Evidence-based Practice Center Review Protocol

Project Title: *Nonpharmacologic Treatment for Maternal Mental Health Conditions*

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(Amendments Details-see Section VIII)

I. Background and Objectives for the Systematic Review

During the perinatal period (defined as pregnancy through 12 months postpartum), individuals may experience various mental health conditions such as depression, anxiety, post-traumatic stress disorder (PTSD), bipolar disorder, and obsessive-compulsive disorder (OCD). Mental health experiences can range in severity, for example from transient postpartum blues to a depressive episode to more persistent depression. Approximately 19% of individuals who were pregnant experience a depressive episode in the first 3 months postpartum, and about 7% to 13% experience depression during the perinatal period.[1] In the United States, the prevalence of postpartum depression varies across geographical regions (e.g., 10% in Illinois vs. 24% in Mississippi[1]) and tends to be higher in people who are under 19 years old, of American Indian/Alaska Native heritage, smoked during pregnancy, experienced various traumas, and self-reported depression before or during pregnancy.[1] Similarly, up to 20% of perinatal individuals meet criteria for an anxiety disorder,[2] 5% may experience perinatal PTSD,[3] and 20% may experience bipolar-spectrum mood disorders.[4] Prevalence of perinatal OCD is less clearly established, but a recent well-controlled study estimated prevalence of 8% during pregnancy and 17% postpartum.[5] Of concern, the prevalence of perinatal mental health conditions has increased during the COVID-19 pandemic.[6]

Lack of treatment or undertreatment of perinatal mental health conditions can have profound and persistent effects on both the mother and the developing fetus and child.[7] Compared with non-depressed pregnant people, those who are depressed are more likely to smoke,[8] use alcohol,[9] and have inadequate gestational weight gain[10] and are less likely to form an attachment to the fetus during the third trimester.[11] Pregnant people who are both depressed and experiencing domestic violence are at particularly high risk for missing prenatal appointments.[12] Depression during pregnancy is also associated with adverse pregnancy outcomes, such as preterm birth, low birth weight, operative deliveries, poorer postpartum pain control, opioid use, and longer pre-delivery hospital stays.[13, 14] Individuals with postpartum depression are more likely than those without depression to have impaired bonding,[15] less likely to be fully responsive to infants' needs,[16] less likely to initiate or maintain breastfeeding,[17-19] and have a greater frequency of missed well-baby check-ups.[20] Postpartum depression may also lead to adverse outcomes for the infant, including impaired child development, including poor cognitive functioning, emotional maladjustment, and behavioral inhibition.[21, 22]

Anxiety disorders during pregnancy have been associated with preterm birth, low birth weight, pre-eclampsia, and miscarriage,[23-29] deficits in bonding, less attunement to infant cues,[30] and have an overall unfavorable impact on infant and child development.[31] Episodes of bipolar disorder during pregnancy and the postpartum period are associated with greater risk of low birth weight, preterm delivery, cesarean section, and diminished prenatal care; following delivery, there is increased risk of impaired bonding and attentiveness to infant cues.[32] Finally, OCD during pregnancy is associated with greater risk of preterm birth and low birthweight[33] and has been shown to have a deleterious impact on infant bonding and attachment.[34]

Given the known deleterious impact of untreated and undertreated perinatal depression, anxiety, PTSD, bipolar disorder, and OCD, early intervention in the perinatal period is paramount.[35] Appropriate pharmacologic treatments for perinatal mental health conditions are an important component of treatment, despite insufficient direct evidence for this population.[36] For example, in partnership with the

American College of Obstetrics and Gynecology (ACOG) and American Psychiatric Association, the Agency for Healthcare Research and Quality (AHRQ) published an systematic review (SR) of pharmacologic treatment for mental health conditions in preconception, antepartum, postpartum, and lactating individuals.[36] The review found few studies conducted in pregnant and postpartum individuals on the benefits of pharmacotherapy; many studies reported on harms but were of low quality. As in the general population, nonpharmacologic treatments for mental health conditions are often preferred over medications,[37] a preference that is amplified for perinatal individuals given pregnancy and breastfeeding concerns.[38, 39] Even when pharmacologic treatment is used, nonpharmacologic treatments may be important adjunctive therapies.

Numerous nonpharmacologic interventions have been considered for perinatal mental health. Common nonpharmacologic psychotherapy treatments for perinatal mental health conditions of interest include cognitive behavioral therapy (CBT)[40] and interpersonal psychotherapy.[41] For mild to moderate depression in the general population, complementary therapies, such as exercise, yoga, bright light therapy, and acupuncture have also shown efficacy and are often utilized.[42] Because a poor marital or primary relationship is associated with perinatal depression,[1] couples or family therapy can be effective as a primary or adjunctive treatment.[43] The delivery of counseling treatments via support groups,[44] home visiting, [44] and specialized psychiatric partial hospital programs[45] have also been investigated. In the general population, nonpharmacologic interventions for PTSD can include exposure therapy, trauma-focused CBT, eye movement desensitization and reprocessing therapy, interpersonal psychotherapy, explorative therapy, and self-hypnosis and relaxation.[46] While pharmacologic interventions are important for the treatment of bipolar disorders, adjunctive nonpharmacologic treatments are important interventions; for example, interpersonal and social rhythm therapy is an effective stand-alone or adjunctive therapy that may be effective in the perinatal population. [47] Other documented effective adjunctive treatments for bipolar disorder include psychoeducation,[48] mindfulness,[49] and cognitive remediation therapy.[50] Finally, nonpharmacologic interventions for OCD may include CBT combined with exposure response prevention, which has shown to be effective in the general population.[51]

Clinical practice guidelines (CPGs) and consensus statements for the general population and perinatal individuals have tended to routinely recommend the use of nonpharmacologic interventions as either frontline interventions or as an adjunctive therapy with pharmacologic interventions.[52-56] However, the CPGs do not include the latest evidence are largely outdated and/or focus on specific therapies. While some SRs exist on nonpharmacologic interventions for perinatal mental health, most focus on single types of interventions and have varying search dates and levels of rigor. Such diversity is challenging for CPG developers to consolidate to inform a single guideline.

Thus, decisionmakers face the following decisional dilemmas:

1) Whether to offer nonpharmacologic interventions alone or in combination with pharmacologic interventions for specific perinatal mental health conditions
2) Which nonpharmacologic interventions (and their possible combinations) for perinatal mental health provide the optimal patient outcomes

A SR of nonpharmacologic treatments (alone or in combination with pharmacologic treatments) for mental health conditions is needed to inform a clinical practice guideline (CPG) for this population.

The topic of this SR was nominated by ACOG in partnership with American Psychiatric Association. This SR will potentially inform future guidance developed by ACOG, American Psychiatric Association, and American Psychological Association for treatment of mental health conditions during the perinatal period.[57]

II. Key Questions

Key Question 1: What are the effectiveness and comparative effectiveness and harms of nonpharmacologic treatments for mental health conditions in perinatal individuals?

a) Depressive disorders
b) Bipolar disorder
c) Anxiety disorders
d) Post-traumatic stress disorder
e) Obsessive-compulsive disorder

Key Question 2: What are the comparative effectiveness and harms of nonpharmacologic treatments compared with pharmacologic treatment alone for mental health conditions in perinatal individuals?

a) Depressive disorders
b) Bipolar disorder
c) Anxiety disorders
d) Post-traumatic stress disorder
e) Obsessive-compulsive disorder

III. Eligibility Criteria

The specific eligibility criteria provided below have been refined based on discussions with a panel of Key Informants (KIs) and a Technical Expert Panel (TEP). These stakeholders included perspectives from patient advocacy, obstetrics and gynecology, social work, doula care, health services research and health disparities research.

Eligibility criteria below applies to all key questions:

Population(s)

- Perinatal individuals
  - Individuals who are pregnant or postpartum (up to 12 months after delivery) with new or preexisting diagnosis of depression disorder, bipolar disorder, anxiety disorders, post-traumatic stress disorder (PTSD), obsessive-compulsive disorder (OCD)
  - Diagnoses must be confirmed via clinical interview or validated screening tool (e.g., Edinburgh Postnatal Depression Scale [EPDS]; Patient Health Questionnaire-9 [PHQ-9) with a commonly accepted threshold
  - EXCLUDE: studies that evaluate patients with depressive or anxiety symptoms in contrast with diagnoses of depression or anxiety, including studies that include patients with screening tool values below a threshold consistent with diagnosis
  - EXCLUDE: populations in which the primary condition is phobia of pregnancy (i.e., tokophobia)
  - EXCLUDE: studies with mixed populations (e.g., perinatal and non-perinatal, mental health condition and non-mental health condition), unless $\geq$90% of the studied population represent an eligible population for the review. This exclusion criterion does not apply to populations with multiple eligible mental health conditions; studies of perinatal individuals with two or more conditions (e.g., studies targeting individuals with both depression and anxiety) will be included.
  - EXCLUDE: Studies of patients with substance use disorders, exclusively.

Intervention

- **Nonpharmacologic modalities**
  To be included, studies must evaluate one or more nonpharmacological modalities such as those listed below. Although the list sought to be comprehensive, it is not intended to be restrictive to

modalities not appearing on the list. If a study otherwise meets eligibility criteria and describes a nonpharmacological intervention involving a form of psychotherapy or complementary/alternative therapy (aside from those specified for exclusion) it will be considered for inclusion.
Note that the list of modalities includes treatments for any of the mental health conditions under consideration, recognizing that not all therapies are appropriate for all conditions.

Psychotherapies
- Cognitive behavior therapy (CBT)
  - Examples: trauma-focused CBT, mindfulness-based, cognitive processing therapy, cognitive restructuring, cognitive remediation therapy, stress inoculation training
- Acceptance and commitment therapy (ACT)
- Psychodynamic therapy
- Interpersonal psychotherapy (IPT)
- Supportive therapy
- Dialectical behavioral therapy (DBT)
- Exposure therapy
  - Example: Narrative Exposure Therapy (NET), prolonged exposure therapy
- Eye movement desensitization and reprocessing therapy
- Imagery rehearsal therapy
- Social rhythm therapy

Psychoeducation
- Trauma affect regulation
- Problem solving

Other
- Electroconvulsive therapy (ECT)

Complementary/alternative therapies
- Yoga
- Tai Chi
- Acupuncture
- Mindfulness
- Exercise
- Relaxation
- Self-hypnosis and relaxation
- Bright light therapy
- Sleep therapy
- Writing, art, music therapy

- EXCLUDE: studies with interventions that are poorly specified or not structured programs (i.e., cannot be reasonably replicated in practice or future research)
- EXCLUDE: unsupervised peer-to-peer or social media interventions
- EXCLUDE: interventions delivered through ingestion or parenterally, and surgical or invasive interventions (with the exception of acupuncture or ECT) (e.g., omega-3 fatty acid, St. John's wort, kava, valerian, theanine)
- EXCLUDE: interventions designed to address issues other than the mental health conditions of interest (e.g., diet changes, weight loss, lactation training, reintroduction of sexual activity)
- EXCLUDE: interventions focused on the processes of delivering of care (e.g., collaborative care model)

Mechanisms of delivery
The above intervention modalities may be delivered in diverse ways in different settings, by different personnel, with different intensities. We will include studies of the above that directly compare different mechanisms of delivery below. We have purposefully separated the content of modalities of interest from means by which they may be delivered since mechanisms of delivery (e.g., telehealth) are not interventions in their own right.

Number of participants
- Individuals
- Group

Type of participants
- Individual
- Couple
- Family

Type of provider
- Professional (e.g., psychotherapist, exercise instructor)
- Community based non-professional or peer
- Not applicable (i.e., self-administered)

Type of modality
- In-person
- Online via computer
- Online via mobile app

Duration
- 'Brief', 'short-term'
- 'Prolonged'
- *N.B. many studies use diverse labels to signify the duration of the intervention delivered. The meaning of these labels will be extracted as part of our intervention extraction process. We will not exclude studies based on their duration.*

Outcomes

Outcomes in bold font, with footnote "a" will be prioritized (i.e., will be included in Evidence Profiles)

- **Scores on psychological assessments**[a] (for each evaluated condition)
  - Including self-assessed symptoms of mental health condition[b]
- **Cure/resolution of symptoms or condition**[a]
- **Parent-infant bonding**[a,b]
- **Suicide**[a,b]
  - **Suicidal thoughts**[a]
  - **Attempted suicide**[a]
  - **Death by suicide**[a]
- **Thoughts of harming the baby, including thoughts of extended suicide**[a,b]
- **Adherence to mental health treatment**[a,b]
- Satisfaction with intervention[b]
- Perceived self-efficacy for parenthood
- Perceived self-efficacy for management of mental health
- Harms of treatment
- Quality of life
- Return to work
- Maternal clinical outcomes (e.g., preeclampsia, preterm delivery)
- Safe family environment
- Fetal/neonatal/pediatric clinical outcomes
  - Live birth
  - Infant feeding success
  - Infant growth
  - Pediatric death
  - Pediatric development (e.g., neurodevelopmental milestones)
  - Pediatric cognitive and academic achievement
  - Pediatric social/emotional wellbeing

[a] Prioritized outcome

[b] From perinatal depression core outcome set (recommended 9 core outcomes) Helberg et al. 2021. PMID 34047454

- Prenatal care utilization. E.g., completion of prenatal visits, completion of recommended prenatal services, unexpected health care utilization (e.g., emergency department/triage visits), postpartum care follow-up

Potential Modifiers

- Pregnancy status (pregnant, postpartum after live birth, postpartum after fetal loss or infant death or needing intensive care, breastfeeding; change of status within study period)
- Severity of mental health conditions (e.g., mild, moderate or severe depression; depression with or without anxiety, psychosis)
- Comorbidities, including other mental health conditions
- Age
- Race/ethnicity
- Religion/faith
- Birthplace (e.g., immigrant from Latin America vs. U.S.-born)
- Gender identification
- Sexual orientation
- Socioeconomic factors
- Geographic region, urbanicity
- Patient-provider congruence (e.g., with respect to racial, ethnic, language, and other socioeconomic factors)
- Use of social media
- Partner support
- Interpersonal violence (including partner violence)
- Availability of family leave, paid or unpaid
- Drug use
- History of abortion
- History of pregnancy loss
- Intended pregnancy
- Parity
- Insurance status
- Accessibility issues (e.g., internet access, in particular for telehealth interventions)
- COVID-19 pandemic (as defined by study authors)

Setting

- Ambulatory with exception of individuals in hospital due to non-mental health pregnancy or postpartum complications (i.e., exclude patients in acute inpatient psychiatric setting)
- Treatment delivery method (all including in-person, telehealth, digital)
- High-income countries (as defined by World Bank as of May 11, 2023)

Design

- Randomized controlled trials
- EXCLUDE: Nonrandomized comparative studies
- EXCLUDE: Single group (noncomparative) studies, including case reports or series
- EXCLUDE: Studies with N<10 per arm
- EXCLUDE: Studies published only in dissertation or conference abstract format

We will collect SRs to identify potentially eligible primary studies (within date restrictions) and possibly to narratively summarize older studies of earlier foundational nonpharmacological interventions.
For topics with robust existing SRs (e.g., non-pharmacological interventions for perinatal depression), we will consider (with partners and our task order officer [TOO]) updating these SRs (relying on the published SRs for all data pertaining to the older primary studies)

Eligibility criteria specific to Key Question 1 (nonpharmacologic vs. nothing/treatment as usual/usual care or vs. other nonpharmacologic)

Intervention

- May include same pharmacologic co-intervention as comparator group

Comparators

- No nonpharmacologic treatment
- Other nonpharmacologic modality
- May include same pharmacologic co-intervention as intervention group

Eligibility criteria specific to Key Question 2 (nonpharmacologic vs pharmacologic**Intervention**

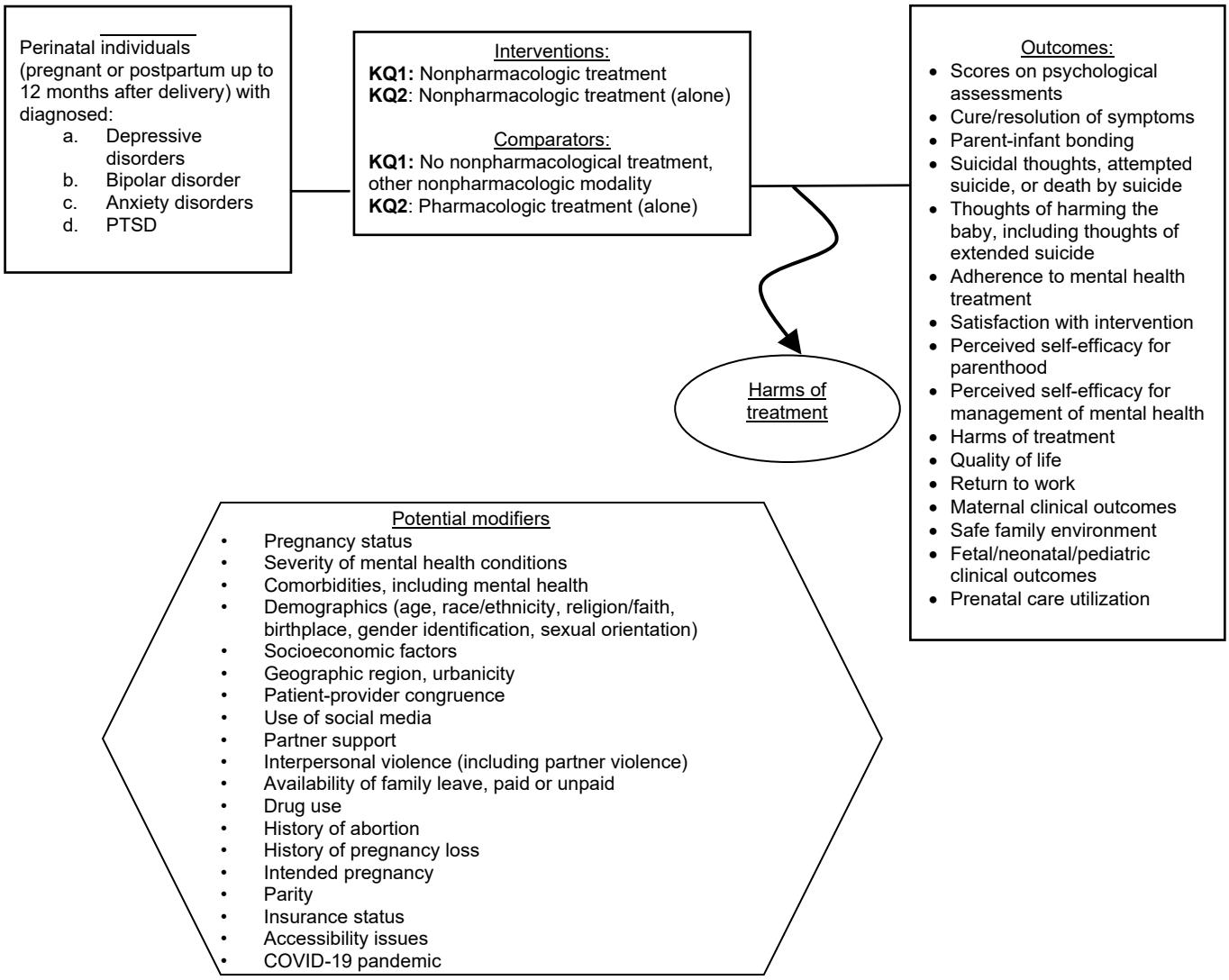
- Nonpharmacologic intervention alone (no use of pharmacologic therapy)

Comparators

- Pharmacologic treatment alone

IV. Analytic Framework

Figure. Analytic Framework for Key Questions 1 and 2: Nonpharmacologic interventions for mental health conditions in perinatal individuals



Abbreviations: KQ = Key Question, OCD = obsessive-compulsive disorder, PTSD = post-traumatic stress disorder

V. Methods

This SR will follow Evidence-based Practice Center (EPC) Program methodology, as described in its Methods Guide, particularly as it pertains to reviews of comparative effectiveness, and complex meta-analyses.

Criteria for Inclusion/Exclusion of Studies in the Review: See Study Eligibility Criteria in Section III.

Literature Search Strategies to identify primary studies for all KQs

We will conduct full literature searches in Medline (via PubMed), Embase, CINAHL, PsycINFO, the Cochrane Register of Clinical Trials and the Cochrane Database of Systematic Reviews. We will also run a search of the ClinicalTrials.gov registry to capture references to published studies the literature searches may have missed. We will not employ language restrictions, but we will limit publication date to studies published ≥2000 as our KIs and TEP agreed this would be most applicable to contemporary practice. We will include filters to remove nonhuman studies and articles that are not primary RCTs or SRs. Our searches will include specific controlled vocabulary terms (MeSH or Emtree), along with specific free-text words for eligible interventions. For non-English language articles, screening and data extraction will be done either by readers of the relevant languages or after translation via Google Translate (https://translate.google.com/), where possible. Searches will be independently peer reviewed by a librarian at another Evidence-based Practice Center.

We will use existing SRs in one of three ways. For topics with robust existing SRs (e.g., non-pharmacological interventions for perinatal depression), we will consider (with partners and TOO) updating these SRs. In such cases, we would extract study-level data from the existing SRs and only extract vital missing data from the primary studies, not including risk of bias assessment. We will use AMSTAR-2[58] to determine whether SRs were well-conducted and reported (including adequate assessment of risk of bias). Only such SRs would be eligible for full inclusion. For all topics without robust SRs, we will use the existing SRs as reference sources. We will also consider summarizing SRs of earlier foundational nonpharmacological interventions (i.e., SR published after 2000 but primary studies were published before 2000).

A Supplemental Evidence and Data for Systematic review (SEADS) portal will be available for this review. Additional articles suggested to us from any source, including peer and public review, will be screened applying identical eligibility criteria. We will update the search during public of the Draft Report.

Screening Process

Citations from all searches will be deduplicated and then entered into Abstrackr software (http://abstrackr.cebm.brown.edu/) to enable title and abstract screening. The team will conduct two or more rounds of pilot screening. During each pilot round, we will all screen the same 100 abstracts and discuss conflicts, with the goal of training the team in the nuances of the eligibility criteria and refining the criteria as needed. After the pilot rounds, we will continue abstract screening in duplicate. The Abstrackr software has machine learning capabilities that predict the likelihood of relevance of each citation. Daily, the list of unscreened abstracts will be sorted so that the most potentially relevant articles are presented first. This process will make screening more efficient and will enable us to capture almost all relevant articles relatively early in the abstract-screening process. Consistent with the approach we have used for all our reviews in the past 5 years, we will use standardized methods to leverage Abstrackr's (http://abstrackr.cebm.brown.edu/) machine learning capacities to constrain the number of citations that need human screening.

We will train the machine learning algorithm as follows: (1) We will include references of known existing potentially relevant studies for each KQ. (2) We will confirm this set of potentially relevant citations was successfully captured by our PubMed search and add the ones that are not. (3) Based on recently published work by Sampson et. al.,[59] we will select the top 500 articles from our search using PubMed's best-match ("most relevant") algorithm. (4) The abstracts from steps (1) and (3) will be entered into Abstrackr and screened by all team members, with resolution of all conflicts in conference. (5) Subsequently, citations found by the full literature searches will be added to the already-screened citations in Abstrackr, and abstract screening will continue in duplicate, with conflicts adjudicated in conference or by a third screener.

Potentially relevant citations will be retrieved in full text. All these articles will be rescreened in duplicate.

Data Extraction and Data Management

We will extract data and conduct risk of bias assessments directly into Systematic Review Data Repository Plus (SRDR+) software (https://srdrplus.ahrq.gov). Data will be entered by one highly experienced researcher and reviewed by at least one other. For each study, we will extract publication identifying data, study design features (including definitions used to define the eligible population), population characteristics, intervention and comparator names and descriptions (including intervention content, duration, modes of delivery, personnel delivering the intervention and setting in which it is delivered), relevant outcomes and their definitions, results, and funding source. We will extract, as available, data on the effect modifiers that are relevant to the KQs being addressed by each study. We will extract data on intervention details in Google sheets and use the approach we used successfully for our recent reviews of complex interventions for substance use disorders and for prehabilitation/rehabilitation interventions.[60, 61] Namely, we will implement an intervention taxonomy to code each intervention which characterizes the intervention content as well as the modes of delivery (described in the eligibility criteria above). Each study will be independently coded by research associates who will be trained by investigators with expertise in complex interventions and nonpharmacologic and behavioral interventions.

Assessment of Methodological Risk of Bias of Individual Studies:

We will evaluate each study for risk of bias and methodological quality. We will incorporate items from the Cochrane Risk of Bias Tool[62] and the National Heart, Lung, and Blood Institute (NHLBI) Quality Assessment Tool.[63] We will use all the items from the Cochrane Risk of Bias Tool, which addresses issues related to randomization and allocation concealment methodology; blinding of patients, study personnel/care providers, objective outcome assessors, and subjective outcome assessors; incomplete outcome data; selective outcome reporting; and other issues that could be related to bias. We will also use items from the NHLBI quality-assessment tool focusing on the adequacy of descriptions of study eligibility criteria, interventions, and outcomes.[63]

Data Synthesis:

Each included study will be described in summary and evidence tables presenting study design features, study participant characteristics, descriptions of interventions (at a high level and at a granular detailed level), outcome results, and risk of bias/methodological quality. We will summarize the evidence of outcome results narratively for all outcomes of interest. Summary tables will briefly describe the studies and their findings, within appropriate groupings of comparisons as relevant.

Due to time and resource restrictions, for topics with large bodies of evidence, we plan to restrict synthesis to comparisons with three or more studies. Our logic is that these are the comparisons researchers have deemed to be of greatest interest and they are the comparisons we are most likely to be able to make conclusions about (beyond “insufficient evidence”), and the restriction will reduce the need to spend resources on extracting and summarizing studies that will only lead to “insufficient” evidence. We will however include a list of these studies with key characteristics and findings in an appendix. We will not impose this restriction for smaller evidence bases (e.g., comparisons of interventions for the treatment of PTSD, bipolar disorder, or OCD).

For prioritized outcomes, if at least three sufficiently similar trials are found, we will conduct standard pair-wise meta-analyses. We may consider conducting network meta-analyses comparing broad intervention groups (e.g., CBT vs. mindfulness) if data allow, as we did in the adolescent substance use review.[61] Should data permit, we will use hierarchical multivariable meta-regression models to estimate the association between predictors of interest (e.g., population, intervention, comparator characteristics) and study outcomes.[64] We may conduct meta-analyses on non-prioritized outcomes as time and resources allow, depending on the potential value of such analyses.

For all stages of the SR, we will closely adhere to up-to-date AHRQ guidance on content, format, and structure. We will include summaries of SR findings and conclusions written for nontechnical readers. We will work with AHRQ and the TEP to design tables and graphics that most clearly transmit information, particularly to fit the needs of any planned CPG development groups. All extracted data will be in SRDR+ and the project will be made publicly available (i.e., published) within SRDR+.

Grading the Strength of Evidence (SoE) for Major Outcomes and Comparisons: We will evaluate the SoE addressing each major comparison of nonpharmacological interventions for each KQ. We expect that these will include the following comparisons for perinatal individuals:

- Relative impact on **psychological assessments** associated with various nonpharmacological interventions
- Relative impact on **cure/resolution of symptoms or condition** associated with various nonpharmacological interventions
- Relative impact on **parent-infant bonding** associated with various nonpharmacological interventions
- Relative impact on **suicidal thoughts, attempted suicide, or death by suicide** associated with various nonpharmacological interventions
- Relative impact on **thoughts of harming the baby, including thoughts of extended suicide** associated with various nonpharmacological interventions
- Relative impact on **adherence to mental health treatment** associated with various nonpharmacological interventions

We will grade the strength of the body of evidence as per the AHRQ Methods Guide on assessing SoE.[65] We will assess SoE for each of the prioritized outcomes. For each SoE assessment, we will consider the number of studies, their study designs, the study limitations (i.e., risk of bias and overall methodological quality), the directness of the evidence to the KQs, the consistency of study results, the precision of any estimates of effect, the likelihood of reporting bias, other limitations, and the overall findings across studies. Based on these assessments, we will assign a SoE rating as being either high, moderate, low, or insufficient evidence to estimate an effect.

Outcomes with imprecise estimates or inconsistent findings across studies that preclude a conclusion or with data from only one study will be deemed to have insufficient evidence to allow for a conclusion (with the exception that a particularly large, low risk of bias, well-generalizable single study could provide at least low SoE). This approach is consistent with the concept that for imprecise evidence "any estimate of effect is very uncertain," the definition of Very Low-quality evidence per GRADE.[66]

We will summarize the data sources, basic study characteristics, and each SoE dimensional rating in an "Evidence Profile" table. This table will detail our reasoning for arriving at the overall SoE rating.

Assessing Applicability:

For each KQ, we will assess the applicability of the included studies to the general population of perinatal individuals with mental health conditions in the U.S. based primarily on the studies' eligibility criteria and their included participants, specifically related to such factors as age, perinatal risk status, accessibility (financial or other resources required) of the intervention, and country.

VI. References

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VII. Abbreviations

AHRQ	Agency for Healthcare Research and Quality
ACOG	American College of Obstetrics and Gynecology
ACT	Acceptance and commitment therapy
APA	American Psychiatric Association
ACT	Acceptance and commitment therapy
CBT	Cognitive behavioral therapy
COI	Conflicts of interest
CPG	Clinical practice guideline
DBT	Dialectical behavioral therapy
DSM	Diagnostic and Statistical Manual
ECT	Electroconvulsive therapy
EPDS	Edinburgh Postnatal Depression Scale
EPC	Evidence-based practice center
IPT	Interpersonal psychotherapy
KQ	Key question
NET	Narrative Exposure Therapy
NHLBI	National Heart, Lung, and Blood Institute
OB/GYN	Obstetrician-gynecologists
OCD	Obsessive compulsive disorder
PHQ-9	Patient Health Questionnaire-9
PSI	Postpartum Support International
PTSD	Posttraumatic stress disorder
RCT	Randomized controlled trial
SEADS	Supplemental Evidence and Data for Systematic review
SoE	Strength of Evidence
SR	Systematic review
TEP	Technical expert panel
TOO	Task order officer

VIII. Summary of Protocol Amendments

Date	Section	Original Protocol	Revised Protocol	Rationale
August 24, 2023	V. Methods / Screening Process / Data Synthesis	*Data Synthesis* Due to time and resource restrictions, for topics with large bodies of evidence, we plan to restrict synthesis to comparisons with three or more studies. Our logic is that these are the comparisons researchers have deemed to be of greatest interest and they are the comparisons we are most likely to be able to make conclusions about (beyond "insufficient evidence"), and the restriction will reduce the need to spend resources on extracting and summarizing studies that will only lead to "insufficient" evidence. We will however include a list of these studies with key characteristics and findings in an appendix. We will not impose this restriction for smaller evidence bases (e.g., comparisons of interventions for the treatment of PTSD, bipolar disorder, or OCD).	[Moved to] *Classification of studies for full data synthesis or appendix evidence map* Given the expected large body of evidence and numerous potentially eligible interventions and comparisons for nonpharmacologic treatments of depression and anxiety, and given time and resource restrictions, we plan to restrict full data synthesis mostly to comparisons with three or more studies. Our logic is that these are the comparisons researchers have deemed to be of greatest interest and they are the comparisons we are most likely to be able to make conclusions about (beyond "insufficient evidence"). We will also include comparisons with at least one large (N≥100 per group), low or moderate risk of bias studies, since these may allow for at least a low strength-of-evidence (SoE) conclusion. We will not impose this restriction for smaller evidence bases (i.e., comparisons of interventions for the treatment of PTSD, bipolar disorder, or OCD). Otherwise eligible (small) studies evaluating uncommonly-analyzed comparisons of interventions for depression and anxiety treatments will be listed in an appendix "evidence map". This appendix will include each study's key characteristics (e.g., interventions, sample size	Improved clarification of the plan to handle the expected large volume of uncommonly reported comparisons of interventions for anxiety and depression. Also clarification of the rationale for this method. Also addition of full review of large, low or moderate risk of bias studies in the full report. More explicit description of how studies included in the appendix evidence map will be handled.

Date	Section	Original Protocol	Revised Protocol	Rationale
			per group, and primary findings. We will extract these data solely from each study's abstract (except, if needed, data on sample size). We will not assess risk of bias for these studies; except that we will assess risk of bias of large studies (N≥100 per group) to determine whether they should be included in the full synthesis. If we determine these large studies are at high risk of bias, we will explain why.	
August 24, 2023	V. Methods / Data Extraction and Data Management	We will extract data and conduct risk of bias assessments directly into Systematic Review Data Repository Plus (SRDR+) software (https://srdrplus.ahrq.gov).	For studies meeting criteria for full data synthesis, we will extract data and conduct risk of bias assessments directly into Systematic Review Data Repository Plus (SRDR+) software (https://srdrplus.ahrq.gov).	Clarification that these methods apply to studies meeting criteria for full data synthesis, not for studies in the appendix evidence map.
August 24, 2023	V. Methods / Data Extraction and Data Management	[No text]	We will also enter studies included only in the evidence map into SRDR+, but will limit data extraction to intervention names, sample sizes, and a text summary of the main findings.	Additional methods for how studies in the appendix evidence map will be processed.
August 24, 2023	V. Methods / Assessment of Methodological Risk of Bias of Individual Studies	We will evaluate each study for risk of bias and methodological quality.	For studies meeting criteria for full data synthesis (and for other large studies [N≥100 per group]), we will evaluate each study for risk of bias and methodological quality.	Clarification that these methods apply to studies meeting criteria for full data synthesis, not for studies in the appendix evidence map.

Date	Section	Original Protocol	Revised Protocol	Rationale
August 24, 2023	V. Methods / Data Synthesis	Each included study will be described in summary and evidence tables…	For studies meeting criteria for full data synthesis, each included study will be described in summary and evidence tables…	Clarification that these methods apply to studies meeting criteria for full data synthesis, not for studies in the appendix evidence map.
August 24, 2023	XV. Registration	Prospero registration number was still pending	The registration number is PROSPERO 2023 CRD42023440650	Prospero registration number added

If we need to further amend this Protocol, we will give the date of each amendment, describe the change, and provide the rationale in this section.

IX. Review of Key Questions

AHRQ posted the Key Questions on the AHRQ Effective Health Care Website for public comment. The EPC refined and finalized them after reviewing of the public comments and seeking input from KIs. This input is intended to ensure that the Key Questions are specific and relevant.

X. Review of Key Questions

We included a panel of KIs during Topic Refinement. The included KIs represented diverse perspectives related to obstetrics and gynecology, clinical psychology, social work, and maternal and child healthcare policy. We also included KIs with expertise in diversity, equity, and inclusion and KIs who offered important patient perspectives.

Within the EPC program, the KIs' role is to provide input into identifying and refining the Key Questions for research that will inform healthcare decisions. The EPC solicits input from KIs when developing questions for systematic review or when identifying high priority research gaps and needed new research. KIs are not involved in analyzing the evidence, writing the report, or reviewing the report, except as given the opportunity to do so through the peer or public review mechanism.

KIs must disclose any financial conflicts of interest greater than $5,000 and any other relevant business or professional conflicts of interest. Because of their role as end-users, individuals are invited to serve as KIs and those who present with potential conflicts may be retained. The Task Order Officer (TOO) and the EPC work to balance, manage, or mitigate any potential conflicts of interest identified.

XI. Technical Experts

Technical Experts constitute a multi-disciplinary group of clinical, content, and methodological experts who provide input in defining populations, interventions, comparisons, or outcomes and identify particular studies or databases to search. The Technical Expert Panel (TEP) is selected to provide broad expertise and perspectives specific to the topic under development. Divergent and conflicting opinions are common and perceived as healthy scientific discourse that fosters a thoughtful, relevant systematic review. Therefore, study questions, design, and methodological approaches do not necessarily represent the views of individual technical and content experts. Technical Experts provide information to the EPC to identify literature search strategies and suggest approaches to specific issues, as requested by the EPC. Technical Experts do not do analysis of any kind; neither do they contribute to the writing of the report.

They do not review the report, except as given the opportunity to do so through the peer or public review mechanism.

Members of the TEP must disclose any financial conflicts of interest greater than $5,000 and any other relevant business or professional conflicts of interest. Because of their unique clinical or content expertise, individuals are invited to serve as Technical Experts and those who present with potential conflicts may be retained. The AHRQ TOO and the EPC work to balance, manage, or mitigate any potential conflicts of interest identified.

XII. Peer Reviewers

Peer reviewers are invited to provide written comments on the Draft Report based on their clinical, content, or methodological expertise. The EPC considers all peer review comments on the Draft Report in preparation of the Final Report. Peer reviewers do not participate in writing or editing of the Final Report or other products. The Final Report does not necessarily represent the views of individual reviewers. The EPC will complete a disposition of all peer review comments. The Disposition of Comments for systematic reviews will be published 3 months after the publication of the Final Report.

Potential peer reviewers must disclose any financial conflicts of interest greater than $5,000 and any other relevant business or professional conflicts of interest. Invited peer reviewers may not have any financial conflict of interest greater than $5,000. Peer reviewers who disclose potential business or professional conflicts of interest may submit comments on Draft Reports through the public comment mechanism.

XIII. EPC Team Disclosures

EPC core team members must disclose any financial conflicts of interest greater than $1,000 and any other relevant business or professional conflicts of interest. Related financial conflicts of interest that cumulatively total greater than $1,000 will usually disqualify EPC core team investigators.

XIV. Role of the Funder

This project is funded by and executed under AHRQ, U.S. Department of Health and Human Services through Contract No. 75Q80120D00001 / 75Q80123F32009 The TOO will review contract deliverables for adherence to contract requirements and quality. The authors of this report will be responsible for its content. Statements in the report should not be construed as endorsement by ACOG, American Psychiatric Association, American Psychological Association, AHRQ, or the U.S. Department of Health and Human Services.

XV. Registration

This Protocol has been registered in the international prospective register of systematic reviews (PROSPERO). The registration number is PROSPERO 2023 CRD42023440650 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42023440650.