of the Riseup-PPD framework to tackle the emerging issues and questions in the field of PPD.

2. Methods

This paper reports findings from a comprehensive narrative synthesis of previously published information on the topic of PPD. A literature search was performed between September and October 2019, to identify relevant publications in the field of PPD. Although no time restrictions were imposed as a search criterion, more attention was given to papers published in the last 15 years. The literature search utilized various databases (e.g., Medline, PsychInfo) using a combination of broad search terms, including peripartum depression (e.g., peripartum depression OR prepartum depression OR postpartum depression), diagnosis (e.g., diagnosis OR diagnostic criteria OR diagnostic tools), prevention (e.g., preventive interventions OR prevention OR prevention approaches), treatment (e.g., psychological treatment OR psychopharmachological treatment OR innovative treatment approaches OR non-invasive neuromodulation) and cost-effectiveness (e.g., cost-effectiveness OR cost-utility). Peer-reviewed articles were considered if their main focus was diagnosis, prevention, treatment or management cost-effectiveness of peripartum depression. Papers addressing bipolar depression in the peripartum period were not included in this narrative review. A representative sample of the existent literature was summarized in the form of a narrative synthesis, coupled with a critical overview of the current issues and questions that should be addressed within the topic of PPD. Particular emphasis was given to a) prior systematic reviews and meta-analyses that systematize the state-of-the-art knowledge concerning diagnosis, prevention, treatment or cost-effectiveness of PPD; and b) empirical studies on PPD which contribute to identifying important challenges or issues that should be further addressed.

3. Results

The literature was summarized and critically discussed in the context of the main challenges (issues and questions) in the PPD field which remain unaddressed, specifically regarding each of the following topics: Diagnosis of PPD, Prevention of PPD, Treatment of PPD and Cost-effectiveness of PPD management.

3.1. Diagnosis of PPD

There are several challenges to the diagnosis of PPD, with the

definition and timing of PPD being a major one. According to the Diagnostic and Statistical Manual of Mental Disorders (DSM-5; American Psychiatric Association [APA], 2013), PPD is diagnosed as any other depressive episode alongside 'a peripartum onset' specifier, if the onset of mood symptoms occurs during pregnancy or within 4 weeks postpartum. However, the WHO defined PPD as an onset of a major depressive episode during pregnancy or within the first 12 months postpartum. The absence of a consensus regarding what constitutes the peripartum period has implications for research and practice, as different time frames (e.g., 4 weeks postpartum, 12 months postpartum) are used for different purposes (O'Hara and McCabe, 2013), as well as for clinical registry of PPD cases.

Moreover, there seems to be substantial heterogeneity in severity. timing of onset (pregnancy vs. postpartum) and history of previous mood or other psychiatric disorders in cases of PPD (Putnam et al., 2015), which raises questions regarding its distinct subtypes. The 'Postpartum Depression: Action Towards Causes and Treatment (PACT) Consortium' identified five distinct subtypes of PPD (severe anxious depression, moderate anxious depression, anxious anhedonia, pure anhedonia, and resolved depression) which signify clear differences in symptom quality and time of onset (Putnam et al., 2017). In addition, general practitioners and obstetric and mental health care providers face difficulties in diagnosing PPD in clinical practice, whether due to the overlap of depressive symptoms with pregnancy or postpartum-related symptoms (e.g., loss of energy, disturbed sleep, and changes in appetite and weight) (Boyd et al., 2011; Ford et al., 2017a) or to women's difficulty in recognizing their experience of depressive symptoms during or after pregnancy. This may occur because of women's difficulty to distinguish between depressive symptoms and normative distress associated with transition to parenthood (Bilszta et al., 2010) or because of feelings of guilt, shame and stigma which result in concealing or denying their condition (Button et al., 2017). Altogether these complexities make it difficult for practitioners to apply the general diagnostic criteria for depression (Ford et al., 2017a).

Finally, assessments tools for identifying and diagnosing PPD vary, making it difficult to reach a consensus regarding PPD diagnosis and prevalence. The most widespread screening instrument is the Edinburgh Postnatal Depression Scale (EPDS), followed by the Patient Health Questionnaire-9 (PHQ-9) and the Beck Depression Inventory (BDI-II) (Moraes et al., 2017). However, these screening instruments focus primarily on symptom severity, and not on duration, impairment or possibility of symptom attribution to other psychiatric or medical conditions; therefore, they should not replace a clinical diagnosis for PPD. As far as we know, no specific standardized instruments and procedures for diagnosing PPD are available for clinical practice and research.

A related important note should be made concerning the clinical assessment of suicidal ideation and suicide attempts, which are diagnostic criterions for a major depressive episode (APA, 2013). Suicidal ideation predicts later suicidal attempts (Mundt et al., 2013) and should therefore be carefully assessed during the perinatal period. The PPD screening tools, e.g., the EPDS or the PHQ-9, contain a one-item question regarding suicidal ideation. However, a proper risk assessment for suicidal ideation among mothers presenting with depressive symptoms may be helpful for identifying mothers at medium (suicidal ideation with a plan or history of suicide attempt, without an immediate intent) or high-risk (suicidal ideation with an immediate intent) suicidal behaviour, enabling a prompt development and implementation of a safety plan (Orsolini et al., 2016).

3.2. Prevention of PPD

A preventive perspective regarding PPD has emerged over the past few years (e.g., O'Connor et al., 2019; Sockol et al., 2013), resulting in implementation of various preventive interventions for PPD and consequently raising important questions concerning their effectiveness.

Numerous studies have examined the effectiveness of preventive interventions for PPD and these findings were synthesized in several literature reviews and/or meta-analyses, which focused primarily on the prevention of postpartum depression. Only a small number of reviews compared the effectiveness of various preventive interventions (Morrell et al., 2016; O'Connor et al., 2019; Sangsawang et al., 2018; Sockol et al., 2013), while others focused on the effectiveness of a specific intervention. The latter include the preventive effect of physical activity (Carter et al., 2019; Davenport et al., 2018; Nakamuraa et al., 2019), various psychotherapeutic models (e.g., Cognitive Behavioral Therapy [CBT], Sockol, 2015; Interpersonal therapy [IPT], Sockol, 2018; or Family Therapy, Cluxton-Keller and Bruce, 2018), dietary supplements (Miller et al., 2013), anti-depressants (Molyneaux et al., 2018) or home-based interventions (Leis et al., 2009).

Overall, these preventive interventions seem promising; however, some of them were examined in only a single study and some lack enough evidence to reach clear-cut conclusions regarding their effectiveness, indicating that more rigorous studies are needed. In addition, a comprehensive synthesis of the current literature is necessary to examine the comparative effectiveness of different types of preventive interventions (e.g., psychological, psychosocial, pharmacological and health behavior interventions) for PPD. Other important gaps in the literature which should be addressed are i) studies on preventive interventions for prepartum depression; ii) studies aimed at understanding which preventive interventions work for low-resourced communities (e.g., immigrants, low-income, ethnically diverse; Clarke et al., 2013); iii) studies examining the comparative effectiveness of preventive interventions delivered in LMIC and HIC; and iv) studies examining cessation of smoking and consumption of caffeine, alcohol and other substances before and during pregnancy for prevention of PPD (Jacka et al., 2012).

Another important challenge that needs to be tackled in the field of PPD prevention is the promotion of women's professional help-seeking for PPD. Several review studies synthesized the literature on professional help-seeking barriers and facilitators for peripartum psychological distress (e.g., Button et al., 2017), PPD (Reilly et al., 2019) or postpartum depression (e.g., Bina, 2019; Dennis and Chung-Lee, 2006; Hadfield and Wittkowski, 2017). These reviews provided an overall summary of intra-personal, interpersonal, communal and system-bases barriers and facilitators to seeking help. As prepartum depression is one of the strongest predictors of postpartum depression (Beck, 2001), there is a need to examine professional help-seeking barriers and facilitators specifically during the prepartum period and compare findings from reviews done in the pre- versus the postpartum periods. Also, as screening programs are being implemented around the world (Milgrom and Gemmill, 2014), there is a need to examine the effect of PPD screening programs on professional help-seeking and mental health outcomes. There is also a need to examine the effect of interventions to increase help-seeking on actual treatment uptake.

Finally, another important challenge in the field is to improve health professional's awareness of PPD, as they can assist in supporting women with early-onset symptoms and refer them early on for help when needed (Bina, 2019). To our knowledge, only one literature review was found regarding general practitioners' awareness and management of PPD (Ford et al., 2017b); however, other front-line workers (e.g., OB/GYN, Nurses, Midwives) also play an important role in its recognition and management. Moreover, there is no evidence concerning the effectiveness of interventions to improve awareness of the impact of PPD, although some individual studies targeted healthcare professionals' awareness, knowledge and attitudes regarding PPD and its screening and management (e.g., Bina et al., 2019).

3.3. Treatment of PPD

3.3.1. Psychopharmacological treatments for PPD

For women with moderate to severe depression in the peripartum period, treatment with psychotropic medications, most commonly antidepressants, is often required. One important challenge to address relates to prescription and use of psychotropic medication during the peripartum period. In Europe, the prevalence of gestational use of antidepressants is between 1-3%, while anxiolytics/sedatives and antipsychotics are less commonly prescribed (range of use <1% to 1%) (Lupattelli et al., 2014; Zoega et al., 2015). Generally, the use of psychotropics decreases substantially from three months before pregnancy to the first trimester, and so forth during pregnancy, increasing slightly in the early postpartum period (Engeland et al., 2018). It is now wellestablished that pregnancy constitutes a major reason for discontinuation of psychotropic medication, even when the drug may be needed. In fact, researchers found that only 10% of women on an antidepressant treatment before pregnancy and 19-38% of those on an antipsychotic treatment still received these pharmacotherapies at the start of the third trimester (Petersen et al., 2011, 2014). Even in the context of continued psychotropic treatment, about half of pregnant women (49%) show low medication adherence (Lupattelli et al., 2015). Not least, postpartum use of psychotropics is associated with lower breastfeeding rates (Leggett et al., 2016). Discordant findings and lack of information regarding neonatal and maternal safety during and after use of psychotropics have posed significant challenges for clinicians and women in assessing the risk of pharmacotherapy versus the risk of non-medicated maternal illness (Howard et al, 2014; Koren and Nordeng, 2012; Spigset and Nordeng, 2016).

Moreover, studies on peripartum women have almost exclusively focused on the risks of psychotropic treatment, with very little attention given to its benefits. The current knowledge gaps, regarding the effectiveness of psychotropic drugs during pregnancy and as a preventive treatment for postpartum mental illness, have major implications for evidence-based decision making by clinicians as well as by women themselves (Molyneaux et al., 2018; Sharma, 2017). To date, only two trials with 81 participants have examined the benefit of antidepressants (nortriptyline and sertraline) on PPD (Molyneaux et al., 2018). This may be one of the reasons why current clinical guidelines regarding treatment with psychotropics in peripartum women are at times discordant (Molenaar et al., 2018). In 2019, the Food and Drug Administration in the US approved the first drug specifically for postpartum depression treatment, the GABA-A receptor modulator brexanolone, and regulatory pathways have been initiated for its approval in Europe. Comparative data between brexanolone infusion and other pharmacotherapies is lacking given its recent approval, but this may eventually constitute an important therapeutic option for women with severe postpartum depression (Kanes et al., 2017). Nevertheless, the riskbenefit ratio of this new pharmacotherapy remains a crucial point to assess for each woman and her newborn individually, while considering the fact that the prolonged administration form (IV infusion over a total of 60 hours) of brexanolone, its elevated cost, and the need for maternal-child interaction monitoring may be detrimental for some new mothers.

3.3.2. Psychological treatments for PPD

Several meta-analyses and systematic reviews have documented the efficacy of psychological treatments for pre- and postpartum depression (Cuijpers et al., 2008; Dennis and Hodnett, 2007; Sockol et al., 2011); however, one important question concerns the comparative effectiveness of different psychotherapeutic models and delivery formats. CBT is the psychotherapeutic model that seems to have the most empirical support for PPD treatment (Huang et al., 2018; Sockol, 2015), although there is also evidence of the effectiveness of IPT (Miniati et al., 2014; Sockol, 2018). Other less investigated psychological approaches include psychodynamic therapy (e.g., Tambelli et al., 2015), psychoeducative

interventions (e.g., Shorey et al. 2015), non-directive counselling (e.g., Ramenzi et al., 2017) or interpersonal therapy interventions to improve the mother-infant relationship (e.g., King et al., 2015). In addition to the most traditional individual face-to-face delivery format, there is some evidence on the effectiveness of group therapy format (grounded in CBT or IPT) in reducing PPD symptoms (Goodman and Santangelo, 2011; Scope et al., 2013), as well as of e-health interventions, which are mostly grounded in CBT models (Ashford et al., 2016). However, these other delivery formats are often not considered in clinical guidelines for PPD management. Finally, the benefits of including the partner in the interventions have also been discussed (Alves et al., 2018), although further evidence is needed.

Despite the progress in the field, there are still other issues that must be addressed. First, it is necessary to identify which therapeutic options (e.g., psychotherapeutic model, delivery format) work best for each person, depending on the onset of symptoms (pre- vs. postpartum), its severity and/or the presence of previous mental health disorders (Navarro et al., 2016). There is also the need to better understand the mechanisms that explain the treatment response (Ammerman et al., 2012). Second, it is important to advance knowledge concerning the long-term effects of psychological interventions for PPD, as well as the prevention of its relapse in future pregnancies (Dennis and Hodnett, 2007). Finally, further evidence is needed concerning the effectiveness of psychological interventions for PPD in specific populaas low-income women (e.g., Gajaria Ravindram, 2018; Munoz et al., 2007), immigrant women who need culturally-adapted interventions (Rojas et al., 2014), adolescent mothers (Yozwiak, 2010), or women with a previous history of substance use, an abuse history, or chronic illness (Ross and Dennis, 2009).

3.3.3. Other innovative approaches for PPD treatment

Due to an increased demand for non-pharmacological approaches to treating PPD, strategies such as non-implantable neuromodulation (NIN), light therapy, exercise or Omega-3 fatty acids have been under scrutiny in the last decade, yet questions remain concerning the efficacy and safety of these innovative approaches.

NINs includes a set of techniques aiming at modulating the brain activity and connectivity patterns using electric currents delivered through the scalp. Whereas non-convulsive NINs are well tolerated and show promising efficacy in treating depressive symptoms in mild to moderate postpartum depression (Kim et al., 2019), convulsive NINs are recommended for clinically severe and treatment-resistant patients, showing high clinical evidence and fast treatment responses (Rundgren et al., 2018) but leading to cognitive side effects (Engel and Kayser, 2016; Semkovska et al., 2012). Due to its effectiveness, good tolerability, safety profile and potential acceptability, non-convulsive NINs have been discussed to manage not only postpartum depression (Ganho-Ávila et al., 2019), but also depression during pregnancy (Cole et al., 2019). Both repetitive transcranial magnetic stimulation (rTMS) (Cole et al., 2019) and transcranial direct current stimulation (tDCS) (Sreeraj et al., 2016; Vigod et al., 2019), showed promising evidence of their effectiveness in reducing depressive symptoms during pregnancy, with no negative outcomes for young mothers or pregnant women, although a potential association with preterm birth in the case of rTMS should be further examined (Kim et al., 2019). Nonetheless, further research is needed to determine the safety and efficacy of nonconvulsive NINs in the peripartum period to gather the needed evidence for its adoption as a treatment approach for PPD. Moreover, the efficacy of photobiomodulation using red/near infra-red light has been suggested in major depressive disorders (Cassano et al., 2016) and should be explored as a non-invasive alternative for PPD.

Light therapy, which is another non-pharmacological alternative to reduce depressive symptoms, is argued to address insufficient light exposure, counteract pathological hormonal and serotonergic profiles and regulate sleep and fatigue (Crowley and Youngstedt, 2012). However, previous data from one open pilot study and four randomized

controlled trials were inconsistent regarding its efficacy in the postpartum period (Swanson et al., 2018). Finally, whereas results from studies assessing the benefits of exercise, mega-3 fatty acids, and acupuncture are mixed, studies assessing the benefits of yoga and perinatal massage do not benefit of unbiased data (Nillni et al., 2018).

3.4. Cost-effectiveness of PPD management

Untreated maternal depression may have important implications regarding the public assistance system (e.g., work disability), health system (e.g., poor health outcomes), early intervention and education systems (e.g., given its impact on the child's development and academic performance), and the child and welfare system (Sontag-Padilla et al., 2013). These implications may translate into high economic costs for society. One important question to be answered is whether these potential costs may be reduced or eliminated by focusing on or adding resources to prevention, identification (screening) and treatment efforts to reduce PPD incidence. A recent systematic review concerning the cost-effectiveness of interventions for PPD included eight studies (four in the UK, two in the USA, one in Australia and one in Canada) and concluded that the methodological heterogeneity across studies makes it difficult to draw conclusions about the cost-effectiveness of interventions for PPD (Camacho and Shields, 2018). It is, therefore, important that further studies assessing screening, prevention and treatment interventions in this field include methodologically sound reports of economic evaluations that facilitate future evidence synthesis.

4. Discussion

This narrative review provided a synthesis of the state-of-the-art knowledge regarding diagnosis, prevention and treatment of PPD, and contributed to the identification of several important questions that remain to be answered concerning these issues. In addition, this review highlighted the impact of these issues on the way PPD is viewed by professionals and researchers, e.g., how the lack of standardized procedures for PPD diagnosis leads to prevalence and epidemiological estimates biases, and on the way this clinical condition is managed by health professionals, considering, for example, the lack of consensus about what interventions are most effective, cost-effective and for whom. Despite the non-systematic nature of this review, which constitutes the main limitation of the present study, the synthesis provided allows us to reflect on the critical challenges and questions that should be addressed within the scope of PPD research and clinical practice. The Pan-European Riseup-PPD multidisciplinary network will significantly contribute to answering some of these questions by adopting a global approach to the understanding of PPD, anchored in four lines of action.

4.1. Riseup-PPD Framework: lines of action

The first line of action aims to provide an updated and comprehensive synthesis of existing knowledge that clearly contributes to informing clinical recommendations and guidelines for PPD management. As noted in the review, this seems particularly important in the context of prevention and psychological treatments for PPD, where several systematic reviews and meta-analyses are already available, sometimes only partially covering the topic of interest. There is a need to move to higher levels of evidence synthesis (e.g., systematic reviews of systematic reviews, umbrella reviews) to gather knowledge on the comparative effectiveness of different types of interventions to prevent PPD (e.g., psychological, psychopharmacological) or different psychotherapeutic models (e.g., CBT, IPT) and delivery formats to treat PPD. The comparative synthesis of the effectiveness of interventions to prevent or treat depression in the pre- vs. the postpartum period is also another important aspect which deserves consideration.

The second line of action aims to clarify inconsistent findings concerning diagnosis, prevention and treatment of PPD. By making use of

the different backgrounds and expertise of this Pan-European multidisciplinary network, we are in a privileged position to design methodologically robust and cross-national research projects aiming to clarify important questions identified in this consensus report such as the epidemiology of PPD (e.g., through a consensus on diagnostic criteria and standardized procedures and gathering large-scale epidemiological evidence), the continuation or tapering of psychotropic medication during pregnancy (e.g., by using randomized studies that clearly take into account both risks and benefits of psychotropic medication), or the (cost-)effectiveness of innovative approaches for treating PPD (e.g., multicenter randomized trials to provide evidence about the effectiveness of NINs).

The third line of action aims to develop a new focus of research in the field of PPD. Some important questions identified in this report to be further investigated concern the distinct subtypes of PPD and how they differ in terms of disease trajectories and response to treatment(s); the moderators and mediators of treatment response (*what works better from whom and how it works?*); and the need to gather information about the effectiveness of interventions for specific populations (e.g., low-resourced communities, LMIC, adolescent mothers), among others.

The fourth line of action aims to develop international recommendations for PPD diagnosis, prevention and treatment. Based on the syntheses of the current evidence concerning PPD diagnosis, on the prevention and treatment (cost-)effectiveness, on the collection of existing guidelines for PPD management in some countries (e.g., Molenaar et al., 2018), and on the critical expertise of the extended network of researchers and health professionals that constitute the Riseup-PPD network, we aim to develop clear guidelines and recommendations to facilitate PPD diagnostic and therapeutic decision-making in clinical practice.

5. Conclusions

There are crucial questions that remain to be answered concerning diagnosis, prevention and treatment of PPD. Within the proposed four lines of action of the Riseup-PPD COST, we expect to globally disseminate the knowledge and outputs, directly and indirectly, resulting from this Pan-European network to the adequate stakeholders, policy-makers and citizens, in order to raise awareness regarding PPD and to play a key role in influencing maternal mental health policy-making at global and local levels.

Compliance with Ethical Standards

Disclosure of potential conflicts of interests: The authors declare that they have no conflict of interest.

Research involving human participants and/or animals: Not Applicable

Informed consent: Not Applicable.

Declaration of Competing Interest

The authors declare no conflict of interest.

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Supplementary materials

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