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Title: Effectiveness of psychological, psychoeducational and psychosocial interventions to prevent postpartum depression: study protocol for a systematic review and meta-analysis of randomized controlled trials.

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ABSTRACT

Introduction: The prevalence of postpartum depression (PPD) is 17%, and the incidence is 12% worldwide. Adverse consequences for mothers and babies have been associated with this disease. To assess the effectiveness of psychological, psychoeducational and psychosocial interventions in preventing PPD, a systematic review and meta-analysis will be conducted.

Method and Analysis: A systematic review and meta-analysis (SR/MA) will be performed following the indications of the PRISMA guidelines. Studies will be identified through MEDLINE (Ovid and PubMed), PsycINFO, Web of Science, Scopus, CINAHL, Cochrane Central Register of Controlled Trials (CENTRAL), Opengrey, Australian New Zealand Clinical Trial Registry, clinicaltrial.gov and evidencebasedtherapy.org. The selection criteria will be as follows: 1) subjects will be females who have given birth in the last 12 months and who were non-depressive at baseline; 2) psychological, psychoeducational and psychosocial interventions; 3) comparator will be usual care, active control, waiting list or no intervention; 4) outcomes will be specific results on PPD and 5) the design of the studies will be randomized controlled trials. No restrictions regarding the year of publication, the setting of the intervention or the language of publication will be considered. Pooled SMDs and 95% confidence intervals will be calculated. The risk of bias of the studies will be assessed through the Cochrane Collaboration risk of bias tool. Heterogeneity between the studies will be determined by the I2 and Cochran's Q statistics. Sensitivity and sub-group analyses will also be performed. Publication bias will be checked with funnel plots and Egger's test. If heterogeneity is relevant, random effects meta-regression will also be performed.

Ethics and dissemination: The results from this study will be presented in international conferences related to this field and disseminated through peer-review publications. Regarding the ethical assessment, it is not required due to the characteristics of this study.

PROSPERO registration number: CRD4201810998

Article Summary

The strengths and limitations of this study are as follows:

- This SR/MA of randomized controlled trials will assess the effectiveness of psychological, psychoeducational and psychosocial interventions in preventing PPD.
- This SR/MA will include results on postpartum depression throughout the whole period considered "postpartum period", up to 12 months after delivery.
- In this study, we will analyse which characteristics of mothers can explain the heterogeneity in the results.
- This study will include only RCTs that have been performed with psychological, psychoeducational and/or psychosocial interventions.
- This study will conform to the PRISMA statement for reporting systematic reviews and meta-analyses to achieve high scientific quality.

INTRODUCTION

Postpartum depression (PPD) is one of the most common postnatal complications following childbirth (1). PPD shares the same diagnostic criteria for major depressive disorders, with an onset specifier of within four weeks after delivery according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-V) (2) or within approximately 6 weeks after delivery according to International Classification of Diseases (ICD-11) (3). Despite these criteria, empirical research considers the "postpartum period" to be from the first hours after delivery to one year after childbirth (4). The most common symptoms of PPD are fatigue, sadness, difficulty concentrating, lack of interest in the baby, feelings of being a bad mother, fear of harming the baby or oneself and a loss of interest or pleasure in life (5). PPD also increases the risk of continuous or recurrent depression in the mother (6). Furthermore, in extreme cases, it can also lead to suicidal ideation, attempted suicide or suicide (7). Moreover, PPD affects the health of children and is associated with an increased risk of their psychological and developmental disturbances (5). Globally, depression is considered a major public health issue that is twice as common in women during childbearing ages than in men (8) and is expected to be the leading cause of disease burden worldwide by 2030 (9). Two recent systematic reviews and meta-analyses (SRs/MAs) have shown that although it varies by nation, the global prevalence of PPD is approximately 17%, and the incidence is 12% (10,11).

Early psychosocial or pharmacological treatments are recommended to reduce the prevalence of PPD, improve the health conditions of females and their families and reduce costs (12,13). While there are effective treatments for PPD (14,15), treatments alone are not sufficient to minimize the development, intensity and duration of maternal depressive symptoms and their potential impact on an infant (5). An additional way to reduce the burden of PPD is to lower the incidence of new cases, which can be achieved through prevention (16).

The prevention of PPD is attracting increasingly more interest. In support of PPD prevention, there are a multitude of randomized controlled trials (RCTs) as well as some SRs/MAs that have addressed this topic. To date, six SRs/MAs on the effectiveness of interventions that prevent PPD, including psychological, psychoeducational and/or psychosocial strategies, have been published (17–22). However, there are some differences between these previous SRs/MAs and this work. First, the majority of the previous SRs/MAs included females with a diagnosis of depression at the beginning of the intervention (18–21) or only excluded the trials in which more than 50% (22) of the females were depressed at baseline. Second, two studies focused on specific kind of psychological interventions, such as family therapeutic interventions and self-help psychological interventions (20,21). Finally, one of the SRs/MAs only included studies conducted in countries ranked as having "very high" human development according to the World Health Organization (22). Additionally, new RCTs on interventions for the prevention of PPD have been recently published. Therefore, robust evidence synthesis that follows methodologically rigorous processes to systematically identify psychological, psychoeducational and psychosocial interventions and

analyse their effectiveness could be considered beneficial in promoting interventions for the prevention of PPD.

Given the aforementioned reasons, the goal of this study is to conduct a SR/MA of randomized controlled trials assessing the effectiveness of psychological, psychoeducational and psychosocial interventions in preventing PPD in females during the first postpartum year.

METHODS AND ANALYSIS

The design of the study followed PRISMA-P (Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols 2015 Statement) (23). The protocol of the study was registered with the International Prospective Register of Systematic Reviews (PROSPERO) on 29 October 2018 and was last updated on 4 September 2019 (registration number: CRD4201810998).

Eligibility criteria

The inclusion and exclusion criteria of the studies (see Table 1) were defined based on the PICOS schema: participants, interventions, comparator, outcome and study design (24). The objective was to determine the effectiveness of psychological, psychoeducational and psychosocial interventions in preventing PPD.

Participants

The participants will be females who had given birth in the previous 12 months. Studies that included females with a diagnosis of depression will not be considered in this SR/MA in order to distinguish the programmes designed to prevent PPD from other possible kinds of interventions. To this end, depression will be required to have been discarded through any of the following criteria at baseline: diagnosis by a mental health specialist, validated scales with standard cut-off points (e.g., PHQ-9) or standardized interviews (e.g., Structured Clinical Interview for DSM Disorder). Studies that include depressed and non-depressed females at baseline will also be included if they provide separate results for the non-depressed participants. If necessary, authors will be asked for this information. Studies with a subset of females with a history of depression will be included.

Criteria	Inclusion criteria	Exclusion criteria
Population	Females who had given birth in the previous 12 months and were not depressed at baseline.	Other populations.
Intervention	Psychological, psychoeducational and psychosocial interventions.	Any other type of intervention such as a pharmacological intervention, acupuncture, aromatherapy or a similar intervention.
Comparator	No intervention, usual care, waiting list, active control.	Any type of intervention with available evidence of its effectiveness in preventing depression.
Outcome	Prevention of postpartum depression (incidence and/or reduction of symptoms).	Different outcomes or trials in which the effect on postpartum depression and other diseases are provided together.
Study design	Randomized controlled trials.	Other designs.
Language	All languages.	None.
Setting	All settings.	None.

Table 1. Inclusion and exclusion criteria.

Type of interventions

Studies will be eligible based on the inclusion of psychological, psychoeducational or psychosocial interventions. In this context, psychological interventions are those focus on changing the thoughts and behaviours of an individual (e.g., cognitive behavioural therapy, interpersonal psychotherapy and psychological debriefing) (17). Psychoeducational interventions aim to inform females regarding postpartum depression without engaging them in an active intervention that has been designed to change their behaviours or moods (e.g., informative sessions and the distribution of fact sheets) (18). The goal of psychosocial interventions is to promote changes through certain links with the social environment (e.g., home visits, telephone support, group interventions and interventions in which the female's partner has been included in session) (17,25). The abovementioned definitions are based on previous SRs/MAs.

Despite this differentiation, psychological, psychoeducational and psychosocial interventions usually overlap in real practice. Interventions carried out before and/or after delivery will be included. Furthermore, studies in which the interventions are focused on couples and/or other family members in addition to the females themselves will be included.

Comparators

The comparator in eligible studies will be any of the following: usual care, active control (which is based on any type of intervention for which there is no available evidence about its effectiveness in preventing postpartum depression) or waiting list. Studies where the control group does not participate in any type of intervention but undergoes the same assessments as the intervention group will also be included.

Outcome

Studies will be included when they report the incidence of new cases of postpartum depression and/or the reduction of postpartum depressive symptoms as a primary or secondary outcome. It will be required that outcomes were measured by validated scales or standardized interviews. If more than one scale was used to measure postpartum depression in the same study, the following action will be taken: a hierarchy will be developed, and the instrument most used across all the studies will be selected. Otherwise, if the instruments used in one study does not have a high frequency of use, it will be selected the best validated instrument for the country and setting in which the study was conducted. This method allows all studies, regardless of the instrument used to measure the outcome, to be included in the meta-analysis, for the sake of optimal power and representativeness (26). When a study provides results of postpartum depression and other diseases together (e.g., anxiety), the authors will be contacted to request these data separately. If the authors do not have this information or they do not reply to the query, the study will be excluded.

Study design

Studies will be eligible when they are original and use a quantitative RCT methodology, including cluster RCT methodology. RCTs will be included because they are a reference standard for clinical trials; they provide more evidence on causality than other types of studies do (27).

Setting and language

No limits will be imposed on the study publication language or publication date.

Information resources and search strategy

A literature search will be systematically conducted by using the following electronic databases: MEDLINE (through Ovid and PubMed), PsycINFO, Web of Science, Scopus, CINAHL, Cochrane Central Register of Controlled Trials (CENTRAL), Opengrey (System for Information on Grey Literature in Europe), Australian New Zealand Clinical Trial Registry, clinicaltrial.gov and evidencebasedtherapy.org. This search will be

performed using medical subject headings and keywords related to randomized controlled trials, prevention and postpartum depression. The Supplementary File shows PubMed´s search strategy, as the search will be developed first in PubMed. Then, the search will be adapted to the rest of the abovementioned databases, always following the PICOS format. In addition, PROSPERO will be searched for similar ongoing or recently completed systematic reviews. Furthermore, to ensure literature saturation, recent systematic reviews and meta-analyses in the field will be hand-searched, and their reference lists will be reviewed, as well as the references from the RCTs included in this SR/MA. Moreover, authors from studies meeting the inclusion criteria and experts in the field will be contacted to identify additional relevant studies missing in our search. No restrictions on the language or setting will be implemented. The time frame of the search will extend until the review is completed.

Study selection

The whole study selection process will be conducted independently by two researchers. This process will be performed in the following consecutive phases: after duplicate records are eliminated, the titles and abstracts of all studies will be reviewed. Studies that do not meet the inclusion criteria will be excluded. Full-text articles from the remaining records will then be screened to assess eligibility. Disagreements will be discussed until a consensus is reached between the two reviewers, or, if necessary, a third independent reviewer will resolve the disagreement. Additional information will be sought from the corresponding author to resolve any questions about eligibility. The Kappa index (28) will be calculated to assess the level of agreement between the studies.

Data extraction

A purposefully designed data extraction sheet will be completed independently by two reviewers to display the most relevant characteristics of each study. Discrepancies will be resolved by a consensus between the two reviewers or by a third independent reviewer. Regarding the qualitative data that will be collected, it will include author/year and country, target population characteristics (whether the females are nulliparous or multiparous, whether they are adolescents or adults, whether they belong to an ethnic minority, and whether they have a previous history of depression), sessions details for the intervention group (type of prevention, type of intervention, orientation, setting and provider, whether there were prenatal or postnatal sessions as well as whether there were other people participating in the intervention, such as fathers or any other relative), sample size (control/intervention) and type of control group. Furthermore, the exclusion criteria regarding the depressive females at baseline and validated instruments used (cut-off if a scale was used), prevention depression outcomes and validated instruments used (cut-off if a scale was used), and follow-up information provided by the RCTs will be collected.

Risk of bias

The Cochrane Collaboration risk of bias tool (24) will be used to assess the quality of the studies included. This tool allows the quality of the studies to be measured by six criteria: 1) random sequence generation,

2) allocation concealment, 3) blinding of the participants and clinicians, 4) blinding of the outcome assessments, 5) incomplete reporting of the outcome data, and 6) selective reporting of the data. In all items, zero points are assigned for low risk of bias, one point is assigned for unclear risk and two points are assigned for high risk. Therefore, the risk of bias score will range between 12 and 0. The quality ratings will be checked by two reviewers, and disagreements will be resolved through discussion and consultation with a third independent reviewer. The inter-rater reliability will be rated using intraclass correlation coefficients (28). The authors from the original articles will be contacted if additional information is required.

Assessment of publication bias

To assess the publication bias, a funnel plot will be examined. Following the approach proposed by Duval and Tweedie (29), the number of studies that are missing from the funnel plot will be estimated, if any. The effect size after the imputation of these missing studies will be estimated by the trim-and-fill method. Begg and Mazumdar's test (30) and Egger's test (31) will also be performed.

Meta-analysis

Quantitative data from each study will be extracted and inserted into an Excel sheet by two independent reviewers. Statistical analyses will be carried out by using the Comprehensive Meta-Analysis (CMA) software package, V.2.2.021 and STATA-Release V.14.2.

Standardized mean differences (SMDs) and 95% confidence intervals (CIs) will be used to calculate the effect sizes, as we expect that most of the RCTs included in our meta-analysis will have reported the differences in symptoms of postpartum depression. For studies that only report the incidence of postpartum depression, comprehensive meta-analysis (CMA) will be used to obtain the equivalent SMD. The first post-intervention measure that was assessed after delivery and reported in the study will be the measure used for the effect size analyses. The effect size will be interpreted by Cohen's proposal: .20 corresponds to a small effect size, .50 corresponds to a medium effect size and .80 corresponds to a large effect size (32). A random effects model will be selected under the assumption that studies included in the meta-analysis have been carried out with heterogeneous populations (24). When studies report multiple intervention groups, they will be recorded as different groups, and the effect sizes will be calculated separately for each intervention and control group. We will inflate the SEs of nested comparisons in the same RCT by following the suggestions of Cates (33).

Heterogeneity of the effect sizes will be estimated through forest plots, the Cochran's Q statistic and its P value. Heterogeneity will also be tested by the I2 statistic, which can quantify the heterogeneity ranging from 0% (no heterogeneity) to 100% (the differences between the effect sizes can completely be explained by chance alone), and the interpretations of the percentages are as follows: 0%-40% indicates potentially unimportant heterogeneity, 30%-60% indicates moderate heterogeneity, 50%-90% indicates substantial heterogeneity and 75%-100% indicates considerable heterogeneity (24).

Sensitivity analyses will be performed using a fixed effects model and a Hedges' g. RCTs from the analysis will be excluded when they have a high risk of bias (a score of 6 points or more) or elicit a large increase in heterogeneity. Furthermore, sensitivity analyses will be performed regarding the average of all follow-ups reported in the studies.

To explore the heterogeneity across studies, sub-group analysis will be performed using a mixed-effects model according to the following variables: previous deliveries (nulliparous/primiparous, nulliparous/primiparous and multiparous together), previous history of depression (yes/no), risk level (females at risk/general population), age (adolescents and adults), ethnicity, type of intervention (psychological, psychoeducational or psychosocial) and intervention timing (prepartum, postpartum or both).

Meta-regressions will be conducted to explain the between-trial heterogeneity. Prior to the data being included in meta-regression analysis, normality of the distribution will be confirmed by skewness and kurtosis normality tests (34), and the pertinent transformations will be performed to obtain approximately normal data distributions when necessary. Risk of bias and sample size will be included in the meta-regression models, and the models will be adjusted for these factors; sample size only will be included if publication bias is detected. Of the covariables considered for subgroup analysis, those with a significance level of P<.15 and those that were not removed from the model due to collinearity will also be included in meta-regression models. CIs and standard errors will be calculated using the Knapp and Hartung method (35). P values will be calculated using the Higgins and Thompson (36) permutation test, taking into account multiplicity adjustments, if necessary. A plot of the standardized shrunken residuals will be used to test goodness of fit in the meta-regression models.

Quality of evidence

To determine whether the estimated effect size is reliable, the Grading of Recommendations Assessment, Development and Evaluation (GRADE) (37) system will be used. This system helps to evaluate the quality of evidence in the domains of risk of bias, consistency, directness, precision and publication bias through four categories: high, moderate, low and very low.

Patient and Public Involvement

No patients or public are involved.

ETHICS AND DISSEMINATION

The results from this systematic review and meta-analysis will be presented at international conferences related to this field and disseminated through peer-review publications. Regarding the ethical assessment, it is not required due to the characteristics of this study.

DISCUSSION

This systematic review and meta-analysis will assess the effectiveness of psychological, psychoeducational and psychosocial interventions in preventing PPD. This study will summarize qualitative and quantitative evidence on this topic and will provide an overview of the current body of knowledge on PPD. A meta-analysis will be performed, and a statistical integration of the results will be used to compute common effect sizes and significance. The effect size, robustness and quality of evidence obtained in this meta-analysis will help to determine whether psychological, psychoeducational and psychosocial interventions can prevent PPD or postpartum depressive symptoms. It is expected that the results found in this study can contribute toward improving the prevention of postpartum depression and can be incorporated into perinatal mental health guidelines.

Author contributions: CM-G is the guarantor. EM and CM-G designed the study, and the other authors collaborated on the design. CM-G and EM drafted the protocol, and PM and JAB revised the manuscript. CM-G, SC-C and HC will independently screen the potential studies, extract the data, assess the risk of bias and complete the data synthesis. CM-G, JAB and PM-P will perform the data analyses. All authors read, provided feedback, discussed and approved the final manuscript.

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Patient consent: Not required.

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Supplementary file: PICOS Search Strategy

PICOS	Population	No restriction
	Intervention	((prevent*[Title/Abstract]) AND ((((intervention*[Title/Abstract]) OR program*[Title/Abstract]) OR strategy*) OR course[Title/Abstract]))
	Comparator	No restriction
	Outcome	(((((((depress*[Title/Abstract]) OR "depressive disorder"[Title/Abstract]) OR "depressive disorder"[MeSH Terms]) OR depression[Title/Abstract]) OR depression[MeSH Terms]) OR depression, postpartum[MeSH Terms])) AND ((((((((((postpartum[Title/Abstract]) OR postnatal[Title/Abstract]) OR puerperal[Title/Abstract]) OR perinatal[Title/Abstract]) OR prenatal[Title/Abstract]) OR antenatal[Title/Abstract]) OR intrapartum[Title/Abstract]) OR pregnancy[Title/Abstract]) OR pregnancy[MeSH Terms]) OR "pregnant women"[Title/Abstract]) OR "pregnant women"[MeSH Terms]) OR matern*[Title/Abstract]))))
	Study design	(((((("randomized controlled trial"[Publication Type]) OR random*[Title/Abstract]) OR controlled [Title/Abstract]) OR trial[Title/Abstract]) OR "clinical trial"[Title/Abstract]) OR "controlled clinical trial"[Publication Type])

No population and comparator restrictions included in the search strategy. The selection was performed using the inclusion and exclusion criteria.

BMJ Open

Effectiveness of psychological, psychoeducational and psychosocial interventions to prevent postpartum depression in adolescent and adult mothers: study protocol for a systematic review and meta-analysis of randomized controlled trials.

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Title: Effectiveness of psychological, psychoeducational and psychosocial interventions to prevent postpartum depression in adolescent and adult mothers: study protocol for a systematic review and meta-analysis of randomized controlled trials.

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ABSTRACT

Introduction: The prevalence of postpartum depression (PPD) is 17%, and the incidence is 12% worldwide. Adverse consequences for mothers and babies have been associated with this disease. To assess the effectiveness of psychological, psychoeducational and psychosocial interventions in preventing PPD, a systematic review and meta-analysis will be conducted.

Method and Analysis: A systematic review and meta-analysis (SR/MA) will be performed following the indications of the PRISMA guidelines. Studies will be identified through MEDLINE (Ovid and PubMed), PsycINFO, Web of Science, Scopus, CINAHL, Cochrane Central Register of Controlled Trials (CENTRAL), Opengrey, Australian New Zealand Clinical Trial Registry, clinicaltrial.gov and evidencebasedtherapy.org from inception until January 31, 2020. Bridging searches will be also conducted until the review is completed. The selection criteria will be as follows: 1) subjects will be pregnant females or females who have given birth in the last 12 months and who were non-depressive at baseline; 2) psychological, psychoeducational and psychosocial interventions; 3) comparator will be usual care, attention control, waiting list or no intervention; 4) outcomes will be specific results on PPD and 5) the design of the studies will be randomized controlled trials. No restrictions regarding the year of publication, the setting of the intervention or the language of publication will be considered. Pooled SMDs and 95% confidence intervals will be calculated. The risk of bias of the studies will be assessed through the Cochrane Collaboration risk of bias tool. Heterogeneity between the studies will be determined by the I^2 and Cochran's Q statistics. Sensitivity and sub-group analyses will also be performed. Publication bias will be checked with funnel plots and Egger's test. If heterogeneity is relevant, random effects meta-regression will also be performed.

Ethics and dissemination: The ethical assessment was not required. The results will be presented at conferences and disseminated through publications.

PROSPERO registration number: CRD42018109981

Keywords: postpartum depression; prevention; systematic review; meta-analysis and study protocol.

Article Summary

The strengths and limitations of this study are as follows:

- This SR/MA of randomized controlled trials will assess the effectiveness of psychological, psychoeducational and psychosocial interventions in preventing PPD.
- This SR/MA will include results on postpartum depression throughout the whole period considered "postpartum period", up to 12 months after delivery.
- In this study, we will analyse which characteristics of mothers can explain the heterogeneity in the results.
- This study will include only RCTs that have been performed with psychological, psychoeducational and/or psychosocial interventions.
- This study will conform to the PRISMA statement for reporting systematic reviews and meta-analyses to achieve high scientific quality.

INTRODUCTION

Postpartum depression (PPD) is one of the most common postnatal complications following childbirth (1). PPD shares the same diagnostic criteria for major depressive disorders, with an onset specifier of within four weeks after delivery according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-V) (2) or within approximately 6 weeks after delivery according to International Classification of Diseases (ICD-11) (3). Despite these criteria, empirical research and reviews consider the "postpartum period" to be from the first hours after delivery to one year after childbirth (4–7). The most common symptoms of PPD are fatigue, sadness, difficulty concentrating, lack of interest in the baby, feelings of being a bad mother, fear of harming the baby or oneself and a loss of interest or pleasure in life (8). PPD also increases the risk of later depression in the mother (9). Furthermore, in extreme cases, it can also lead to suicidal ideation, attempted suicide or suicide (10). Moreover, PPD affects the health of children and is associated with an increased risk of their psychological and developmental disturbances (8). Globally, depression is considered a major public health issue that is twice as common in women during childbearing ages than in men (11). The burden of disease in terms of years lived with disability attributable to major depression are increasing, ranking third in the world in high-income countries(12). Two recent systematic reviews and meta-analyses (SRs/MAs) have shown that although it varies by nation, the global prevalence of PPD is approximately 17%, and the incidence is 12% (13,14).

Early psychosocial or pharmacological treatments are recommended to reduce the prevalence of PPD, improve the health conditions of females and their families and reduce costs (15,16). While there are effective treatments for PPD (17,18), treatments alone are not sufficient to minimize the development, intensity and duration of maternal depressive symptoms and their potential impact on an infant (8). An additional way to reduce the burden of PPD is to lower the incidence of new cases, which can be achieved through prevention (19). The majority of preventive interventions for depression available are based on psychological, psychoeducational or psychosocial approaches (20)

The prevention of PPD is attracting increasingly more interest. In support of PPD prevention, there are a multitude of randomized controlled trials (RCTs) as well as some SRs/MAs that have addressed this topic. To date, six SRs/MAs on the effectiveness of interventions that prevent PPD, including psychological, psychoeducational and/or psychosocial strategies, have been published (20–25). However, there are some differences between these previous SRs/MAs and this work. First, the majority of the previous SRs/MAs included females with a diagnosis of depression at the beginning of the intervention (22–25) or only excluded the trials in which more than 50% (20) of the females were depressed at baseline. Second, two studies focused on specific kind of psychological interventions, such as family therapeutic interventions and self-help psychological interventions (24,25). Finally, one of the SRs/MAs only included studies conducted in countries ranked as having "very high" human development according to the World Health Organization (20). Additionally, new RCTs on interventions for the prevention of PPD have been recently published. Therefore, robust evidence synthesis that follows methodologically rigorous

processes to systematically identify psychological, psychoeducational and psychosocial interventions and analyse their effectiveness could be considered beneficial in promoting interventions for the prevention of PPD.

Given the aforementioned reasons, the goal of this study is to conduct a SR/MA of randomized controlled trials assessing the effectiveness of psychological, psychoeducational and psychosocial interventions in preventing PPD in females during the first postpartum year.

METHODS AND ANALYSIS

This is a protocol for an SR/MA whose design has followed PRISMA-P (Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols 2015 Statement) (26). The protocol of the study was registered with the International Prospective Register of Systematic Reviews (PROSPERO) on 29 October 2018 and was last updated on 4 September 2019 (registration number: CRD4201810998).

Eligibility criteria

The inclusion and exclusion criteria of the studies (see Table 1) were defined based on the PICOS schema: participants, interventions, comparator, outcome and study design (27). The objective was to determine the effectiveness of psychological, psychoeducational and psychosocial interventions in preventing PPD.

Participants

The participants will be adolescents and adult mothers who had given birth in the previous 12 months. Since some interventions may begin before delivery, pregnant women will also be included when the study reports a measure of PPD after delivery. Studies that included females with a diagnosis of depression will not be considered in this SR/MA in order to distinguish the programmes designed to prevent PPD from other possible kinds of interventions. To this end, depression will be required to have been discarded through any of the following criteria at baseline: diagnosis by a mental health specialist, validated scales with standard cut-off points (e.g., PHQ-9 or Edinburgh Postnatal Depression Scale) or standardized interviews (e.g., Structured Clinical Interview for DSM Disorder or Composite International Diagnostic Interview). Studies that include depressed and non-depressed females at baseline will also be included if they provide separate results for the non-depressed participants. If necessary, authors will be asked for this information. Studies with a subset of females with a history of depression will be included. It is not required that psychiatric disorders other than depression have been ruled out at baseline.

Table 1. Inclusion and exclusion criteria.

[a]Pregnant females will be included when the study reports a measure of depression after delivery.

Criteria	Inclusion criteria	Exclusion criteria
Population	Adolescents and adult mothers [a]who had given birth in the previous 12 months and were not depressed at baseline.	Other populations.
Intervention	Psychological, psychoeducational and psychosocial interventions.	Any other type of intervention such as a pharmacological intervention, acupuncture, aromatherapy or a similar intervention.
Comparator	No intervention, usual care, waiting list attention control,.	Any type of intervention with available evidence of its effectiveness in preventing depression.
Outcome	Prevention of postpartum depression (incidence and/or reduction of symptoms).	Different outcomes or trials in which the effect on postpartum depression and other diseases are provided together.
Study design	Randomized controlled trials.	Other designs.
Language	All languages.	None.
Setting	All settings.	None.

Type of interventions

Studies will be eligible based on the inclusion of psychological, psychoeducational or psychosocial interventions. In this context, psychological interventions are those focus on changing the thoughts and behaviours of an individual (e.g., cognitive behavioural therapy, interpersonal psychotherapy and psychological debriefing) (21). Psychoeducational interventions aim to inform females regarding postpartum depression without engaging them in an active intervention that has been designed to change their behaviours or moods (e.g., informative sessions and the distribution of fact sheets) (22). The goal of psychosocial interventions is to promote changes through certain links with the social environment (e.g., home visits, telephone support, group interventions and interventions in which the female's partner has been included in session) (21,28). The abovementioned definitions are based on previous SRs/MAs. Despite this differentiation, psychological, psychoeducational and psychosocial interventions usually overlap in real practice. Interventions carried out before and/or after delivery will be included. Furthermore, studies in which the interventions are focused on couples and/or other family members in addition to the females themselves will be included.

Comparators

The comparator in eligible studies will be any of the following: usual care, attention control (which is based on any type of intervention for which there is no available evidence about its effectiveness in preventing postpartum depression) or waiting list. Studies where the control group does not participate in any type of intervention but undergoes the same assessments as the intervention group will also be included.

Outcome

Studies will be included when they report the incidence of new cases of postpartum depression and/or the reduction of postpartum depressive symptoms during the first year postpartum as a primary or secondary outcome. It will be required that outcomes were measured by validated scales or standardized interviews. If more than one scale was used to measure postpartum depression in the same study, the following action will be taken: a hierarchy will be developed, and the instrument most used across all the studies will be selected. Otherwise, if the instruments used in one study does not have a high frequency of use, it will be selected the best validated instrument for the country and setting in which the study was conducted. This method allows all studies, regardless of the instrument used to measure the outcome, to be included in the meta-analysis, for the sake of optimal power and representativeness (29). When a study provides results of postpartum depression and other diseases together (e.g., anxiety), the authors will be contacted to request these data separately. If the authors do not have this information or they do not reply to the query, the study will be excluded.

Study design

Studies will be eligible when they are original and use a quantitative RCT methodology, including cluster RCT methodology. Other kinds of design such as cross-over trials or quasi-randomised trials will be excluded from this RS/MA. RCTs will be included because they are a reference standard for clinical trials; they provide more evidence on causality than other types of studies do (30). Characteristics such as sample size, study duration and the number of treatment sessions have no limitations and will be described in the qualitative analysis. The blinding also does not have limitation, but it will be assessed through the Cochrane Collaboration risk of bias tool.

Setting and language

No limits will be imposed on the study publication language or publication date.

Information resources and search strategy

A literature search will be systematically conducted by using the following electronic databases: MEDLINE (through Ovid and PubMed), PsycINFO, Web of Science, Scopus, CINAHL, Cochrane Central Register of Controlled Trials (CENTRAL), Opengrey (System for Information on Grey Literature in Europe), Australian New Zealand Clinical Trial Registry, clinicaltrial.gov and evidencebasedtherapy.org. This search will be performed using medical subject headings and keywords related to randomized controlled trials, prevention and postpartum depression. The Supplementary File shows PubMed´s search strategy, as the search will be developed first in PubMed. Then, the search will be adapted to the rest of the abovementioned databases, always following the PICOS format. In addition, PROSPERO will be searched for similar ongoing or recently completed systematic reviews. Furthermore, to ensure literature saturation, recent systematic reviews and meta-analyses in the field will be hand-searched, and their reference lists will be reviewed, as well as the references from the RCTs included in this SR/MA. Moreover, authors from studies meeting the inclusion criteria and experts in the field will be contacted to identify additional relevant studies missing in our search. No restrictions on the language or setting will be implemented. It is expected that the time frame of the search will extend from inception to January 31, 2020. Bridging searches will also be conducted to capture literature until the review is completed.

Study selection

The whole study selection process will be conducted independently by two researchers. This process will be performed in the following consecutive phases: after duplicate records are eliminated, the titles and abstracts of all studies will be reviewed. Studies that do not meet the inclusion criteria will be excluded. Full-text articles from the remaining records will then be screened to assess eligibility. Disagreements will be discussed until a consensus is reached between the two reviewers, or, if necessary, a third independent reviewer will resolve the disagreement. Additional information will be sought from the corresponding author to resolve any questions about eligibility. The Kappa index (31) will be calculated to assess the level of agreement between the studies.

Data extraction

A purposefully designed data extraction sheet will be completed independently by two reviewers to display the most relevant characteristics of each study. Discrepancies will be resolved by a consensus between the two reviewers or by a third independent reviewer. Regarding the qualitative data that will be collected, it will include author/year and country, target population characteristics (whether the females are nulliparous or multiparous, whether they are adolescents or adults, whether the intervention is aimed explicitly at females who belong to a specific ethnic minority, and whether they have a previous history of depression), sessions details for the intervention group (type of prevention, type of intervention, orientation, setting and provider, intervention duration (number of sessions and estimated contact hours, frequency of sessions), whether there were prenatal or postnatal sessions as well as whether there were other people participating in the intervention, such as fathers or any other relative), sample size (control/intervention) and type of control group. Furthermore, the exclusion criteria regarding the depressive females at baseline and validated instruments used (cut-off if a scale was used), prevention depression outcomes and validated instruments used (cut-off if a scale was used), and follow-up information provided by the RCTs will be collected.

Risk of bias

The Cochrane Collaboration risk of bias tool (27) will be used to assess the quality of the studies included. This tool allows the quality of the studies to be measured by six criteria: 1) random sequence generation, 2) allocation concealment, 3) blinding of the participants and clinicians, 4) blinding of the outcome assessments, 5) incomplete reporting of the outcome data, and 6) selective reporting of the data. In all items, zero points are assigned for low risk of bias, one point is assigned for unclear risk and two points are assigned for high risk. Therefore, the risk of bias score will range between 12 and 0. The quality ratings will be checked by two reviewers, and disagreements will be resolved through discussion and consultation with a third independent reviewer. The inter-rater reliability will be rated using intraclass correlation coefficients (31). The authors from the original articles will be contacted if additional information is required.

Assessment of publication bias

To assess the publication bias, a funnel plot will be examined. Following the approach proposed by Duval and Tweedie (32), the number of studies that are missing from the funnel plot will be estimated, if any. The effect size after the imputation of these missing studies will be estimated by the trim-and-fill method. Begg and Mazumdar's test (33) and Egger's test (34) will also be performed.

Meta-analysis

Quantitative data from each study will be extracted and inserted into an Excel sheet by two independent reviewers. Statistical analyses will be carried out by using the Comprehensive Meta-Analysis (CMA) software package, V.2.2.021 and STATA-Release V.14.2.

Standardized mean differences (SMDs) and 95% confidence intervals (CIs) will be used to calculate the effect sizes, as we expect that most of the RCTs included in our meta-analysis will have reported the differences in symptoms of postpartum depression. For studies that only report the incidence of postpartum depression, comprehensive meta-analysis (CMA) will be used to obtain the equivalent SMD. The first post-intervention measure that was assessed after delivery and reported in the study will be the measure used for the effect size analyses. The effect size will be interpreted by Cohen's proposal: .20 corresponds to a small effect size, .50 corresponds to a medium effect size and .80 corresponds to a large effect size (35). A random effects model will be selected under the assumption that studies included in the meta-analysis have been carried out with heterogeneous populations (27). When studies report multiple intervention groups, they will be recorded as different groups, and the effect sizes will be calculated separately for each intervention and control group. We will inflate the SEs of nested comparisons in the same RCT by following the suggestions of Cates (36).

Heterogeneity of the effect sizes will be estimated through forest plots, the Cochran's Q statistic and its P value. Heterogeneity will also be tested by the I^2 statistic, which can quantify the heterogeneity ranging from 0% (no heterogeneity) to 100% (the differences between the effect sizes can completely be explained by chance alone), and the interpretations of the percentages are as follows: 0%-40% indicates potentially unimportant heterogeneity, 30%-60% indicates moderate heterogeneity, 50%-90% indicates substantial heterogeneity and 75%-100% indicates considerable heterogeneity (27).

Sensitivity analyses will be performed using a fixed effects model and a Hedges' g. RCTs from the analysis will be excluded when they have a high risk of bias (a score of 6 points or more) or elicit a large increase in heterogeneity. Furthermore, sensitivity analyses will be performed regarding the average of all follow-ups reported in the studies.

To explore the heterogeneity across studies, sub-group analysis will be performed using a mixed-effects model according to the following variables: previous deliveries (eg. primiparous only versus primiparous and multiparous), previous history of depression (females without previous history of depression only versus females with and without history of depression), risk level (females with specific risk factors versus general population), age (adolescents versus adolescents and adults), ethnicity (intervention aims to females from a specific ethnic group versus not), and intervention timing (prepartum only versus prepartum and postpartum versus postpartum only).

Meta-regressions will be conducted to explain the between-trial heterogeneity. Prior to the data being included in meta-regression analysis, normality of the distribution will be confirmed by skewness and kurtosis normality tests (37), and the pertinent transformations will be performed to obtain approximately normal data distributions when necessary. Risk of bias and sample size will be included in the meta-regression models, and the models will be adjusted for these factors; sample size only will be included if publication bias is detected. Of the covariables considered for sub-group analysis, those with

a significance level of P<.15 and those that were not removed from the model due to collinearity will also be included in meta-regression models. CIs and standard errors will be calculated using the Knapp and Hartung method (38). P values will be calculated using the Higgins and Thompson (39) permutation test, taking into account multiplicity adjustments, if necessary. A plot of the standardized shrunken residuals will be used to test goodness of fit in the meta-regression models.

Quality of evidence

To determine whether the estimated effect size is reliable, the Grading of Recommendations Assessment, Development and Evaluation (GRADE) (40) system will be used. This system helps to evaluate the quality of evidence in the domains of risk of bias, consistency, directness, precision and publication bias through four categories: high, moderate, low and very low.

Patient and Public Involvement

No patients or public are involved.

ETHICS AND DISSEMINATION

Due to the characteristics of this study, the ethical assessment was not required. The results from this systematic review and meta-analysis will be presented at international conferences related to this field and disseminated through peer-review publications.

DISCUSSION

This systematic review and meta-analysis will assess the effectiveness of psychological, psychoeducational and psychosocial interventions in preventing PPD. This study will summarize qualitative and quantitative evidence on this topic and will provide an overview of the current body of knowledge on PPD. A meta-analysis will be performed, and a statistical integration of the results will be used to compute common effect sizes and significance. The effect size, robustness and quality of evidence obtained in this meta-analysis will help to determine whether psychological, psychoeducational and psychosocial interventions can prevent PPD or postpartum depressive symptoms. It is expected that the results found in this study can contribute toward improving the prevention of postpartum depression and can be incorporated into perinatal mental health guidelines.

Author contributions: CM-G is the guarantor. EM and CM-G designed the study, and PM-P, JAB, SC-C, HC-P, IG-G, AR and IB collaborated on the design. CM-G and EM drafted the protocol, and PM-P and JAB revised the manuscript. CM-G, SC-C and HC-P will independently screen the potential studies, extract the data, assess the risk of bias and complete the data synthesis. CM-G, JAB and PM-P will perform the data analyses. CM-G, PM-P, JAB, SC-C, HC-P, IG-G, AR, IB and EM read, provided feedback, discussed and approved the final manuscript.

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Supplementary file: PICOS Search Strategy

PICOS	Population	No restriction
	Intervention	((prevent*[Title/Abstract]) AND ((((intervention*[Title/Abstract]) OR program*[Title/Abstract]) OR strategy*) OR course[Title/Abstract]))
	Comparator	No restriction
	Outcome	(((((((depress*[Title/Abstract]) OR "depressive disorder"[Title/Abstract]) OR "depressive disorder"[MeSH Terms]) OR depression[Title/Abstract]) OR depression[MeSH Terms]) OR depression, postpartum[MeSH Terms])) AND ((((((((((postpartum[Title/Abstract]) OR postnatal[Title/Abstract]) OR puerperal[Title/Abstract]) OR perinatal[Title/Abstract]) OR prenatal[Title/Abstract]) OR antenatal[Title/Abstract]) OR intrapartum[Title/Abstract]) OR pregnancy[Title/Abstract]) OR pregnancy[MeSH Terms]) OR "pregnant women"[Title/Abstract]) OR "pregnant women"[MeSH Terms]) OR matern*[Title/Abstract]))))
	Study design	(((((("randomized controlled trial"[Publication Type]) OR random*[Title/Abstract]) OR controlled [Title/Abstract]) OR trial[Title/Abstract]) OR "clinical trial"[Title/Abstract]) OR "controlled clinical trial"[Publication Type])

No population and comparator restrictions included in the search strategy. The selection was performed using the inclusion and exclusion criteria.

Section and topic	Item No	Checklist item	Page
Administrative information			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	-
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	2,5
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	11
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	-
Support:			
Sources	5a	Indicate sources of financial or other support for the review	11
Sponsor	5b	Provide name for the review funder and/or sponsor	-
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	11
Introduction			
Rationale	6	Describe the rationale for the review in the context of what is already known	4,5
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	5
Methods			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	5-7
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	7,8
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	7,8
Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	8
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	8,9
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	8,9
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	8,9
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	9,10
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	8,9
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesized	10
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2, Kendall's, τ)	10
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	9,10
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	-
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	9
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	11