



# VA/DoD CLINICAL PRACTICE GUIDELINE FOR THE MANAGEMENT OF PREGNANCY

# Department of Veterans Affairs Department of Defense

#### **QUALIFYING STATEMENTS**

The Department of Veterans Affairs (VA) and the Department of Defense (DoD) guidelines are based on the best information available at the time of publication. The guidelines are designed to provide information and assist decision making. They are not intended to define a standard of care and should not be construed as one. Neither should they be interpreted as prescribing an exclusive course of management.

This clinical practice guideline (CPG) is based on a systematic review of both clinical and epidemiological evidence. Developed by a panel of multidisciplinary experts, it provides a clear explanation of the logical relationships between various care options and health outcomes while rating both the quality of the evidence and the strength of the recommendation.

Variations in practice will inevitably and appropriately occur when providers consider the needs of individual patients, available resources, and limitations unique to an institution or type of practice. Therefore, every health care professional using these guidelines is responsible for evaluating the appropriateness of applying them in the setting of any particular clinical situation with a patient-centered approach.

These guidelines are not intended to represent VA or DoD policies. Further, inclusion of recommendations for specific testing, therapeutic interventions, or both within these guidelines does not guarantee coverage of civilian sector care.

Version 4.0 - 2023

# Prepared by Management of Pregnancy Work Group

With support from

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and

**Clinical Quality Improvement Program, Defense Health Agency** 

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Based on evidence reviewed through June 1, 2022

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<sup>&</sup>lt;sup>a</sup> VA/DoD Clinical Practice Guideline. (2023). Management of Pregnancy Work Group. Washington, DC: U.S. Government Printing Office.

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# I. Introduction

The VA and DoD Evidence-Based Practice Work Group (EBPWG) was established and first chartered in 2004, with a mission to advise the VA/DoD Health Executive Committee "on the use of clinical and epidemiological evidence to improve the health of the population . . ." across the Veterans Health Administration (VHA) and Military Health System (MHS), by facilitating the development of CPG for the VA and DoD populations.(1) Development and update of VA/DoD CPGs is funded by VA Evidence Based Practice, Office of Quality and Patient Safety. The system-wide goal of evidence-based CPGs is to improve patient health and wellbeing.

In 2018, VA and DoD published a CPG for the Management of Pregnancy (2018 VA/DoD Pregnancy CPG), which was based on evidence reviewed through May 18, 2017. Since the release of that CPG, the evidence base on pregnancy has expanded. Consequently, the EBPWG initiated the update of the 2018 VA/DoD Pregnancy CPG in 2022. This updated CPG's use of Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach reflects a more rigorous application of the methodology than previous iterations.(2) Therefore, the strength of some recommendations might have been modified because of the confidence in the quality of the supporting evidence (see Evidence Quality and Recommendation Strength).

This CPG provides an evidence-based framework for evaluating and managing care for pregnant patients toward improving clinical outcomes. Successful implementation of this CPG will

- Assess the patient's condition and collaborate with the patient, family, and caregivers to determine optimal management of patient care;
- Emphasize the use of patient-centered care and shared decision making;
- Minimize preventable complications and morbidity; and
- Optimize individual health outcomes and quality of life (QoL).

# II. Background

# A. Description of Pregnancy

Pregnancy is the reproductive time during which a developing embryo or fetus grows inside the uterus. It is a time of dramatic change for a developing embryo or fetus and a pregnant person.

Although pregnancy and birth are normal physiological events, pregnancy is a period of increased risk for a range of conditions for the pregnant patient. It is also a time of more frequent interaction or interactions with the health care system, affording an opportunity to optimally manage chronic health conditions and provide preventive care. The goal of the health care team is to support the pregnant person to have as healthy a pregnancy as

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possible and ideally to have an uncomplicated full-term birth. The physical, psychological, and social support that the pregnant person receives during this time can help reduce health problems in their own life and that of their child. Evidence-based care during pregnancy can have a life-long impact on both the pregnant person and their child.

Patients receiving care from VHA and the Defense Health Agency (DHA) share some similarities with the general pregnant population in the United States (U.S.) but also have unique characteristics that distinguish them from their civilian counterparts. The next sections provide a brief context of key epidemiologic trends in the U.S. pregnant population that will contextualize more specific data and background that follows about the pregnant patients cared for by VHA and DHA.

# B. Current Trends in Pregnancy Epidemiology in the United States General Population

# a. Rates of Reproduction

Since 2007, both the number of births and the birth rate in the U.S. general population have been down trending. For example, in 2014, there were 3,988,076 births (12.5 births/1,000 persons capable of pregnancy), but in 2021 there were 3,664,292 births (11 births/1,000 persons capable of pregnancy). Of note, the years 2019–20 saw an increased decline over prior or subsequent years because births declined approximately 4% (versus the 1–2% decline otherwise over this period).(3) The COVID-19 pandemic appears, in emerging literature, to be a contributor to this increased decline in 2019–20.(4, 5) Alongside this downward trend in birth rates is an upward trend in the mean age at first birth as well as the median age of giving birth.(6, 7) In 2021, the mean age at first birth was 27.3, up from 27.1 in 2020.(3) The median age at which people give birth has also increased, from 27 in 1990 to 30 in 2019.(8)

Multifactorial reasons likely account for both the decrease in birth rates and increase in older people giving birth. These reasons include increased educational and career opportunities before having children and improved access to contraception and reproductive health services as well as constraints on ideal family size because of economic challenges and more recently the COVID-19 pandemic. Many of these factors are potentially interrelated.(9, 10)

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# b. Maternal Mortality, Pregnancy-Related Mortality, and Severe Maternal Morbidity – Current Trends in the General United States Population

Despite advances in medical knowledge, the U.S. has the unfortunate distinction of having rising numbers of maternal deaths<sup>b</sup> as well as rising pregnancy-related mortality<sup>c</sup> and severe maternal morbidity<sup>d</sup> (SMM) rates. In 2021, there were 1,205 maternal deaths in the U.S. compared with 861 in 2020 and 754 in 2019. The maternal mortality rate for 2021 was 32.9 deaths per 100,000 live births, compared with a rate of 23.8 in 2020 and 20.1 in 2019.(11) Likewise, since the implementation of the Pregnancy Mortality Surveillance System, the number of reported pregnancy-related deaths in the U.S. increased from 7.2 deaths per 100,000 live births in 1987 to 17.6 deaths per 100,000 live births in 2019.(12)

These deaths are distributed unequally across all pregnant patients in the U.S. Notable disparities exist both for differences in rates of pregnancy-related deaths among differing racial and ethnic groups as well as for birthing persons living in rural versus more urban areas. For example, during 2017–19, there were 62.8 deaths per 100,000 live births among non-Hispanic Native Hawaiian or Other Pacific Islander persons, 39.9 deaths per 100,000 live births among non-Hispanic Black persons, and 32.0 deaths per 100,000 live births among non-Hispanic American Indian or Alaska Native persons. In contrast, there were significantly lower rates in other ethnic and racial groups, including 14.1 deaths per 100,000 live births among non-Hispanic White persons, 12.8 deaths per 100,000 live births among non-Hispanic Asian persons, and 11.6 deaths per 100,000 live births among Hispanic persons.(12) Over the same period of 2017–19, leading causes of pregnancy-related deaths included cardiovascular conditions (excluding cardiomyopathy), infection or sepsis, cardiomyopathy, hemorrhage, thromboembolic events, hypertensive disorders of pregnancy (HDP), amniotic fluid embolism,

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Maternal Death: A maternal death is defined by the World Health Organization as "the death of a woman while pregnant or within 42 days of termination of pregnancy, irrespective of the duration and the site of the pregnancy, from any cause related to or aggravated by the pregnancy or its management, but not from accidental or incidental causes."
(https://www.cdc.gov/nchs/data/hestat/maternal-mortality/2021/maternal-mortality-rates-2021.pdf)
Maternal Mortality Rate: The number of maternal deaths per 100,000 live births

Pregnancy Related Mortality: A death during or within one year of pregnancy, from a pregnancy complication, a chain of events initiated by pregnancy, or the aggravation of an unrelated condition by the physiologic effects of pregnancy. (<a href="https://reviewtoaction.org/learn/definitions">https://reviewtoaction.org/learn/definitions</a>); Pregnancy Related Mortality Ratio: Pregnancy-related death (per above definition) per 100,000 live births

Severe Maternal Morbidity: SMM includes unexpected outcomes of labor and delivery that result in significant short- or long-term consequences to a woman's health.

(https://www.cdc.gov/reproductivehealth/maternalinfanthealth/severematernalmorbidity.html#anchor R eferences Severe maternal morbidity: screening and review. Obstetric Care Consensus No. 5.

American College of Obstetricians and Gynecologists. Obstet Gynecol 2016;128:e54–60.); NB: this document has aimed for inclusive language, however specific terms including maternal death and maternal mortality rate that incorporate "maternal" are not wholly interchangeable with "pregnancy" because of differences in definitions of these terms, so in these cases maternal has not been changed for a more sex neutral term.

cerebrovascular accident, other non-cardiovascular medical conditions and, very rarely, anesthesia complications.(12)

Likewise, a recent study using 2016–19 data from the Centers for Disease Control and Prevention (CDC) found that birthing persons in rural areas were more likely to be admitted to the intensive care unit (ICU) and to have a maternal mortality rate almost twice that of their urban counterparts, although maternal mortality rates rose for both groups over the study period.(13)

Severe maternal morbidity, characterized as unexpected outcomes of labor and delivery that result in significant short- or long-term consequences to a birthing person's health, follows similar trends to maternal deaths and pregnancy-related deaths. (14) Examples of SMM include blood transfusions, intubation, and hysterectomy. A study examining rates of SMM from 2012–15 using the National Inpatient Sample found that SMM including blood transfusions occurred at higher rates in all non-White ethnic groups when compared with White birthing persons; when blood transfusions were excluded from the SMM category, Black birthing people had persistently higher rates of SMM versus White birthing people. The same study noted that patients with medical comorbidities were more likely to experience SMM, and the disparity between rates of SMM for Black versus White birthing people was most stark for Black persons with multiple medical comorbidities.(15)

Severe pregnancy-related morbidity affects approximately 65,000 patients in the U.S. each year.(16) Key behavioral conditions, such as major depression, suicide, substance use disorder, intimate partner violence (IPV), and social determinants of health, are also significant contributors to pregnancy-related morbidity and mortality in addition to the medical conditions previously described.(17-19) Multiple factors might contribute to rising rates of SMM, including increased maternal age, pre-pregnancy obesity, increased rates of preexisting chronic conditions among pregnant persons, and an increasing number of cesarean deliveries. Additionally, pregnant people are impacted by increasing rates of suicidality and suicide, drug and alcohol overdose, and violence, including homicide.(17) Furthermore, given the disparities in rates of maternal deaths, pregnancy-related deaths, and SMM among racial and ethnic groups in the U.S., community, provider, and systemic factors might also play a role. These factors include differential access to both high-quality health care and the socioeconomic resources that can directly impact health and health care use. Implicit bias within the health care system and broader structural racism leading to systemic disadvantage of specific groups' access to housing, education, and economic resources are additional factors contributing to perinatal health disparities.(20)

In contrast to the trend of increasing maternal deaths, pregnancy-related deaths, and SMM among birthing persons in the U.S., the infant mortality rate, defined as the number of deaths during the first of life per 1,000 live births, declined 2.9% between

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2019 and 2020 and remained stable in 2021.(21, 22) The CDC indicated the following were the five leading causes of infant death in ranked order in 2021:

- Birth defects;
- Preterm birth or low birth weight;
- Sudden infant death syndrome (SIDS);
- Unintentional injuries (e.g., accidental suffocation); and
- Maternal complications of pregnancy.

This list of causes highlights the close interplay among the health of the pregnant patient, pregnancy complications, and neonatal morbidity and mortality; for example, HDP is associated with fetal growth restriction and preterm birth, low birth weight, or both. Beyond implications for infant mortality, the gestational age at birth can help predict neonatal outcomes, as shown in Table 1.(23, 24)

Table 1. Gestational Age at Birth Predicts Offspring Outcomes (23-25)

Term	Gestational Age at Birth	Outcomes		
		Increased risk for adverse outcomes such as respiratory, gastrointestinal, and neurological complications		
		Decreased risk for adverse outcomes compared with other preterm infants but increased risk for adverse outcomes compared with term infants		
Early- term	37 0/7–38 6/7 weeks	Increased risk of adverse outcomes, particularly respiratory, compared with full-term infants		
Full-term	39 0/7–40 6/7 weeks	Fully developed lungs, brains, and liver; better health outcomes than infants born outside this period		
Late-term	41 0/7–41 6/7 weeks	Increased risk of adverse neonatal outcomes compared with full-term infants		
Post-term	>41 6/7 weeks	Significant risk of adverse neonatal outcomes compared with full-term infants		

In 2021, preterm birth (birth before 37 completed weeks of gestation) occurred in approximately 10% of infants born in the U.S. The preterm birth rate rose 4% in 2021, from 10.1% in 2020 to 10.5% in 2021. Preterm birth rates, like SMM and pregnancy-related death rates, were notable for racial and ethnic disparities. In 2021, the rate of preterm birth among African American women (14.8%) was about 50% higher than the rate of preterm birth among White or Hispanic women (9.5% and 10.2% respectively).(22)

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# C. Pregnancy in the Department of Defense and the Department of Veterans Affairs Populations

This VA/DoD Pregnancy CPG is relevant to providers within the VA and DoD health care systems as well as providers in the broader community who care for VA and DoD beneficiaries.

#### a. Location of Care

# 1. Department of Defense

Pregnant Service members and dependents might receive their pregnancy care through the DoD health care system or through civilian providers within the community, depending on local availability of services and policies. Active duty Service members are expected to receive maternity services at their Military Treatment Facility (MTF), when available. The Defense Health Agency is engaged in several efforts to improve care during and after pregnancy. In 2022, DHA published four clinical practice recommendations to enhance and standardize care rendered during and after pregnancy to optimize health outcomes in the military health system. The topics included (1) behavioral health screening and referral in pregnancy and postpartum; (2) pelvic health evaluation, treatment, and referral for patients; (3) pregnancy and postpartum rehabilitation services; and (4) optimizing postpartum care.

#### 2. Veterans Affairs

State of Reproductive Health, Vol II: VA Reproductive Health Diagnoses and Organization of Care outlines the scope of care provided for women and sex-diverse pregnant Veterans. (26) Because VHA provides no routine prenatal or pregnancy care within VA health care facilities, pregnancy care is provided in the community via referral. Maternity care for Veterans is contracted to community providers outside VHA through the Office of Community Care. These system-level factors might lead to fragmentation of care and have been associated with poor pregnancy outcomes. VHA has implemented processes to address pregnancy care coordination needs, including assigning VHA-based Maternity Care Coordinators (MCC) to pregnant Veterans to help coordinate care, provide support, and place referrals requested by providers through pregnancy. Currently VA is expanding the MCC program to include the first year postpartum. In addition, educational programs for community providers describe the unique needs and characteristics of Veterans. Because of the nature of the provision of pregnancy care and ongoing care coordination, communication among providers is critical to ensure that each Service or family member or both and each Veteran is receiving the care coordination during pregnancy and postpartum and that all providers are fully aware of information relevant to the pregnant person's individual health and treatment plan.

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# b. Rates of Reproduction

# 1. Department of Defense

Between 2015 and 2021, there were 94,534 live births to active duty Service members. The number of live births annually has remained stable over that time, with only a slight decrease from the highest number of 13,854 births in 2020 to 12,841 births in 2021. Of the total births during this period, 67.6% (63,906) occurred in an MTF and the remainder occurred in civilian medical facilities. In addition, 562,318 live births occurred among dependents over the same time. In contrast to the stable live birth rate of active duty Service members, a nearly 20% decrease has occurred in the number of deliveries resulting in live birth for dependents, from 89,326 births in 2015 to 71,900 births in 2021. Only 32.9% of dependents delivered in an MTF during this period. This information was taken from the Department of Defense Birth and Infant Health Research (BIHR) program: Select reproductive health outcomes, 2015-2021; BIHR response to data request, December 9, 2022.

## 2. Veterans Affairs

Between fiscal years 2011 and 2021, VA covered an estimated total of 46,500 deliveries through community providers. Over this period, the number of deliveries covered by VA increased from approximately 2,577 in 2011 to more than 5,800 in 2021.(27) As the number of childbearing-age Veterans increases, the demand for use of pregnancy and newborn care will continue to increase. Veterans might be at especially high risk for adverse pregnancy outcomes because the prevalence of comorbid conditions is higher among Veterans than among their civilian counterparts.(28-30) System-level and provider-level factors might also impact pregnancy outcomes among Veterans.(26)

#### c. Pregnancy Complications

Although Service members and Veterans experience many of the same challenges during pregnancy as does the general population, they also have unique pregnancy care needs relative to their civilian counterparts.

# 1. Military Service Exposures

Service members and Veterans' military service experience might have included involvement in combat and attendant trauma, including sequelae such as physical injury or posttraumatic stress disorder (PTSD), or environmental/occupational exposures (e.g., fumes from burn pits, chemical toxicants). Additionally, service-related stressors might amplify the physical and psychological stresses of pregnancy for both active duty Service members and Veterans.(29, 31, 32) A 2022 peer reviewed publication reporting a survey of Veterans based on self-reported experiences of military sexual trauma (MST) and birth outcomes suggested that MST experiences might also impact perinatal outcomes.(33) Although current information is limited regarding the impact of this range of exposures on reproductive health outcomes, efforts are ongoing to assess the

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possible health impacts of military experience on active duty Service members and Veterans and their implications for obstetric health care.(34, 35)

### d. Behavioral Health

Similarly, to the general population, pregnant Veterans and Service members might be affected by both behavioral and physical health complications, which can lead to adverse outcomes.

# 1. Department of Defense

Certain military assignments, deployments, and removal from a support network might affect mental health outcomes of pregnant Service members. Nearly one in eight pregnant people in the military, compared with approximately one in nine in the general population, develop postpartum depression. Postpartum depression can, in turn, be complicated by other psychosocial factors, such as poor relationship satisfaction and low self-esteem.(36-38)

#### 2. Veterans Affairs

A study conducted between 2008 and 2012, compared the mental health of women Veterans who had experienced a pregnancy with women Veterans who had never experienced pregnancy. The results showed that anxiety, depression, and PTSD were twice as likely among women Veterans who had experienced a pregnancy as opposed to those without prior pregnancy history.(29) Reproductive aged Veterans who become pregnant might also have additional risk factors for increased behavioral health needs in the peripartum period, including history of MST, trauma, and social determinants of health needs, including housing.

# e. Physical Health

#### Department of Defense

The following data relate to complications experienced in pregnancies of active duty Service members, which appear to be similar to those of the dependent spouses of active duty Service members.(39, 40) Between 2012 and 2016, preterm labor, obesity-related complications, preeclampsia, and gestational diabetes mellitus (GDM) affected 17.7%, 9.2%, 6.8%, and 6.3% of live births, respectively. During this time, the percentage of live births affected by preeclampsia and GDM remained relatively stable, while the percentages of live births affected by preterm labor decreased and the percentage of live births affected by obesity-related complications increased.(40)

#### 2. Veterans Affairs

Significant perinatal complications affect Veterans, and similarly to the general U.S. population, these complications affect Veterans of color more than their White counterparts. The population of women or sex diverse Veterans is more racially or ethnically diverse than the general U.S. population. Of the Veteran population, Black and Hispanic women or sex-diverse Veterans are, on average, younger than their

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White counterparts and more likely to be in their reproductive years (18–44 years old).(26) Additionally, a single cross-sectional analysis of a longitudinal, prospective, multisite, observational cohort study of pregnant and postpartum Veterans receiving community-based obstetrical care examined pregnancy experiences in VA and found that pregnant persons of color were more likely to deliver by cesarean section than their White counterparts. (41) This background suggests that the pregnant population served by the VHA is at higher risk for significant pregnancy complications. Emerging data from two studies using CDC criteria to define SMM from the VHA supports this idea. Combellick et al. (2020) evaluated SMM and pregnancy-related mortality in pregnant Veterans who used VHA pregnancy benefits.(42) The study focused on 9,829 pregnancies among 91,061 post-9/11 Veterans between January 2014 and December 2016. Using individual chart review to confirm findings of SMM, the study followed Veterans through the first year postpartum. Results echoed those described in the section on SMM in the general population. Notable among Veterans who experienced life-threatening pregnancy-related events were high rates of mental health conditions, obesity, and rurality; the study also noted racial disparities in SMM among Veterans. Forty-eight percent of all SMM events occurred in the postpartum period following discharge from the hospital, with the majority of these occurring during the first week. The most common morbidity events included systemic infection, high blood pressure disorders, blood clots, blood transfusion requiring more than four units of blood products, and heart failure.(42) Quinn et al. (2021) identified 31,592 pregnancy outcomes among Veterans who used VHA and pregnancy benefits during fiscal years 2010–17.(43) One or more severe pregnancy-related morbidity (SPRM) events from the last menstrual period to within 1 year of pregnancy outcome (for this study, pregnancy outcome included ectopic pregnancy, spontaneous abortion, still birth, or live birth) were recorded for 2.5% of pregnancies (n=806). An SPRM event complicated 3.4% of pregnancies among Black Veterans, 2.4% of pregnancies among White Veterans, and 1.7% of pregnancies among Hispanic Veterans (p<0.001). Excluding transfusion, the most common morbidity events included systemic infection, blood clots, acute heart failure, bleeding disorders, and the need for life support such as ventilators. Black Veterans were 46% more likely than White Veterans to experience SPRM (OR: 1.46; 95% CI: 1.2–1.70).(43) Researchers have also attempted to examine the intersection of behavioral health and physical health conditions on perinatal outcomes. Using a database of all VA-covered deliveries between 2000 and 2012, Shaw et al. (2017) explored the possible relationship between PTSD and GDM and preeclampsia diagnoses in that population. (28) The team reported associations between Veterans diagnosed with PTSD and GDM (RR: 1.4; 95% CI: 1.2-1.7), preeclampsia (RR: 1.3; 95% CI: 1.1–1.6), prolonged hospitalization (RR: 1.2; 95% CI: 1.01–1.4), and repeat hospitalization (RR: 1.4; 95% CI: 1.2–1.6).(28) Furthermore, disparities exist within patients' postpartum reconnection to primary care, which is a primary way to address the ongoing effects of pregnancy complications related to hypertension (HTN), diabetes mellitus (DM), and behavioral health needs. One-half of Veterans reengage in VA primary care after childbirth, with significant racial differences in this care transition.

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Reengagement for those with common pregnancy complications, such as HDP and GDM, is only slightly higher and remains fewer than 60%.(44)

Other VA/DoD CPGs provide guidance regarding care for the following conditions.

- Screening and Management of Obesity and Overweight (VA/DoD Obesity CPG)
- Management of Posttraumatic Stress Disorder and Acute Stress Disorder (VA/DoD PTSD CPG)<sup>e</sup> (NB: To avoid overlap with other existing CPGs, evidence for and use of psychiatric medications to treat conditions, including depression and PTSD, perinatally were not covered in depth; more information on the evidence and use of these important treatments for pregnant persons can be found in the VA/DoD PTSD CPG and VA/DoD Major Depressive Disorder CPG.)

# III. Scope of This Guideline

This CPG is based on published clinical evidence and related information available through June 1, 2022. It is intended to provide general guidance on best evidence-based practices (see <a href="Appendix A">Appendix A</a> for additional information on the evidence review methodology). Although the CPG is intended to improve the quality of care and clinical outcomes (see <a href="Introduction">Introduction</a>), it is not intended to define a standard of care (i.e., mandated or strictly required care).

# A. Guideline Audience

This CPG is intended for use by VA and DoD providers and other providers involved in the care of pregnant patients. Additionally, this CPG is intended for community-based providers involved in the care of pregnant Service members, beneficiaries, or Veterans.

# **B.** Guideline Population

The patient population of interest for this CPG is pregnant patients who are eligible for care in the VA or DoD health care delivery systems, and those who receive care from community-based providers. It includes Veterans and Service members as well as their dependents.

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See the VA/DoD Clinical Practice Guideline for the Management of Posttraumatic Stress Disorder and Acute Stress Disorder. Available at: https://www.healthquality.va.gov/guidelines/MH/ptsd/

# IV. Highlighted Features of This Guideline

# A. Highlights in This Guideline

An update to the 2018 VA/DoD Pregnancy CPG, the current document includes the following noteworthy updates, making it important that providers review this version of the CPG.

 New pregnancy care algorithm to better reflect tailoring of care to individual patients' medical, behavioral, and social determinants of health needs to optimize prenatal and postpartum care and reduce maternal morbidity

This version added new guidance on preventive care in pregnancy, including updated recommendations for the COVID-19 vaccine as well as other vaccines, pelvic floor muscle training (PFMT), and use of low-dose aspirin in patients at risk for developing preeclampsia.

More rigorous application of GRADE methodology

Medical literature reflects a growing understanding and evidence that optimal pregnancy and postpartum care requires tailored attention to medical and behavioral health conditions as well as to the social needs of each individual patient. This growth includes the use of telehealth<sup>f</sup> and telemedicine<sup>g</sup> technologies to deliver care and new advances in testing and treatment. This CPG introduces new recommendations based on evidence-based literature reviews. These reviews progressed from key clinical questions developed by the Work Group, with a particular focus on topics relevant to VA and DoD patients and the providers that care for them. A sample of the pertinent new recommendations for the care of VA and DoD pregnant patients included in this guideline are the following.

- Assessment of all patients for behavioral health needs and use of evidence-based interventions for depression, including cognitive behavioral therapy (CBT), peer support, yoga, and mindfulness (NB: This guideline reviewed evidence related to specific key questions related to the listed interventions. However, pharmacotherapy plays a key role in treating depression for many pregnant patients. Guidance on pharmacotherapy for depression in pregnancy and postpartum can be found in the <a href="VA/DoD Major Depressive Disorder CPG">VA/DoD Major Depressive Disorder CPG</a>, specifically Recommendation 23.)
- Evaluation of pelvic floor muscle function and provision of basic instruction in pelvic floor muscle exercises for all patients during pregnancy
- Screening after pregnancy for pelvic muscle dysfunction, specifically urinary incontinence with referral to pelvic health rehabilitation

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In this CPG, telehealth is defined as a broad term that includes remote non-provider health services and remote clinical services between a provider and patient.

<sup>&</sup>lt;sup>9</sup> In this CPG, telemedicine is defined as remote clinical services between a provider and patient.

- Prenatal risk assessment of all patients for conditions that impact initiation and continuation of lactation, including obesity, depression, inappropriate gestational weight gain, and GDM
- Use of telehealth and telemedicine as part of pregnancy and postpartum care
- Superiority of non-invasive prenatal testing (NIPT) over other modalities for patients desiring prenatal genetic screening

The Work Group consisted of a multidisciplinary team of VA and DoD professionals (see <u>Guideline Development Team</u>) with experience in evaluating and managing the pregnancies of active duty Service members and Veterans. The recommendations, discussion sections, algorithm, and other clinical elements of this CPG were created with the evidence obtained from the literature reviews and by applying the GRADE approach. The 2023 VA/DoD Pregnancy CPG used a more rigorous application of the methodology than previous iterations, which resulted in the exclusion or downgrading of data used in previous versions of this CPG. This approach impacted the strength of some recommendations (e.g., *Strong for* downgraded to *Weak for*) despite a similar evidence base. For additional information on GRADE or CPG methodology, see <u>Appendix A</u>. The CPG included patient focus group input on critical care priorities. In addition, this CPG provides expanded recommendations on research needed to strengthen future guidelines.

# B. Components of This Guideline

This CPG provides clinical practice recommendations for the care of patients who are pregnant (see <u>Recommendations</u>). In addition, the <u>Algorithm</u> incorporates the recommendations in the context of the flow of patient care. This CPG also includes <u>Research Priorities</u>, which list areas the Work Group identified as needing additional research.

To accompany this CPG, the Work Group also developed toolkit materials for providers and patients, including a provider summary, a patient summary, and a quick reference guide, which can be found at <a href="https://www.healthquality.va.gov/index.asp">https://www.healthquality.va.gov/index.asp</a>.

# C. Racial and Ethnic Demographic Terminology in This Guideline

Demographic terms referring to an individual's race or ethnicity (e.g., Hispanic, Latino or Latina, Asian, Native American, Black, African American, White, Caucasian) can be ambiguously defined and understood, reflecting diverse geographies, histories, cultures, and experiences. Aligned with the recent Executive Order on Further Advancing Racial Equity and Support for Underserved Communities through the Federal Government, he Work Group used terms such as Black rather than African American and White rather than Caucasian to avoid presumptions about ancestry and to promote inclusivity,

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h Executive Order on Further Advancing Racial Equity and Support for Underserved Communities Through the Federal Government | The White House

clarity, and consistency. However, to represent accurately the evidence on which this CPG is based, the Work Group generally deferred to racial and ethnic terminology as reported in the published systematic reviews (SR), clinical trials, and other studies comprising that evidence when summarizing or otherwise referring to those studies. Consequently, usage of demographic terms in this CPG might appear inconsistent.

# D. Sex Terminology in This Guideline

Sex terminology is an area of rapidly evolving language and understanding within the health care sphere. The Work Group strove to use sex inclusive language throughout the guideline and notes that trans-identifying and nonbinary individuals might desire, seek, and experience pregnancy. However, to represent accurately the evidence on which this CPG is based, the Work Group generally deferred to sex terminology as reported in the published SRs, clinical trials, and other studies comprising the evidence when summarizing or otherwise referring to those studies. Consequently, sex inclusive language use might appear to vary in this CPG.

# E. Topics Considered outside the Scope of This Guideline

In recognizing that this CPG serves as a comprehensive guideline for routine pregnancy care, the Work Group felt it was important to call attention to several important components beyond the scope of this resource.

- The scope of this guideline is specifically for prenatal and postpartum care;
   therefore, recommendations for intrapartum and delivery management, except for recommendations for delivery timing, were excluded.
- Although this resource does provide guidance on initial evaluation and management to include referral indications to an advanced prenatal care provider, it does not include extensive guidance on the comprehensive management of complicated pregnancies.
- Because of the complexity of alternative birthing options as an emerging topic in obstetrical care, guidance on this subject, such as home births, is not included. The Work Group would defer to recommendations published by national organizations as well as would recommend staying abreast of new research and evidence for these topics.
- Although the Work Group recognizes that abortion care is a critical component of
  comprehensive pregnancy health care that plays a major role in reducing
  maternal morbidity and mortality and in promoting reproductive justice and
  freedom, specific guidance on the provision of abortion care was considered
  outside the scope of this guideline.

# F. Guideline Development Team

The VA Evidence Based Practice, Office of Quality and Patient Safety, in collaboration with the Clinical Quality Improvement Program, DHA, identified the following four

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providers to serve as Champions (i.e., leaders) of this CPG's Work Group: Carrie Kairys, DNP, and Elizabeth Patton, MD, MPhil, MSc, FACOG from VA; and Dalia Wenckus, MD, FACOG, and Michael Clark, MD, FACOG, from DoD.

The Work Group comprised individuals with the following areas of expertise: physical therapy, social work, nursing, obstetrics/gynecology, pharmacy, psychology, psychiatry, dietetics, family medicine, reproductive endocrinology, and maternal-fetal medicine.

Table 2 lists the Work Group and Guideline Development Team members. This CPG Work Group, led by the Champions, was tasked with

- Determining the scope of the CPG;
- Crafting clinically relevant key questions (KQs) to guide the systematic evidence review:
- Identifying discussion topics for the patient focus group and considering the patient perspective;
- Providing direction on inclusion and exclusion criteria for the systematic evidence review and the assessment of the level and quality of evidence; and
- Developing evidence-based clinical practice recommendations, including determining the strength and category of each recommendation.

The Lewin Team, including The Lewin Group, ECRI, Sigma Health Consulting, and Duty First Consulting, was contracted by VA to help develop this CPG.

Table 2. Guideline Work Group and Guideline Development Team

Organization	Names*		
	Carrie Kairys, DNP, FNP-BC (Champion)		
	Elizabeth W. Patton, MD, MPhil, MSc, FACOG (Champion)		
	Alicia Christy, MD, MHSCR		
	Sophia Hill-Smith, MSN, RN		
Department of Veterans Affairs	Ashley Lauria, MA, RD, LDN, IBCLC		
	Lisa Longo, PharmD, BCPS		
	Laura Miller, MD		
	Lauren Pachl, LCSW, CLC		
	Tammy Tenace, BSN, MS, ARNP-BC		
	Michael Clark, MD, FACOG (Champion)		
	Dalia Wenckus, MD, FACOG (Champion)		
Department of Defense	Colleen C. Blosser, MSN, RN		
	Michael Bybel, DO, FAAFP		
	Christine Higgins, DNP		

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Organization	Names*
	Adam Edward Lang, PharmD
Department of Defense	Leigh Anne Lechanski, PT, DPT, OCS
(cont.)	Amanda Owens, DO, FACOG
	Kristi Shearer, PhD
	James Sall, PhD, FNP-BC
VA Evidence Based Practice, Office of Quality and Patient Safety	Jennifer Ballard-Hernandez, DNP, RN, FNP-BC
Veterans Health Administration	René Sutton, BS, HCA
	Eric Rodgers, PhD, FNP-BC
	Elaine P. Stuffel, MHA, BSN, RN
Clinical Quality Improvement Program Defense Health Agency	Cynthia F. Villarreal, BSN, RN
	Isabella M. Alvarez, MA, BSN, RN
	Clifford Goodman, PhD
	Jennifer Weil, PhD
	Erika Beam, MS
The Lewin Group	Savannah Kucera, MPH, RN
	Amanda Heinzerling, MS
	Kristen Godwin, MPH
	Andrea Dressel, BS
	Stacey Uhl, MS
ECRI	Kelley Tipton, MPH
	Laura Koepfler, MLS
Sigma Health Consulting	Frances M. Murphy, MD, MPH
Sigina riealth Consulting	James Smirniotopoulos, MD
	Kate Johnson, BS
Duty First Consulting	Rachel Piccolino, BA
	Anita Ramanathan, BA

<sup>\*</sup>Additional contributor contact information is available in Appendix E.

# VI. Summary of Guideline Development Methodology

The methodology used in developing this CPG follows the *Guideline for Guidelines*, an internal document of the VA/DoD EBPWG updated in July 2019 that outlines procedures for developing and submitting VA/DoD CPGs.(45) The *Guideline for Guidelines* is available at <a href="http://www.healthquality.va.gov/policy/index.asp">http://www.healthquality.va.gov/policy/index.asp</a>. This CPG also aligns with the National Academy of Medicine's (NAM) principles of trustworthy CPGs (e.g., explanation of evidence quality and strength, management of potential conflicts of interest [COI], interdisciplinary stakeholder involvement, use of SR and

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external review).(46) Appendix A provides a detailed description of the CPG development methodology.

# A. Evidence Quality and Recommendation Strength

The Work Group used the GRADE approach to craft each recommendation and determine its strength. Per the GRADE approach, recommendations must be evidence based and cannot be made based on expert opinion alone. The GRADE approach uses the following four domains to inform the strength of each recommendation (see <a href="Determining Recommendation Strength">Determining Recommendation Strength and Direction</a>).(47)

- 1. Confidence in the quality of the evidence
- 2. Balance of desirable and undesirable outcomes
- 3. Patient values and preferences
- Other considerations, as appropriate (e.g., resource use, equity, acceptability, feasibility, subgroup considerations)

Using these four domains, the Work Group determined the relative strength of each recommendation (*Strong* or *Weak*). The strength of a recommendation is defined as the extent to which one can be confident that the desirable effects of an intervention outweigh its undesirable effects and is based on the framework above, which incorporates the four domains.(48) A *Strong* recommendation generally indicates *High* or *Moderate* confidence in the quality of the available evidence, a clear difference in magnitude between the benefits and harms of an intervention, similar patient values and preferences, and understood influence of other implications (e.g., resource use, feasibility).

In some instances, insufficient evidence exists on which to base a recommendation for or against a particular therapy, preventive measure, or other intervention. For example, the systematic evidence review might have found little or no relevant evidence, inconclusive evidence, or conflicting evidence for the intervention. The manner in which this finding is expressed in the CPG might vary. In such instances, the Work Group might include among its set of recommendations a statement of insufficient evidence for an intervention that might be in common practice although it is unsupported by clinical evidence and particularly if other risks of continuing its use might exist (e.g., high opportunity cost, misallocation of resources). In other cases, the Work Group might decide to exclude this type of statement about an intervention. For example, the Work Group might remain silent where an absence of evidence occurs for a rarely used intervention. In other cases, an intervention might have a favorable balance of benefits and harms but might be a standard of care for which no recent evidence has been generated.

Using these elements, the Work Group determines the strength and direction of each recommendation and formulates the recommendation with the general corresponding text, as shown in <u>Table 3</u>.

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Table 3. Strength and Direction of Recommendations and General Corresponding Text

Recommendation Strength and Direction	General Corresponding Text
Strong for	We recommend
Weak for	We suggest
Neither for nor against	There is insufficient evidence to recommend for or against
Weak against	We suggest against
Strong against	We recommend against

That a recommendation's strength (i.e., *Strong* versus *Weak*) is distinct from its clinical importance (e.g., a *Weak* recommendation is evidence based and still important to clinical care) is important to note. The strength of each recommendation is shown in Recommendations.

This CPG's use of GRADE reflects a more rigorous application of the methodology than previous iterations; the determination of the strength of the recommendation is more directly linked to the confidence in the quality of the evidence on outcomes that are critical to clinical decision making. The confidence in the quality of the evidence is assessed using an objective, systematic approach independent of the clinical topic of interest. Therefore, recommendations on topics for which designing and conducting rigorous studies might be inherently more difficult (e.g., randomized controlled trials [RCT]) are typically supported by lower quality evidence and, in turn, *Weak* recommendations. Recommendations on topics for which rigorous studies can be designed and conducted might more often be *Strong* recommendations. Per GRADE, if the quality of evidence differs across the relevant critical outcomes, the lowest quality of evidence for any of the critical outcomes determines the overall quality of the evidence for a recommendation.(2, 49) This stricter standard provides a consistent approach to determining recommendation strengths. For additional information on GRADE or CPG methodology, see Appendix A.

# B. Categorization of Clinical Practice Guideline Recommendations

Evidence-based CPGs should be current. Except for an original version of a new CPG, staying current typically requires revision of a CPG's previous versions based on new evidence or as scheduled subject to time-based expirations.(50) For example, the USPSTF has a process for monitoring the emergence of new evidence that could prompt an update of its recommendations, and it aims to review each topic at least every 5 years for either an update or reaffirmation.(51)

Recommendation categories were used to track how the previous CPG's recommendations could be reconciled. These categories and their corresponding definitions are similar to those used by the National Institute for Health and Care Excellence (NICE, England).(52, 53) Table 4 lists these categories, which are based on

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whether the evidence supporting a recommendation was systematically reviewed, the degree to which the previous CPG's recommendation was modified, and whether a previous CPG's recommendation is relevant in the updated CPG.

Additional information regarding these categories and their definitions can be found in <u>Recommendation Categorization</u>. The 2023 CPG recommendation categories can be found in <u>Recommendations</u>. <u>Appendix D</u> outlines the 2018 VA/DoD Pregnancy CPG's recommendation categories.

Table 4. Recommendation Categories and Definitions<sup>a</sup>

Evidence Reviewed	Recommendation Category	Definition		
	New-added	New recommendation		
	New-replaced	Recommendation from previous CPG was carried forward and revised		
Reviewed <sup>b</sup>	Not changed	Recommendation from previous CPG was carried forward but unchanged		
	Amended	Recommendation from previous CPG was carried forward with a nominal change		
	Deleted	Recommendation from previous CPG was deleted		
	Not changed	Recommendation from previous CPG was carried forward but unchanged		
Not Reviewed <sup>c</sup>	Amended	Recommendation from previous CPG was carried forward with a nominal change		
	Deleted	Recommendation from previous CPG was deleted		

<sup>&</sup>lt;sup>a</sup> Adapted from the NICE guideline manual (2012)(52) and Garcia et al. (2014)(53)

Abbreviation: CPG: clinical practice guideline

# C. Management of Potential or Actual Conflicts of Interest

Management of COIs for the CPGs is conducted as described in the *Guideline for Guidelines*.(45) Further, the *Guideline for Guidelines* refers to details in the VHA Handbook 1004.07 Financial Relationships between VHA Health Care Professionals and Industry (November 2014, issued by the VHA National Center for Ethics in Health Care)(54) as well as to disclosure statements (i.e., standard disclosure form completed at least twice by CPG Work Group members and the guideline development team).(45) The disclosure form inquires regarding relevant financial and intellectual interests or other relationships with, for example, manufacturers of commercial products, providers of commercial services, or other commercial interests. The disclosure form also inquires regarding any other relationships or activities that could be perceived to have

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<sup>&</sup>lt;sup>b</sup> The topic of this recommendation was covered in the evidence review carried out as part of the development of the current CPG.

<sup>&</sup>lt;sup>c</sup> The topic of this recommendation was not covered in the evidence review carried out as part of the development of the current CPG.

influenced, or that give the appearance of potentially influencing, a respondent's contributions to the CPG. In addition, instances of potential or actual COIs among the CPG Work Group and the guideline development team were subject to random webbased identification via standard electronic means (e.g., Centers for Medicare & Medicaid Services Open Payments, ProPublica). No COIs were identified among the CPG Work Group or the guideline development team.

# D. Patient Perspective

When developing a CPG, consideration should be given to patient perspectives and experiences, which often vary from those of providers.(49, 55) Focus groups can be used to help collect qualitative data on patient perspectives and experiences. VA and DoD Leadership arranged a virtual patient focus group on March 23, 2022. The focus group aimed to gain insights into patients who are pregnant of potential relevance and incorporate these insights into the CPG, as appropriate. Topics discussed included the patients' priorities, challenges they have experienced, information they have received regarding their care, and impacts of their care on their lives.

The patient focus group comprised a convenience sample of eight people. There were zero males and eight females. Five participants received care from both VA and DoD health systems. The Work Group acknowledges this convenience sample is not representative of all patients who are pregnant within the VA and DoD health care systems and, thus, findings are ungeneralizable and do not comprise evidence. For more information on the patient focus group methods and findings, see <a href="Appendix B">Appendix B</a>. The patient focus group participants were provided the opportunity to review the final draft and provide additional feedback.

#### E. External Peer Review

The Work Group drafted, reviewed, and edited this CPG using an iterative process. For more information, see <a href="Drafting and Finalizing the Guideline">Drafting and Finalizing the Guideline</a>. Once the Work Group members completed a near-final draft, they identified experts from VA and DoD health care systems and outside organizations generally viewed as experts in the respective field to review it. The draft was sent to those experts for a 14-business-day review and comment period. The Work Group considered all feedback from the peer reviewers and modified the CPG where justified, in accordance with the evidence. Detailed information on the external peer review can be provided by the VA Office of Quality and Patient Safety.

# F. Implementation

This CPG and algorithm are designed for adaptation by individual health care providers with respect to unique patient considerations and preferences, local needs, and resources. The algorithm serves as a tool to prompt providers to consider key decision points in the care for a patient with pregnancy. The Work Group submits suggested performance metrics for VA and DoD to use when assessing the implementation of this

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CPG. Robust implementation is identified in VA and DoD internal implementation plans and policies. Additionally, implementation would entail wide dissemination through publication in the medical literature, online access, educational programs, and, ideally, electronic medical record programming in the form of clinical decision support tools at the point of care.

# VII. Approach to Care in the Department of Veterans Affairs and the Department of Defense

# A. Patient-Centered Care

Intended to consider patient needs and preferences, guideline recommendations represent a whole/holistic health approach to care that is patient centered, culturally appropriate, and available to people with limited literacy skills and physical, sensory, or learning disabilities. VA/DoD CPGs encourage providers to use a patient-centered, whole/holistic health approach (i.e., individualized treatment based on patient needs, characteristics, and preferences). This approach aims to treat the particular condition while also optimizing the individual's overall health and wellbeing.

Regardless of the care setting, all patients should have access to individualized evidence-based care. Patient-centered care can decrease patient anxiety, increase trust in providers, and improve treatment adherence.(56, 57) A whole/holistic health approach (https://www.va.gov/wholehealth/) empowers and equips individuals to meet their personal health and wellbeing goals. Good communication is essential and should be supported by evidence-based information tailored to each patient's needs. An empathetic and non-judgmental approach facilitates discussions sensitive to sex, culture, ethnicity, and other differences.

# **B.** Shared Decision Making

This CPG encourages providers to practice shared decision making, a process in which providers, patients, and patient care partners (e.g., family, friends, caregivers) consider clinical evidence of benefits and risks as well as patient values and preferences to make decisions regarding the patient's treatment.(58) Shared decision making is emphasized in *Crossing the Quality Chasm,* an Institute of Medicine, now NAM, report in 2001 (59) and is inherent within the whole/holistic health approach. Providers must be adept at presenting information to their patients regarding individual treatments, expected risks, expected outcomes, and levels or settings of care or both, especially where patient heterogeneity in weighing risks and benefits might exist. VHA and MHS have embraced shared decision making. Providers are encouraged to use shared decision making to individualize treatment goals and plans based on patient capabilities, needs, and preferences.

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# C. Patients with Co-occurring Conditions

Co-occurring conditions can modify the degree of risk, impact diagnosis, influence patient and provider treatment priorities and clinical decisions, and affect the overall approach to managing pregnancy. Many Veterans, active duty Service members, and their families have one or more co-occurring conditions. Because pregnancy is sometimes accompanied by co-occurring conditions, managing pregnancy collaboratively with other care providers is often best. Some co-occurring conditions might require early specialist consultation to determine necessary changes in treatment or to establish a common understanding of how care will be coordinated. This approach might entail reference to other VA/DoD CPGs (e.g., for Suicide Risk, Substance Use Disorder, Opioids, Major Depressive Disorder, PTSD, or Schizophrenia).

### VIII. Recommendations

The evidence-based clinical practice recommendations listed in <u>Table 5</u> were developed using a systematic approach considering four domains as per the GRADE approach (see <u>Summary of Guideline Development Methodology</u>). These domains include confidence in the quality of the evidence, balance of desirable and undesirable outcomes (i.e., benefits and harms), patient values and preferences, and other implications (e.g., resource use, equity, acceptability).

Table 5. Evidence-Based Clinical Practice Recommendations with Strength and Category

Topic	Sub- topic	#	Recommendation	Strength <sup>a</sup>	Category <sup>b</sup>	
Routine Care	iploidy sening	Aneuploidy Screening	1.	We recommend offering non-invasive prenatal testing as the prenatal screening test of choice for all patients with singleton pregnancies who choose aneuploidy screening.	Strong for	Reviewed, New-added
	Aneupl	2.	We suggest non-invasive prenatal testing for patients with twin pregnancies who choose aneuploidy screening.	Weak for	Reviewed, New-added	
	tion	3.	We suggest assessing all patients for risk factors that impact initiation and continuation of lactation, including obesity, depression, inappropriate gestational weight gain, and gestational diabetes mellitus.	Weak for	Reviewed, New-added	
	Lactation	4.	We suggest individual or group lactation education delivered via in-person, telemedicine, or multimedia modalities be provided for all pregnant and postpartum patients to improve the probability of initiating and continuing lactation.	Weak for	Reviewed, New- replaced	

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i The VA/DoD Clinical Practice Guidelines are available at: https://www.healthquality.va.gov/

Topic	Sub- topic	#	Recommendation	Strength <sup>a</sup>	Category <sup>b</sup>			
	Pelvic Floor Health	5.	We suggest all patients have an early prenatal evaluation of pelvic floor muscle function and receive pelvic floor muscle exercise instruction during pregnancy for the prevention of urinary incontinence in late pregnancy and up to 6 months postpartum.	Weak for	Reviewed, New-added			
nt.)	Pelvic .	6.	We suggest referral to pelvic health rehabilitation for patients with reported urinary incontinence in the postpartum period.	Weak for	Reviewed, New-added			
Routine Care (cont.)	su	7.	We recommend offering scheduled delivery to patients who reach 41 weeks and 0/7 days undelivered. Antepartum fetal testing should begin at 41 weeks and 0/7 days if not delivered.	Strong for	Not reviewed, Amended			
Routin	Selected Conditions	8.	We suggest that patients with uncomplicated pregnancies may continue a standard work schedule throughout their pregnancy.	Weak for	Not reviewed, Amended			
	lected	9.	We suggest offering telemedicine as a complement to usual perinatal care.	Weak for	Reviewed, New-added			
	/eS	10.	There is insufficient evidence to recommend for or against specific interventions that would diminish disparities in perinatal care access and maternal and childbirth outcomes.	Neither for nor against	Reviewed, New-added			
	reterm Delivery	Preterm Delivery	ivery	ivery	11.	We recommend considering fetal fibronectin testing as a part of the evaluation strategy in patients between 24 0/7 and 34 6/7 weeks' gestation with signs and symptoms of preterm labor, particularly in facilities where the result might affect management of delivery.	Strong for	Not reviewed, Amended
SS			12.	We suggest vaginal progesterone or cerclage for singleton pregnancy with short cervix, history of spontaneous preterm birth, or both depending on patient characteristics and preferences.	Weak for	Reviewed, New-added		
Obstetri	1	13.	There is insufficient evidence to recommend for or against the use of aspirin to reduce recurrent spontaneous preterm birth.	Neither for nor against	Reviewed, New-added			
Complicated Obstetrics	ſS	rs	rs	14.	We recommend initiating aspirin therapy at or before 16 weeks' gestation in patients at risk of developing preeclampsia.	Strong for	Reviewed, New- replaced	
Сомр	Disorde	15.	We suggest low-dose aspirin of 100–150 mg daily for patients at risk of preeclampsia.	Weak for	Reviewed, New- replaced			
	Hypertensive Disorders	16.	We suggest patients with cardiometabolic disorders (e.g., gestational diabetes mellitus, hypertension, and obesity) be counseled on the benefits of following the Dietary Approaches to Stop Hypertension diet.	Weak for	Reviewed, New-added			
	Hy	17.	There is insufficient evidence to recommend for or against self-monitoring for blood pressure during pregnancy and the postpartum period.	Neither for nor against	Reviewed, New-added			

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Topic	Sub- topic	#	Recommendation	Strength <sup>a</sup>	Category <sup>b</sup>			
Complicated Obstetrics (cont.)	Bariatric Surgery	18.	We suggest patients who have undergone bariatric surgery be evaluated for nutritional deficiencies and the need for nutritional supplementation where indicated (e.g., vitamin B12, folate, iron, calcium).	Weak for	Not reviewed, Amended			
	Bariatri	19.	There is insufficient evidence to recommend for or against the routine supplementation of vitamins A, D, E, or K for pregnant patients who have undergone bariatric surgery.	Neither for nor against	Not reviewed, Amended			
	ľ	20.	We recommend screening for use of tobacco and nicotine products, alcohol, cannabis, illicit drugs, and inappropriate use of prescription medication. See VA/DoD Substance Use Disorders CPG.	Strong for	Not reviewed, Amended			
	Screening	Screening	Screening	Screening	21.	We recommend screening for depression periodically using a standardized tool, such as the Edinburgh Postnatal Depression Scale or the 9-item Patient Health Questionnaire, during pregnancy and postpartum.	Strong for	Not reviewed, Not changed
			22.	We suggest screening patients with posttraumatic stress disorder (PTSD) for active PTSD and offering PTSD treatment. See VA/DoD PTSD CPG.	Weak for	Reviewed, New-added		
Mental Health	Treatment	ant	23.	We recommend offering individual or group Interpersonal Psychotherapy or cognitive behavioral therapy for pregnant patients at risk of perinatal depression.	Strong for	Reviewed, New-added		
/ental			24.	We recommend offering Interpersonal Psychotherapy for treating depression during pregnancy or postpartum.	Strong for	Reviewed, New-added		
2			25.	We suggest offering cognitive behavioral therapy for treating depression during pregnancy or postpartum.	Weak for	Reviewed, New-added		
		26.	We suggest offering peer support for people with perinatal depression or risk of perinatal depression to improve depressive symptoms.	Weak for	Reviewed, New-added			
		27.	We suggest exercise, mindfulness, yoga, or any combination of these interventions for depressive symptoms in perinatal patients.	Weak for	Reviewed, New-added			
		28.	We suggest offering psychotherapies (e.g., cognitive behavioral therapy, Interpersonal Psychotherapy) or yoga or both for anxiety symptoms during and after pregnancy.	Weak for	Reviewed, New-added			

<sup>&</sup>lt;sup>a</sup> For additional information, see <u>Determining Recommendation Strength and Direction</u>.

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<sup>&</sup>lt;sup>b</sup> For additional information, see <u>Recommendation Categorization</u>.

### A. Routine Care

# a. Aneuploidy Screening

#### Recommendation

 We recommend offering non-invasive prenatal testing as the prenatal screening test of choice for all patients with singleton pregnancies who choose aneuploidy screening.

(Strong for | Reviewed, New-added)

2. We suggest non-invasive prenatal testing for patients with twin pregnancies who choose aneuploidy screening.

(Weak for | Reviewed, New-added)

#### **Discussion**

Evidence suggests that NIPT, with cell-free fetal deoxyribonucleic acid screening for aneuploidy, is a superior screening test for aneuploidy. Diagnostic accuracy parameters for detecting aneuploidy, such as sensitivity, specificity, positive predictive value, and negative predictive value, are higher for NIPT compared with aneuploidy screening methods, such as the serum quad screen, serum sequential screen, and serum integrated screen, with or without the addition of nuchal translucency in patients within a generally low-risk population or unselected pregnant patients. (60) Non-invasive prenatal testing demonstrated a sensitivity of at least 99.2% and specificity of 100% for the detection of trisomy 21 in an unselected pregnant population compared with a traditional screening sensitivity of 78.9% and specificity of 94.6%. Additionally, NIPT demonstrated excellent sensitivity and specificity for the detection of trisomy 18 and trisomy 13 compared with standard screening methods. The confidence intervals were noted to be wider for these outcomes because of a very low population prevalence of trisomy 18 and trisomy 13. A second SR, Rose et al. (2022), reported a negative predictive value for chromosomal anomalies in a general/low risk population of 99-100%, making this screening test optimal because of its extremely low false negative rate. (61) The SR by Badeau et al. (2017) also demonstrated high sensitivity and specificity for the detection with screening for sex chromosomal abnormalities, another set of relatively common conditions within the general population. (60) Sex chromosomal conditions are not screened for by the other traditional genetic screening tests.

For patients who choose aneuploidy prenatal screening, the benefits of NIPT far outweigh the potential risks. The superior sensitivity and specificity of the testing make for high aneuploidy detection rates with lower false positive rates compared with traditional screening methods. Although the positive predictive value does decrease dependent on the prevalence of the condition screened, it does so for all prenatal screening options, and, therefore, NIPT remains the superior test. The risks of NIPT testing are like those of any screening tests: it can result in significant anxiety when test results are positive, and patients must then choose whether to pursue diagnostic

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testing. Because NIPT is a screening test only, no decision to terminate a pregnancy should be made on the results of NIPT alone.

The SR by Badeau et al. (2017) also compared screening NIPT with actual diagnostic testing (via a pooled combination of amniocentesis and chorionic villus sampling in a mixed-risk population).(60) Diagnostic testing was found to have superior detection of the number and types of chromosomal anomalies. NIPT does not replace diagnostic testing and cannot detect all the genetic conditions that diagnostic testing can detect. The Work Group reinforces previous recommendations that suggest making prenatal diagnostic testing available to all pregnant patients.

Evidence suggests that for the general/low risk twin gestation, NIPT is the superior screening testing for the detection of trisomy 21, trisomy 18, and trisomy 13, based on diagnostic accuracy parameters in the 2022 SR by Rose et al.(61) The sensitivity and specificity remained high overall for all three conditions, with the highest being for the detection of trisomy 21. The sensitivity did decrease for both trisomy 18 and trisomy 13. No direct comparisons were made in this study with any of the other traditional prenatal screening options, which limits the quality of the data. We suggest offering NIPT as the test of choice when aneuploidy screening is desired in this population because the identified sensitivity and specificity appear to exceed the limited published values for traditional screening tests.

The benefits to the patient with twins undergoing prenatal screening with NIPT outweigh the risks. The benefits are the result of an accurate screening test to best inform the patient. The risks of being tested include the higher rate of test failure in twins, the uncertainty of which twin might be affected in the setting of a positive test, and the way or ways prenatal identification of a single aneuploid fetus might affect pregnancy management. All these things should be discussed with a patient in the pretest counseling.

Patient values and preferences vary significantly regarding genetic screening. All patients should be offered prenatal screening, diagnostic testing, or no testing and should be allowed to decide what fits with their personal values and preferences. First, patients need informative counseling on prenatal screening risks and benefits to make the most informed choice for themselves. This message can be lost in the difficulty of attempting to counsel patients on all their available aneuploidy screening options. The Work Group recommends simplifying and streamlining prenatal aneuploidy screening by recommending NIPT as the primary screening test in individuals who desire prenatal screening, so it is available to all people. It is the prenatal screening available at the earliest timeframe within the first trimester and can be performed at any time in pregnancy, in addition to having the highest sensitivity and specificity. Because it is not a two-part test, it does not require coordination of the correct timing of the blood draw and can be completed in one visit, an important consideration for mobile populations, such as VA/DoD patients. Providers should be aware of the interpretation of cfDNA

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screening test results, including counseling patients on the positive and negative predictive values of the test and recommending diagnostic testing (chorionic villus sampling or amniocentesis) before any irreversible decisions about the pregnancy. Predictive value calculators are available to assist providers.

Individuals with low fetal fraction or no-call cfDNA results should be referred to maternal-fetal medicine (MFM) physicians for counseling and offered diagnostic testing because of the 3% aneuploidy rate. Furthermore, individuals with suspected malignancy on cfDNA screening tests should also be referred to MFM physicians for additional evaluation and counseling.

The Work Group acknowledges that the other traditional prenatal screening methods might identify a broader scope of conditions than does NIPT, such as conditions associated with an elevated alpha-fetoprotein (e.g., spina bifida, gastroschisis, omphalocele, conditions associated with unexplained elevated alpha-fetoprotein), for which younger people might be at greater risk than for aneuploidy. Given this fact, patients should continue to be offered additional screening for measuring alpha-fetoprotein between 15 and 20 weeks of gestation. The Work Group also acknowledges that there are additional recommendations from professional societies to offer carrier screening to all pregnant people for specific genetic conditions (e.g., CF, SMA, hemoglobinopathies). Such tests, if performed, need not be repeated in each pregnancy. Counseling should include residual risk estimates of having an affected child.

The Work Group systematically reviewed evidence related to these recommendations.(60, 61) Therefore, they are categorized as *Reviewed, New-added*. The Work Group's confidence in the quality of the evidence was moderate to low. The limitations in the evidence were secondary to the low prevalence of chromosomal anomalies. This finding reduces the overall quality of the evidence because of larger variations in confidence intervals. The benefits of NIPT for aneuploidy screening in singleton and, to a lesser extent, twin gestation because of superior test performance parameters outweighed the potential harm of anxiety associated with false positive testing. However, the false positive results in the setting of NIPT are also reduced compared with traditional screening. Patient values and preferences varied somewhat because of differing preferences surrounding genetic testing. Thus, the Work Group made the following recommendations: We recommend offering non-invasive prenatal testing as the prenatal screening test of choice for all patients with singleton pregnancies who choose aneuploidy screening. We suggest non-invasive prenatal testing for patients with twin pregnancies who choose aneuploidy screening.

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#### b. Lactation

#### Recommendation

 We suggest assessing all patients for risk factors that impact initiation and continuation of lactation, including obesity, depression, inappropriate gestational weight gain, and gestational diabetes mellitus.

(Weak for | Reviewed, New-added)

#### **Discussion**

Searches identified three SRs and two prospective cohort studies that examined risk factors associated with lactation or breastfeeding, which includes any breastfeeding, exclusive breastfeeding, mixed formula and breastfeeding, cessation of breastfeeding, and time to first formula. Providers should be aware of risk factors suspected to impact lactation. Bringing awareness to these risk factors enables the provider to help patients meet their individual goals. Our searches have shown confidence in the quality of this evidence to be low to fair; however, the findings carry substantial weight and are very important to mention. The evidence identified risk factors, such as obesity and overweight, depression and anxiety, metabolic dysfunction (GDM), and inappropriate gestational weight gain. Glover et al. (2018) found that with every two-unit increase in BMI, participants were 8% more likely to experience early lactation cessation. (62) Lactogenesis is delayed among patients with BMI categorized as overweight or obese as well as those diagnosed with GDM.(62-64) Those categorized as either underweight, overweight, or obese were less likely to initiate breastfeeding or lactation, per Huang et al. (2019) and Nomura et al. (2020).(63, 64) Additionally, Huang et al. (2019) found that inappropriate gestational weight gain, both excessive and inadequate weight gain, were found to reduce initiation and impede continuation of breastfeeding. Inappropriate gestational weight gain is defined as not meeting or exceeding recommended weight gain per BMI category (see Table 10 for recommendations on weight gain).

Stuebe et al. (2019) and Kim et al. (2022) found that patients who experienced depression, anxiety, or both demonstrated earlier cessation of breastfeeding and were more likely to introduce formula.(65, 66) Nomura et al. (2020) also found that those with BMI categorized as overweight or obese often reported postpartum depression.(64) The previous 2018 VA/DoD Pregnancy CPG included findings by Fairlie et al. (2009) that suggest patients with prenatal depressive symptoms were less likely to plan to breastfeed.(67)

Patients who present with these risk factors and desire to breastfeed might need additional support or referral to ensure lactation success. The reviewed studies did not clearly define those who desired to breastfeed nor did the studies elaborate whether these risk factors were the sole cause of breastfeeding non-initiation or early cessation. The Work Group would like to emphasize that this list of risk factors is not comprehensive but encompasses those found to have supportive evidence.

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The patient focus group found that patients desire comprehensive multidisciplinary care. Not all VA/DoD facilities have the means to provide lactation services; however, it is a health goal that warrants support. Further research is needed to identify subpopulations and reasons for non-initiation and early cessation of breastfeeding, which would allow for development of targeted interventions for each subgroup.

The Work Group systematically reviewed evidence related to this recommendation. (62-66) Therefore, it is categorized as Reviewed, New-added. The Work Group's confidence in the quality of the evidence was very low. The body of evidence had some limitations, including self-reporting of BMI, mood symptoms, and breastfeeding/feeding mode. The prospective cohort study by Glover et al. (2018) was limited because it included only women diagnosed with GDM.(62) Of note, the measure of BMI is not a standard international measure. Based on the critical outcome measures of initiation of breastfeeding, continuing breastfeeding, mixed breastfeeding, and exclusive breastfeeding, the evidence had a low confidence in the quality of the strength of evidence based on the GRADE criteria. The benefits outweighed the harms, although no harms were identified. Patient values and preferences varied somewhat because of patients' desire to receive multidisciplinary care by their obstetric provider and stigma related to overweight/obesity or mental health conditions. These patients might be less forthcoming or willing to discuss the identified risk factors. Thus, the Work Group made the following recommendation: We suggest assessing all patients for risk factors that impact initiation and continuation of lactation, including obesity, depression, inappropriate gestational weight gain, and gestational diabetes mellitus.

#### Recommendation

4. We suggest individual or group lactation education delivered via in-person, telehealth, or multimedia modalities be provided for all pregnant and postpartum patients to improve the probability of initiating and continuing lactation.

(Weak for | Reviewed, New-replaced)

### **Discussion**

The World Health Organization recommends initiation of human milk feeding within the first hour of life, with exclusive human milk feeding for at least 6 months. (68) Significant health benefits are linked to lactation for both the patient and the infant. Human milk feeding has been shown to lower the risk of type 2 DM, certain types of breast cancer, and ovarian cancer in patients and to reduce asthma, childhood leukemia, and type 2 DM in children. (69) Education is provided and offered to patients in various ways. Lactation education differs immensely across clinical settings. That education should be provided prenatally (ideally at the first visit) and continued throughout the pregnancy is apparent, including to the pregnant patient's family or chosen support people, and it should be continued through the postpartum period. Lactation education offers the opportunity for patients to make an informed choice about their feeding decisions and meet their personal goals.

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Evidence suggests that individual or group lactation education delivered via in-person, telehealth, or multimedia modalities increased the probability that pregnant and postpartum patients would initiate and continue lactation.(70-79) The systematic evidence review identified five SRs and nine RCTs. The modality of how the education was provided, however, varied among the evidence retrieved.

Varying types of lactation education (telephone, in-person, multimedia) provided individually might increase the likelihood of exclusive lactation at 6 months postpartum compared with TAU.(70, 71) Evidence also suggests that group lactation education might increase the probability of initiating and continuing lactation when compared with TAU.(73, 74, 79) Robinson et al. (2018) specifically found that group lactation education resulted in a greater likelihood of lactation initiation among African American women, which corresponded to the general study sample findings.(72) Findings from multiple other studies, conducted in a variety of patient populations, have been consistent with this finding.(80-82)

The success of lactation education was also impacted by who specifically was providing the education. Evidence found that women who were provided lactation consultant support might be more likely to engage in any amount of lactation compared with TAU at 6 months.(75) It was also indicated that Hispanic patients provided with lactation consultant support were more likely to use *only* breastmilk at 10 months postpartum.(76) There was also evidence that peer telephone support programs might increase the likelihood of any or exclusive breastfeeding at 6 months compared with TAU.(77) More specifically, evidence from one RCT suggested that peer support increased the likelihood of exclusive breastfeeding among Hispanic patients at 6 months when compared with TAU.(78) An RCT by Kellams et al. (2018) demonstrated that giving low-income patients a lactation video to watch did not affect the likelihood of exclusive or continuation of any lactation at 6 months,(83) demonstrating that education should be provided in a more hands-on approach by an experienced and trained provider rather than self-study.

Regardless, lactation education should be tailored to the needs of the individual patient and the resources available in the community. A provider should approach the topic with sensitivity and foster a supportive environment. A lactation education program that uses open-ended questions focusing on the patient's beliefs about lactation—for example, "Have you thought about how you are going to feed your baby?"—is effective in increasing lactation rates.(84)

Patient preferences varied regarding how lactation education is provided, which can impact the likelihood of initiating and continuing lactation. The patient focus group noted that lactation education was appreciated and provided benefits. Sometimes a stigma can be associated with lactation. In some circumstances, counseling patients who do not want to lactate might lead to their feeling ashamed. Patients might also have underlying issues, such as trauma or substance use, which might affect their willingness

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to initiate or discuss lactation or both. Further, availability of resources needed to provide lactation education as well as trained lactation professionals might be limited at various facilities. Patients who live in rural areas might have limited access to lactation services. Moreover, the education level and expertise of the providers offering the education varies. Subgroup populations should also be considered. Robinson et al. (2019) found that group lactation education resulted in a greater likelihood of lactation initiation among African American women.(72) Also, Hispanic women provided lactation consultant support were most likely to use *only* breastmilk at 10 months postpartum.(76) Similarly, one RCT found that peer support increased the probability of Hispanic women's exclusive breastfeeding at 6 months when compared with TAU.(78)

The Work Group systematically reviewed evidence related to this recommendation and considered the assessment of the evidence put forth in the 2018 VA/DoD Pregnancy CPG.(70-83) Therefore, it is categorized as Reviewed, New-replaced. The Work Group's confidence in the quality of the evidence was very low. The body of evidence had some limitations, including blinding of participants and personnel, imbalances between intervention and comparator groups, and lack of details on intervention or randomization.(70, 72, 75, 82) Maternal mental health is also impacted by lactation and can be considered both a benefit and potential harm.(85) A positive association exists between lactation and improved mental health outcomes. Lactation challenges, failing to meet lactation expectations, or both, however, are associated with negative mental health outcomes. (85) Overall, the benefits of individual and group lactation education on the probability of initiating and continuing lactation outweighed the potential harms. Patient values and preferences varied because some patients might feel pressured or guilty if they do not want to lactate but are counseled on the topic. Also, some patients might have underlying issues, such as a history of trauma or substance use. Thus, the Work Group made the following recommendation: We suggest individual, or group lactation education delivered via in-person, telehealth, or multimedia modalities be provided for all pregnant and postpartum patients to improve the probability of initiating and continuing lactation.

#### c. Pelvic Floor Health

#### Recommendation

5. We suggest all patients have an early prenatal evaluation of pelvic floor muscle function and receive pelvic floor muscle exercise instruction during pregnancy for the prevention of urinary incontinence in late pregnancy and up to 6 months postpartum.

(Weak for | Reviewed, New-added)

#### **Discussion**

Moderate evidence suggested that PFMT exercise initiated during early pregnancy (mixed prevention and treatment) reduced the prevalence of urinary incontinence for all patients in late pregnancy and up to 6 months postpartum (86-88) This recommendation

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is based on findings from two SRs and one RCT.(86-88) See <u>Pelvic Muscle Function</u> section for instructions on pelvic floor muscle examination and training.

Woodley et al. (2020) conducted a Cochrane SR from the findings of 46 total overall poor-quality RCTs (n=10,832) on various types of PFMT interventions and outcomes during and after pregnancy.(86) Specifically, the SR found evidence in 15 RCTs that favored initiation of PFMT in early pregnancy compared with controls of no PFMT (four trials), TAU (nine trials), or an unspecified control (two trials) for the mixed prevention and treatment of urinary incontinence in both primiparous and multiparous women. (86) The impact of PFMT on the outcome of fecal incontinence was uncertain because of a low number of studies (two trials). Eleven trials confirmed a correct voluntary pelvic floor muscle contraction by a provider via a pelvic examination before the initiation of various forms of PFMT treatment program types (group: two trials; individualized: seven trials; independent: three trials; no PFMT: eight trials). Studies were also stratified based on health care provider contact as low (fewer than five contacts - three trials), moderate (6-12 contacts - four trials), and high (more than 12 contacts - five trials). Most PFMT intervention programming described focused on strength training of the pelvic floor and adjacent muscles. Studies that used PFMT combined with bladder training, drug therapy, or standalone electrical stimulation were excluded, while studies combined with biofeedback, electrical stimulation, and multimodal exercise programs typically conducted in pelvic health rehabilitation were included.

Yang et al. (2022) conducted an SR from the findings of five overall fair-quality RCTs (n=1,132) that found the group-based PFMT exercise training sessions (online, face-to-face [FTF], or combination) during pregnancy significantly reduced the prevalence of urinary incontinence in both the pregnancy and postpartum periods.(87) The intervention was provided by physical therapists or midwives and was compared with TAU (information on PFMT or no further instruction) ranging from 6–16 weeks in duration with weekly to occurring once every two weeks sessions. The population studied consisted of pregnant and postpartum women older than age 18 with or without incontinence (mixed prevention and treatment). Studies were excluded if the intervention included PFMT with electrical stimulation or electromyography biofeedback training interventions that would be found only in individualized pelvic health rehabilitation programs.

Johannessen et al. (2021) conducted an RCT secondary analysis (n=722) of The Training in Pregnancy trial that assessed the efficacy of an antenatal training program. (88) This program consisted of a group class (30–35 minutes) led by a physical therapist once weekly and a home exercise program conducted twice weekly (20–25 minutes) for 12 weeks using a standardized program of strengthening exercises using the limbs, back extensors, deep abdominals, and pelvic floor muscles with light stretching, breathing exercises, and relaxation. (89) The pelvic floor muscle exercises were of moderate intensity and included endurance hold and quick flick muscle contractions (8–12 repetitions for 6–8 seconds holds with three fast contractions at the

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end). The population studied consisted of healthy women older than age 18 with uncomplicated singleton pregnancies. The control was TAU using only a handout about pelvic floor muscle exercises. All patients were individually educated on pelvic anatomy and how to correctly conduct a pelvic floor muscle contraction via a vaginal palpation examination by a provider at the start of care in early pregnancy. The main outcomes measured were the prevalence of urinary incontinence at 18–22 weeks of pregnancy and at 3 months postpartum using the Sandvik Severity Index. Patients in the group exercise cohort had a significantly lower prevalence of urinary incontinence compared with the control group until 3 months postpartum.(89)

Evidence indicated no significant reported harms or adverse outcomes associated with PFMT exercises in the reviewed studies.(86-88) Woodley et al. (2020) cited two reports of mild pelvic floor pain with exercises.(86) This intervention is considered low risk and a key component of conservative care for the management of urinary incontinence in the general population.(90) The benefits of PFMT exercise include improved QoL with urinary continence and reduced health care costs and requirements that outweigh the harms and burdens of pelvic floor muscle examination and exercise training that can be conducted independently or with supervision.

Patient values and preferences varied somewhat regarding this treatment because patients might not want to undergo a pelvic floor muscle function examination (e.g., history of trauma), might have competing demands that interfere with the ability to consistently conduct or attend exercise programming, might not want to do the pelvic floor muscle exercises, or any combination of these objections. The 2023 VA/DoD Pregnancy CPG patient focus group findings cited patient desires for enhanced consideration of co-occurring health conditions and improved education on topics such as exercise during pregnancy.

Further implications that should be considered for this recommendation are resource use, acceptability, and feasibility. Pelvic floor muscle evaluation and training might increase the workload requirements of the primary provider managing a pregnant patient. Pelvic muscle function examinations might not be conducted routinely outside pelvic health rehabilitation or pelvic medicine and reconstructive surgery providers. Some medical providers managing pregnancy might require additional training on the proper evaluation of pelvic muscle function and instruction of patients on conducting an appropriate muscle activation without compensatory strategies via single-digit palpation and verbal cueing if unfamiliar.(91) Most of the studies reviewed initiated PFMT intervention with a medical provider first conducting a pelvic examination to confirm that patients were able to appropriately activate their pelvic floor muscles via single-digit palpation and validating the absence of compensatory muscles or bearing down (e.g., Valsalva maneuver). See Routine Pregnancy Care Section of Pelvic Muscle Function for further details on how to conduct this type of examination.

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Application of this recommendation might potentially require enhanced availability of resources such as qualified personnel to provide consistent and standardized training in various forms when feasible and indicated. The systematic evidence review established that enhanced patient supervision in pelvic muscle training showed better outcomes.(87, 88) However, to refer every pregnant patient to pelvic health rehabilitation for individual care is infeasible because of the limited availability of pelvic health therapists in the U.S. This intervention shows positive treatment and prevention effects that have the potential to reduce overall health care costs and to improve QoL in the long term for patients during and after pregnancy in patients with and without symptoms of urinary incontinence.

The education and training interventions in the reviewed studies were highly variable, including with provider education on pelvic muscle training exercises ranging from individually, self-directed home programs, group exercise sessions, or both. A patient education handout or discussion in the absence of pelvic floor muscle examination with instruction training on how to properly perform pelvic floor muscle activation is likely insufficient according to the systematic evidence review, although it is common practice in many primary care and specialty (non-rehabilitation) clinics. PFMT can be accomplished via home exercise program education instruction during pelvic examination by providing verbal and tactile feedback on appropriate muscle activation, exercise education in a group prenatal care program, independent exercise/self-care strategies, or any combination of these approaches.

The Work Group systematically reviewed evidence related to this recommendation. (86-88) Therefore, it is categorized as Reviewed, New-added. The Work Group's confidence in the quality of the evidence was low. The body of evidence had some limitations, including challenges with blinding active interventions, short-term follow-up periods, diversity of intervention methodologies, and variability in the outcome measurement tools used. These studies overall concluded that the conduct of PFMT exercises supported by a confirmation examination of pelvic muscle function and with training (individual, home program, or group) for the mixed prevention and treatment of incontinence when initiated in early pregnancy reduces the incidence of urinary incontinence in late pregnancy and up to 6 months postpartum compared with TAU routine care (no PFMT exercises or self-directed care without provider muscle activation confirmation and training). These studies evaluated the primary outcome of urinary incontinence by assessing the prevalence of any level of urinary incontinence in patients. These studies used self-report questionnaires or tools during and after pregnancy using mixed prevention and treatment with a variety of training techniques, frequency, duration, and settings. The benefits of PFMT exercises outweigh the potential harm (no significant adverse events reported), but the burden of increased care requirements for the patient and provider should be considered. Patient values and preferences vary somewhat as some patients might not want to or are unable to have an internal pelvic floor examination or to conduct pelvic muscle training consistently.

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Thus, the Work Group made the following recommendation: We suggest all patients have an early prenatal evaluation of pelvic floor muscle function and receive pelvic floor muscle exercise instruction during pregnancy for the prevention of urinary incontinence in late pregnancy and up to 6 months postpartum.

#### Recommendation

6. We suggest referral to pelvic health rehabilitation for patients with reported urinary incontinence in the postpartum period.

(Weak for | Reviewed, New-added)

#### **Discussion**

Recent evidence suggested that pelvic health rehabilitation improved symptoms and the QoL in postpartum patients with urinary incontinence(86, 92, 93). This recommendation is based on the findings of one Cochrane SR review and two small individual RCTs.(86, 92, 93)

Woodley et al. (2020) conducted a large Cochrane SR from the findings of 46 total overall poor-quality RCTs (n=10,832) on various types of PFMT interventions and outcomes during and after pregnancy. (86) Specifically, the SR evaluated the evidence in 3 RCTs on the efficacy of postnatal PFMT that favored the treatment of urinary incontinence in the late postnatal period (>6–12 months). (94-96) The intervention of PFMT in the late postnatal period for the treatment of incontinence was compared with the control (no PFMT or TAU). The primary outcome measured was the prevalence of urinary and incontinence specific QoL measures. It should be noted that 2 of the RCTs were self-directed exercise (94, 95) and only 1 RCT(96) provided supervised and highintensity PFMT for the treatment of urinary incontinence. The individual data analysis of these 3 RCTs listed above is found in the "Analysis 4.1" table (Comparison 4: Postnatal PFMT versus control for the treatment of incontinence, Outcome 1: Urinary incontinence late postnatal period) that favored PFMT for the reduction of urinary incontinence in the late postnatal period. A 2018 Cochrane SR (n=1,817) on the efficacy of PFMT in the general population for the treatment of urinary incontinence was consistent with these individual analysis findings that favor this intervention. (90)

Sniezek et al. (2021) conducted a small RCT (n= 56) that assessed the efficacy of a 6-week physical therapy course of care initiated at 6–8 weeks after delivery using the BeBo Pelvic Floor Training Concept.(92) This program was provided to primiparous women with a natural (vaginal) childbirth event for pelvic floor muscle strengthening and endurance training. Individualized treatment sessions with a physical therapist were 60 minutes in duration (10 minutes' education, 50 minutes' exercise) and occurred two times per week. The intervention was compared with a control group that consisted of no treatment. The outcome measures were pelvic floor strength, using the PERFECT scheme testing scale and a perinometer, standardized QoL outcome measure questionnaires using the Urinary Distress Inventory Short Form and the International Consultation of Incontinence Questionnaire Short Form (ICIQ-SF), and prevalence rates of urinary incontinence. All

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study participants showed improvements in both groups (intervention and control) for incontinence and QoL measure, but the exercise group had statistically significant improvements in ICIQ-SF scores and prevalence rates of incontinence with an 85% improvement in patients with symptoms of urinary incontinence at the start of treatment. No difference in pelvic floor muscle objective strength was found between intervention and control groups, but both groups had statistically significant changes from baseline over time that were attributed to natural recovery.

Sigurdardottir et al. (2019) conducted a small RCT (n=84) that assessed the efficacy of PFMT in the early postpartum period for the outcomes of urinary and fecal incontinence, related bother, and pelvic floor strength at 6 and 12 months after delivery in adult primiparous women with incontinence (urinary or fecal).(93) The treatment intervention started at approximately 9 weeks postpartum with individualized physical therapist—guided PFMT care with biofeedback consisting of 12 weekly rehabilitation treatment sessions. The control group received no instruction in PFMT. All participants received an initial assessment of pelvic floor muscle function examination with a single-digit vaginal palpation for muscle activation confirmation and objective strength tests vaginally and rectally with a manometer device. Postpartum PFMT reduced the rates of urinary incontinence and related bother and increased pelvic floor muscle strength and endurance at 6 months postpartum, but no difference between groups was found by 12 months. The PFMT training had no significant effects on fecal (anal) incontinence but improved pelvic floor muscle and anal sphincter strength values overall.

Evidence indicates no reported significant harms or adverse outcomes associated with PFMT in rehabilitation from the reviewed studies.(86, 92, 93) The SR by Woodley et al. (2020) cited two reports of pelvic floor pain with exercises.(86) This intervention is considered low risk and a key component of conservative care for the management of urinary incontinence in the general population.(90) The benefits of PFMT exercise include improved QoL with urinary continence and reduced health care costs and requirements that outweigh the harms and burdens of pelvic health rehabilitation programs.

Patient values and preferences varied somewhat regarding this treatment because patients might not want to undergo a pelvic muscle function examination and rehabilitation (e.g., history or trauma), might have competing demands as a new parent that interfere with the ability to consistently adhere to treatment requirements or attend rehabilitation, or both. Patients, however, might want to maximize conservative intervention first in lieu of medication or surgical interventions that might carry more inherent risks than rehabilitation, especially during childbearing years. The patient focus group findings cited desires for enhanced consideration of co-occurring health conditions and improved access to rehabilitation resources in the postpartum period. Access to this type of specialty care is limited nationwide because of a paucity of trained providers in pelvic health rehabilitation, which is the smallest cohort of board certification specialties in the physical therapy profession. (97) The factor of rehabilitation availability alone did not influence the strength of the recommendation.

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The Work Group systematically reviewed evidence related to this recommendation. (86, 90, 92-96) Therefore, it is categorized as *Reviewed, New-added*. The Work Group's confidence in the quality of the evidence was very low. The body of evidence had some limitations, including challenges with blinding active interventions, short-term follow-up periods, diversity of intervention methodologies, and variability in the outcome measurement tools used. The benefits of supervised pelvic muscle training by a rehabilitation provider improved rates of urinary incontinence and QoL measure scores that outweighed the potential harms (no reported significant adverse outcomes) or burdens (increased health care use rates). Patient values and preferences varied somewhat because some patients might not want to or are unable to participate in rehabilitation care because of increased life responsibilities as a new parent. Thus, the Work Group made the following recommendation: We suggest referral to pelvic health rehabilitation for patients with reported urinary incontinence in the postpartum period.

# d. Selected Conditions

### Recommendation

7. We recommend offering scheduled delivery to patients who reach 41 weeks and 0/7 days undelivered. Antepartum fetal testing should begin at 41 weeks and 0/7 days if not delivered.

(Strong for | Not reviewed, Amended)

#### **Discussion**

Perinatal and maternal complications increase as a pregnancy extends beyond term. Multiple studies demonstrated that perinatal mortality steadily increased with gestational age past 41 weeks.(98, 99) Previously reviewed evidence suggested that induction of labor at 41 weeks was associated with a decrease in perinatal mortality without negatively impacting other neonatal and maternal outcomes.(100, 101) A national cohort study showed a significant reduction in perinatal mortality from 1.3-0.8% (p=0.033) following the implementation of an induction or fetal surveillance policy starting at 41 weeks.(100) An SR also showed that induction of labor at 41 weeks was associated with a significant reduction in cesarean delivery rates and a trend toward lower perinatal mortality rates.(101) Although not part of the previous systematic evidence review from the 2018 VA/DoD Pregnancy CPG, subsequent studies continued to support the findings that induction of labor at 41 weeks is associated with a reduction in perinatal mortality and a reduction in rates of cesarean section. (102, 103) Additionally, a recent RCT published in 2018 evaluating the outcomes of elective induction starting at 39 weeks showed no increased risk of maternal or perinatal adverse outcomes while demonstrating a reduction in cesarean deliveries. Although there was also no demonstration of improved maternal or perinatal outcomes by offering induction at this time, this finding would suggest that providers could consider offering elective delivery starting at 39 weeks without increasing the risk of cesarean delivery. Based on the moderate quality of evidence from the 2018 systematic evidence review, the Work Group makes a strong recommendation for offering patients a scheduled

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delivery at 41 weeks' gestation if undelivered. For patients who choose to continue their pregnancy past 41 weeks, we recommend starting antepartum fetal testing.

Counseling patients to make an informed decision about scheduled inductions or antepartum fetal monitoring without induction will help prioritize each individual's values. Some patients might value immediate delivery, although others might prefer to wait. The costs associated with induction include increased length of hospital stay and increased nursing contact time versus costs incurred by outpatient monitoring followed by induction if spontaneous labor does not occur. However, medical costs and resource allocation associated with perinatal complications are also high, making this approach valuable in reducing negative outcomes and costs. Some patient variability in values will be noted in this approach because some patients highly value deliveries without intervention and have limited time for antenatal monitoring. These patients might find this approach less acceptable than those who highly value the reduction of risk.

The Work Group considered the assessment of the evidence put forth in the 2018 VA/DoD Pregnancy CPG related to this recommendation.(98-101) Therefore, it is categorized as *Not reviewed, Amended*. The Work Group's confidence in the quality of the evidence was moderate in support of offering scheduled delivery for people undelivered at 41 weeks 0/7 days for the outcome of decreased perinatal mortality. The benefits of delivery by 41 weeks to improve maternal and perinatal outcomes, such as decreased cesarean section rates (101) and reduced perinatal mortality (98, 101), outweighed the potential harms of increased medical interventions associated with induction. Further studies since the original evidence review have only added to support for this recommendation.(102, 103) Patient values and preferences varied somewhat for the reasons mentioned above. Thus, the Work Group made the following recommendation: We recommend offering scheduled delivery to patients who reach 41 weeks and 0/7 days undelivered. Antepartum fetal testing should begin at 41 weeks and 0/7 days if not delivered.

# Recommendation

8. We suggest that patients with uncomplicated pregnancies may continue a standard work schedule throughout their pregnancy.

(Weak for | Not reviewed, Amended)

# **Discussion**

If a pregnant patient's work is strenuous or if they spend long periods on their feet, they should avoid periods of prolonged standing, limit their workday, or shift, and limit their workweek to 40 hours during the last trimester (beginning at 28 weeks) or earlier if determined to be medically necessary by a provider. Physically demanding work and prolonged standing increase the risk of preterm birth and HTN or preeclampsia.(104-108)

Active duty Service members should continue to follow their service-specific limited duty policies. Before a specific evidence-based recommendation can be made regarding

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particular work limitations, further high-quality studies are needed to examine the association between strenuous or prolonged work activities and adverse pregnancy outcomes.

The Work Group considered the assessment of the evidence put forth in the 2018 VA/DoD Pregnancy CPG related to this recommendation.(104-107) Therefore, it is categorized as *Not reviewed, Amended*. The Work Group's confidence in the quality of the evidence was moderate. The benefits of this recommendation slightly outweighed the potential harms for patients with uncomplicated pregnancies. Patient values and preferences varied somewhat because some patients might need to work, although others might prefer to lessen work burden. Thus, the Work Group made the following recommendation: We suggest that patients with uncomplicated pregnancies may continue a standard work schedule throughout their pregnancy.

# Recommendation

9. We suggest offering telemedicine as a complement to usual perinatal care. (Weak for | Reviewed, New-added)

### **Discussion**

The systematic evidence review identified three SRs and four RCTs that compared telemedicine with usual perinatal care for pregnant or postpartum patients. All studies compared different interventions via different modalities, but none were solely telehealth.(109-115) The three SRs focused on any type of telemedicine, which included email, text messaging, virtual visits, telephone calls, or any combination of these modes of communication. The use of telemedicine in these SRs was to evaluate the effectiveness of different modalities of telemedicine interventions for pregnant patients with GDM(109) or to provide health care decision support to pregnant patients at risk of GDM, HTN, or other chronic disorders of pregnancy in conjunction with TAU.(110, 111) Two RCTs focused on an app-based intervention along with health care provider support via either telephone or online communication.(112, 113) One RCT compared a text message program and an at-home blood pressure monitoring with usual in-person care visits.(114) The last RCT compared regular health coaching telephone calls in addition with regular office visits alone to provide additional care to patients who were overweight or obese.(115)

Search criteria used the U.S. Department of Health and Human Services' definition of telemedicine, which broadly defines telemedicine as the use of electronic information and telecommunications technologies to support and promote long-distance clinical health care. Technologies include videoconferencing, the internet, store-and-forward imaging, streaming media, and terrestrial and wireless communications. The Work Group also included studies that assessed electronic applications (or apps). However, the Work Group considered studies in which the app involved only two-way communication between patient and provider.

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Three studies rated fair in overall quality included Laursen et al. (2022), which explored telemedicine encompassing text messaging, telephone, or app-based communication versus TAU for pregnant patients with DM.(109) Gunes Ozturk et al. (2021) explored telemedicine communication through smartphones, two-way video, email, or SMS versus TAU for pregnant patients at risk for GDM.(110) And Lau et al. (2017) investigated telemedicine, including email, SMS, or other app-based communication versus TAU for overweight or obese pregnant patients or both.(111) Watson et al. (2021) studied the QUiPP telemedicine app with email or telephone communication versus TAU for pregnant patients, and Hirshberg et al. (2018) researched text messaging versus prenatal office visits for the pregnant patient with HTN.(112, 114)

Two studies rated good in overall quality include Butler-Tobah et al. (2019), which explored the OB Nest telemedicine program with virtual health care provider communication versus TAU for pregnant patients and Van Horn et al. (2018), which explored health coaching calls versus TAU for pregnant patients.(113, 115)

For most critical outcomes, the evidence suggested no difference between telemedicine and TAU. Moderate-quality evidence indicated that the use of telemedicine interventions lead to fewer overall number of required care visits compared with TAU.(110, 112, 113) Also, patients provided care through telemedicine interventions expressed greater satisfaction with care compared with those who received TAU.(113)

Patient preferences varied somewhat regarding this treatment. The patient focus group findings highlighted preferences for continuity of care and feelings that telemedicine might help provide continuity when FTF visits are difficult or impossible. Some evidence showed high patient satisfaction with telemedicine (e.g., focus group]); however, some patients might prefer FTF care. Further implications for consideration included variation in access to telemedicine modalities (e.g., smart phones, text messages) and how regulations around telemedicine might affect billing or reimbursement or both. The Work Group noted that telemedicine might be especially helpful in particular subpopulations (e.g., pregnant patients with HTN, DM, obesity). Factoring in the cost of supplying medical equipment for telemedicine (e.g., fetal dopplers, blood pressure cuffs) is essential to consider, as well.

The Work Group systematically reviewed evidence related to this recommendation.(109-115) Therefore, it is categorized as *Reviewed*, *New-added*. The Work Group's confidence in the quality of the evidence was low. The body of evidence had some limitations, including that the methodological quality of the studies was limited because of concerns around randomization and blinding procedures, moderate to high attrition, wide confidence intervals, lack of clarity around randomization, allocation concealment, and blinding of patients, study personnel, and assessors. The benefits of telemedicine moderately improved care visits and patient satisfaction rates and led to fewer overall required care visits. Neither demonstrated a difference nor supported telemedicine as an adjunct to TAU. No harms were reported in the studies. Patient

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values and preferences varied somewhat because some might desire FTF visits. In addition, almost one-quarter of all Veterans in the U.S., 4.7 million, choose to reside in rural communities after their military service and might benefit from enhanced telemedicine technologies as a complement to TAU. Thus, the Work Group made the following recommendation: We suggest offering telemedicine as a complement to usual perinatal care.

#### Recommendation

10. There is insufficient evidence to recommend for or against specific interventions that would diminish disparities in perinatal care access and maternal and childbirth outcomes

(Neither for nor against | Reviewed, New-added)

#### **Discussion**

Evidence reporting the prevalence and negative impact of disparities in pregnancy and childbirth in the U.S. is abundant. Maternal mortality rates have continued to rise for the last two decades, increasing from 9.9 deaths per 100,000 live births in 1999 to 23.8 in 2020. Racial disparities stand out in the data, with Black women experiencing a 2.9 times higher risk of maternal mortality compared with White women. Additional risk factors for increased maternal mortality rates include unmarried status, lower education, and living in a low-income area.(116-118) Disparities in care can be reported in a variety of ways. Some quality metrics include the proportion of women accessing first-trimester care, rates of preterm birth, cesarean delivery, postpartum infection, and hemorrhage. Consistent with maternal mortality data, these metrics vary by race with the largest impact on Black patients.(119)

The systematic evidence review identified six RCTs comparing interventions with standard care in pregnant and postpartum patients at increased risk of adverse pregnancy outcomes, highlighting a paucity of data assessing interventions to address the problem.(77, 120-124) The trial defined "interventions" included home visits, with or without doula services, patient navigation plus behavioral incentives, provision of practical resources for effective postpartum parenting, Rotterdam reproduction risk reduction (R4U) score card plus a list of obstetric indications (LOI), or standardized electronic messages with or without nurse contact.

The six RCTs from the systematic evidence review varied greatly in terms of patient population, intervention, and standard of care comparator, which makes drawing general conclusions from this body of evidence difficult; however, several themes did emerge.

The rate of preterm delivery was addressed in our search. No difference was found in preterm birth (<37 weeks' gestation) between the patient navigation + behavioral incentives (PNBI) group and assessment + standard care (ASC) control groups in African American patients at risk for adverse birth outcomes.(120) Similarly, the incidence of

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preterm delivery among patients in urban areas of the Netherlands with an overrepresentation of adverse pregnancy outcomes did not differ between patients in the R4U plus LOI group compared with the LOI plus individual care group or in the study assessing doula care services compared with case management.(123) In this particular group, readmission was also evaluated and noted to be similar between groups.(123) Rates of cesarean delivery were assessed in two studies; no difference in the mode of delivery occurred in the study comparing patients with R4U plus LOI. Similar findings were noted in a doula home visiting services versus case management study.(123)

Patient engagement in care was also assessed in several studies, either as a primary or a secondary outcome. Evidence from one RCT suggests that Hispanic pregnant patients at or below 26 weeks' gestation in the maternal infant health outreach worker group received more referrals from community providers, connected with more referral resources, and received more new services than patients in the minimal education intervention group.(77) In addition, an RCT by Svikis et al. (2022) assessed an African American population by comparing PNBI and ASC.(120) Patients in the PNBI group were paired with a patient care navigator to learn how to access and advocate for services to reduce adverse outcomes and received incentives for attending prenatal care visits. Patients in the PNBI group showed no difference in the number of prenatal visits but a modest increase in attendance of postpartum visits.(120) The average age of study participants was 18.4 years, calling into question the generalizability of this study to the VA/DoD population. A third RCT involving low-income families compared home visit plus doula care with case management. Patients in the home visit plus doula care group were more likely to attend childbirth education classes.(123)

Overall, drawing conclusions from this evidence is difficult because of the heterogeneity of interventions and comparators. Only one RCT was rated as fair quality based on the randomization method, leaving concerns regarding unclear allocation methods, serious limitations in the blinding process, and low attrition-rates.(77) The five other RCTs were rated as poor quality because of a lack of clarity around randomization, allocation concealment, and blinding.(120-124) There remains a paucity of RCTs that evaluate the impact of interventions to address racial and health care disparities, despite the ubiquitous nature of this problem.

Patient preferences varied largely regarding interventions to reduce disparities given the diversity of affected subgroups. This topic aligns with the patient focus group's expression of interest in comprehensive education options. Education was provided via doula services, peer support, and patient navigators. Extended postpartum care was also preferred by the focus group, addressed by nurse contact via text messaging in the postpartum period.

The Work Group systematically reviewed evidence related to this recommendation.(77, 120-124) Therefore, it is categorized as *Reviewed, New-added*. The Work Group's confidence in the quality of the evidence was very low. The body of evidence had multiple

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limitations, including lack of clarity in randomization and blinding, overall small sample size, and high attrition rate. In addition, the type of intervention varied in each study as did the comparator. An accurate assessment of the risks and benefits of strategies or interventions to reduce health care and racial disparities could not be assessed given the mix of neutral and weak study findings. Patient values and preferences varied largely because of the unique needs, cultural beliefs, and values of each at-risk subgroup. Thus, the Work Group made the following recommendation: There is insufficient evidence to recommend for or against specific interventions that would diminish disparities in perinatal care access and maternal and childbirth outcomes.

# **B.** Complicated Obstetrics

# a. Preterm Delivery

# Recommendation

11. We recommend considering fetal fibronectin testing as a part of the evaluation strategy in patients between 24 0/7 and 34 6/7 weeks' gestation with signs and symptoms of preterm labor, particularly in facilities where the result might affect management of delivery.

(Strong for | Not reviewed, Amended)

#### **Discussion**

The evaluation of patients between 24 0/7 and 34 6/7 weeks' gestation with signs and symptoms of preterm labor includes a pooled consideration of individual patient historical factors, clinical history, and presenting symptoms in conjunction with laboratory assessment for infections and examination to include cervical length screening in settings where clinical expertise to accomplish this assessment exists. Fetal fibronectin testing has a narrowly defined role in obstetric evaluation and, therefore, should be used only when it has the potential to alter care. The potential value of fetal fibronectin testing in the setting of evaluation or triage of preterm labor is to more precisely discriminate between the subset of women who have true preterm labor versus false labor.(125) In a woman at low risk for preterm delivery presenting with preterm contractions, a negative test might inform the decision to use or avoid tocolytics and corticosteroids.(126) Alternatively, a positive test might allow providers at some facilities to arrange the transfer of patients identified as at higher risk of preterm delivery to facilities better suited to manage the complications of preterm birth. Routine screening for preterm delivery using fetal fibronectin test in asymptomatic patients is not recommended.

Patient preferences varied little regarding fetal fibronectin use. As an additional test within a standard preterm labor workup, it places no extra burden on the patient. The Work Group finds potential value in fetal fibronectin testing at VA/DoD facilities where management of results could impact decisions to transfer to higher levels of care, and testing could have a positive impact on the associated resource use while concomitantly mitigating potential burdens of unnecessary transfers to the patient.

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The Work Group considered the assessment of the evidence put forth in the 2018 VA/DoD Pregnancy CPG related to this recommendation.(125, 126) Therefore, it is categorized as *Not reviewed, Amended*. The Work Group's confidence in the quality of the evidence was moderate. The body of evidence had some limitations, including a small sample size and confounders in the analysis. The benefits of fetal fibronectin outweighed the potential harm of false negative testing, which is rare. Patient values and preferences were similar because fetal fibronectin is an insignificant additional burden to a standard preterm labor assessment when used in properly selected patients. Thus, the Work Group made the following recommendation: We recommend considering fetal fibronectin testing as a part of the evaluation strategy in patients between 24 0/7 and 34 6/7 weeks' gestation with signs and symptoms of preterm labor, particularly in facilities where the result might affect management of delivery.

# Recommendation

12. We suggest vaginal progesterone or cerclage for singleton pregnancy with short cervix, history of spontaneous preterm birth, or both depending on patient characteristics and preferences.

(Weak for | Reviewed, New-added)

# **Discussion**

Evidence suggested vaginal progesterone reduces the risk of spontaneous preterm birth in patients with a short cervix, a history of spontaneous preterm birth, or both. Care et al. (2022), a large SR including 61 RCTs (n=17,273 pregnant patients), contributed data for outcomes to include preterm birth <37 weeks, preterm birth <34 weeks, perinatal death, neonatal death, respiratory distress syndrome, neonatal sepsis, and neonatal intensive care unit (NICU) admission.(127) The systematic evidence review evaluated multiple interventions to reduce asymptomatic spontaneous preterm birth, including vaginal progesterone, intramuscular progesterone (17-OHPC), oral progesterone, various cerclage types, and pessaries.(127) This SR was consistent with conclusions from additional recently published SRs.(128) Vaginal progesterone is the intervention that has demonstrated the most benefit compared with other intervention modalities to reduce the risk of spontaneous preterm birth in patients with the highest risk of spontaneous preterm birth, namely patients with a history of prior spontaneous preterm birth or patients with a short cervix, defined as fewer than 25 mm. Although individual studies have been mixed regarding benefits in reduction of preterm birth occurrence—and the various studies do use different formulations and dosages of vaginal progesterone—when evaluated together in this SR, vaginal progesterone is shown to significantly reduce preterm birth <37 weeks, preterm birth <34 weeks, and perinatal death rates.

Evidence also suggested that cervical cerclage reduced the risk of spontaneous preterm birth in patients with a short cervix alone or in patients with a history of spontaneous preterm birth and a short cervix. The SR by Care et al. (2022) reviewed

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13 RCTs that evaluated the intervention of cerclage to reduce the risk of preterm birth.(127) The population within the 13 RCTs included nulliparous patients with a short cervix and also patients with a history of spontaneous preterm birth and a short cervix, along with other "high risk" for preterm birth conditions. Preterm birth <34 weeks was found to be reduced with the placement of a Shirodkar cerclage. Moreover, NICU admission was found to be significantly reduced with McDonald cerclage. A trend toward a reduction in perinatal death was noted with the placement of a McDonald cerclage. Serious quality limitations, as well as serious indirectness and imprecision, arose within the cerclage literature. However, when taken as a whole, the evidence does suggest a benefit in particular clinical scenarios for the use of cerclage as an intervention to reduce the risk of preterm birth. The overall evidence does not appear to favor one type of vaginal cerclage over another. Finally, indirect comparisons of cerclage with vaginal progesterone within the SR by Care et al. (2022) found no difference for the outcomes of preterm birth <34 weeks and perinatal death.(127)

Vaginal progesterone should be considered as a treatment option and should be discussed with patients who have a history of spontaneous preterm birth <37 weeks and a short cervix <2.5 cm. Standard practice indicates that patients with a history of spontaneous preterm birth should undergo serial cervical length surveillance between 16 and 24 weeks, usually at an interval of every 2 weeks. If a cervical length is ≤25 mm, the patient should be counseled on the significantly increased risk for preterm birth with these two risk factors and should be offered vaginal progesterone or, in certain clinical circumstances, cerclage placement. If a patient is nulliparous or has never had a preterm birth, a routine cervical length assessment either transabdominally or transvaginally during the anatomic survey is standard. If the cervix is found to be short at ≤25 mm, the patient should be offered vaginal progesterone as a treatment that appears to reduce the risk for spontaneous preterm birth. In addition, evidence exists that if the cervix is very short at <10 mm, cerclage may be offered as an intervention to reduce the risk of preterm birth.

In fall 2022, 17-OHPC underwent a Food and Drug Administration (FDA) review of its accelerated approval pathway, and the FDA advisory board voted for its removal. The confirmatory recent RCT required after the accelerated approval process failed to show any benefit versus placebo.(129) Previously, intramuscular progesterone has been an intervention modality offered to patients with a history of spontaneous preterm birth. Most recently since 2021, it was offered interchangeably with vaginal progesterone in that group of patients with a history of spontaneous preterm birth, to start around 16 weeks. The preponderance of evidence appears to favor the benefits of vaginal progesterone over 17-OHPC, especially the evidence that involves patients with a short cervix. However, head-to-head trials with vaginal progesterone versus 17-OHPC do not appear to show a difference.(127) Subsequently, the company that made the patented version of 17-OHPC (Makena) voluntarily withdrew the drug from the market in March of

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2023, and the final ruling for removal from the market was issued by the FDA in April 2023.

Preterm birth is among the most important challenges in obstetrics, and prematurity accounts for three-quarters of perinatal mortality and more than one-half of long-term neonatal morbidity at significant social and economic costs.(130) One-half of preterm births are spontaneous.(131, 132) Prior spontaneous preterm birth and short cervix are the greatest contributing risk factors to spontaneous preterm birth. Interventions that reduce the risk of spontaneous preterm birth can help reduce this burden on patients. Currently, no significant evidence exists that progesterone causes harm, either to the pregnant patient or the fetus. However, long-term data is still being evaluated and research is being conducted on long-term effects.

It is important to note here that vaginal and oral progesterone are different than 17 alpha-hydroxyprogesterone caproate (17-OHPC), the intramuscular progesterone. Vaginal and oral progesterone are natural progestogens, with chemical structures similar to those produced by living organisms. However, 17-OHPC is synthetic, and its structure has been modified and does not correspond to a naturally occurring steroid. The human body does not make the caproate molecule. Progesterone and 17-OHPC have different physiologic properties and different pharmacologic profiles.(133)

Large variations will be anticipated in patient preferences regarding both progesterone and cerclage for the reduction of spontaneous preterm birth. Although preterm birth is a significant issue, some patients do not view the problem the same way. Some patients with a prior spontaneous preterm birth might have had an early preterm birth <34 weeks with a neonate that was admitted to the NICU for several weeks, although others might have had a preterm birth at 36 weeks, where the neonate was not admitted to the NICU and where no complications were noted. Although a patient with a spontaneous preterm birth is at significantly increased risk of recurrent preterm birth, as well as risk for earlier preterm birth, patients' prior experience might make them less likely to choose an intervention such as progesterone. Vaginal progesterone is a gel or a suppository used nightly for up to 21 weeks, depending on when it is started. Vaginal discharge might increase significantly, and it can be messy as well as potentially increasing vaginal symptoms such as pruritis or odor. In addition, patients might be wary of hormonal treatment. Regarding cerclage placement, surgery involves risks that include preterm labor or ruptured membranes, infection, or damage to the maternal bladder or bowel. Although these risks are low, they do increase with the severity of the cervical shortening or dilation. In addition, although cerclage might significantly prolong pregnancy, it might also prolong pregnancy only to the threshold of viability, where preterm labor and delivery might then result in the birth of a severely premature infant. These complex conversations with patients must balance the potential benefits of these two interventions and address the uncertainty in the literature as well as recognize the difficulty of estimating how much these interventions might reduce preterm birth risk.

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There are other implications to consider, as well. The Work Group's recommendation to support vaginal progesterone over other types of progesterone and the removal of 17-OHPC from the market do simplify decision making and counseling as well as reduce the cost of treatment compared with other modalities of progesterone. That vaginal progesterone is available in all MTFs caring for pregnant patients as well as available in the civilian or community sector for VA patients when obstetric care is outsourced would be imperative. Preterm birth history might be complex and confusing, and providers might have different viewpoints on early versus late preterm birth and when and to whom the intervention should be offered, especially when cerclage might also be an important intervention to consider based on the clinical picture. Some obstetric practitioners might feel comfortable placing cerclages, and some might wish to refer out to a higher-level provider, such as an MFM specialist or an obstetrician. This variability could result in a delay in care or patients not being presented with a shared decision making process on whether to pursue an intervention.

The Work Group systematically reviewed evidence related to this recommendation.(127, 128) Therefore, it is categorized as *Reviewed*, *New-added*. The Work Group's confidence in the quality of the evidence was low for vaginal progesterone and very low for cerclage. The body of evidence had some limitations, including study quality with risk of bias within some of the reviewed RCTs within the SR, as well as indirectness in comparison of interventions, and imprecision.(127, 128) However, vaginal progesterone and cerclage appeared to reduce preterm birth as well as perinatal death, and this finding outweighed the potential harms that might exist with cerclage or the currently theoretical risks with vaginal progesterone (none are currently identified). Patient values and preferences will vary somewhat because of their own prior preterm birth experience, concerns for a hormonal intervention, or concerns regarding the benefits of cerclage. Thus, the Work Group made the following recommendation: We suggest vaginal progesterone or cerclage for singleton pregnancy with short cervix, history of spontaneous preterm birth, or both depending on patient characteristics and preferences.

# Recommendation

13. There is insufficient evidence to recommend for or against the use of aspirin to reduce recurrent spontaneous preterm birth.

(Neither for nor against | Reviewed, New-added)

#### **Discussion**

Evidence from one randomized, placebo-controlled trial did not demonstrate that daily aspirin was effective in reducing spontaneous preterm birth in patients with prior spontaneous preterm birth.(134) In Landman et al. (2022), 387 women with a singleton pregnancy and a prior spontaneous preterm birth were initiated on aspirin 80 mg or placebo between 8 and 16 weeks of gestation and continued to 36 weeks of gestation.(134) No significant difference in the primary endpoint of preterm birth fewer

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than 37 weeks of gestation was found between the aspirin and placebo groups. Because of lower-than-expected preterm birth rates in the trial, the study was underpowered to detect a difference in the primary endpoint. No significant differences in the secondary perinatal outcomes, including fetal death, hospital or ICU admission, or a composite of poor neonatal outcomes were identified. There was an excess number of poor neonatal outcome events in the aspirin group, though the number of events was small. No difference in reports of maternal serious adverse events was noted between the aspirin and placebo groups.

Two additional meta-analyses were included in the systematic evidence review that evaluated daily aspirin during pregnancy; however, both meta-analyses focused on the use of aspirin for the indication of preeclampsia prevention in patients at risk (e.g., chronic HTN, cardiovascular or endocrine disease, pregnancy HTN).(135, 136) Substantial overlap occurred between the RCTs included in the two meta-analyses. Evidence suggests that daily aspirin might reduce preterm birth, perinatal mortality, and intrauterine growth restriction when used in preeclampsia prevention. Yip et al. (2022) identified an increased risk of postpartum hemorrhage in patients who received aspirin, but Choi et al. (2021) found no significant elevated risk of bleeding events (maternal or neonatal) with aspirin treatment.(135, 136)

For patients at risk of developing preeclampsia, there is a role for daily aspirin to reduce the risk of preeclampsia and adverse pregnancy outcomes, including preterm birth, intrauterine growth restriction, and perinatal mortality. In patients without risk factors for preeclampsia, the USPSTF Guidelines for Aspirin Use to Prevent Preeclampsia do not recommend aspirin.(137) See Recommendations 14 and 15 in this CPG for further discussion on the use of aspirin in patients at risk for preeclampsia.

The Work Group systematically reviewed evidence related to this recommendation.(134) Therefore, it is as categorized as *Reviewed, New-added*. The Work Group's confidence in the quality of the evidence was low. The body of evidence had some limitations, including small sample size and only one relevant RCT.(134) Aspirin reduced adverse outcomes, including preterm birth, in pregnant patients at risk for preeclampsia. The benefits and harms of aspirin for the population of patients with prior spontaneous preterm birth were unknown. Patient values and preferences varied somewhat because different patients might be more or less willing to take medications during pregnancy. Thus, the Work Group made the following recommendation: There is insufficient evidence to recommend for or against the use of aspirin to reduce recurrent spontaneous preterm birth.

# b. Hypertensive Disorders

#### Recommendation

14. We recommend initiating aspirin therapy at or before 16 weeks' gestation in patients at risk of developing preeclampsia.

(Strong for | Reviewed, New-replaced)

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15. We suggest low-dose aspirin of 100–150 mg daily for patients at risk of preeclampsia.

(Weak for | Reviewed, New-replaced)

#### **Discussion**

Preeclampsia, a hypertensive disorder affecting up to 8% of all pregnancies, is associated with serious maternal and fetal risks to include accounting for approximately one-sixth of all premature births. The evidence reviewed showed that in patients at high risk, low-dose aspirin resulted in a significant reduction in the development of preeclampsia.(138-142) An SR involving 23 RCTs (n=26,952) showed that aspirin with daily doses ranging from 50-150 mg was associated with a reduction in the risk of preeclampsia.(138) In regard to the timing of initiation, a greater chance of risk reduction also occurred when initiated at fewer than 16 weeks' gestation. In addition to a reduction in preeclampsia risk, daily aspirin was associated with lower risks of perinatal mortality, preterm birth, and intrauterine growth restriction. Several studies showed no differences in the risk of miscarriage, maternal bleeding (e.g., vaginal bleeding, epistaxis) postpartum hemorrhage, placental abruption, or fetal intracranial hemorrhage.(138-140) Although not part of this review, there is a common set of risk factors cited by ACOG and USPSTF to determine who would be a candidate for aspirin therapy.(137, 143) See the routine pregnancy care section on Preeclampsia for further information. Based on the systematic evidence review, the Work Group recommends initiating low-dose aspirin starting at or before 16 weeks' gestation in patients at risk of developing preeclampsia.

With regard to dosing, the current guideline from the USPSTF based on data from the SR(138) makes a recommendation for the use of aspirin 81 mg daily initiated at 12 weeks for the prevention of preeclampsia.(137) This recommendation aligns with the ones endorsed by ACOG and the Society for Maternal-Fetal Medicine.(143) However, based on subgroup analysis within the SR, the Work Group recognized that doses greater than or equal to 100 mg daily were more likely to be associated with a reduction in the risk of preeclampsia.(138). In the review of the individual studies within the SR, Rolnik et al. (2017) suggested the reasoning behind choosing 150 mg for their study was because of prior studies showing no therapeutic response based on laboratory markers of approximately 30% of women with daily dosage of 81 mg, which decreased to only 5% when the dose was increased to 162 mg.(144) Also, a single RCT (n=50) using 80 mg in twin pregnancies did not show a reduction in preeclampsia, with authors suggesting the dose was insufficient to generate the desired effect.(139) Based on the systematic evidence review, the Work Group suggests using low-dose aspirin of 100–150 mg in patients at increased risk for developing preeclampsia.

The current dosing availability within the U.S. might lead practitioners to choose to use 120 mg (1.5 tablets) or 162 mg (2 tablets) as the prescribed daily dose. Although recognizing a gap in the current systematic evidence review in that no quality studies specifically are using 162 mg, the Work Group felt considering these doses (120 mg or

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162 mg) might be reasonable because the studies within the SR using 150 mg daily showed significant risk reductions without an increase in adverse effects, especially in patients considered at especially high risk for preterm preeclampsia.(138) Also important to point out is that although the evidence suggests using higher doses than those commercially available and recommended by national organizations, this finding does not extend to other standard dosing forms such as 325 mg. Although the mechanism of preeclampsia prevention by aspirin is poorly understood, the evidence suggests a relationship to the inhibition of platelet aggregation and the anti-inflammatory effects of suppressing the production of prostaglandins and thromboxane(145, 146), accomplished by the inactivation of the COX-1 enzyme, which is selectively and irreversibly accomplished at doses fewer than 300 mg.(147)

Because of the discrepancy between this recommendation and that of the other national organizations, there might be acceptability implications from some providers who will choose to continue to use 81 mg dosing. In addition to the need for further research to fill those gaps, adoption of this recommendation might require systematic education of providers detailing the rationale behind it. Patient preferences vary little regarding this treatment, given the general compliance with daily medication and limited side-effect profile. Because of the heterogeneity of the studies within the SR and the lack of data directly comparing different dosing regimens, the Work Group decided to split the previous recommendation into two separate recommendations.

For Recommendation 14, the Work Group systematically reviewed evidence related to these recommendations (138-140, 144) and considered the assessment of the evidence put forth in the 2018 VA/DoD Pregnancy CPG.(141, 142). Therefore, it is categorized as *Reviewed, New-replaced*. The confidence in the quality of the evidence was moderate to support the use of low-dose daily aspirin initiated before 16 weeks' gestation. The benefits of aspirin therapy outweighed the potential harms of miscarriage or stillbirth, small size for gestational age, vaginal bleeding, maternal bleeding, placental abruption, and fetal intracranial bleeding. Patient values and preferences were similar because of the low risk of adverse side effects and the general acceptability of daily medication compliance. Thus, the Work Group made the following recommendation: We recommend initiating aspirin therapy at or before 16 weeks' gestation in patients at risk of developing preeclampsia.

For Recommendation 15, the Work Group systematically reviewed evidence related to these recommendations (138-140, 144) and considered the assessment of the evidence put forth in the 2018 VA/DoD Pregnancy CPG.(141, 142) Therefore, is categorized as *Reviewed, New-replaced*. The confidence in the quality of the evidence was low because of the indirectness of subgroup analysis, heterogeneity in the included studies, and lack of direct comparisons of different dosing regimens. However, despite these limitations, the Work Group felt that the evidence supports the recommendation of higher doses (100–150 mg) with reasonable extrapolation to 162 mg based on dosing availability. The evidence suggests that doses greater than 100 mg daily were

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associated with greater degree of risk reduction for preeclampsia without increasing the risk of adverse events such as maternal bleeding, placental abruption, and fetal intracranial bleeding. Thus, the Work Group made the following recommendation: We suggest low-dose aspirin of 100–150 mg daily for patients at risk of preeclampsia.

#### Recommendation

16. We suggest patients with cardiometabolic disorders (e.g., gestational diabetes mellitus, hypertension, and obesity) be counseled on the benefits of following the Dietary Approaches to Stop Hypertension diet.

(Weak for | Reviewed, New-added)

#### **Discussion**

The Dietary Approaches to Stop Hypertension (DASH) diet promotes the consumption of fruit, vegetables, fat-free or low-fat dairy, whole grains, nuts, and legumes, while limiting the intake of saturated fat, cholesterol, refined sugar, sodium, and red and processed meats. This diet was originally recommended for controlling HTN. Increased intake of whole grains, fruits, vegetables, low-fat dairy products, nuts, and reduced consumption of sugary foods demonstrated an inverse relationship between risk of CVD, total cancers, and all-causes of mortality in non-pregnant populations.(148)

An SR of six RCTs by Li et al. (2020) showed a lower incidence of preeclampsia with the DASH diet and found no difference among other outcomes.(148)

Based on the evidence reviewed, pregnant patients who followed the DASH diet were found to have a lower incidence of preeclampsia than those who followed an alternative prescribed diet or those who received general dietary advice.(148)

The DASH diet has emerged as a potential therapeutic option for conditions such as HDP, pre-pregnancy obesity, or gestational weight gain given its beneficial effect on metabolic risk factors. Cardiovascular and metabolic risk factors can influence maternal and fetal outcomes during pregnancy. The reviewed SRs and meta-analyses found a significant inverse association between DASH diet adherence and CVD, cancer, all-cause, and cause-specific mortality in non-pregnant populations.(148)

Patient preferences varied somewhat regarding this treatment. The DASH diet can be difficult to adhere to because of the cost associated with buying needed grocery items or having limited options while dining out. Further, there might be a lack of available RDNs to provide education or counseling to patients on this diet, a lack of other resources (e.g., Healthy Teaching Kitchen through Whole Health Initiative-VA), or Veterans and Service members living in food deserts. Moreover, lack of patient adherence to this diet might be linked to patient-disordered eating or eating disorders (e.g., anorexia or bulimia).

The Work Group systematically reviewed evidence related to this recommendation.(148) Therefore, it is categorized as *Reviewed, New-added*. The Work

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Group's confidence in the quality of the evidence was low. The body of evidence had some limitations, including the quality of evidence being based on the lowest GRADE rating for preeclampsia. The benefits of the DASH diet outweighed the potential harms and burdens. Patient values and preferences varied somewhat because following this diet (e.g., cost associated with buying groceries, having limited options when eating out) might be difficult for patients. Patient lack of adherence to this diet might be linked to patient-disordered eating or eating disorders (e.g., anorexia or bulimia). Further, there might be a lack of available RDNs to provide education or counseling to patients on this diet, a lack of other resources (e.g., Healthy Teaching Kitchen through Whole Health Initiative in VA), or Veterans and Service members living in food deserts. Thus, the Work Group made the following recommendation: We suggest patients with cardiometabolic disorders (e.g., gestational diabetes mellitus, hypertension, and obesity) be counseled on the benefits of following the Dietary Approaches to Stop Hypertension diet.

#### Recommendation

 There is insufficient evidence to recommend for or against self-monitoring for blood pressure during pregnancy and the postpartum period.
 (Neither for nor against | Reviewed, New-added)

# **Discussion**

Evidence suggests that there might be no benefit to self-monitoring blood pressure (SMBP) at home as a supplement to routine clinic blood pressure assessments.(<u>149-152</u>).

Tucker et al. (2022) conducted an RCT that compared SMBP with TAU with TAU alone in pregnancies at risk for preeclampsia.(152) They found no statistically significant difference in the timing of clinic-based blood pressure detection of HTN and no difference in the incidence of preeclampsia, eclampsia, transient ischemic attack, or stroke.(152) In a similar and linked RCT, Chappell et al. (2022) compared SMBP with TAU with TAU alone in pregnancies with diagnosed HTN(150) and found no statistically significant difference in clinic-based blood pressure control and no difference in the incidence of preeclampsia, severe HTN, or maternal death.(150)

Two SRs echoed these findings in comparing SMBP with TAU with TAU alone in populations that included pregnant and postpartum people with and without HTN.(149, 151) Ashworth et al. (2020) found no statistically significant difference in preeclampsia, eclampsia, or maternal death.(149) Kalafat et al. (2020) found no difference in the incidence of preeclampsia and no difference in prenatal or postpartum readmissions.(151)

Patient preferences vary regarding SMBP. Some patients, particularly those with a history of preeclampsia, might wish to learn and perform SMBP between clinic-based visits. Other patients might prefer traditional clinic-based care only. Further, home blood

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pressure monitoring requires equipment. Some patients might be provided a home blood pressure cuff, although other patients who wish to perform SMBP might be required to purchase a home blood pressure monitor device and might find this cost prohibitive.

Home blood pressure monitoring requires additional clinic resources to educate patients on the use of the equipment, frequency of monitoring, and communication of blood pressure assessments. Consideration should be given to clinic resources required to initiate home monitoring and support ongoing review of SMBP assessments. Although no difference was found in the outcomes of interest for this recommendation, additional evidence does suggest that in postpartum patients with HTN, SMBP used in conjunction with telehealth in place of an in-office visit might improve compliance with timely postpartum visits in the first 10 days following birth.(114) See Recommendation 9 for further details.

The Work Group systematically reviewed evidence related to this recommendation. (149-152) Therefore, it is categorized as *Reviewed, New-added*. The Work Group's confidence in the quality of the evidence was very low. The body of evidence had some limitations, including methodological quality of the included studies and imprecision based on small sample sizes or wide confidence intervals. Moreover, the identified critical outcomes were likely too uncommon to be captured on a large scale in the evidence. (149-152) Additionally, some studies used home blood pressure monitors that might not have been validated for use in pregnancy. (149, 150) No clear benefits nor harms were identified in self-monitoring for blood pressure in addition to TAU, so the benefits were balanced with harms. Patient values and preferences varied because some patients prefer not to self-monitor. Thus, the Work Group made the following recommendation: There is insufficient evidence to recommend for or against self-monitoring for blood pressure during pregnancy and the postpartum period.

# c. Bariatric Surgery

# Recommendation

18. We suggest patients who have undergone bariatric surgery be evaluated for nutritional deficiencies and the need for nutritional supplementation where indicated (e.g., vitamin B12, folate, iron, calcium).

(Weak for | Not reviewed, Amended)

19. There is insufficient evidence to recommend for or against the routine supplementation of vitamins A, D, E, or K for pregnant patients who have undergone bariatric surgery.

(Neither for nor against | Not reviewed, Amended)

# **Discussion**

The prevalence of obesity doubled from 1980 to 2008, and an increasing number of patients are becoming pregnant after bariatric surgery. (66) Recent CDC data, which

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was not included in the systematic evidence review and did not influence the strength of the recommendation, reports that the U.S. obesity prevalence was 41.9% between 2017 and March 2020. As noted in the VA/DoD Obesity CPG, many non-surgical treatments for obesity are available; however, obese patients are often unable to achieve substantial weight loss. Bariatric surgery has been proven to be an effective obesity treatment. However, the impact of bariatric surgery on pregnancy has been inadequately studied. Pregnancies after bariatric surgery might require additional care other than routine prenatal care because unique risks might be present. Bariatric surgeries might create a risk for nutritional deficiencies during pregnancy. Thus, patients might be advised to defer pregnancy for at least 18 months after bariatric surgery.

Although obesity is common and use of bariatric surgery has been increasing, very little high-quality evidence exists to support best practices during pregnancy. In the previous systematic evidence review conducted for the 2018 VA/DoD Pregnancy CPG, interventions considered for patients who have undergone bariatric surgery included nutritional screening, nutritional medicine referrals, nutritional management, and additional micronutrient supplementation.

We suggest that patients who have undergone bariatric surgery should be evaluated for nutritional deficiencies, most commonly vitamin B12, folate, iron, and calcium, and need for nutritional supplementation where indicated. The evidence supporting this recommendation was determined to be of low quality because of small sample sizes(153, 154), significant non-compliance with prescribed supplement regimens, and heterogeneous bariatric surgery types with some having restrictive versus malabsorptive procedures.(153)

According to the VA/DoD Obesity CPG, the risk for nutritional deficiencies might vary depending on the type of surgery performed. The VA/DoD Obesity CPG states, "Specifically after Roux-en-Y gastric bypass, several nutritional deficiencies are common and supplementation at higher than the usual recommended daily dose may be required. Typical doses of elemental calcium are 1,200–2,000 mg daily, preferably as calcium citrate, which is better absorbed in the absence of gastric acid. The optimal dose of vitamin B12 is not known. While all forms of delivery are effective, poor absorption is common, and sublingual or intramuscular injection may be required. Iron deficiency is common and typically all patients receive prophylactic therapy in conjunction with vitamin C to enhance absorption."

In the studies reviewed, no serious adverse events were related to evaluation and supplementation. Potential benefits greater for neonatal outcomes might exist, but study sample sizes did not provide power to demonstrate. Minimal risks and potential benefits are associated with evaluation and supplementation for vitamin B12, folate, iron, and calcium.

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For Recommendation 18, the Work Group considered the assessment of the evidence put forth in the 2018 VA/DoD Pregnancy CPG.(153, 154) Therefore, it is categorized as *Not Reviewed, Amended*. The Work Group's confidence in the quality of the evidence was very low. The body of evidence had some limitations (because of small sample sizes and vague reporting regarding supplementation regimens used) in support of evaluation for nutritional deficiencies and nutritional supplementation when indicated for women who have had bariatric surgery. (153, 154) The benefits were determined to outweigh the burdens because there is a benefit to supplementation if a patient has documented deficiency; however, it is noted that supplements might cause digestive issues if too much is taken. Patient values and preferences were similar because bariatric patients have undergone counseling that explains they might require supplementation throughout their life. Thus, the Work Group made the following recommendation: We suggest patients who have undergone bariatric surgery be evaluated for nutritional deficiencies and the need for nutritional supplementation where indicated (e.g., vitamin B12, folate, iron, calcium).

For Recommendation 19, the Work Group considered the assessment of the evidence put forth in the 2018 VA/DoD Pregnancy CPG.(153, 154) Therefore, it is categorized as *Not reviewed, Amended*. The Work Group's confidence in the quality of the evidence was very low. The body of evidence had some limitations because of small sample sizes and vague reporting regarding supplementation regimens used. It was determined the harms of routine supplementation outweighed the benefits. If a patient is not vitamin deficient and routinely supplemented, potential harm could occur (e.g., vitamin A has been documented to cause birth defects). Patients might have variations in values, preferences, or both regarding supplementation, depending on the number of specialists they see. They might be receiving conflicting guidance, and enhanced collaboration between their providers would be helpful to promote patient safety and optimal outcomes. Thus, the Work Group made the following recommendation: There is insufficient evidence to recommend for or against the routine supplementation of vitamins A, D, E, or K for pregnant patients who have undergone bariatric surgery.

# C. Mental Health

# a. Screening

### Recommendation

 We recommend screening for use of tobacco and nicotine products, alcohol, cannabis, illicit drugs, and inappropriate use of prescription medication. See VA/DoD Substance Use Disorders CPG.

(Strong for | Not reviewed, Amended)

#### **Discussion**

Evidence from the previous CPG has supported screening for the use of tobacco and nicotine products, alcohol, cannabis, illicit drugs, and inappropriate use of prescription medications.(155-166) Additional evidence presented throughout this narrative did not

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meet inclusion criteria for the current systematic evidence review but was included in this narrative to provide updated information and context to support the previous evidence. Substance use during pregnancy can influence fetal and maternal outcomes. Tobacco and nicotine products, alcohol, cannabis, and illicit drugs are the most commonly misused addictive substances during pregnancy.(167) Compiled data from the National Survey on Drug Use and Health from 2015–18 demonstrates that 9.8% of pregnant patients reported current alcohol use, and 4.5% reported binge drinking. Of those respondents who used alcohol, 38.2% also reported use of at least one other substance, including tobacco, marijuana, opioids, and other substances.(168) Substance use among Veterans might be higher than in the general population. Among Veterans of childbearing age, an estimated 27–43% have had heavy episodic drinking (defined as four or more standard drinks on at least one occasion), 24–26% have had daily cigarette use, 12–29% have reported illicit drug use in the past year, and 6–14% have reported misuse of prescription drugs.(169, 170)

Prenatal exposure to some substances might increase the risk of congenital anomalies and long-term adverse effects. However, other risky behaviors (e.g., use of multiple substances, lack of prenatal care, and other stressors in the antepartum period) confound attempts to assign causality.(171)

The best available evidence indicates that prenatal smoking could impact pregnancy outcomes, increasing the risk of miscarriage, fetal growth restrictions, preterm birth, placental abnormalities, and stillbirth. Additionally, in utero exposure to tobacco products can lead to impaired lung function and visual difficulties.(172)

Alcohol is a known teratogen. The effects of prenatal alcohol exposure are wide ranging and reflect the extent of exposure and susceptibility. Moreover, no safe drinking limit during pregnancy has been established.(170) Prenatal alcohol exposure causes several abnormalities in the heart, kidney, liver, gastrointestinal tract, endocrine system, and brain.(173) The term fetal alcohol spectrum disorder describes the broad range of adverse sequelae of fetal alcohol exposure, with fetal alcohol syndrome and its characteristic triad of problems with facial features, growth, and central nervous system as its most severe expression. Fetal alcohol exposure might cause low birth weight, preterm birth, small for gestational age neonates, and early pregnancy loss.

Emerging evidence suggests negative health consequences of cannabis use during pregnancy and lactation, including leading to impaired cognition, difficulty learning, and behavioral problems.(174, 175)

Opioids in general have not been considered teratogenic, although a higher incidence of congenital anomalies in infants born to mothers exposed to codeine, methadone, or heroin has been reported.(171) In utero exposure to opioids is associated with neonatal abstinence syndrome (NAS), defined as a constellation of symptoms in newborns including central nervous system irritability, gastrointestinal dysfunction, and

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temperature instability.(<u>176</u>) The incidence of NAS has increased by almost 300% from 1999–2013, reflecting increases in the use of opioid prescription medications and heroin among women of reproductive age.(<u>177</u>, <u>178</u>)

Methods used to screen patients for alcohol, tobacco, and drug use vary and might include validated questionnaires or patient interviews. Validated screening tools exist that can be provider- or self-administered either in-person or electronically. Screening for these substances should be done for all pregnant patients.(179) In the case of screening for prenatal alcohol exposure, the reference standard is maternal self-reporting.(180) This approach can be limiting given that women might be less likely than men to disclose alcohol use to a primary care provider, resulting in women being less likely to receive an effective intervention.(181) No reliable laboratory test exists to screen for alcohol use in pregnancy.(180, 182) Because of potential legal and other consequences when positive laboratory tests are found for any of these substances, informed consent must be obtained before their use, except in the case of a medical emergency when the pregnant person is unconscious and unable to consent. Legal implication varies by state and local laws, and it is important for providers to be aware of these.

The Work Group considered the assessment of the evidence put forth in the 2018 VA/DoD Pregnancy CPG related to this recommendation.(155-166) Therefore, it is categorized as Not reviewed, Amended. The Work Group's confidence in the quality of the evidence was moderate. The body of evidence had some limitations particularly related to confounders and heterogeneity. The benefits of screening for use of harmful substances, specifically tobacco, alcohol, cannabis, illicit drugs, and unauthorized use of prescription medication include opportunities for timely counseling, intervention, and treatment as needed (see VA/DoD Substance Use Disorders CPG). These effects outweighed the potential harm of screening, acknowledging that patients might feel shame or stigma related to disclosure. Patient values and preferences varied largely because of the varied social acceptance and legality of the specific substance and potential for implications with Child Protective Services, custody impacts, and additional considerations for Service members. Thus, the Work Group made the following recommendation: We recommend screening for use of tobacco and nicotine products, alcohol, cannabis, illicit drugs, and inappropriate use of prescription medication. See VA/DoD Substance Use Disorders CPG.

#### Recommendation

21. We recommend screening for depression periodically using a standardized tool, such as the Edinburgh Postnatal Depression Scale or the 9-item Patient Health Questionnaire, during pregnancy and postpartum.

(Strong for | Not reviewed, Not changed)

### **Discussion**

In general, studies have found that screening patients during pregnancy and the postpartum period for depression using a validated screening tool is more effective than

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usual clinical assessment in detecting depressive symptoms.(183) The EPDS and the PHQ-9 are among the depression screening tools validated for perinatal use. In an RCT reviewed by the Work Group comparing these two screening tools, moderate quality evidence suggests an 83% concordance between the two scales when scores are dichotomized between "normal" and "increased risk of depression."(184) Concordance is greatest at the highest score levels, and concordance for suicidal thoughts is very high.

The systematic evidence review found no harm associated with perinatal depression screening. Potential harms of screening include time spent on screening and discomfort with screening questions.

Patient preferences varied somewhat regarding perinatal depression screening. Participants in the patient focus group noted that they are familiar with depression screening, do not object to it, and want to discuss mental health concerns with their providers. This finding is congruent with research findings that perinatal depression screening is acceptable to most women. (185)

Depression screening tools are readily and consistently available across VA/DoD health systems. The availability of interventions for people with positive screens might vary across facilities, which could affect the consistency and utility of screening.

The Work Group considered the assessment of the evidence put forth in the 2018 VA/DoD Pregnancy CPG related to this recommendation.(184) Therefore, it is categorized as *Not reviewed, Not changed*. The Work Group's confidence in the quality of the evidence was moderate, with no major concerns regarding study limitations, consistency, or directness but some imprecision in reporting statistical findings. The benefits of perinatal depression screening (improved detection of depression) outweighed the potential harms (time spent on screening, discomfort with screening questions). Patient values and preferences varied somewhat, yet the VA/DoD patient focus group findings suggested that perinatal patients want to discuss mental health concerns with their providers and do not object to depression screening. Screening tools and mental health treatment resources are available in VA and DoD. Thus, the Work Group made the following recommendation: We recommend screening for depression periodically using a standardized tool, such as the Edinburgh Postnatal Depression Scale or the 9-item Patient Health Questionnaire, during pregnancy and postpartum.

# Recommendation

22. We suggest screening patients with posttraumatic stress disorder (PTSD) for active PTSD and offering PTSD treatment. See VA/DoD PTSD CPG. (Weak for | Reviewed, New-added)

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### **Discussion**

Evidence suggests that Veterans with active symptoms of PTSD during pregnancy were at higher risk for postpartum depression, preeclampsia, and preterm birth; however, evidence was less clear for active duty pregnant people.(28, 186, 187) Nillni et al. (2020) proactively examined Veteran populations with a PTSD diagnoses (all types of PTSD were combined).(186) In this study, pregnant Veterans were recruited and followed by mail throughout their pregnancies and beyond. Results showed that participants with active PTSD symptoms, "moral injury" (believing to have acted or witnessed others acting against moral beliefs), or both had a higher rate of preterm birth, preeclampsia, and miscarriage, whereas only active PTSD symptoms predicted postpartum depression and anxiety. In addition, Nillni et al. (2020) identified that the concept of active PTSD combined with moral injury predicted adverse perinatal outcomes better than active PTSD alone.(186) This prospective study was deemed to be of low quality partially because of the use of self-reported medical outcomes versus chart review. Similarly, Shaw et al. (2017) retrospectively reviewed 15,986 singleton deliveries, 2,977 of which were mothers with a PTSD diagnosis. (28) Shaw et al. (2017) found that in the Veteran population, a current diagnosis of PTSD increased the risk for GDM (RR: 1.4; 95% CI: 1.2–1.7), preeclampsia (RR: 1.3; 95% CI: 1.1–1.6), prolonged hospital stay (RR: 1.2; 95% CI: 1.01–1.4), and repeat hospitalization (RR: 1.4; 95% CI: 1.2–1.6).(28) The systematic evidence review suggests that a current PTSD diagnosis increased the risk of pregnancy complications in Veteran populations, whereas active symptoms of PTSD increased the risk of postpartum depression. The current research does not suggest a causal relationship between PTSD and complications, rather just a higher incidence of complications. Given the risk of complications, it is suggested that PTSD diagnoses and symptoms be identified and treated as per the VA/DoD PTSD CPG.

Another large study on active duty pregnant women had different findings. Lutgendorf et al. (2021) found no overall association between preterm birth and "active PTSD." (187) Lutgendorf et al. (2021) reviewed 103,221 retrospective records and compared 1,657 patients who had a diagnosis of PTSD within 1 year or less of pregnancy with 101,564 other pregnancies. (187) Results suggested a weak correlation between those with PTSD, who also under-use prenatal care, and preterm birth. However, no association was found between the larger PTSD group and its non-PTSD comparators. Of note, this retrospective study by Lutgendorf et al. (2021) used a definition of PTSD as defined by a recent diagnosis within the military medical record system. (187) This definition of PTSD might have missed those with active PTSD symptoms who did not have a recent diagnosis or those who had long-standing PTSD.

The research reviewed by the Work Group documented a connection between PTSD and perinatal complications in pregnant Veterans, although the association between PTSD and perinatal complications has not been directly identified in an active duty population.(28, 186, 187) However, the Work Group decided to suggest that both groups be offered treatment if symptoms/diagnoses are identified.(187) Many factors

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were considered when developing this recommendation, including patient preferences, availability of treatment, and feasibility. Patient preferences might vary regarding being identified as a person with PTSD and given treatment for PTSD during pregnancy. Some individuals might have already undergone treatment, do not care to engage in treatment at this time, or might already be seeking treatment. As with any mental health treatment, some stigma might be attached to being identified as a person with a mental health condition. However, members of the patient focus group noted they wanted whole-person treatment during their pregnancy; adding an option for treatment of PTSD during pregnancy would take steps in this direction. It is noted that there is a higher incidence of PTSD in military/Veteran populations and, thus, PTSD is screened for in routine medical care in both medical systems.(188) The availability of this information might make it easier to identify individuals with PTSD during pregnancy. This recommendation does place an additional burden on providers to do additional chart reviews or interviews. But resources are in place in both systems to provide treatment if a person chooses to accept it.

The Work Group systematically reviewed evidence related to this recommendation.(28, 186, 187) Therefore, it is categorized as *Reviewed, New-added*. The Work Group's confidence in the quality of the evidence was low. The body of evidence had some limitations, including methodological restrictions, retrospective reviews, and confounders in the analysis; however, all studies were directly focused on active duty personnel or Veteran populations and had large sample sizes. Patient values and preferences were noted to vary somewhat because some patients prefer not to be identified as a person with a mental health condition. The benefits of identifying a pregnant person with a PTSD diagnosis and referring them to treatment were determined to outweigh the potential harm. It was noted that a stigma exists in acknowledging a PTSD diagnosis for patients; however, great benefit can be found if identification and treatment or alternative management can lead to less preterm delivery, preeclampsia, or postpartum depression. Thus, the Work Group made the following recommendation: We suggest screening patients with posttraumatic stress disorder (PTSD) for active PTSD and offering PTSD treatment. See VA/DoD PTSD CPG.

#### b. Treatment

#### Recommendation

23. We recommend offering individual or group Interpersonal Psychotherapy or cognitive behavioral therapy for pregnant patients at risk of perinatal depression. (Strong for | Reviewed, New-added)

#### **Discussion**

Evidence is growing that Interpersonal Psychotherapy (IPT) or CBT is beneficial for pregnant patients at risk for perinatal depression.(<u>189-191</u>) Although these interventions are known to treat diagnosed mental health conditions, our systematic evidence review strongly indicated that treating those at risk for postpartum depression led to benefits

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from these treatments. Supporting data for this recommendation was found in two SRs as well as 1 RCT. O'Connor et al. (2019) systematically reviewed 50 RCTs evaluating the benefits and harm of interventions to prevent perinatal depression.(189) Twenty of those studies suggested that IPT and CBT, when offered to at-risk populations, reduced the incidence of depression and depressive symptoms postpartum.(189) Waqas et al. (2021), although relevant, reviewed many of the same RCTs used in O'Connor et al. (2019).(191) Waqas et al. (2021) reached the same conclusion regarding the prevention of postpartum depression and treatment.(191) However, the main focus of Waqas et al. (2021) was other preventive variables and, thus, not as directly related to this recommendation. The systematic evidence review was deemed to be of moderate quality with little to no inconsistencies, indirectness, or imprecision.

These findings are particularly important in the military and Veteran populations because the prevalence of mental health conditions is higher among women who have served in the military than in civilian counterparts.(192) In addition, nearly one in eight women in the military (compared with approximately one in nine in the general population) develop postpartum depression.(29, 36-38). Therefore, applying this robust finding to active duty Service members and the Veteran population might be highly beneficial.

In multiple studies, the incidence of depression, distress, and anxiety were all decreased by the intervention.(193) The body of literature supporting the benefit was so compelling that the USPSTF also recommended that providers either counsel pregnant and postpartum persons at increased risk of perinatal depression or refer them to counseling interventions.(193) A limitation of the majority of the studies, however, was the lack of a universal definition of "at risk." In the reviewed research, at risk was defined as a history of a mental health diagnosis, a current mental health diagnosis, or a subclinical elevation on a mental health screener (i.e., EPDS or PHQ-9). This lack of a consistent definition did not eliminate the robustness of the findings, indicating that preventive IPT or CBT counseling has a positive impact on at-risk mothers. The Work Group believed that using already available mental health screeners (see Recommendation 21) and a history of mental health conditions is the least burdensome way to identify at-risk populations for this recommendation. Another limitation was variability in the diagnostic criteria for postpartum depression.

Research shows that perinatal depression is associated with increased likelihood of preterm birth, low birth weight, and intrauterine growth restriction (194) and impaired offspring development.(195) Thus, reducing these risks might lead to a healthier pregnancy. Patient preferences varied somewhat regarding mental health treatment. As with all mental health treatment, patients might be more or less willing or able to engage in treatment. The patient focus group noted that they are interested in more whole-person pregnancy care, which prevention of mental health complications might work to improve.(196) It is noted that treatment, whether in a group or an individual format, can be burdensome because it requires frequent visits and trained providers. However, as noted in Recommendation 9 above, telemedicine might help provide continuity when

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FTF visits are difficult or impossible so the patient can still receive care. Further, currently preventive mental health services are not uniformly offered across all VA/DoD health care facility locations. Given the variability of resources, applying such services equitably in all locations might be difficult.

The Work Group systematically reviewed evidence related to this recommendation.(189-191) Therefore, it is categorized as *Reviewed, New-added*. The Work Group's confidence in the quality of the evidence was high. The body of evidence was consistent across multiple large studies, and the research base had minor limitations, including methodological restrictions. Patient values and preferences might vary somewhat when it comes to treatment; however, the benefits of recommending treatment outweighed the harms identified. Thus, the Work Group made the following recommendation: We recommend offering individual or group Interpersonal Psychotherapy or cognitive behavioral therapy for pregnant patients at risk of perinatal depression.

# Recommendation

- 24. We recommend offering Interpersonal Psychotherapy for treating depression during pregnancy or postpartum.
  - (Strong for | Reviewed, New-added)
- 25. We suggest offering cognitive behavioral therapy for treating depression during pregnancy or postpartum.

(Weak for | Reviewed, New-added)

# **Discussion**

Two types of psychotherapy were examined for their role in treating perinatal depression. IPT focuses on role transitions, interpersonal disputes, loss, and social support.(197) CBT aims to help people identify, evaluate, challenge, and modify maladaptive beliefs and behaviors.(198) The efficacy of IPT and CBT for treating general depression is well established (see VA/DoD Major Depressive Disorder CPG).

Evidence shows that IPT reduced depressive symptoms in patients with depressive symptoms during pregnancy or postpartum.(199, 200) In an SR, Sockol et al. (2018) found that treatment with IPT was associated with a significant reduction in depressive symptoms over time in 14 of 15 studies.(199) Among 7 included studies that assessed the difference in the change in depressive symptoms between treatment and comparison conditions, most found significantly larger reductions in depressive symptoms in the treatment condition. Findings from a subsequent RCT of telephone-based nurse-delivered IPT were consistent with the findings from the SR.(200)

Evidence shows that CBT reduced depressive symptoms in patients with depressive symptoms during pregnancy or postpartum.(201-203) An SR of 45 RCTs of CBT for patients with depressive symptoms who were pregnant or within the first year postpartum found that treatment with CBT was associated with a significant reduction in

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depressive symptoms immediately post-intervention and longer-term, to the end of follow-up.(202) Findings from an SR of therapist-supported internet-based CBT were consistent with this result; treatment was associated with a significant improvement in depressive symptoms. Similarly, an RCT of nurse-delivered group CBT for people with postpartum depression found significantly greater reductions in depressive symptoms in the treatment group than in a control group receiving TAU.(203)

Though IPT and CBT were not compared directly with one another, the evidence base was found to be stronger for IPT as a treatment of depression. In the studies of IPT, better consistency and less attrition was found than in the studies of CBT. The limitations of the systematic evidence review for both IPT and CBT included unclear blinding of outcome assessors.

Although IPT and CBT can both be adapted to address common perinatal concerns, that such adaptation happened less often in studies of CBT might be relevant. Specific parental cognitions during pregnancy were strongly correlated with perinatal depressive symptoms (expecting negative judgment from others about parenting, intense parental responsibility, and parental role idealization).(204) The included studies on CBT did not specifically adapt CBT to address these cognitions.

No treatment-related adverse events were noted in the studies of IPT or CBT. Data about psychotherapy for general depression indicated that time commitment and stigma are potential harms or burdens.(205)

Patient preferences varied somewhat regarding any type of psychotherapy, including IPT and CBT. Patient focus group participants stated that more consideration of their mental health needs by their care team would be beneficial throughout pregnancy and the postpartum period. Data about psychotherapy for general depression indicated that time commitment and stigma might be reasons some patients would not prefer psychotherapy.(205) Technology-enabled delivery might reduce these barriers for some patients. For example, in the RCT of telephone-based IPT, 97.9% of participants in a satisfaction questionnaire reported liking the telephone treatment; 94.9% found it convenient.(200) Although some patients might prefer antidepressant medication to psychotherapy, data suggested that more pregnant women prefer psychotherapy.(206)

Both IPT and CBT are offered in VA and DoD, though access to these treatments might vary among individual facilities. Access to specific delivery modes (e.g., in-person, internet-based, telephone-based) might differ among patients. Evidence suggests efficacy across multiple delivery modes, which could improve access and equity.

The Work Group systematically reviewed evidence related to IPT.(199, 200) Therefore, is categorized as *Reviewed*, *New-added*. The Work Group's confidence in the quality of the evidence was moderate. The body of evidence had some limitations including unclear blinding of outcomes assessors and moderate attrition in some studies included in this SR. The benefits of IPT (e.g., reduction in depressive symptoms) outweighed the

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potential harms (e.g., stigma, time commitment). Patient values and preferences varied somewhat because some patients prefer other treatments for depression, such as medication. Thus, the Work Group made the following recommendation: We recommend offering Interpersonal Psychotherapy for treating depression during pregnancy or postpartum.

The Work Group systematically reviewed evidence related to CBT.(201-203) Therefore, it is categorized as *Reviewed*, *New-added*. The Work Group's confidence in the quality of the evidence was low. The body of evidence had some limitations including, unclear blinding of outcomes assessors and attrition in more than one-half of the studies included in the main SR.(202) The benefits of cognitive behavioral therapy (e.g., reduction in depressive symptoms) outweighed the potential harms or burdens (e.g., stigma, time commitment). Patient values and preferences varied somewhat because some patients prefer other treatments for depression, such as medication. Thus, the Work Group made the following recommendation: We suggest offering cognitive behavioral therapy for treating depression during pregnancy or postpartum.

### Recommendation

26. We suggest offering peer support for people with perinatal depression or risk of perinatal depression to improve depressive symptoms.

(Weak for | Reviewed, New-added)

# **Discussion**

Evidence from the systematic evidence review suggests peer support that extends into the postpartum period reduces perinatal depressive symptoms. Fang et al. (2022) systematically reviewed 16 RCTs on the benefit of peer support.(207) Fang et al. (2022) was judged to have a well-executed methodology and statistical analysis but was deemed to potentially not be generalizable to the VA or DoD populations (207) The participants were pregnant patients or patients within 1 year of giving birth with a formal diagnosis of perinatal depression or risk of perinatal depression (e.g., those with serious pregnancy complications, adverse birth outcomes). In addition, Fang et al. (2022) divided interventions into three intervention groups and divided by periods of intervention: prenatal, perinatal (second trimester extending into postpartum), and postpartum.(207) Peer support that continued into the postpartum period varied in length from up to 6 months postpartum to 3 years postpartum. Fang et al. (2022) found that peer support has a more robust effect on depression scores as interventions move toward the postpartum period.(207) Though all studies reviewed by Fang et al. (2022) favored peer support as an intervention for perinatal depressive symptoms, interventions that do not extend into postpartum might be ineffective.(207)

Many factors in addition to the research were considered in developing this recommendation, including patient preferences, focus group outcomes, and cost and benefit concerns. It is acknowledged that some variation might occur in patient preferences regarding this treatment. Patients generally value peer support (e.g., group

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prenatal care).(208, 209) Some might not want to participate or share with peers, although others might prefer peer support over other interventions. Peer support for some patients will have less stigma compared with other interventions (e.g., two mothers meeting). Social support has been shown to improve outcomes during pregnancy.(210) The patient focus group shared the importance of access to comprehensive education options, which includes peer support. Further, VA provides peer specialists with opportunities for reproductive women's mental health training. Systemized peer support is unavailable uniformly at DoD but might be expanded from programs already in place. Peer support might be offered through many different modalities/forms, which makes it more feasible. Group peer support might be more efficient from a provider's perspective.

The Work Group systematically reviewed evidence related to this recommendation.(207) Therefore, it is categorized as a *Reviewed, New-added*. The Work Group's confidence in the quality of the evidence was low. The body of evidence had some limitations, including the location where these studies were conducted (i.e., Middle East, Near East, and east Asia). Additionally, socioeconomic status, racial representations, and demographics of the study samples might or might not represent U.S. Service member or Veteran populations or both. The benefits of peer support outweighed the potential harms. Patient values and preferences varied somewhat because some patients might prefer peer support over other interventions, and some might not want to share their condition or engage with peers. Thus, the Work Group made the following recommendation: We suggest offering peer support for people with perinatal depression or risk of perinatal depression to improve depressive symptoms.

# Recommendation

27. We suggest exercise, mindfulness, yoga, or any combination of these interventions for depressive symptoms in perinatal patients.

(Weak for | Reviewed, New-added)

# **Discussion**

Three types of non-pharmacologic approaches—including complementary and integrative health modalities—were examined for their role in reducing perinatal depressive symptoms: exercise, mindfulness, and yoga.

Evidence suggests that exercise reduces depressive symptoms in patients with depressive symptoms during pregnancy or postpartum.(211-213) In an SR of 14 RCTs, Morres et al. (2022) found that low to moderate-intensity aerobic exercise during pregnancy or the first 6 months after giving birth reduced depressive symptoms compared with TAU, waitlist controls, or instructional controls.

Findings from a prior SR including only postpartum patients were consistent with these findings.(211) Carter et al. (2019) included 17 RCTs and found that exercise reduced postpartum depressive symptoms compared with TAU, waitlist, or active controls.(211)

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By contrast, an RCT of exercise for patients with postpartum depressive symptoms who lived inside a city found no significant change in depression scores.(212)

The quality of studies on exercise as an intervention for perinatal depression was fair to poor, with limitations including lack of patient or assessor blinding, high attrition, unclear randomization, selective reporting, and potential bias. The type, frequency, and intensity of exercise varied among studies and included walking, other aerobic exercises, and strength training.

Evidence suggests that mindfulness-based interventions reduced depressive symptoms in patients with depressive symptoms during pregnancy or postpartum.(214) In an SR and meta-analysis of 11 RCTs, Corbally & Wilkinson (2021) found that mindfulness-based interventions during pregnancy or the first year after giving birth reduced depressive symptoms compared with TAU or non-mindfulness-based interventions.(214) The quality of included studies was fair to poor, with limitations including lack of patient or assessor blinding, unclear randomization, and lack of trained therapists in some studies. The type of mindfulness-based intervention varied among studies and included Mindfulness-Based Cognitive Therapy, Mindfulness-Based Stress Reduction®, Acceptance and Commitment Therapy, and mindfulness-based interventions.

Evidence suggests that yoga reduced depressive symptoms in patients with depressive symptoms during pregnancy.(215) In an SR and meta-analysis of 12 RCTs, Corrigan et al. (2022) found that yoga during pregnancy was associated with a reduction in depressive symptoms compared with TAU.(215) The quality of included studies was fair to poor, with limitations including lack of blinding, unclear randomization, incomplete outcome data, and possible bias. The type, frequency, and duration of yoga interventions varied among included studies. Results showed consistent positive benefits from yoga.

No treatment-related adverse events were noted in the reviewed studies of exercise, mindfulness-based interventions, or yoga. Depending on individual vulnerability factors and the type and intensity of exercise, potential adverse effects of exercise, in general, include injuries, asthma, MIs, sudden cardiac death, and over-exercising in the context of an eating disorder. Potential adverse effects of mindfulness-based interventions, in general, include anxiety, flashbacks, derealization, and dissociation.(216) In a non-perinatal study of yoga, adverse effects included soreness, pain, muscle injuries, and fatigue.(217)

Patient preferences varied somewhat regarding exercise, mindfulness-based interventions, and yoga for depression. Patient focus group participants stated that more consideration of their mental health needs by their care team would be beneficial throughout pregnancy and the postpartum period. Nationally representative surveys in the U.S. of respondents who identified as women (218) and of any sex (219) found

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that most respondents with depression used complementary and integrative health interventions within the year before the surveys.

Access to some forms of exercise, mindfulness-based interventions, yoga, or any combination of these interventions is widely available, though some people experience barriers to access. Some individuals require modifications of technique based on medical or mental health conditions or both.

The Work Group systematically reviewed evidence related to this recommendation.(211-215) Therefore, it is categorized as *Reviewed, New-added*. The Work Group's confidence in the quality of the evidence was low. The body of evidence had some limitations, including lack of blinding, unclear randomization, selective reporting, potential bias, attrition, lack of trained therapists, and incomplete outcome data. The benefits of exercise, mindfulness-based interventions, and yoga (e.g., reduction in depressive symptoms) outweighed the potential harms, especially when techniques were modified according to individual needs. Patient values and preferences varied because some patients prefer standard treatments for depression, such as other psychotherapies or medication. Thus, the Work Group made the following recommendation: We suggest exercise, mindfulness, yoga, or any combination of these interventions for depressive symptoms in perinatal patients.

# Recommendation

28. We suggest offering psychotherapies (e.g., cognitive behavioral therapy, Interpersonal Psychotherapy) or yoga or both for anxiety symptoms during and after pregnancy.

(Weak for | Reviewed, New-added)

# **Discussion**

The driver of this recommendation was the finding from an SR of 13 prospective observational studies by Grigoriadis et al. (2019), which included more than 11,514 participants, 1,708 of whom had antenatal anxiety.(220) The SR found an association between antenatal anxiety and postpartum depression, with an odds ratio of 2.64.(220) Because of this association and the potential for serious harm to both the patient and child that depression can cause, the Work Group felt that addressing the evidence on managing anxiety during and after pregnancy was important.

Based on the systematic evidence review, three different interventions showed efficacy. The evidence suggests that CBT, IPT, and yoga improve symptoms of anxiety among pregnant and postpartum patients.(199, 202, 215) An SR by Corrigan et al. (2022) showed yoga was favored over TAU for reducing symptoms of anxiety based on 11 RCTs.(215) An SR by Li et al. (2022) found CBT alone was associated with improvements in symptoms of anxiety at both short-term and long-term follow-ups (less than 1 month and a mean of 2.5 months respectively).(202) Sockol et al. (2018) found, based on 5 RCTs, that IPT reduced symptoms of anxiety compared with TAU.(199) Of

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note, the Work Group did not review evidence on pharmacologic interventions for anxiety or other mental health conditions during pregnancy given the scope of the guideline and the evaluation of these conditions in other VA/DoD CPGs.

Patient preferences varied somewhat regarding these interventions. The patient focus group indicated that patients wanted more support and consideration around mental health during pregnancy. Although some patients enjoy yoga, others might not enjoy this activity, and some might have physical conditions that limit their participation in yoga. Psychotherapy interventions are also preferred by some because they are an alternative to medications in many cases; however, others might feel that a stigma is related to this type of treatment, and active duty Service members might be concerned about how having this treatment on record could affect their promotion ability. Access to some forms of yoga are widely available, though some people experience barriers to access. Both IPT and CBT are offered in VA and DoD, though access to these treatments might vary among individual facilities. Access to specific delivery modes (e.g., in-person, internet-based, telephone-based) might differ among patients. Evidence suggests efficacy across multiple delivery modes, which could improve access and equity.

The Work Group systematically reviewed evidence related to this recommendation. (199, 202, 215, 220) Therefore, it is categorized as *Reviewed, New-added*. The Work Group's confidence in the quality of the evidence was low. The body of evidence had some limitations including lack of blinding, unclear randomization of allocation concealment methods, incomplete outcome data, unclear blinding of outcome assessors, and moderate to high attrition rates. (199, 202, 215, 220) The benefits of using yoga, CBT, or IPT as interventions for anxiety symptoms outweighed the potential harms, which were small. Patient values and preferences varied somewhat because some patients do not prefer certain types of physical activity, and a stigma against psychotherapy still exists in the military and Veteran populations. (221) Thus, the Work Group made the following recommendation: We suggest offering psychotherapies (e.g., cognitive behavioral therapy, Interpersonal Psychotherapy) or yoga or both for anxiety symptoms during and after pregnancy.

# IX. Algorithm

This algorithm is designed to inform providers of the recommended interventions and appropriate timing of each of the recommended interventions for pregnant patients during pregnancy and in the postpartum period. The interventions included in the algorithm are paired with the corresponding recommendation in the VA/DoD Clinical Practice Guideline for the Management of Pregnancy. Following the algorithm, the Routine Pregnancy Care section provides additional information.

# A. Algorithm Key

Table 6 displays the key to the algorithm symbols and their meanings.

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# Table 6. Algorithm Key

Symbol	Meaning
Р	Action to be carried out by obstetric provider
R	Referral to be made to an advanced prenatal care provider (e.g., obstetrician, maternal-fetal medicine physician) or other allied health professional
L	Lab or labs to be ordered
Dotted	Pregnant patient to receive this action at this time (Timing is not ideal, but it is still helpful for the patient rather than not at all.)
V1	First visit
PP	Postpartum visit

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# B. Interventions by Weeks' Gestation

<u>Table 7</u> presents a week-by-week guide to prenatal care, including all interventions for a healthy pregnancy.

Table 7. Interventions by Weeks' Gestation

	Weeks' Gestation			
	First Trimester	Second Trimester	Third Trimester	
Interventions	V1 8 9 10 11 12 13	14 15 16 17 18 19 20 21 22 23 24 25 26 27	28 29 30 31 32 33 34 35 36 37 38 39 40 41	PP
Screen for tobacco and nicotine products, alcohol, cannabis, illicit drugs, caffeine use, herbal supplements, and inappropriate use of prescription medication; if positive, recommend cessation, and offer assistance. See <a href="Recommendation 20">Recommendation 20</a> .		Р		
Provide prenatal education (e.g., dental health, breastfeeding, exercise, weight gain, work schedules, dietary supplementation). See <a href="Education"><u>Education</u></a> .		Р		
Recommend influenza vaccination (seasonal) for pregnant patients and family. See <a href="Immunization">Immunization</a> <a href="Assessment">Assessment</a> .		Р		
Recommend COVID-19 vaccination. See <a href="Immunization Assessment">Immunization Assessment</a> .		Р		
Screen for indications for referral to advanced prenatal care provider. See <a href="Table 11">Table 11</a> .		R		
Screen for intimate partner violence using a validated tool (e.g., HITS). See <a href="IPV Screening">IPV Screening</a> .	Р		P	P
Screen for depression using a standardized tool (e.g., EPDS, PHQ-9). See Recommendation 21.	Р		Р	Р
Perform routine prenatal lab evaluation for all pregnant patients and selective labs as indicated. See <u>Table 8</u> .	L			
Screen for infectious diseases; treat or manage as indicated. See <u>Infectious Disease Screening</u> .	L			

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	Weeks' Gestation											
	F	irst Trimester		Secor	nd Trime	ester			Third T	rimeste	er	
Interventions	V1	8 9 10 11 12 13	3 14 1	5 16 17 18 19	20 21 22	23 24 25 26	6 27	28 29 30 3 <sup>-</sup>	1 32 33 3	4 35 36 37	7 38 39 40 41	PP
Screen for Rh status, anemia, and hemoglobinopathies.	L											
Evaluate for nutritional deficiencies in patients who have undergone bariatric surgery. See Recommendations 18 and 19.	P L											
Refer patients who have undergone bariatric surgery or are on a restrictive diet to an RDN. See <u>Table 13</u> .	R											
Perform dating ultrasound. See <u>Early (Dating)</u> <u>Ultrasound</u> .		Р										
Perform pelvic muscle function evaluation and provide training on pelvic muscle exercises during pregnancy. See Recommendation 5.		P										
Offer group model of prenatal care. See Group Prenatal Care.		Р										
Offer prenatal screening for aneuploidy with NIPT and common genetic disorders. See Recommendation 1.		Р										
Offer prenatal diagnostic testing for aneuploidy as an accepted alternative to screening.		Р										
Initiate low-dose aspirin therapy for patients at risk for preeclampsia. See Recommendations 14 and 15.		Р										
Offer MSAFP screening for open spine defects to pregnant patients who did not have serum aneuploidy screening or who had NIPT.				L								
Offer antenatal progesterone therapy in consultation with an advanced prenatal care provider for patients at high risk for recurrent spontaneous preterm delivery. See Recommendation 12.				Р								

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	Weeks' Gestation					
	First Trimester	Second Trin	Third Trimester			
Interventions	V1 8 9 10 11 12 13	14 15 16 17 18 19 20 21 2	22 23 24 25 26 27	28 29 30 31 32 33 34	35 36 37 38 39 40 41	PP
Complete fetal anatomy ultrasound. See Anatomy (Dating) Ultrasound.		P				
Measure fundal height. See Fundal Assessment.				Р		
Screen for GDM with one-hour GCT (use patterned glucose monitoring for patients at risk for dumping syndrome).			L			
Perform fetal fibronectin test for patients with signs or symptoms of preterm labor if test would change clinical management. See Recommendation 11.			L			
Assess and educate patients regarding fetal movements, signs/symptoms of preterm labor or ROM, and signs/symptoms of preeclampsia.				Р		
For patients with a prior cesarean delivery, assess the plans for delivery and provide TOLAC counseling for those who are candidates.						
Recommend Tdap vaccination. See Immunization Assessment.				Р		
Discuss family planning and contraception. See <u>Education</u> .				Р		Р
Assess the plans for infant feeding and provide a breast pump prescription to patients who desire it.				Р		
Screen for group B strep carrier status. See Infectious Disease Screening.					L	
Initiate HSV prophylaxis, if indicated.					Р	
Assess fetal presentation.					Р	

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	Weeks' Gestation			
	First Trimester	Second Trimester	Third Trimester	
Interventions	V1 8 9 10 11 12 13	14 15 16 17 18 19 20 21 22 23 24 25 26 27	28 29 30 31 32 33 34 35 36 37 38 39 40 41	PP
Assess and educate patients regarding fetal movements, signs/symptoms of labor, and signs/symptoms of preeclampsia.			P	
Offer scheduled delivery or initiate antepartum fetal testing if undelivered. See Recommendation 7.			P	
Educate patients about lifetime risk of CVD and DM for patients with GDM, HTN, preeclampsia or any combination of these problems.				Р
Screen for current vaccination status in accordance with CDC guidance. See <a href="Immunization Assessment">Immunization Assessment</a> .				Р
Screen for type 2 DM with a 2-hour GCT in patients who had GDM.				Р
Screen for pelvic floor dysfunction and urinary incontinence; refer to Pelvic Health Rehabilitation if positive. See Recommendation 6.				P R

Abbreviations: CDC: Centers for Disease Control and Prevention; COVID-19: coronavirus disease of 2019; CVD: cardiovascular disease; DM: diabetes mellitus; EPDS: Edinburgh Postnatal Depression Scale; GCT: glucose challenge test; GDM: gestational diabetes mellitus; HITS: Hits, Hurts, Insult, Threaten, Scream tool; HSV: herpes simplex virus; HTN: hypertension; IPV: intimate partner violence; MSAFP: maternal serum alpha-fetoprotein; NIPT: non-invasive prenatal testing; PHQ-9: 9-item Patient Health Questionnaire; RDN: registered dietician nutritionist; rh: rhesus; ROM: rupture of membranes; Tdap: tetanus, diphtheria, pertussis; TOLAC: trial of labor after cesarean

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# X. Routine Pregnancy Care

This CPG does not address every aspect of routine pregnancy care and is not intended to be a comprehensive guide to all care needed in pregnancy. In some cases, clinically important and part of the generally accepted standard of pregnancy care interventions do not have sufficient high-quality evidence to support a standalone recommendation. Additionally, some recommendations included in past versions of this CPG were determined by the Work Group to consistently be supported by the evidence to warrant inclusion as accepted standards of care without needing further evidence review. Lastly, the scope of the Work Group was limited to selected priority topics based on the needs of pregnant patients served by the VA and DoD health systems, which precluded review of all potentially relevant aspects of pregnancy care. The below information can be used to help guide providers during the routine aspects of the management of pregnancy.

#### A. Initial Prenatal Visit

### a. Routine Lab Screening

The following panel of labs is recommended for all patients at the beginning of pregnancy to be done in conjunction with the initial prenatal visit. There are also optional labs that should be offered to all patients and some selective labs performed in response to the presence of certain risk factors. <u>Table 8</u> lists the three types of prenatal lab panels.

**Table 8. Prenatal Lab Panels** 

Prenatal Lab Panels						
Prenatal Lab Pai	Tels					
Recommended for All Patients	<ul> <li>Blood type</li> <li>Antibody screen</li> <li>Complete blood count</li> <li>Rubella status</li> <li>Varicella status</li> <li>Hepatitis B surface antigen</li> </ul>	<ul><li>Hepatitis C antibody</li><li>HIV status</li><li>Syphilis screen</li><li>Urine culture</li><li>Gonorrhea screen</li><li>Chlamydia screen</li></ul>				
Offered to All Patients	<ul><li>Hemoglobin electrophoresis</li><li>Aneuploidy screening</li><li>Cystic fibrosis carrier screening</li></ul>	<ul> <li>Spinal muscle atrophy carrier screening</li> <li>Maternal serum alpha fetoprotein (15-22 weeks)</li> </ul>				
Selective Labs	<ul> <li>Cervical cytology, with or without HPV DNA</li> <li>Comprehensive metabolic panel</li> <li>Urine spot protein/creatinine ratio</li> <li>1-hour 50 gm oral glucose challenge test</li> <li>Hemoglobin A1C</li> <li>Thyroid stimulating hormone test</li> </ul>	<ul> <li>If due for screening or surveillance</li> <li>At risk for developing preeclampsia</li> <li>At risk for developing preeclampsia</li> <li>Increased risk for GDM</li> <li>Pregestational diabetes mellitus</li> <li>Pregestational diabetes mellitus, thyroid disease</li> </ul>				

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Prenatal Lab Panels						
Selective Labs (cont.)	<ul><li>Free thyroxine test</li><li>Fragile X screening</li></ul>	Thyroid disease Family history of related disorder, or suggestive intellectual disability				

Abbreviations: GDM: gestational diabetes mellitus; HIV: human immunodeficiency virus; HPV: human papillomavirus

## b. Early (Dating) Ultrasound

Accurate dating is crucial to the management of pregnancy because it drives the milestones and decision making for the application of appropriate monitoring and intervention as the pregnancy proceeds. The estimated due date is initially established by calculating 280 days from the first day of the last normal menstrual period. This practice has the potential to produce an inaccurate due date because only about 50% of patients accurately recall the date of the last menstrual period or because menstrual cycles might be shorter or longer than 28 days or might be irregular.(222) The Work Group advises a first-trimester ultrasound to establish or confirm the gestational age and estimated birth date and to confirm the presence of cardiac activity. For pregnant patients who present after the first trimester, we advise performing a dating and anatomical ultrasound at the earliest opportunity, preferably before 22 weeks. Besides confirming or establishing an estimated due date, there are other indications for performing an ultrasound early in pregnancy, including evaluation of vaginal bleeding, confirmation of an intrauterine location, presence and chronicity of multiple gestations, presence of uterine anomalies, or presence of other pelvic pathology. Patients with complaints of bleeding or pain should be referred for immediate ultrasound on presentation.

## c. Genetic Screening

The many different methods for screening for fetal aneuploidy are offered at different times during a pregnancy. Although considered optional, prenatal fetal aneuploidy screening and diagnostic testing should be offered to all pregnant patients, regardless of risk of aneuploidy. Offering prenatal screening and diagnostic testing for aneuploidy, regardless of maternal age or risk factors, respects the values and preferences of patients who make this choice. See <a href="Recommendations 1">Recommendations 1</a> and 2 for further information on screening recommendations.

In addition to tests that screen for aneuploidy, maternal serum alpha-fetoprotein (MSAFP) can be used to screen for neural tube defects (NTD) such as open spina bifida. When performed between 15 and 22 weeks, this test is not a part of NIPT (prenatal cell-free DNA screening [cfDNA]) and should, therefore, be offered to patients who choose to undergo NIPT for their aneuploidy screening test. That MSAFP might have limited use on its own as a screening test is important to note given studies suggesting high-quality ultrasound has a higher detection rate for NTDs.(223) However, unexplained elevated MSAFP (elevated MSAFP unrelated to a diagnosis of open NTD or other anatomic malformation) is associated with an increased risk of adverse

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outcomes, such as preterm birth, preterm rupture of membranes (ROM), preeclampsia, fetal growth restriction, abnormal placentation, and intrauterine fetal death.(224, 225) Therefore, we advise that pregnant patients with an unexplained elevation of MSAFP be evaluated and counseled by an advanced prenatal care qualified obstetric provider because of the increased risk for adverse perinatal outcomes. If cfDNA testing is chosen for aneuploidy screening, and MSAFP testing is desired, providers should *not* order serum screening (e.g., quad screen) with MSAFP because additional aneuploidy screening increases the risk of false positives and inconsistent lab results with no additional benefit.

In contrast to aneuploidy screening and MSAFP, genetic testing (e.g., parental carrier testing) can be done before or during pregnancy without need to repeat in a future pregnancy. These genetic tests include hemoglobin electrophoresis (to screen for hemoglobinopathy), carrier screening for cystic fibrosis (CF) and spinal muscular atrophy (SMA), which should be offered to all patients. In addition, fragile X carrier screening should be offered to patients at increased risk of the condition based on personal or family history of fragile X–related disorders (e.g., premature ovarian insufficiency, elevated follicle stimulating hormone level before age 40, a known FMR1 premutation, family history of intellectual disability suggestive of fragile X syndrome). A more comprehensive carrier screen panel may be considered for patients of Ashkenazi Jewish ancestry.(226)

## d. Infectious Disease Screening

Screening for infectious diseases, listed below, during pregnancy per current guidance from the CDC is recommended. Appropriate follow-up treatment, prophylaxis treatment, or both depending on the history, known exposure, and symptoms of infectious disease are necessary.

- Gonorrhea
- Chlamydia
- Syphilis
- Human immunodeficiency virus (HIV)
- Hepatitis B virus
- Hepatitis C virus
- Rubella

- Varicella
- Human papillomavirus (HPV) (if the patient has a history of an abnormal cervical screen)
- Herpes simplex virus (HSV)
- Asymptomatic bacteriuria
- Tuberculosis
- Group B streptococcus (GBS)

Infectious diseases during pregnancy can cause significant morbidity and mortality in both the pregnant patient and the fetus. According to the CDC, screening for infectious diseases, counseling, and treatment can improve maternal and fetal outcomes.(227)

Group B streptococcus infections are the leading cause of serious neonatal infections (e.g., sepsis, meningitis, pneumonia) within the first 7 days of life (early-onset infection).

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Antenatal screening is recommended for all pregnant patients between 36 0/7–37 6/7 weeks, except for patients already identified as candidates for GBS prophylaxis based on urine culture or history of a prior affected infant. Because new exposures and infectious agents can emerge (e.g., Zika, COVID, monkeypox), referring to the most recent CDC guidance is important. Screening can lead to diagnosis in asymptomatic persons and can allow pregnant patients an opportunity to be treated.

#### e. Obstetric Risk Factor Assessment

Many conditions can adversely impact the outcome of a pregnancy, potentially placing the patient and fetus at risk for complications. Although this resource is not intended to provide guidance on the management of high-risk pregnancies, it does identify conditions that should be managed in consultation with an advanced prenatal care provider, as detailed in <u>Tables 11.1–11.3</u>. As part of the initial evaluation, the primary obstetric provider must assess for certain risk factors early in the pregnancy because interventions, monitoring, and education throughout the pregnancy can have a positive impact on outcomes.

## f. Preeclampsia

Given that preeclampsia is one of the leading causes of maternal morbidity and mortality, early identification of patients at risk for developing it is important. As detailed in Recommendations 14 and 15, patients at high risk for developing preeclampsia should be treated with low-dose aspirin therapy to reduce that risk. An early evaluation might also consist of a complete metabolic panel and urine protein/creatinine ratio in patients at risk for having underlying hepatic or renal disease. Table 9 delineates risk factors associated with developing preeclampsia. Patients with one or more high-risk factors or two or more moderate-risk factors should be offered low-dose aspirin therapy between 12 and 28 weeks' gestation (optimally before 16 weeks) and should be continued daily until delivery.

Table 9. Clinical Risk Factors for Preeclampsia (137)

High Risk Factors	Moderate Risk Factors
History of preeclampsia	Nulliparity
Multifetal gestation	Obesity (body mass index >30)
Chronic hypertension	Family history of preeclampsia
Pregestational Type 1 or 2 diabetes mellitus	Black persons (due to social, rather than biological, factor <sup>a</sup> )
Renal disease	Lower income
Autoimmune disease	Age 35 years or older
(e.g., antiphospholipid syndrome, systemic	In vitro conception
lupus erythematosus)	Personal risk factors

<sup>&</sup>lt;sup>a</sup> These factors are associated with increased risk due to environmental, social, and historical inequities shaping health exposures, access to health care, and the unequal distribution of resources, not biological propensities.

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<sup>&</sup>lt;sup>b</sup> Low birth weight, previous adverse pregnancy outcomes, >10 years since last pregnancy

### g. Diabetes Mellitus

With increasing rates of both pregestational diabetes mellitus and GDM in the pregnant population in the U.S., providers might encounter patients who potentially benefit from early identification of GDM or new diagnoses of pregestational diabetes mellitus made in early pregnancy. Gestational diabetes mellitus affects about 4% of all pregnancies, and risk factors include having a prior pregnancy affected by GDM; having a prior delivery of a baby weighing more than 9 pounds at birth; being overweight or obese; having a family history of DM; being African American, Hispanic, American Indian, Alaska Native, Native Hawaiian, or Pacific Islander; being treated for HIV. (228) The Work Group did attempt to specifically examine the evidence on the utility of early GDM screening to reduce the incidence of gestational hypertension (GHTN), preeclampsia, or GDM. With this focused, narrow prompting question, only one pragmatic RCT met review criteria, which randomized 922 obese patients with a BMI greater than 30 to either early screening (14-20 weeks) or treatment as usual (TAU) (GDM screening at 24-28 weeks).(229) The results showed a potentially associated increased risk for GHTN and preeclampsia in the early GDM screening group, but the confidence intervals around the effect estimates for each of the three outcomes were wide and crossed 1.0, such that the differences between early care and TAU screening groups did not reach statistical significance. Future research is needed to define more clearly the benefits and harms of early GDM screening, optimal diagnostic thresholds and testing strategies for early screening, and potentially the patients who benefit most.

When considering early GDM screening for patients with multiple risk factors for GDM, providers should use clinical judgment regarding the benefits and harms of offering such early screening depending on individual patient characteristics. The Work Group also notes that American College of Obstetricians and Gynecologists (ACOG) and the United States Preventative Services Task Force (USPSTF) both offer guidance on early GDM screening for patients with multiple risk factors to support provider decision making regarding early GDM screening for patients with risk factors.(230, 231)

### h. Spontaneous Preterm Birth

Affecting nearly 1 in 10 newborns, preterm birth is a major cause of perinatal morbidity and mortality. One-half of preterm births are related to spontaneous preterm labor. Although many risk factors are associated with spontaneous preterm birth, the strongest predictor is the history of spontaneous preterm birth. Other strong risk factors include prior preterm pre-labor ROM, multiple gestation, and short cervix. Given the time-sensitive nature to implement preventive strategies, the primary obstetric provider should assess the patient's risk for preterm birth at the initial prenatal visit. Patients at high risk for subsequent spontaneous preterm delivery should be counseled on the options for prevention. Women experiencing psychological distress related to high-risk status of having a spontaneous preterm birth or because of a history of spontaneous preterm birth should be offered mental health treatment. See <a href="Recommendation 12">Recommendation 12</a> for further information.

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## i. Screening for Intimate Partner Violence

Women who have served in the military are at higher risk of experiencing IPV than those who have never served in the military.(232) Women who experience IPV have a higher likelihood of unintended pregnancies and shorter interpregnancy intervals, in part because of reproductive coercion and reduced access to contraception.(233-236) Experiencing IPV during pregnancy is associated with reduced prenatal care and increased use of addictive substances.(237, 238) Independent of those factors, experiencing IPV while pregnant is associated with an increased risk of preterm birth, low birth weight, perinatal loss, and death by homicide or suicide.(239-241)

Perinatal care providers are especially well positioned to screen for IPV because of the frequency of health care contacts and opportunities for privacy.(242) It is important to screen more than once because individuals might feel unready to disclose initially. Several IPV screening tools have been validated, including the Modified E-HITS (Extended Hurt – Insult – Threaten – Scream), which has been validated for use with women Veterans.(243, 244) For patients who screen positive for IPV, we recommend completing an assessment and providing information, intervention, referrals, or any combination of these supports, as needed.

## j. Depression Screening

Screening pregnant and postpartum patients for depression using a validated screening tool is more effective than usual clinical assessment in detecting depression and in reducing depressive symptoms, particularly when performed with access to interventions such as treatment protocols, care management, and trained providers. (183) Providers should screen patients at the first presentation, week 28 of gestation, and at the postpartum visit.

The Edinburg Postnatal Depression Scale (EPDS) and the Patient Health Questionnaire-9 (PHQ-9) are among the screening tools validated for perinatal use. Both screening tools are readily available in VA and DoD clinical settings. See Recommendation 21 for further information.

#### k. Substance Use Assessment

Perinatal use of alcohol, cigarettes, cannabis, illicit drugs, or unauthorized use of prescription medication is common and might be associated with adverse effects. Screening for use of these substances should occur at each prenatal and postpartum visit followed by additional evaluation and treatment based on screening results. See Recommendation 20 for further information.

### I. Immunization Assessment

All pregnant and breastfeeding patients should be immunized according to current CDC schedules for vaccination. Immunizations of the birthing patient decrease the risk of life-or fetus-threatening diseases during pregnancy. Pregnant people are relatively

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immunocompromised and can be severely affected by influenza, COVID-19, and other infectious pathogens. Immunizations help protect the birthing patient from infection. They also enhance the passive immunity of infants to pathogens that cause lifethreatening illnesses.(245) Pertussis and influenza vaccines are recommended to be given during each pregnancy. Some patients might have concerns about the safety of vaccination in pregnancy; therefore, providers should be well versed in the safety and benefits of vaccine administration. In addition, providers should discuss with patients the immunization recommendations for the baby's family members and caregivers as provided by the CDC.(246)

Although the following list represents recommended vaccines to receive as a part of routine prenatal and postpartum care, active duty Service members are required to obtain many more vaccines for mission readiness. That pregnant Service members consult with their perinatal care provider is important to determine which vaccines are safe to take during pregnancy and which ones should be delayed until the postpartum period.

## 1. Given during Pregnancy

- **Pertussis:** Also known as whooping cough, pertussis is a highly contagious bacterial disease that can cause coughing and difficulty breathing. Pertussis poses a significant burden on infants and can be very serious or deadly, especially in those younger than 1 year. Pertussis-related hospitalizations and deaths are highest in infants younger than 2 months.(245) People who are pregnant should receive the Tdap (tetanus, diphtheria, and pertussis) vaccine during each pregnancy to provide passive immunity to infants, who would not otherwise routinely receive it until 2 months of age.(247) Although a pregnant person can receive the Tdap vaccine at any time during pregnancy, the optimal time to receive the vaccine is from 27–36 weeks' gestation, maximizing maternal antibody response and passive antibody transfer to the newborn. People who do not receive the Tdap vaccine during pregnancy should receive it in the immediate postpartum period if they had never received a prior dose. People who did not receive the Tdap vaccine during pregnancy but had received a prior dose of Tdap in their lifetime should not receive Tdap postpartum.(248)
- Influenza: Patients who acquire influenza during pregnancy are at increased risk for spontaneous abortion, maternal morbidity, and even death.(249) For this reason, all people who are or will be pregnant during influenza season should receive the influenza vaccine (an inactivated virus). According to the CDC, influenza vaccination is safe for both the pregnant patient and the fetus, regardless of gestational age. Influenza immunization has also been proven to protect both the birthing parent and child from influenza for several months after birth.(250)
- **COVID-19:** Pregnant and recently pregnant patients are more likely to develop severe illness from COVID-19 compared with people who are not pregnant. The CDC recommends COVID-19 vaccination and staying up-to-date with boosters

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for everyone age 6 months and older, including pregnant and lactating patients.(251) COVID-19 infection during pregnancy is associated with an increased likelihood of adverse pregnancy outcomes including preterm birth and stillbirth.(252) Accumulating evidence supports the safety and effectiveness of COVID-19 vaccination during pregnancy. No increased risk of miscarriage, stillbirth, or birth defects have been identified with mRNA COVID-19 administration. No safety concerns were observed in animal studies. COVID-19 vaccination has been shown to reduce the risk of severe illness because of COVID-19 during pregnancy when comparing vaccinated versus nonvaccinated populations. Preliminary data suggest that there might be passive immunity and protection of infants, but more study is needed.(245)

## 2. Given Following Pregnancy

- Varicella: People with varicella infection during pregnancy have a 10–20% risk of developing pneumonia, a significant risk factor for maternal mortality, which is estimated to be as high as 40%.(253) In pregnancy, varicella might cross the placenta, resulting in congenital or neonatal varicella infection. Infection during the first half of pregnancy has been associated with congenital varicella syndrome.(254) Neonatal varicella zoster virus (VZV) infection is associated with a high neonatal death rate.(255) If the pregnant patient is determined to be notimmune by titers or other screening method (e.g., history of vaccination or disease), vaccination is recommended during the postpartum period. The vaccine is contraindicated during pregnancy. According to the CDC, patients who get the varicella vaccine may continue to breastfeed.(256-258)
- Rubella: Infection in the first 16 weeks of pregnancy can cause miscarriage or congenital rubella syndrome. (259) Because of concerns about possible teratogenicity and the theoretical risk to the fetus in administering a live vaccine to a pregnant patient, the measles, mumps, and rubella (MMR) vaccination is not recommended during pregnancy. (260, 261) Patients who are not immune to rubella should be vaccinated postpartum. According to the CDC, MMR vaccine is safe to receive during breastfeeding. (262)
- Human papillomavirus: The HPV vaccine is not recommended during pregnancy. It is not known to cause harm in a pregnant patient or fetus, but no specific studies evaluating the safety in the pregnant population exist.
   Vaccination should be delayed until after pregnancy. The vaccine may be administered to patients who are lactating.(263)

#### m. Medication and Supplement Review

Taking medicines during pregnancy is common; about 9 in 10 women take at least one medicine during pregnancy, and 7 in 10 take at least one prescription medication.(264) Medication review and reconciliation should occur at every prenatal visit and should include screening for potentially teratogenic medications, newly prescribed medications

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since the last prenatal visit, over-the-counter medications, supplements, vitamins, and dietary or herbal products. The CDC has partnered with other federal agencies and non-federal partners to improve the health of pregnant people and fetuses by working to identify the safest treatment options for the management of common conditions before and during pregnancy.(265) As potentially teratogenic medications are identified, we recommend referral to a maternal-fetal medicine specialist.

#### n. Pelvic Muscle Function

A brief pelvic floor muscle evaluation should be conducted early in pregnancy, using a single-digit palpation to assess pelvic muscle strength, with follow-up instructions on how to properly facilitate an appropriate muscle contraction without compensatory patterns (e.g., gluteal or adductor muscle activation). If a patient is unable to activate their pelvic floor musculature, referral to a pelvic health rehabilitation specialist for PFMT would be appropriate. See <u>Table 12</u> and <u>Recommendation 5</u> and <u>Recommendation 6</u> for further details.

A pelvic floor muscle activation exercise involves a muscle contraction and upward/inward movement of at least the following muscles: levator ani, obturator internus, transverse perineal, bulbocavernosis, ischiocavernosis, and anal sphincters.(266) Adjacent supporting muscle groups include the adductors, gluteals, and abdominal wall musculature commonly activated using compensatory strategies when pelvic floor muscle weakness or mobility limitations exist. The quality of the pelvic muscle contraction can be documented with the Laycock Pelvic Floor Manual Muscle Test Scale, which uses a 6-point Oxford scale (0=no contraction, 1=flicker, 2=weak, 3=moderate, 4=good [with lift], and 5=strong) during the internal examination to measure pelvic floor muscle strength in women.(91, 267) Defined as repeated voluntary muscle contractions, PFMT can be conducted independently or with supervision by trained providers as part of a comprehensive exercise program during pregnancy. Provider feedback training on proper pelvic floor muscle activation is critical before prescribing PFMT to patients.

Providers should also screen and adhere to trauma-informed care concepts while considering a patient's receptivity to pelvic examinations. Rates of sexual trauma are known to be high in military female Veterans and Service members.(268) (35) The recommended examination and training can be conducted easily in a short amount of time during an early pregnancy visit concurrent with a cervical cancer screening or ultrasound examination. If the patient is unable to appropriately activate the pelvic floor musculature or has a significant weakness, referral to a pelvic health rehabilitation specialist for further evaluation and treatment would be suitable (Table 12).

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## **B.** Subsequent Prenatal Visits

## a. Actions at Every Visit

The frequency of obstetric visits should be individualized. Typically, a patient with an uncomplicated first pregnancy is examined every 4 weeks until 28 weeks' gestation, every 2 weeks from 28–36 weeks' gestation, and then every week until delivery. People with medical or obstetric complications might require closer surveillance, and parous people without medical or obstetric complications, who have had prior normal pregnancy outcomes, may be seen less frequently as long as additional appointments are available as needed.(269)

Certain actions should be completed consistently at every visit, but other actions will be more specific to the gestational age.

During each regularly scheduled visit, the obstetric provider should evaluate the blood pressure, patient weight, uterine size for progressive growth and consistency with gestational age, and presence of fetal heart activity at appropriate gestational ages. After the pregnant patient reports quickening and at each prenatal visit thereafter, the obstetric provider should ask about fetal movement.(269)

#### b. Blood Pressure

Routinely measuring blood pressure at every visit is important in the early detection and continued management of HDP.(269, 270) Hypertensive disorders of pregnancy are associated with severe maternal complications, including myocardial infarction (MI) and stroke, and are a leading cause of pregnancy-related death in the U.S.(271) Early identification of HDP through blood pressure measurement can reduce morbidity, mortality, and severe complications, including death, through timely intervention and treatment.

## c. Weight Gain

Routinely measuring weight for pregnant patients at every visit is useful in monitoring appropriate weight gain and allows the provider to offer interventions that can improve the short-term and long-term health of a pregnant patient and their fetus. Patients who are overweight or obese are at greater risk for adverse health conditions during the preconception, antepartum, and postpartum periods. Patients with low body mass index (BMI) are also at risk for adverse maternal and neonatal outcomes. Inadequate weight gain is a risk factor for spontaneous abortion, preterm birth, fetal growth restriction, HDP, and poor perinatal outcomes. Patients with anorexia nervosa might be identified by a low initial BMI, inadequate antepartum weight gain, or both.(272) This screening is particularly important in the military and Veteran population because studies have suggested that this population might be at greater risk for BMI-associated obstetrical complications.(273) More information regarding recommended weight gain is shown in Table 10.

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Table 10. Weight Gain Recommendations for Singletons and Twins(274)

Pre-pregnancy Weight (BMI in kg/m²)	Singletons	Twins
Underweight (BMI <18.5)	12.7-18.2 kgs (28-40 lbs)	22.7–28.1 kgs (50–62 lbs)
Normal Weight (BMI 18.5–24.9)	11.3–15.9 kgs (25–35 lbs)	16.8–24.5 kgs (37–54 lbs)
Overweight (BMI 25.0–29.9)	6.8–11.3 kgs (15–25 lbs)	14.1–22.7 kgs (31–50 lbs)
Obese (BMI ≥30.0)	5.0-9.1 kgs (11-20 lbs)	11.3–19.1 kgs (25–42 lbs)

Abbreviations: BMI: body mass index; kg/m<sup>2</sup>: kilograms per square meter; kgs: kilograms; lbs: pounds

### d. Fundal Assessment, Fetal Heart Tones, Fetal Movement

Assessment of the fundal height at each visit, beginning at 20 weeks' gestation, is a simple, inexpensive test to monitor expected growth. Fetal heart tones are recommended at each antenatal visit to confirm a viable fetus and to provide psychological reassurance to the pregnant patient. The pregnant patient's perception of fetal movements is the oldest and most commonly used method to assess fetal wellbeing as decreased fetal movement has been associated with an increased risk of stillbirth.(275)

## e. Anatomy (Dating) Ultrasound

An integral part of routine antenatal care, antenatal ultrasonography is widely used in pregnancy to assess fetal growth and anatomy and to detect fetal anomalies. It is recommended as an accurate method of determining gestational age, fetal number, viability, anatomic survey, placental location, amniotic fluid, and assessment of pelvic organs. The optimal timing of the complete fetal anatomy ultrasound is in the second trimester between 18 and 22 weeks' gestation. Ultrasonography should be performed by technologists or providers who have undergone specific training and only when a valid medical indication for examination is present.

The diagnosis of a fetal anomaly significantly reduces perinatal mortality and morbidity and maternal morbidity. Prenatal diagnosis enables a psychologically less traumatic and early medical termination of pregnancy for patients who choose abortion. It also enables planning for specific fetal palliative care for patients who elect to continue pregnancy. It decreases probable complications of continuation of pregnancy and labor, prevents an unnecessary cesarean section for a fetus with lethal anomalies diagnosed too late for medical termination of pregnancy, allows planning delivery at the optimal time in a well-equipped tertiary care center with necessary neonatal care facilities, and allows in utero therapy in selected cases. Based on evidence currently available, routine clinical scanning of every pregnant patient using real-time B-mode (2-D) imaging is not contraindicated.

The standard ultrasound evaluation includes the evaluation of fetal presentation, amniotic fluid volume, fetal cardiac activity, placental position, fetal biometry, and fetal number plus an anatomic survey.

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#### f. 24-28 Weeks

### 1. Family Planning

The ideal time to begin an in-depth discussion with the patient with respect to family planning goals is 24–28 weeks' gestation. Formulating these goals at this point better prepares the patient for an optimal individualized plan in the event of a preterm delivery or if immediate postpartum contraception is desired. See the <a href="Education">Education</a> section for additional details on family planning.

#### 2. Gestational Diabetes Mellitus

Screening for GDM using the 1-hour 50 gram oral glucose challenge (GCT) test is recommended for all pregnant patients beginning at 24 weeks of pregnancy. (276) Screening is ideally completed by 28 weeks of pregnancy. Patients who screen positive should undergo a 3-hour 100 gram oral glucose tolerance test to establish a diagnosis. See the section on Diabetes Mellitus which discusses the potential role of GDM screening before 24–28 weeks. Should a diagnosis of GDM be established during the pregnancy, maternity care providers should take care to perform a 2-hour 75 gram oral glucose tolerance test at the 6–8 weeks postpartum visit to ensure resolution of the GDM. Given the increased lifetime risk for progression to type 2 DM, communication of this pregnancy complication to subsequent primary care providers is important and affects subsequent lifetime DM screening recommendations.

## 3. Complete Blood Count - Anemia

Because of plasma volume expansion and increased iron requirements during pregnancy, all pregnant patients should be rescreened for anemia between 24–28 weeks of pregnancy.(277) In the second trimester, hemoglobin and hematocrit values below 10.5 and 32.0, respectively, warrant further investigation and treatment. Values below 11.0 and 33.0 in the third trimester require additional investigation and treatment.

#### 4. Tdap

Pregnant patients should receive the Tdap vaccine during each pregnancy to provide passive immunity through breastmilk to newborns, who would not otherwise routinely receive it until 2 months of age.(247) Although a pregnant patient can receive the Tdap vaccine at any time during pregnancy, the optimal time to receive the vaccine is from 27–36 weeks' gestation, maximizing maternal antibody response and passive antibody transfer to the newborn.

#### 5. Rho(D) Immune Globulin

Rhogam for the prevention of Rh(D) alloimmunization should be given to all Rh-negative pregnant patients at the 28-weeks prenatal visit.

"The USPSTF recommends repeated Rh(D) antibody testing for all unsensitized Rh(D)-negative women at 24 to 28 weeks' gestation unless the biological father is known to be Rh(D)-negative."(278)

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## 6. Depression Screening

Pregnant patients should be screened for depression using validated instruments (e.g., EPDS, PHQ-9) at approximately 28 weeks. See Recommendation 21 for further details.

## g. 36 Weeks

## 1. Group B Streptococcus Screening

Group B streptococcus is the leading cause of early-onset sepsis in newborns, the primary risk factor being maternal colonization of the genitourinary and gastrointestinal tracts. Antenatal screening is recommended for all pregnant patients between 36 0/7–37 6/7 weeks, except for patients already identified as candidates for GBS prophylaxis based on urine culture or history of a prior affected infant.(279) A single vaginal and rectal swab should be used to collect the sample for culture, and antibiotics should be initiated in labor for patients who screen positive.(280) Samples collected by a provider or patient self-collected are acceptable methods of screening.(281) GBS culture is highly predictive of colonization within 5 weeks of collection; repeat screening should be considered if more than 5 weeks have elapsed before the onset of labor.(279)

#### 2. Fetal Presentation

Assessment of fetal presentation should take place at 36 weeks' gestation, ideally, with the use of ultrasound for confirmation.(282, 283) Cephalic presentation will be found in many patients; in the case of non-cephalic presentation, counseling and intervention are recommended. If a breech presentation is found, an external cephalic version (ECV) should be offered at 37 weeks if there is no contraindication.(284) This timing allows adequate opportunity for spontaneous cephalic version, minimizes the chance of reversion if successful, and reduces the chance of iatrogenic preterm delivery. Potential benefits of this management include improving vaginal delivery rates and reducing the morbidity associated with cesarean delivery. ECV can be offered to patients with or without a previous cesarean birth.(285)

# C. Postpartum

To optimize the current and future health of recently pregnant patients and their neonates, postpartum care should be treated as an ongoing process, instead of a single encounter. The care should be tailored to the patient's individual needs.(286)

Ideally, all patients should have initial contact with their obstetric provider within 3 weeks of birth; this initial assessment can be done either in-person or via telehealth. By the end of this visit, a plan for individualized postpartum follow-up care should be determined.

Prioritizing early in-person follow-up rather than telehealth alone should be considered for individuals with a high risk of postpartum depression, high risk of cesarean wound infection or perineal wound infection (from third- or fourth-degree lacerations), lactation difficulties, or chronic conditions likely to require postpartum medication titration.

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All individuals with HDP should be assessed no later than 7–10 days after delivery. Individuals with severe HTN should additionally have a blood pressure evaluation within 72 hours of hospital discharge after birth.

All patients should have a comprehensive postpartum visit with their obstetric provider no later than 12 weeks after birth. The timing of this visit should be individualized, and patient centered and should take into account insurance coverage for postpartum care but usually occurs 6–12 weeks following birth. The comprehensive postpartum visit should include an interval history and assessment of physical wellbeing as well as screening and assessment of mood and social wellbeing factors, infant care and feeding, sexual function, contraception, birth spacing, sleep and fatigue, physical recovery from birth, pelvic floor disorders, chronic disease management, and health maintenance.

Individuals with uncomplicated medical histories, deliveries, and postpartum courses will generally transition to ongoing routine care with their primary care provider following the comprehensive postpartum visit with their obstetric provider. This ongoing follow-up and adequate transition from obstetric care to primary care is important for all patients, but it is especially important for individuals who experienced complications during pregnancy and in the postpartum period. Hypertensive disorders of pregnancy, preterm delivery, and GDM are associated with a higher lifetime risk of maternal cardiometabolic disease and warrant additional counseling. Hypertensive disorders, DM, thyroid disorders, renal disease, mood disorders, obesity, substance use disorders, and complex social determinants of health needs warrant communication from the obstetric care provider to the primary care provider and team to coordinate ongoing and long-term follow-up care. Within the VA system, MCCs—patient navigators specifically designated to work with pregnant patients and coordinate their care—contact patients postpartum and assess for medical complications of pregnancy as well as ongoing medical, behavioral, and social determinants of health needs. Based on this assessment, the MCC makes appropriate referrals including mental health, social work, and primary care follow-up, highlighting key issues to the primary care team.

### a. Postpartum Contraception

Contraceptive counseling should be initiated during prenatal care, and a plan should be made for postpartum contraception before delivery. Patients should be counseled on all available contraceptive options tailored to the patient's preference and medical history. Counseling should include immediate postpartum long-acting reversible contraceptives (LARC).(287) Immediate postpartum LARC, for people who desire them, may support these patients to receive their preferred contraceptive while avoiding the logistical complexity of attending an in-person visit during the first weeks postpartum. Removing these barriers for patients at high risk of future medical complications in future pregnancies might be particularly beneficial.(288)

Contraception should be addressed with all patients during their postpartum visits to make any needed adjustments to the postpartum contraceptive care plan. (287)

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### D. Education

## a. Breastfeeding/Chestfeeding

Current guidelines endorsed by multiple medical organizations recommend exclusive breastfeeding/chestfeeding for 6 months and continued breastfeeding/chestfeeding for up to 2 years or beyond with the addition of complementary foods per the desires and goals of the parent or parents. Birthing parent benefits of breastfeeding/chestfeeding include positive impacts on a person's risk of breast cancer, ovarian cancer, hypertensive heart disease, and DM. Child benefits include reduced risk of otitis media, SIDS, childhood leukemia, obesity, and many other acute and chronic disorders.(289, 290) Even with these known benefits and recommendations, more than one-half of women in the U.S. stop breastfeeding earlier than they desire.(291) Breastfeeding rates of Service members are lower than the national average in the U.S. general population by 7% at 6 months (51%) and 10% at 12 months (25%).(292) We advise health care providers to incorporate mechanisms and processes within their practice to enable people to achieve their infant feeding goals, including patient education throughout pregnancy, access to lactation specialists, community support, and active mitigation of potential barriers. See Recommendation 3 and Recommendation 4 for further information.

#### b. Oral Health

Pregnancy presents a unique opportunity for health care professionals to positively impact the oral health of patients. Occurring in up to 40% of pregnant people, periodontal disease is associated with adverse perinatal outcomes, including preterm delivery, low birth weight, fetal grown restriction, and preeclampsia.(293, 294) Although recommendations for treatment of periodontal disease cannot be endorsed specifically at this time to decrease these outcomes, evidence indicates that treatment is safe and is associated with the improvement in maternal oral health.(293-295) Pregnancy is not a significant contraindication to most dental services, though some procedures requiring general anesthesia might be deferred to the postpartum period. Oral health care is not just a component of a healthy pregnancy; evidence suggests that most infants and young children acquire caries-causing bacteria from their mothers.(296) Routine dental care, including x-rays (with proper anatomic shielding) and periodontal therapy, along with good oral hygiene, should be encouraged throughout pregnancy.(296, 297)

### c. Family Planning and Contraception

Assessment of future reproductive goals during the prenatal period is important to allow for adequate education and planning for the implementation of desired contraceptive therapies during the postpartum period. Providers should counsel patients on the recommendations for interpregnancy intervals to optimize their overall health and reduce the risk of adverse perinatal outcomes in subsequent pregnancies.(298) Given that 70% of pregnancies occurring within 1 year after delivery are unintended, access to and initiation of reliable forms of contraception to include emergency contraception during the postpartum period are essential to ensure women meet their reproductive

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and family-planning goals.(299) These measures include access to the immediate postpartum placement of LARCs and postpartum sterilization, where appropriate, because these methods are associated with lower rates of unintended pregnancies in active duty Service members.(300) Contraceptive education and counseling should be an integral part of routine prenatal care to optimize the provision of contraceptive and family-planning services during the postpartum and interpregnancy periods.

#### d. Exercise and Work

The U.S. Department of Health and Human Services recommends that pregnant patients engage in at least 150 minutes of moderate-intensity aerobic activity each week during pregnancy and postpartum barring no complications that would prevent otherwise.(301) Benefits of exercising during pregnancy include an increased chance for a vaginal delivery and reductions in weight gain, GDM, gestational HDP, preterm birth, low birth rate, and cesarean birth.(302) We recommend that all healthy, pregnant patients without known contraindications participate in regular mild to moderate exercise sessions, three or more times per week. We suggest that patients be provided with education on the safety and benefits of maintaining appropriate levels of activity and exercise during the pregnancy and postpartum period. We also suggest that patients with uncomplicated pregnancies may continue a standard work schedule throughout their pregnancy. See Recommendation 8 for more details. Patients should be instructed to conduct pelvic floor muscle exercises during and after pregnancy to improve function and reduce the risk of developing urinary incontinence during and after pregnancy. See Recommendation 5 for more details.

#### e. Vitamins

We suggest a daily multivitamin that includes at least 400 micrograms of folic acid be taken starting 1 month before conception and continued throughout pregnancy and lactation. People in the U.S. commonly supplement their diet with vitamins and minerals during pregnancy. Supplementation with multivitamins and minerals has also been associated with improved outcomes, including lower risks of preeclampsia and three forms of childhood cancer (pediatric brain tumors, neuroblastomas, and leukemia).(303, 304) Studies have found that preconception folic acid supplements, either alone or combined with other vitamins or minerals (e.g., in a multivitamin), reduce the risk of NTDs and should be continued through the first trimester of pregnancy.(305-307) Higher doses of folic acid are recommended in certain patients at high risk for NTDs (e.g., patients with a history of an NTD-affected pregnancy).

## f. Group Prenatal Care

A group model of prenatal care can be an acceptable alternative to individual provider appointments. Evidence exists that group prenatal care is associated with lower rates of preterm delivery, especially among African-American women.(308-310) Also, no evidence of harm through participation in group prenatal care has been found. Given that patient preferences and values might affect a patient's desire to pursue

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individualized care versus group care, offering group prenatal care would allow patients to choose how they engage in health care and could potentially lead to increased patient satisfaction in their care. It also might allow for more efficient use of resources to include low-density specialists who can offer preventive education and support (e.g., pelvic health rehabilitation providers, registered dietician nutritionists [RDN], lactation consultants). Patients should be educated on these potential benefits and offered a group model option of prenatal care, where available, as an acceptable alternative to individual appointments.

## XI. Referral Indications

### A. Advanced Prenatal Care Provider

This referral may be consultation, co-management, or transfer to a higher level of obstetric care. Tables 11.1–11.3 list potential indications for such referrals.

Table 11.1. Potential Maternal Indications for Referral to Advanced Prenatal Care Provider<sup>j,k,l</sup>

Potent	ial Maternal Indications for Referral to Advanced Prenatal Care Provider
>	Bariatric surgery within the past 18 months
to	Bowel resection or other significant abdominal-pelvic surgery
T S	Cervical surgery (e.g., LEEP, cone biopsy)
<u> </u>	Myomectomy or other significant uterine surgery (e.g., septum resection, cornual surgery)
Surgical History	Organ transplant
our	Prior cesarean section (e.g., low transverse, classical incisions)
0,	Increased risk for abnormal placentation/accreta (e.g., previa with prior cesarean delivery)
S	Cardiovascular disorders
ÖÜ	History of preeclampsia, eclampsia, GHTN, or HELLP
Chronic Medical Conditions	History of stroke, CVD (e.g., CHF, MI, arrythmia, congenital heart disease), or hypertensive disorders (e.g., chronic hypertension)
S =	Endocrine disorders
edica	Pregestational diabetes mellitus and GDM diagnosed on early screening and GDM requiring medication or insulin management or both
<b>Σ</b>	Thyroid disease
onic	Gastrointestinal disorder
ļ.	Chronic hepatitis B or C
O	Crohn's or inflammatory bowel disease

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J Might benefit from referral to relevant medical specialist in addition to prenatal care consultation/referral

<sup>&</sup>lt;sup>k</sup> Might benefit from referral to relevant behavioral health specialist in addition to or instead of prenatal care consultation/referral pending patient needs

Beyond or not captured by prenatal screening

## Potential Maternal Indications for Referral to Advanced Prenatal Care Provider **Hematologic conditions** Cell line disorders (e.g., sickle cell anemia, Idiopathic Thrombocytopenia Purpura), gestational thrombocytopenia Hypercoagulation disorders (e.g., inherited thrombophilia, current or history of DVT/PE requiring anticoagulation) Hypo-coagulation disorders (e.g., von Willebrand's disease) Chronic Medical Conditions (cont.) Immunologic conditions Cancer, current or recurrent Rheumatologic disease (e.g., Sjogren's syndrome, APLAS, SLE, rheumatoid rthritis) Maternal infectious disease Abnormal cervical cancer screening, high-risk HPV positive, or both HIV TORCH infections **Maternal exposures** Known teratogens Radiation, toxic chemical exposure, or both **Neurologic disorders** · Epilepsy or seizure disorder Other chronic neurologic conditions (e.g., MS, MG) Stroke or CVA **Pulmonary disorders** Chronic disorders impacting function and with likely pregnancy exacerbation (e.g., pulmonary hypertension, idiopathic pulmonary fibrosis, severe or sub-optimally treated asthma) **Behavioral** Alcohol or other substance use disorder Depression Health ADHD OCD · Anxiety disorder PTSD Bipolar disorder Other mental health conditions Obstetric Conditions History of abruption History of intrauterine fetal demise Preterm delivery (e.g., PPROM, preterm labor, medically indicated preterm delivery) · Short cervix, cervical insufficiency, or both, including history of cerclage Family history of genetic condition Conditions Genetic · Parent affected by genetic condition Prior child affected by genetic condition or fetal anomaly Parental carrier of known genetic condition Prior pregnancy affected by genetic condition

Abbreviations: ADHD: attention-deficit/hyperactivity disorder; APLAS: antiphospholipid antibody syndrome; CHF: congestive heart failure; DVT/PE: deep vein thrombosis and pulmonary embolism; GDM: gestational diabetes mellitus; GHTN: gestational hypertension; HELLP: hemolysis, elevated liver enzymes, low platelet count; HIV: human immunodeficiency virus; HPV: human papillomavirus; ITP: immune thrombocytopenia; LEEP: loop electrosurgical excision procedure; MG: myasthenia gravis; MI: myocardial infarction; MS: multiple sclerosis; OCD: obsessive-compulsive disorder; pprom: preterm premature ruptures of membranes; PTSD: posttraumatic stress disorder;

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SLE: systemic lupus erythematosus; TORCH: toxoplasmosis, other (syphilis, varicella-zoster, parvovirus B19), rubella, cytomegalovirus (CMV), and herpes infections

Table 11.2 Potential Placental Indications for Referral to Advanced Prenatal Care Provider

Potent	ial Placental Indications for Referral to Advanced Prenatal Care Provider
	Fluid abnormalities
w	Oligohydramnios
ons	Polyhydramnios
nio	Signs of twin-to-twin transfusion syndrome or twin anemia polycythemia sequence
Amniotic Conditions	Membrane conditions
O	Amniotic bands
	Uncertain twin categorization
	Abruption
Structural Conditions	• Low-lying placenta (with vaginal bleeding or ≥28 weeks)
iti o	Placenta previa (with vaginal bleeding or ≥28 weeks)
ng in	Suspected or confirmed placenta accreta spectrum
လ လ	Vasa previa
	Velamentous cord insertion

### Table 11.3 Potential Fetal Indications for Referral to Advanced Prenatal Care Provider

### Potential Fetal Indications for Referral to Advanced Prenatal Care Provider

#### Abnormal prenatal screening

- Parental known carrier status (e.g., CF, sickle cell)
- Result in previous or current pregnancy (e.g., aneuploidy risk, open NTD, carrier screening-CF, SMA, inheritable anemias)

Malpresentation at >34-36 weeks

Multifetal gestation

### Fetal growth abnormality

- Fetal growth restriction
- · Suspected fetal macrosomia
  - Estimated fetal weight >4,500 g (diabetic)
  - Estimated fetal weight >5,000 g (non-diabetic)

#### Fetal congenital abnormality

Suspected or known in previous or current pregnancy

Alloimmunization with or without fetal anemia, hydrops, or both

#### Intrauterine fetal demise

Current or history in prior pregnancy, including second trimester pregnancy loss

Abbreviations: CF: cystic fibrosis; g: grams; NTD: neural tube defect; SMA: spinal muscular atrophy

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## B. Rehabilitation Care Provider

Pelvic health rehabilitation encompasses services conducted by physical therapists, occupational therapists, or other professionals with documented specialized training and competencies in evaluating and treating conditions related to pelvic (floor) muscle dysfunction. It is a first-line, conservative treatment option in the pregnancy and postpartum periods for managing urinary or fecal incontinence, voiding dysfunctions, pain in the pelvis and adjacent regions, or any combination of the foregoing complaints. Contraindications for pelvic health rehabilitation might include an indwelling catheter, active pelvic infection, open pelvic wounds or sutures, impaired cognitive function, and menorrhagia or hematochezia without prior evaluation. Pelvic health (floor) rehabilitation is a minimally invasive, low-risk treatment approach that can reduce or eliminate symptoms of pelvic muscle dysfunction. (86, 311-313) To improve function and QoL, treatment strategies are designed to strengthen, relax, or facilitate proper coordination of the pelvic floor and trunk muscles or to achieve any combination of these objectives.(311, 314, 315) Strategies can include internal pelvic floor evaluation and treatment using therapeutic exercise, electrical stimulation, biofeedback training, manual therapy, behavioral education, or any combination of these interventions. (311, 316) Pelvic health rehabilitation that includes professional individualized instruction from a therapist and intensive exercise training with personalized feedback demonstrates superior outcomes to generalized education or self-care. (311, 313, 317, 318) A validated assessment questionnaire might be helpful to providers as a screening tool for the presence of pelvic muscle dysfunction during and after pregnancy. (313). The DHA uses the Cozean Screening Tool as referenced in the 2022 DHA Practice Recommendation "Pelvic Health Pregnancy and Postpartum Rehabilitation Services." See Recommendation 5 and Recommendation 6 for further information.

Also, important to highlight is that should a pregnant patient experience musculoskeletal pain or dysfunction during pregnancy, providers should consider early referral to rehabilitation services (e.g., physical therapy, occupational therapy) to conservatively manage these conditions. The presence of multiple musculoskeletal pain conditions is common in pregnancy, especially in the third trimester. (319) Pregnancy is not an absolute contraindication to rehabilitation care, and the completion of pregnancy alone will likely fail to resolve pain chronic symptoms. For example, evidence suggests that patients who experience low back/pelvic girdle pain during pregnancy are at higher risk for postpartum depression and chronic pain.(320, 321) Providers should also consider a postpartum referral to rehabilitation services should the patient continue to experience persistent postpartum symptoms of pelvic muscle dysfunction, musculoskeletal pain, or both, especially if a traumatic birth injury occurred. Rehabilitation providers can provide evidenced-based treatment and education for patients with musculoskeletal conditions that support the safe conduct of physical activity goals during and after pregnancy. Table 12 lists rehabilitation referral guidelines for common specific pregnancy-related musculoskeletal conditions.

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Table 12. Potential Indications for Referral to Pelvic Health (Floor) Rehabilitation

Symptom	Common Pelvio	C Health Condition
Pelvic Pain*	<ul><li>Dyspareunia</li><li>Vaginismus</li><li>Pelvic organ prolapse</li><li>Coccydynia</li><li>Pregnancy-related pelvic girdle pain</li></ul>	<ul> <li>Pregnancy-related sacroiliac joint pain</li> <li>Athletic pubalgia</li> <li>Sacroiliac pain, dysfunction, or both</li> <li>Myofascial pain</li> <li>Pelvic fracture</li> </ul>
Voiding Dysfunction*	<ul><li>Incontinence (urinary, fecal, or both)</li><li>Urgency (urinary, fecal, or both)</li><li>Incomplete emptying</li><li>Constipation</li></ul>	<ul> <li>Obstructed urination or defecation (dysynergia)</li> <li>Bladder or bowel retention</li> <li>Overactive bladder</li> </ul>
Abdominal Pain/ Weakness**	<ul><li>Diastasis rectus abdominus</li><li>Post-surgical pain</li><li>Costochondritis</li></ul>	
Hip and Back Pain**	<ul><li>Facet arthropathy</li><li>Disc pathology</li><li>Radiculopathy</li></ul>	<ul><li> Myofascial pain</li><li> Pain during or after pregnancy</li></ul>
Upper Extremity***	<ul><li>Carpal tunnel syndrome</li><li>Shoulder, hand, wrist, or elbow pain</li></ul>	

<sup>\*</sup>Referral depends on local availability of rehabilitation resources and patient preference to enroll in a pelvic health rehabilitation therapy program.

# C. Registered Dietitian

We suggest that pregnant patients on restrictive diets (e.g., vegetarians, bariatric surgery) consult with an RDN. The Academy of Nutrition and Dietetics recommends screening for the nutritional risks and subsequent assessment by an RDN to evaluate the pregnant patient for nutritional adequacy during this life phase.(322) Appointments with RDNs might be infeasible at some locations, but telemedical nutrition therapy might be a cost-effective option in some instances. The conditions listed in Table 13 are at higher risk of nutritional complications and should, therefore, be considered for referral to a dietitian for nutritional counseling and education. See Recommendations 18 and 19 for further information regarding nutritional deficiencies in patients who have undergone bariatric surgery.

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<sup>\*\*</sup>These routine orthopedic conditions can be managed by most physical therapy clinics and alone do not require access to a pelvic health rehabilitation specialist because evaluation and treatment do not require an internal pelvic floor muscle assessment for initial management.

<sup>\*\*\*</sup>Upper extremity musculoskeletal conditions can be referred to either physical or occupational therapy services based on local treatment facility clinical referral guidelines and availability.

#### Table 13. Indications for Referral to Registered Dietitian

### Indications for Referral to Registered Dietitian

- Previous bariatric surgery
- · Vegetarian or vegan
- Avoidance of certain foods (e.g., because of allergies, cultural reasons, fad diets)
- · Breast feeding while pregnant
- Underweight with a BMI <18.5 kg/m²</li>
- Younger than age 17
- Multiple gestations
- History of hypertension, hyperlipidemia, or diabetes mellitus
- · Gestational diabetes mellitus
- · History of or current eating disorder
- Identified as food insecure (defined by USDA as household-level economic and social condition of limited or uncertain access to adequate food) (323)

Abbreviations: BMI: body mass index; kg/m<sup>2</sup>: kilograms per square meter; USDA: United States Department of Agriculture

# **XII. Emerging Topics**

## A. Reproductive Health and Epidemics

Infectious disease outbreaks put a burden on sexual activity(324, 325), birthrates(326-328), and outcomes in both pregnant people and their offspring (329-334) These issues might impact people of diverse socioeconomic backgrounds differently. (326) Stress and depression related to pregnancy are also major concerns that must be addressed. (335) Additionally, health care services not deemed emergent were significantly curtailed during much of 2020 after the start of the COVID-19 pandemic, likely causing reductions in needed care for people seeking assistance for reproductive health. (336) Patients interested in pregnancy might need assistance in navigating how infectious diseases might affect this process, including learning to cope with the added stress associated with these concerns and understanding how to proceed as safely as possible and to include immunization education. Various online resources are available for those who are planning pregnancy, are pregnant, or are breastfeeding and the relationship of these processes to COVID-19.(337-339) With the likelihood of pandemics predicted to increase in the coming decades (340), continuing to build on reproductive health education, resources, and services will be critical to limit impacts on birth rates and outcomes.

# **B.** Health Care Disparities

In contrast to other developed nations, rates of maternal mortality continue to rise in the U.S., despite health care advancements and increased awareness.(341) Racial and ethnic minorities are disproportionally impacted. According to data from the National Vital Statistics System, the maternal mortality rate for non-Hispanic Black people was

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55.3 deaths per 100,000 live births, which is 2.9 times higher than rates for non-Hispanic White people.(118) Recognizing that these trends are seen in cases of severe maternal morbidity, which occurs 50–100 times more often than maternal death, is important.(342)

Explanations for this trend have been offered, including access to care concerns in rural communities, increased cesarean delivery rates, and a relatively high immigrant population. None of these factors, even taken collectively, can fully account for the disparities in maternal mortality, highlighting the complex nature of this national problem.(341) Concurrently, medical comorbidities of obesity, DM, and HTN have increased in the U.S.(343) An observational study looking at mortality rates across the country suggests social determinants and ethnicity are the primary contributors to regional variation in outcomes; 26% of the difference in statewide mortality was attributed to ethnicity.(344) That minority race alone is not a risk factor for maternal mortality or health inequity is important to note. It is the disparate social and economic opportunities and conditions created by structural policies and practices based on race and class that culminate in poor health outcomes.(345)

Unfortunately, evidence from a study of outcomes in the MHS shows these disparities persist despite equal access to care. Particularly, increased rates of cesarean section, intensive care admission, and rates of severe maternal morbidity were seen in Black patients compared with their White counterparts.(346)

Continued research is needed to determine the most effective interventions to combat these disparities in the U.S. and with focused attention including DHA and VHA beneficiary populations.

#### C. Telemedicine

Telemedicine technologies continue to improve and expand throughout the federal health care system. In 2021, VA served 2 million Veterans via telehealth for patients at home, in the clinic, and in the hospital.(347) On a U.S. national level, telemedicine was used by 37% of adults in 2021, and use increased with age. Its use was more prevalent among women (42%) compared with men (31.7%) and was lower as urbanization level decreased.(348) In terms of reproductive health, telemedicine can expand services to people in certain populations who have limited access otherwise. These populations include those who live in rural areas, who have barriers related to childcare, or who have difficulty with transportation. Telemedicine can improve access to interactions between the provider and patient but also between providers and generally makes the location of each party nominal. Interventions using telemedicine can be set up on, but are not limited to, monitoring devices, cell phones, computers, and tablets. Telemedicine services for contraception, medical abortion, prenatal care, obstetrics, mental health, sexually transmitted infections, sexual health, and sexual assault are currently available in the U.S. Although telemedicine has significant potential, various logistical challenges remain. Many telemedicine services require costs for technology,

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which might create a barrier for some health care facilities. Additionally, different needs for provider licensing and malpractice insurance might exist as well as the need to maintain Health Insurance Portability and Accountability Act compliance.(349) Some patients might have reduced access to telemedicine services, as well. One-third of people living in rural areas have no home internet connection(350), and in the general population, Black and Hispanic adults are less likely to own a computer than White adults.(351) Although telemedicine will likely continue to expand its role in reproductive health care, infrastructure and logistics barriers still limit how it is used currently.

# D. Trans-Identifying and Nonbinary Persons' Experience of Pregnancy

Evidence-based understanding of the experiences and needs of trans-identifying and nonbinary persons' experiences of pregnancy is currently limited, but it is a rapidly evolving area of research and clinical enquiry. Current known best practices include an emphasis on seeking patient preferences for sex pronouns, discussion of anatomic structures, and actions relevant to pregnancy and postpartum (e.g., some transidentifying and non-binary patients might prefer the term chestfeeding rather than breastfeeding).(352, 353) Provider and staff training to ensure a welcoming, non-stigmatizing clinical environment throughout pregnancy care is also key to patient-centered pregnancy care. Also essential is that providers appropriately counsel transidentifying and non-binary individuals on the value of important preventive care, including cervical cancer screenings and postpartum contraception, for those individuals retaining their uterus, even if desiring to use sex affirming hormone therapy postpartum. (354) Additional research is needed to better understand the facilitators of and barriers to optimal pregnancy care for trans-identifying and non-binary persons. See research priorities for additional details.

#### XIII. Research Priorities

During the development of the 2023 VA/DoD Pregnancy CPG, the Work Group identified topics needing additional research, including areas requiring stronger evidence to support current recommendations and research exploring new areas to guide future CPGs. In addition, the Work Group recognized the need to complement these recommendations with participatory action research that would engage individuals with pregnancy and their families in reviewing these guidelines, identifying gaps in the recommendations and in current care as well as in dialog to translate recognition of gaps into areas for research.

# A. Prenatal Screening

- Comparative effectiveness of different non-invasive prenatal testing (NIPT) technologies (targeted versus shotgun versus full genome)
- Cost-benefit analysis
- Exploration of benefits of genetic counseling via telemedicine

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- Comparison of prenatal screening uptake with NIPT versus other screening modalities
- Comparison of NIPT versus other screening modalities for the twin population
- Exploration of barriers and limitations in obtaining NIPT within the VA/DoD population and which patients are most easily obtaining testing

#### **B. Preterm Labor**

- Comparative effectiveness of types of cerclage and cerclage techniques
- Determination of which patient characteristics and risk factors would most benefit from cerclage placement
- Determination of which patient characteristics and risk factors would most benefit from progesterone therapy
- Comparative effectiveness of cerclage versus vaginal progesterone
- Comparative effectiveness of cerclage plus vaginal progesterone with cerclage alone or vaginal progesterone alone
- Comparison of preterm birth outcomes in the subpopulations of racial and ethnic minorities, rural population, economically disadvantaged, and active duty Service members and Veterans
- Exploration of whether aspirin is of benefit in reducing risk of preterm birth in population of patients with a history of spontaneous preterm labor resulting in preterm birth
- Cost-benefit analysis of fetal fibronectin usage versus admission or transfer for evaluation of preterm labor in VA/DoD population obtaining care at remote MTFs

# C. Hypertension in Pregnancy

- Identification of which subpopulations of pregnant and postpartum patients might benefit from self-monitoring of blood pressure
- Comparative effectiveness of telehealth visits versus treatment as usual (TAU)/standard screening in identification and management of hypertension in pregnant and postpartum patients
- Description of patients' perceptions of blood pressure monitoring in pregnancy and postpartum

# D. Low-Dose Aspirin Therapy

- Comparative effectiveness studies to determine optimal dose
- Studies that identify patients at risk for developing preeclampsia
- Evidence-based studies that validate aspirin benefits among patients categorized as high or moderate risk

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 Exploration of aspirin dosage management for preeclampsia prevention during pregnancy to support use of 162 mg dosing given this dose is the available >100 mg dose in U.S.

#### E. Gestational Diabetes

- Identification of which patient characteristics and risk factors benefit from early gestational diabetes mellitus (GDM) screening
- Determination of an optimal screening test for detection of early GDM
- Determination of optimal diagnostic thresholds for early GDM screening
- Comparison of outcomes among patients who require insulin therapy and who undergo early GDM screening versus routine GDM screening
- Comparison of outcomes for patients who undergo early GDM screening and early intervention with diet and exercise versus routine GDM screening

# F. Mental Health Screening and Assessment

- Identification of measures that are valid and reliable for perinatal anxiety screening
- Examination of effectiveness of anxiety screening during pregnancy with a Veteran population
- Determination of whether the use of Screening Brief Intervention Referral Treatment is helpful for pregnant patients in military and Veteran populations

# **G. Prevention of Postpartum Depression**

- Identification of secondary outcomes of postpartum depression, such as maternal bonding, distress symptoms, breast feeding engagement, rapid short interpregnancy interval pregnancy, and chronic health conditions
- Determination of whether prevention of postpartum depression reduces use total cost (e.g., unnecessary health visits, longer stays in hospital)
- Determination of whether preventing postpartum depression improves outcomes for child offspring (e.g., developmental milestones)
- Examination of whether peer support alleviates depressive symptoms
- Replication of Fang et al. (2020 outcomes) in a military and Veteran population
- Determination of what timeframe of initiation of prevention services is most effective (early pregnancy, mid-pregnancy, late pregnancy, or postpartum)

### H. Perinatal Mental Health Treatment

- Effectiveness of interventions by racial and ethnic groups and subgroups
- Optimal training for peer support specialists

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- Relative effectiveness and acceptability of group versus individual perinatal mental health treatment
- Examination of more specific exercise interventions, including type and frequency
- Examination of whether treatment for PTSD and anxiety disorders can reduce negative perinatal and mental health outcomes
- Comparative effectiveness of cognitive behavioral therapy to Interpersonal Psychotherapy with depression in pregnant and postpartum patients

## I. Alternate Forms of Care Delivery

- Examination of different types of telemedicine delivery and modalities (i.e., text message, app, telephone call)
- Evaluation of differences and similarities between definitions and terminology in field
- Determination of whether telemedicine can be used as a replacement for TAU and face-to-face (FTF) visits or just as an adjunct
- Examination of efficacy and acceptability of doula-delivered perinatal supportive interventions
- Patient and provider preferences for type of visits via telemedicine or FTF

## J. Equitable Outcomes

- Important maternal outcomes and engagement by subgroups (i.e., Hispanic population is heterogenous by country of origin)
- Interventions with varying resources or low resource areas
- Implicit bias and microaggression in health care settings
- Interventional studies to address structural racism within health care

# K. Pelvic Floor Muscle Training

- Efficacy of investigating pelvic floor dysfunction among multiparous people that undergo pelvic floor muscle training (PFMT)
- PFMT studies with quantitative outcomes
- Impact of PFMT during and after pregnancy on standardized fitness testing scores at 1 year postpartum
- Practice patterns of VA/DoD women's health providers in screening for pelvic muscle dysfunction, referral patterns to rehabilitation, and pelvic examination for pelvic muscle dysfunctions

# L. Non-pharmacologic Intervention: Cardiometabolic Disorders

Comparative effectiveness of the DASH diet and other nutritional interventions

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Role of physical activity programs and coaching in pregnancy and postpartum

## M. Lactation

- Identification of the root causes of risk factors for reduced initiation and continuation of breastfeeding or breast milk expression and continued lactation
- Evaluation of the efficacy of targeted interventions on subpopulations
- Development of a screening tool for assessing risk factors that impact initiation of breastfeeding or breast milk expression and continuation of lactation
- Evaluation of the use of a standardized curriculum or program
- Investigation of the motivations for human milk feeding or donor milk feeding
- Comparative effectiveness of different interventions to support breastfeeding or breast milk expression, including types of providers, individuals, or both delivering the intervention

# MI. 41 Weeks' Gestation Delivery

- Atypical versus typical delivery indications for delivery at and beyond the 41<sup>st</sup> week
- Acceptability of outpatient induction of labor
- Optimal modes of outpatient induction of labor for patients desiring low intervention delivery at the 41<sup>st</sup> week of gestation

# MII. Trans-Identifying and Nonbinary Persons' Experience of Pregnancy

- Research to understand trans-identifying and nonbinary persons' experience with family building, pregnancy, and postpartum care, including preferences for care delivery and language
- Research to understand system, provider- and patient-level facilitators, and barriers to optimal pregnancy care for trans-identifying and nonbinary persons
- Development of evidence-based guidelines for the clinical pregnancy care of trans-identifying and nonbinary individuals
- Research to understand the impact of sex affirming hormone therapy use before pregnancy on subsequent pregnancy, fertility, or both

#### MIII. Other

- Evaluation of the association between strenuous work or prolonged work and adverse pregnancy outcomes
- Identification of which occupations are associated with positive pregnancy outcomes and which occupations are associated with adverse pregnancy outcomes

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# **Appendix A: Guideline Development Methodology**

# A. Developing Key Questions to Guide the Systematic Evidence Review

To guide this CPG's systematic evidence review, the Work Group drafted 12 key questions (KQ) on clinical topics of the highest priority for the VA and DoD populations. The KQs followed the population, intervention, comparison, outcome, timing, and setting (PICOTS) framework, as established by the Agency for Healthcare Research and Quality (AHRQ). Table A-1 lists and describes the PICOTS elements.

**Table A-1. PICOTS (355)** 

PICOTS Element	Description
Population or Patients	Patients of interest. It includes the condition or conditions, populations or sub- populations, disease severity or stage, co-occurring conditions and other patient characteristics or demographics.
Intervention or Exposure	Treatment (e.g., drug, surgery, lifestyle changes), approach (e.g., doses, frequency, methods of administering treatments), or diagnostic or screening test or both used with the patient or population.
Comparator	Treatment or treatments (e.g., placebo, different drugs) or approach or approaches (e.g., different dose, different frequency, standard of care) being compared with the intervention or exposure of interest described above.
Outcomes	Results of interest (e.g., mortality, morbidity, QoL, complications). Outcomes can include short, intermediate, and long-term outcomes.
Timing, if Applicable	Duration or follow-up of interest for the particular patient intervention and outcome to occur (or not occur).
Setting, if Applicable	Setting or context of interest. Setting can be a location (e.g., primary, specialty, inpatient care) or a type of practice.

Abbreviations: PICOTS: population, intervention, comparison, outcome, timing, and setting

Because of resource constraints, all KQs of interest to the Work Group could not be included in the systematic evidence review. Thus, the Work Group selected the 12 highest priority KQs for inclusion (see <u>Table A-2</u>).

Using the GRADE approach, the Work Group rated each outcome on a 1-9 scale (7-9, critical for decision making; 4-6, important, but not critical, for decision making; and 1-3, of limited importance for decision making). Critical and important outcomes were included in the evidence review (see <a href="Outcomes">Outcomes</a>); however, only critical outcomes were used to determine the overall quality of evidence (see <a href="Determining Recommendation">Determining Recommendation</a> <a href="Strength and Direction">Strength and Direction</a>).

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# a. Populations

Key Question	Population
1, 2, 3, 4, 5, and 12	Standard population
6	Pregnant patients at risk for gestational hypertension (GHTN)
7, 8, 9	Pregnant patients
10, 11	Pregnant, antepartum, and postpartum patients

# b. Interventions and Comparators

KQs	Interventions	Comparators
KQs	<ul> <li>Interventions to promote/support mental health (prevention focus)</li> <li>Survivor Moms</li> <li>Reach Out, Stay Strong, Essentials for new mothers (ROSE)</li> <li>Perinatal IPT-P, (interpersonal therapy, prenatal) (perinatal depression prevention)</li> <li>CBT (mother-baby) (perinatal depression prevention)</li> <li>Social support (peer support groups for new moms)</li> <li>Education: in-person, online, or self-study classes related to pregnancy, childbirth, parenting, breastfeeding, and perinatal mental health.</li> </ul>	Standard care, other listed strategy, or no strategy
	<ul> <li>Peer groups</li> <li>Self-care/self-help:         <ul> <li>Sleep (sleep maintenance, e.g., getting enough sleep)</li> <li>Exercise (only moderate to light aerobic exercise in the form of walking, stationary biking, swimming, exercise classes, yoga)</li> <li>Nutrition (healthy eating for pregnant individuals; no overly specialized diets (e.g., KETO) or studies with poorly defined diets)</li> </ul> </li> <li>Note: include frequency and/or duration of interventions in tables if reported</li> </ul>	
2	Assessment of pelvic muscle dysfunction  Referral to PFPT  Pelvic muscle (floor) training/ physical therapy  Biofeedback  Medication  Relaxation techniques  Surgery  Education on pelvic muscle exercise	Routine care or another intervention listed to the left

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KQs	Interventions	Comparators
3	<ul> <li>BP screening schedule</li> <li>Telehealth BP screening (audio only versus audio and video)</li> <li>Bluetooth enabled BP cuff</li> </ul>	Standard screening (e.g., in-person screening at every visit)
4	Prenatal and postpartum care via telemedicine (videoconference, telephone)     Care coordinated home telehealth (CCHT)	Standard in-person care  Note: Using the U.S. Department of Health and Human Services definition of telehealth, which defines telehealth as the use of electronic information and telecommunications technologies to support and promote long-distance clinical health care. Technologies include videoconferencing, the internet, store-and-forward imaging, streaming media, and terrestrial and wireless communications.  We will only include studies assessing electronic applications or apps in which the app involves two-way communication between patient and provider(s).  The primary focus is on the use of telehealth for routine care visits (especially as used during COVID), and the following special conditions: GHTN, GDM, prevention of preterm birth, and postpartum depression.
5	Risk factors:  Anxiety Trauma (e.g., interpersonal) Distress PTSD	No risk factors or other risk factors
6	Interventions to prevent GHTN:  Aspirin  Weight management/ loss  Nutrition/diet control  Sleep hours/sleep schedule  Stress management	Standard care, other listed intervention, or no intervention
7	<ul> <li>Aneuploidy screening</li> <li>Maternal serum screening</li> <li>Non-invasive prenatal screening/testing (NIPT)</li> <li>Ultrasound</li> <li>Amniocentesis (gold standard)</li> <li>Chorionic villus sampling</li> </ul>	Another screening method from the intervention list

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KQs	Interventions	Comparators
8	Any GDM test earlier than 24 weeks	Any GDM test between 24-28 weeks
9	<ul> <li>Progesterone therapy</li> <li>Cervical cerclage and pessary</li> <li>Cervical length screening</li> <li>Smoking cessation</li> <li>Addressing racial disparities</li> <li>Aspirin</li> </ul>	Standard care or other listed intervention
10	Risk factors (mother):  Prior history of breastfeeding success or failure Prior history of breast surgery or augmentation Nipple protrusion Tagged nipples Other physiological characteristics of the breast Presence of depressive symptoms Postpartum hemorrhage Intimate partner violence Family/ partner support Impaired glucose tolerance/DM/ GDM Parity (first pregnancy or not) Mode of delivery (c/s vs NSVD) Maternal BMI c/w obesity Thyroid dysfunction Delayed onset of lactogenesis II (milk production) Unintended pregnancy WIC participation Lack of education on lactation History of low milk supply in prior pregnancy Risk factors (baby): Latching difficulties Retrognathia Tongue tie Gestational age Formula supplementation	Absence of factors: no history obtained, no surgery, no nipple protrusion or tagged nipples, no characteristics, no depression

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KQs	Interventions	Comparators
11	Interventions:  Breastfeeding education delivered by provider Group lactation education classes Employer support of pumping Breast examination Lactation consultant during prenatal and postpartum period (not isolated to postpartum) Self-study Peer/family support (e.g., La Leche League)	No intervention or one of the interventions listed
12	Other supportive care interventions:  Doula care Care coordination/ care navigation Provider education on racial bias Diverse provider pool Group prenatal care Unconscious bias training Peer and family support and education (pregnancy and childbirth classes) employment support Home visits Telephone video support Lactation supplies Lactation consultant home visits Lactation clinic appointment in PP Including fathers in group prenatal care Promotional materials Removal of race/ethnicity in management calculators (i.e., VBAC calculator)	Standard of care

### c. Outcomes

KQ	Critical Outcomes(s)	Important Outcomes
1	<ul><li>Suicide risk/suicide</li><li>Depression</li><li>Anxiety</li><li>Hospitalization for mental health diagnosis</li></ul>	<ul> <li>Maternal connection to child/bonding</li> <li>Overall health/measures of general sense of wellbeing (e.g., social adjustment, social support, relationship quality, maternal self-efficacy)</li> <li>Quality of life</li> </ul>

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KQ	Critical Outcomes(s)	Important Outcomes
2	<ul> <li>Incontinence: fecal and urinary (including stress incontinence)</li> <li>Pain: pelvic pain, back pain, hip pain, lumbar pain, Coccydynia, etc.</li> <li>Dyspareunia</li> </ul>	<ul> <li>Other GU issues: urinary retention, overactive bladder, painful bladder syndrome, etc</li> <li>Pelvic surgery post- operative care (e.g., hysterectomy, sling procedures, laparoscopy)</li> <li>Pelvic organ prolapse</li> <li>Other GI issues: constipation, etc.</li> </ul>
3	<ul><li>Preeclampsia/eclampsia</li><li>Stroke</li><li>Maternal death</li><li>Hospital readmission</li></ul>	Triage visits (e.g., OB ED) Management of HTN medications
4	<ul> <li>Gestational HTN</li> <li>Maternal morbidity (e.g., ICU admissions, blood transfusions)</li> <li>Engagement with care (e.g., care visits, missed appointments); compliance with prenatal care</li> <li>Gestational DM</li> </ul>	<ul><li>Preterm delivery</li><li>NICU admission</li><li>Patient satisfaction</li></ul>
5	<ul> <li>Postpartum depression with antenatal anxiety, trauma, or distress</li> <li>Stillbirth/perinatal loss</li> <li>Preterm labor and/or delivery (&lt;37 weeks)</li> </ul>	<ul><li>Substance use disorder</li><li>Preeclampsia</li><li>Bonding postpartum</li><li>NICU admission</li><li>Low birth weight</li></ul>
6	<ul> <li>Preeclampsia with and without severe features, eclampsia, "Hemolysis, Elevated Liver enzymes, and Low Platelets (HELLP)") B61</li> <li>Adverse events (including stroke, cardiac events, pulmonary edema, acute kidney injury, requirement for anti-hypertensive therapy, abruption, DIC, need for transfusion</li> <li>Fetal outcomes including oligohydramnios, fetal growth restriction, fetal demise (IUFD), and small for gestational age</li> </ul>	<ul> <li>HTN control (reduction in blood pressure, change in BP from baseline, achievement of lower BP goals)</li> <li>Preterm delivery (&lt;37 weeks) (Indicated or spontaneous)</li> <li>NICU admission</li> <li>Placental abruption</li> </ul>
7	<ul> <li>Specificity</li> <li>Sensitivity</li> <li>Positive predictive value (PPV)</li> <li>Negative predictive value (NPV)</li> </ul>	<ul> <li>Impact on patient decision making (decision to continue or terminate pregnancy, decision regarding delivery method) as defined by the scale of decisional conflict</li> <li>Rates of uptake of amniocentesis (including genetic diagnosis)</li> <li>Counseling (based on results, patient accepted counseling)</li> </ul>
8	<ul><li>Diagnosis of gestational DM</li><li>Diagnosis of preexisting type 2 diabetes</li></ul>	Preeclampsia     Gestational HTN

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KQ	Critical Outcomes(s)	Important Outcomes
9	<ul> <li>Preterm delivery (&lt;37 weeks)</li> <li>Neonatal morbidity and mortality</li> <li>Adverse events including those related to complications of cerclage (e.g., ruptured membranes, infection) and those related to progesterone therapy (e.g., diabetes, developmental effects in offspring [teratogenesis], risk of cancer in offspring)</li> </ul>	Peri-viable delivery     Prolonged pregnancy duration from previous gestation
10	<ul> <li>Initiation of breastfeeding/lactation</li> <li>Continuing breastfeeding/lactation</li> <li>Mixed breastfeeding/formula</li> <li>Exclusive breastfeeding/lactation for 6 months</li> </ul>	Number of post-natal consultations for breastfeeding/lactation
11	<ul> <li>Initiation of breastfeeding/lactation</li> <li>Continuing breastfeeding/lactation</li> <li>Mixed breastfeeding/formula</li> <li>Exclusive breastfeeding/lactation for 6 months</li> </ul>	Number of post-natal consultations for breastfeeding/lactation
12	<ul> <li>Maternal morbidity (e.g., ICU admissions, blood transfusions) and maternal mortality</li> <li>Maternal mortality</li> <li>Hypertension disorders of pregnancy (i.e., gestational HTN or preeclampsia spectrum)</li> <li>Preterm delivery (&lt;37 weeks)</li> </ul>	<ul> <li>Engagement with care (e.g., care visits, missed appointments)</li> <li>Depression</li> <li>Delivery modes (vaginal or caesarean)</li> </ul>

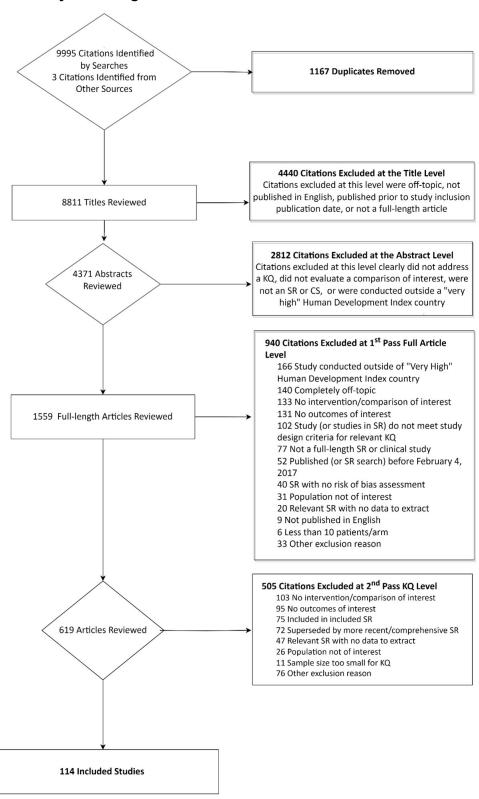
## **B.** Conducting the Systematic Review

Based on the Work Group's decisions regarding the CPG's scope, KQs, and PICOTS statements, the Lewin Team produced a systematic evidence review protocol before conducting the review. The protocol detailed the KQs, PICOTS criteria, methodology to be used during the systematic evidence review, and the inclusion and exclusion criteria to be applied to each potential study, including study type and sample size. The Work Group reviewed and approved the protocol.

<u>Figure A-1</u> below outlines the systematic evidence review's screening process (see also the <u>General Criteria for Inclusion in Systematic Review</u>. In addition, <u>Table A-2</u> indicates the number of studies that addressed each of the questions.

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Figure A-1. Study Flow Diagram



Abbreviations: KQ: key question; SR: systematic review; CS: cohort study

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#### **Alternative Text Description of Study Flow Diagram**

<u>Figure A-1. Study Flow Diagram</u> is a flow chart with nine labeled boxes linked by arrows that describe the literature review inclusion-exclusion process. Arrows point down to boxes that describe the next literature review step and arrows point right to boxes that describe the excluded citations at each step (including the reasons for exclusion and the numbers of excluded citations).

- 1. Box 1: 9,995 citations identified by searches. 4 citations identified from other sources.
  - a. Right to Box 2: 1,187 duplicates removed
  - b. Down to Box 3
- 2. Box 3: 8,812 titles reviewed
  - a. Right to Box 4: 4,440 citations excluded at the title level
    - Citations excluded at this level were off topic, not published in English, published prior to study inclusion publication date, or not a full-length article
  - b. Down to Box 5
- 3. Box 5: 4,372 abstracts reviewed
  - a. Right to Box 6: 2,811 citations excluded at the abstract level
    - Citations excluded at this level did not address a KQ, did not evaluate a comparison of interest, were not an SR or CS, or were conducted outside a "very high" Human Development Index (HDI) country
  - b. Down to Box 7
- 4. Box 7: 1,561 full-length articles reviewed
  - a. Right to Box 8: 940 citations excluded at first pass full article level
    - i. 166 study conducted outside HDI country
    - ii. 140 completely were off topic
    - iii. 133 no intervention/comparison of interest
    - iv. 131 no outcomes of interest
    - v. 102 study (or studies in SR) do not meet study design criteria for relevant KQ
    - vi. 77 not a full-length SR or clinical study
    - vii. 52 published (or SR search) before February 4, 2017
    - viii. 40 SRs with no risk of bias assessment
    - ix. 31 population not of interest

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- x. 20 Relevant SR with no data to extract
- xi. 9 not published in English
- xii. 6 less than 10 patients/arm
- xiii. 33 other exclusion reason
- b. Down to Box 9
- 5. Box 9: 621 articles reviewed
  - a. Right to Box 10: 505 Citations excluded at second pass KQ level
    - i. 103 no intervention/comparison of interest
    - ii. 95 no outcomes of interest
    - iii. 75 included in included SR
    - iv. 72 superseded by more recent/comprehensive SR
    - v. 47 relevant SR with no data to extract
    - vi. 26 population not of interest
    - vii. 11 sample size too small for KQ
    - viii. 77 other exclusion reason
  - b. Down to Box 11
- 6. Box 11: 113 included studies (116 reports)

Table A-2. Evidence Base for KQs

KQ Number	KQ	Number and Study Type
KQ1	In pregnant and postpartum patients, what is the effectiveness of interventions to promote and support maternal mental health?  What is the frequency and/or duration of interventions?	SRs:14 RCTs: 10
KQ2	In pregnant and postpartum patients, what is the effectiveness and comparative effectives of pelvic muscle physical therapy/training in patients during the pregnancy and postpartum period?	SRs: 2 RCTs: 5
KQ3	What is the optimal blood pressure screening frequency in patients with hypertension?	SRs: 2 RCTs: 2
KQ4	What is the impact of prenatal and postpartum care delivered through telemedicine on maternal and neonatal outcomes?  Do outcomes differ for the following subpopulations: racial/ethnic minorities, rural, economically disadvantaged, Military/ Veterans?	SRs: 3 RCTs: 4
KQ5	What is the effect of anxiety, trauma (including interpersonal), and distress on perinatal outcomes?	SR: 1 Cohort studies: 11
KQ6	Among pregnant patients at-risk for gestational hypertension (GHTN), what is the effectiveness of interventions in preventing hypertensive disorders in pregnancy?	SRs: 6 RCTs: 2

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KQ Number	KQ	Number and Study Type
KQ7	What is the comparative accuracy and safety of screening methods (including NIPT) used to screen for aneuploidy in pregnant patients?	SRs: 2 RCTs: 3 Diagnostic accuracy studies: 2 Retrospective cohort study: 1
KQ8	What is the impact of early screening (before 24 weeks) for gestational diabetes compared to routine screening at 24 to 28 weeks?	1 RCT
KQ9	What is the effectiveness and safety of interventions to reduce the risk of preterm delivery?  Do outcomes differ for the following subpopulations: racial/ethnic minorities, rural, economically disadvantaged, Military/ Veterans?	SRs: 8 RCTs: 10
KQ10	In pregnant and postpartum patients, what factors impact initiating and continuing breastfeeding or lactation?	SRs: 3 Cohort studies: 2
KQ11	In pregnant and postpartum patients, what is the effectiveness or comparative effectiveness of interventions that impact the probability of initiating and continuing breastfeeding or lactation?  Do outcomes differ for the following subpopulations: racial/ethnic minorities, rural, economically disadvantaged, Military/ Veterans?	SRs: 5 RCTs: 10
KQ12	What is the effectiveness of strategies to reduce healthcare/racial disparities in pregnancy and childbirth?	RCTs: 6
	Total Evidence Base	113 (116 publications) *

Abbreviations: KQ: key question; RCT: randomized controlled trials; SR: systematic review

#### a. General Criteria for Inclusion in Systematic Evidence Review

- RCTs or systematic reviews published February 4, 2017, through June 1, 2022, if
  not listed otherwise in <u>Table A-2</u>. If multiple systematic reviews addressed a key
  question, we selected the most recent and/or comprehensive review. If
  applicable, systematic reviews were supplemented with RCTs published after the
  systematic review.
- Studies must have been published in English.
- Publication must have been a full clinical study or systematic review; abstracts alone were not included. Similarly, letters, editorials, other non-full-length publications, or non-peer-reviewed publications were not included.
- Systematic reviews must have searched at least MEDLINE or EMBASE for eligible publications, perform risk of bias assessment of included studies, and assess the quality of evidence using a rigorous rating system (e.g., GRADE, the Strength of Evidence grading used by the Evidence-based Practice Centers of the Agency for Healthcare Research and Quality). If an existing review did not

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assess the overall quality of the evidence, evidence from the review must have been reported in a manner that allowed the ECRI team to judge the overall quality, consistency, directness, and precision of evidence. Otherwise, the systematic review was not included.

- Unless otherwise specified, study must have enrolled at least 20 patients (10 per study group for treatment studies). Small sample size is associated with increased risk of bias, and we downgraded small studies in the GRADE domain of precision: one downgrade for imprecision of a single study with <200 patients per study arm.
- Study must have enrolled at least 80% of patients who met the study population criteria.
- Study must have reported on at least one outcome of interest.

#### b. Key Question Specific Criteria for Inclusion in Systematic Evidence Review

- KQ 5 and 10: included prognostic cohort studies that statistically compared outcomes for patients who have relevant risk factors and patients who lack these factors. Prognostic studies had to include at least 200 patients in a multivariate analysis.
- KQ 7: included diagnostic studies with at least 200 patients.

#### c. Literature Search Strategy

Information regarding the bibliographic databases, date limits, and platform, provider, or both can be found in <u>Table A-3</u>. See <u>Appendix E</u> for additional information on the search strategies, including topic-specific search terms and search strategies.

Table A-3. Bibliographic Database Information

Name		Date Limits	Platform or Provider
	EMBASE (Excerpta Medica) and MEDLINE	February 4, 2017, through June 10, 2022	Elsevier
Bibliographic Databases	PsycINFO (for selected KQs)  February 4, 2017, through June 10, 2022		Ovid
	PubMed (In-process and Publisher records)	February 4, 2017, through June 10, 2022	National Library of Medicine
Grey	Agency for Healthcare Research and Quality (AHRQ)	February 4, 2017, through June 10, 2022	AHRQ
Literature	U.S. Department of Veterans Affairs (VA) Evidence Synthesis Program	February 4, 2017, through June 10, 2022	VA

#### d. Rating the Quality of Individual Studies and the Body of Evidence

The Lewin Team assessed the methodological risk of bias of individual diagnostic, observational, and interventional studies using the U.S. Preventive Services Task Force

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(USPSTF) method. Each study is assigned a rating of *Good*, *Fair*, or *Poor* based on a set of criteria that vary depending on study design. Detailed lists of criteria and definitions appear in Appendix VI of the USPSTF procedure manual.(356)

Next, the Lewin Team assessed the overall quality of the body of evidence for each critical and important outcome using the GRADE approach. This approach considers the following factors: overall study quality (or overall risk of bias or study limitations), consistency of evidence, directness of evidence, and precision of evidence. The overall quality of the body of evidence is rated as *High*, *Moderate*, *Low*, and *Very Low*.

#### C. Developing Evidence-Based Recommendations

In consultation with the VA Office of Quality and Patient Safety and the Clinical Quality Improvement Program, Defense Health Agency, the Lewin Team convened a 3 day inperson recommendation development meeting from October 25–27, to develop this CPG's evidence-based recommendations. Two weeks before the meeting, the Lewin Team finalized the systematic evidence review and distributed the report to the Work Group; findings were also presented during the recommendation development meeting.

Led by the Champions, the Work Group interpreted the systematic evidence review's findings and developed this CPG's recommendations. The strength and direction of each recommendation were determined by assessing the quality of the overall evidence base, the associated benefits and harms, patient values and preferences, and other implications (see Determining Recommendation Strength and Direction).

#### a. Determining Recommendation Strength and Direction

Per GRADE, each recommendation's strength and direction is determined by the following four domains.(47) Information on each domain, questions to consider, and the resulting judgment can be found in <u>Table A-4</u>.

#### 1. Confidence in the Quality of the Evidence

Confidence in the quality of the evidence reflects the quality of the body of evidence supporting a recommendation (see <u>Rating the Quality of Individual Studies and the Body of Evidence</u>). The options for this domain include *High*, *Moderate*, *Low*, or *Very Low*. These four ratings are a direct reflection of the GRADE ratings for each relevant critical outcome in the evidence review (see <u>Outcomes</u>). Per GRADE, if the quality of evidence differs across the relevant critical outcomes, the lowest quality of evidence for any of the critical outcomes determines the overall quality of the evidence for a recommendation.(2, 49)

The recommendation strength generally aligns with the confidence in the quality of evidence. For example, *Strong* recommendations are typically supported by *High* or *Moderate* quality evidence. However, GRADE permits *Low* or *Very Low* quality evidence to support a *Strong* recommendation in certain instances (e.g., life-threatening situation).(47)

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#### 2. Balance of Desirable and Undesirable Outcomes

The balance of desirable and undesirable outcomes (i.e., benefits and harms) refers to the relative magnitudes or tradeoffs of anticipated benefits (e.g., increased longevity, reduced morbidity, improved QoL, decreased resource use) and harms (e.g., decreased longevity, increased complications, impaired QoL). The options for this domain include benefits outweigh harms/burdens, benefits slightly outweigh harms/burdens, benefits and harms/burdens are balanced, harms/burdens slightly outweigh benefits, and harms/burdens outweigh benefits. This domain assumes most providers will offer patients an intervention if its advantages exceed the harms. The Work Group's understanding of the benefits and harms associated with the recommendation influenced the recommendation's strength and direction.

#### 3. Patient Values and Preferences

Patient values and preferences is an overarching term that includes patients' perspectives, beliefs, expectations, and goals for health and life as they might apply to the intervention's potential benefits, harms, costs, limitations, and inconvenience. The options for this domain include *similar values*, *some variation*, and *large variation*. For instance, there might be *some variation* in patient values and preferences for a recommendation on the use of acupuncture because some patients might dislike needles. When patient values seem homogeneous, this domain might increase the recommendation's strength. Alternatively, when patient values seem heterogeneous, this domain might decrease a recommendation's strength. As part of this domain, the Work Group considered the findings from the patient focus group carried out as part of this CPG update (see <u>Appendix B</u>).

#### 4. Other Implications

Other implications encompass the potential consequences or other impacts that might affect the strength or direction of the recommendation. The options for this domain, for example, include resource use, equity, acceptability, feasibility, and subgroup considerations. The following are example implications related to equity and subgroup considerations, respectively: some of the indicated population might be geographically remote from an intervention (e.g., complex radiological equipment); a drug might be contraindicated in a subgroup of patients.

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Table A-4. GRADE Evidence to Recommendation Framework

Decision Domain	Questions to Consider	Judgment
Confidence in the quality of the evidence	Among the designated critical outcomes, what is the lowest quality of relevant evidence?  How likely is further research to change the confidence in the estimate of effect?	High Moderate Low Very Low
Balance of desirable and undesirable outcomes	What is the magnitude of the anticipated desirable outcomes? What is the magnitude of the anticipated undesirable outcomes? Given the best estimate of typical values and preferences, are you confident that benefits outweigh harms/burdens or vice versa?	Benefits outweigh harms/burdens Benefits slightly outweigh harms/burdens Benefits and harms/burdens are balanced Harms/burdens slightly outweigh benefits Harms/burdens outweigh benefits
Patient values and preferences	What are the patients' values and preferences?  Are values and preferences similar across the target population?  Are you confident about typical values and preferences?	Similar values Some variation Large variation
Other implications (e.g., resource use, equity, acceptability, feasibility, subgroup considerations)	What are the costs per resource unit? Is this intervention generally available? What is the variability in resource requirements across the target population and settings? Are the resources worth the expected net benefit from the recommendation? Is this intervention and its effects worth withdrawing or not allocating resources from other interventions?	Various considerations

#### b. Recommendation Categorization

A summary of the recommendation categories and definitions is available in Table 4.

#### 1. Categorizing Recommendations with an Updated Review of the Evidence

Reviewed refers to recommendations on topics included in this CPG's systematic evidence review. Reviewed, New-added recommendations are original, new recommendations (i.e., not included in the previous CPG). These recommendations are based entirely on evidence included in the current CPG's systematic evidence review.

Reviewed, New-replaced recommendations were in the previous CPG but revised based on the updated evidence review. These recommendations may have clinically relevant edits. Reviewed, Not changed recommendations were carried forward from the previous CPG unchanged. Reviewed, Amended recommendations were carried forward

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from the previous CPG with a nominal change. This allowed for the recommendation language to reflect GRADE approach and any other not clinically meaningful edits deemed necessary. These recommendations can be based on a combination of evidence included in the current CPG's systematic evidence review and the evidence base that supported the recommendation in the previous CPG.

Reviewed, Deleted refers to recommendations from the previous CPG that were deleted after a review of the evidence. This may occur if the evidence supporting the recommendation is outdated (e.g., there is no longer a basis to recommend use of an intervention and/or new evidence suggests a shift in care), rendering the recommendation obsolete.

## 2. Categorizing Recommendations without an Updated Review of the Evidence

There were also cases in which it was necessary to carry forward recommendations from the previous CPG without an updated review of the evidence. Given time and resource constraints, the systematic evidence review carried out for this CPG update could not cover all available evidence on pregnancy; therefore, its KQs focused on new or updated research or areas not covered in the previous CPG.

For areas in which the relevant evidence was not changed and for which recommendations made in the previous CPG were still relevant, recommendations could have been carried forward to the updated CPG without an updated review of the evidence. The evidence supporting these recommendations was thus also carried forward from the previous CPG. These recommendations were categorized as *Not reviewed*. If evidence had not been reviewed, recommendations could have been categorized as *Not changed*, *Amended*, or *Deleted*. *Not reviewed*, *Not changed* recommendations were carried forward from the previous CPG unchanged. *Not reviewed*, *Amended* recommendations were carried forward from the previous CPG with a nominal change. *Not reviewed*, *Deleted* recommendations were determined by the Work Group to not be relevant. A recommendation may not be relevant if it, for example, pertained to a topic (e.g., population, care setting, treatment) outside of the updated CPG's scope or if it was determined to be common practice.

The recommendation categories for the current CPG are noted in the <u>Recommendations</u>. The recommendation categories from the 2018 VA/DoD Pregnancy CPG are noted in Appendix E.

## D. Drafting and Finalizing the Guideline

The Work Group wrote, reviewed, and edited three drafts of the CPG using an iterative review process to solicit feedback on and make revisions to the CPG. The first and second drafts were posted online for 20 and 14 business days, respectively, for the Work Group to provide feedback. Draft 3 was made available for a 14-day peer review and comment (see <a href="External Peer Review">External Peer Review</a>). The Work Group reviewed all feedback

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submitted during each review period and made appropriate revisions to the CPG. Following the Draft 3 review and comment period, the Work Group reviewed external feedback and created a final draft of the CPG. The Champions then presented the CPG to the VA/DoD EBPWG for approval. The Work Group considered the VA/DoD EBPWG's feedback and revised the CPG, as appropriate, to create the final version. To accompany the CPG, the Work Group produced toolkit products, including a provider summary, quick reference guide, and patient summary. The VA/DoD EBPWG approved the final CPG and toolkit products in July 2023.

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## **Appendix B: Patient Focus Group Methods and Findings**

#### A. Methods

VA and DoD Leadership recruited eight participants for the focus group, with support from the Champions and other Work Group members, as needed. Although participant recruitment focused on eliciting a range of perspectives likely relevant and informative in the CPG development process, the patient focus group participants were not intended to be a representative sample of VA and DoD patients. The participants were not incentivized for participation or reimbursed for travel expenses. The Work Group, with support from the Lewin Team, identified topics on which patient input was important to consider in developing the CPG. The Lewin Team developed and the Work Group approved a patient focus group guide covering these topics. The focus group facilitator led the discussion, using the guide to elicit patient perspectives about their treatment and overall care. Given the limited time and the range of interests of the focus group participants, not all questions were addressed.

### **B.** Patient Focus Group Findings

- a. Participants stated that continuity and coordination of their pregnancy care by their providers (e.g., OBGYN, primary care providers, specialists, doulas, Maternity Care Coordinators [MCC]) within and across treatment settings was of utmost importance to them; they valued access to comprehensive, multidisciplinary care.
- Participants wished to have the same care team throughout their pregnancy, and if possible, the same provider.
- Participants desired to have the opportunity to consult with a wide range of providers (e.g., specialist, doulas, MCCs, midwives).
- Some participants expressed that the continuity of their care was disrupted by the need to switch between different providers across VA, DoD, and community care.
- b. Participants expressed a desire for more frequent, detailed communication with their care team throughout pregnancy, delivery, and the postpartum period, with the ultimate goals of improving understanding of their pregnancy, their treatment plan, and treatment decisions as well as improving shared decision making.
- Some participants shared that they felt anxious when they were unsure about
  why certain clinical decisions were made during their pregnancy or delivery. They
  expressed a desire for their providers to communicate with them in real-time and
  give them an opportunity to ask questions.
- Participants noted that they wanted to be involved in the decision making process throughout their pregnancy and delivery. They noted open

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- communication with their providers and opportunities to make informed decisions about their care plan made them feel empowered.
- c. Participants shared the importance of access to comprehensive education options (e.g., courses, literature, discussions with care team or MCCs, support groups) and expressed different preferences for education format and frequency, depending on individual needs and preferences.
- Participants recognized the importance of educational opportunities to learn about their pregnancy, its impact on their life, and care plan options.
- Some participants expressed a desire for more options regarding content areas, such as courses on pain management, nutrition, lactation, and exercise.
- Participants shared that pregnancy levies a heavy emotional toll; structured opportunities to connect with other pregnant participants would be helpful.
- d. Participants stated that more consideration of their co-occurring health needs and risk factors (e.g., mental health, chronic pain, co-occurring medical conditions, age) by their care team would be beneficial throughout pregnancy and the postpartum period; participants expressed a desire for these discussions to be more central in their pregnancy care planning.
- Participants shared that it seemed as though there was inadequate consideration
  of their co-occurring conditions and risk factors in their pregnancy care plans.
  They expressed often feeling unsure about how to effectively manage these
  conditions during pregnancy (e.g., what medications were safe to take while
  pregnant or lactating).
- Participants noted the importance of mental health needs during pregnancy and the postpartum period. They expressed that adequate evaluation and support were vital, especially for those at increased risk for postpartum depression.
- e. Participants expressed a preference for more comprehensive postpartum care for a longer period (e.g., more frequent postpartum care visits, referrals for postpartum visits with an OBGYN provider instead of a primary care provider, lactation consultants, mental health support, post-surgical treatment and rehabilitation).
- Some participants stated that extended postpartum care would have improved their recovery and overall experience. Other participants noted that the immediate postpartum care provided to them could have been improved.
- Participants expressed a desire to be seen by an OBGYN provider for an extended period in the postpartum period before returning to primary care.

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## **Appendix C: Evidence Table**

Table C-1: Evidence Table a,b,c,d

#	Recommendation	2018 Strength of Recommendation	Evidence	2023 Strength of Recommendation	Recommendation Category
1.	We recommend offering non-invasive prenatal testing as the prenatal screening test of choice for all patients with singleton pregnancies who choose aneuploidy screening.	Not applicable	( <u>60</u> , <u>61</u> )	Strong for	Reviewed, New- added
2.	We suggest non-invasive prenatal testing for patients with twin pregnancies who choose aneuploidy screening.	Not applicable	( <u>60</u> , <u>61</u> )	Weak for	Reviewed, New- added
3.	We suggest assessing all patients for risk factors that impact initiation and continuation of lactation, including obesity, depression, inappropriate gestational weight gain, and gestational diabetes mellitus.	Not applicable	(62-66) Additional Reference (67)	Weak for	Reviewed, New- added

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<sup>&</sup>lt;sup>a</sup> 2018 Strength of Recommendation column: The 2018 VA/DoD Pregnancy CPG was developed using the GRADE approach to determine the strength of each recommendation. Inclusion of more than one 2018 strength of recommendation indicates that more than one 2018 VA/DoD Pregnancy CPG recommendation is covered by the 2023 recommendation. "Not applicable" indicates that the 2023 VA/DoD Pregnancy CPG recommendation was a new recommendation, and therefore does not have an associated 2018 strength of recommendation.

Evidence column: The first set of references listed in each row in the evidence column constitutes the evidence base for the recommendation. To be included in the evidence base for a recommendation, a reference had to be identified through a systematic evidence review carried out as part of the development of this CPG. The second set of references in the evidence column (called "Additional References") includes references that provide additional information related to the recommendation but that were not identified through the systematic evidence review. These references were, therefore, not included in the evidence base for the recommendation and did not influence the strength and direction of the recommendation.

<sup>&</sup>lt;sup>c</sup> 2023 Strength of Recommendation column: The VA/DoD Pregnancy CPG was developed using the GRADE approach to determine the strength of each recommendation. Refer to the Determining Recommendation Strength and Direction section for more information.

d Recommendation Category column: Refer to the Recommendation Categorization section for more information on the description of the categorization process, the categories, and their definitions.

#	Recommendation	2018 Strength of Recommendation	Evidence	2023 Strength of Recommendation	Recommendation Category
4.	We suggest individual or group lactation education delivered via in-person, telehealth, or multimedia modalities be provided for all pregnant and postpartum patients to improve the probability of initiating and continuing lactation.	Strong for	( <u>70-83</u> )  Additional  References ( <u>68</u> , <u>69</u> , <u>84</u> , <u>85</u> )	Weak for	Reviewed, New- replaced
5.	We suggest all patients have an early prenatal evaluation of pelvic floor muscle function and receive pelvic floor muscle exercise instruction during pregnancy for the prevention of urinary incontinence in late pregnancy and up to six months postpartum.	Not applicable	( <u>86-88</u> ) Additional References ( <u>89-91</u> )	Weak for	Reviewed, New- added
6.	We suggest referral to pelvic health rehabilitation for patients with reported urinary incontinence in the postpartum period.	Not applicable	(86, 90, 92-96)  Additional Reference (97)	Weak for	Reviewed, New- added
7.	We recommend offering scheduled delivery to patients who reach 41 weeks and 0/7 days undelivered. Antepartum fetal testing should begin at 41 weeks and 0/7 days if not delivered.	Strong for	( <u>98-101</u> )  Additional References ( <u>102</u> , <u>103</u> )	Strong for	Not reviewed, Amended
8.	We suggest that patients with uncomplicated pregnancies may continue a standard work schedule throughout their pregnancy.	Weak for	(104-107) Additional Reference (108)	Weak for	Not reviewed, Amended
9.	We suggest offering telemedicine as a complement to usual perinatal care.	Not applicable	(109-115)	Weak for	Reviewed, New- added
10.	There is insufficient evidence to recommend for or against specific interventions that would diminish disparities in perinatal care access and maternal and childbirth outcomes.	Not applicable	( <u>77</u> , <u>120-124</u> )  Additional  References  ( <u>116-119</u> )	Neither for nor against	Reviewed, New- added

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#	Recommendation	2018 Strength of Recommendation	Evidence	2023 Strength of Recommendation	Recommendation Category
11.	We recommend considering fetal fibronectin testing as a part of the evaluation strategy in patients between 24 0/7 and 34 6/7 weeks' gestation with signs and symptoms of preterm labor, particularly in facilities where the result might affect management of delivery.	Strong for	( <u>125</u> , <u>126</u> )	Strong for	Not reviewed, Amended
	We suggest vaginal progesterone or cerclage for		( <u>127</u> , <u>128</u> )		
12.	singleton pregnancy with short cervix, history of spontaneous preterm birth, or both depending on patient characteristics and preferences.	Not applicable	Additional References (129-133)	Weak for	Reviewed, New- added
			<u>(134</u> )		
13.	There is insufficient evidence to recommend for or against the use of aspirin to reduce recurrent spontaneous preterm birth.	Not applicable	Additional References ( <u>135</u> , <u>136</u> )	Neither for nor against	Reviewed, New- added
			( <u>138-142</u> , <u>144</u> )		
14.	We recommend initiating aspirin therapy at or before 16 weeks' gestation in patients at risk of developing preeclampsia.	Strong for	Additional References ( <u>137</u> , <u>143</u> , <u>145-147</u> )	Strong for	Reviewed, New- replaced
			( <u>138-142</u> , <u>144</u> )		
15.	We suggest low-dose aspirin of 100–150 mg daily for patients at risk of preeclampsia.	Weak for	Additional References ( <u>137</u> , <u>143</u> , <u>145-147</u> )	Weak for	Reviewed, New- replaced
16	We suggest patients with cardio-metabolic disorders (e.g., gestational diabetes mellitus, hypertension, and obesity) be counseled on the benefits of following the Dietary Approaches to Stop Hypertension diet.	Not applicable	( <u>148</u> )	Weak for	Reviewed, New- added

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#	Recommendation	2018 Strength of Recommendation	Evidence	2023 Strength of Recommendation	Recommendation Category
17.	There is insufficient evidence to recommend for or against self-monitoring for blood pressure during pregnancy and the postpartum period.	Not applicable	( <u>149-152</u> ) Additional Reference ( <u>114</u> )	Neither for nor against	Reviewed, New- added
18.	We suggest patients who have undergone bariatric surgery be evaluated for nutritional deficiencies and the need for nutritional supplementation where indicated (e.g., vitamin B12, folate, iron, calcium).	Weak for	(153, 154) Additional Reference (66)	Weak for	Not reviewed, Amended
19.	There is insufficient evidence to recommend for or against the routine supplementation of vitamins A, D, E, or K for pregnant patients who have undergone bariatric surgery.	Neither for nor against	(153, 154) Additional Reference (66)	Neither for nor against	Not reviewed, Amended
20.	We recommend screening for use of tobacco and nicotine products, alcohol, cannabis, illicit drugs, and inappropriate use of prescription medication. See VA/DoD Substance Use Disorders CPG.	Strong for	( <u>155-166</u> )  Additional References ( <u>167-182</u> )	Strong for	Not reviewed, Amended
21.	We recommend screening for depression periodically using a standardized tool, such as the Edinburgh Postnatal Depression Scale or the 9-item Patient Health Questionnaire, during pregnancy and postpartum.	Strong for	( <u>184</u> ) Additional References ( <u>183</u> , <u>185</u> )	Strong for	Not reviewed, Not changed
22.	We suggest screening patients with posttraumatic stress disorder (PTSD) for active PTSD and offering PTSD treatment. See VA/DoD PTSD CPG.	Not applicable	(28, <u>186</u> , <u>187</u> )  Additional  Reference  ( <u>188</u> )	Weak for	Reviewed, New- added
23.	We recommend offering individual or group Interpersonal Psychotherapy or cognitive behavioral therapy for pregnant patients at risk of perinatal depression.	Not applicable	( <u>189-191</u> )  Additional References ( <u>29</u> , <u>36-38</u> , <u>192-196</u> )	Strong for	Reviewed, New- added

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#	Recommendation	2018 Strength of Recommendation	Evidence	2023 Strength of Recommendation	Recommendation Category	
	M/s managed off miner labour and all		( <u>199</u> , <u>200</u> )			
24.	We recommend offering Interpersonal Psychotherapy for treating depression during pregnancy or postpartum.	Not applicable	Additional References	Strong for	Reviewed, New- added	
	programay or postpartam.		( <u>197</u> , <u>204-206</u> )			
			(201-203)			
25.	We suggest offering cognitive behavioral therapy for treating depression during pregnancy or postpartum.	Not applicable	Additional References	Weak for	Reviewed, New- added	
			( <u>198</u> , <u>204-206</u> )			
	We suggest offering peer support for people with perinatal depression or risk of perinatal depression to improve depressive symptoms.		( <u>207</u> )			
26.		Not applicable	Additional References	Weak for	Reviewed, New- added	
			( <u>208-210</u> )			
	We suggest exercise, mindfulness, yoga, or any		( <u>211-215</u> )			
27.	combination of these interventions for depressive symptoms in perinatal patients.	Not applicable	Additional References	Weak for	Reviewed, New- added	
			( <u>216-219</u> )			
	We suggest offering psychotherapies (e.g.,		( <u>199</u> , <u>202</u> , <u>215</u> , <u>220</u> )			
28.	cognitive behavioral therapy, Interpersonal Psychotherapy) or yoga or both for anxiety symptoms during and after pregnancy.	Not applicable	Additional Reference	Weak for	Reviewed, New- added	
			( <u>221</u> )			

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## **Appendix D: 2018 Recommendation Categorization Table**

Table D-1. 2018 Pregnancy CPG Recommendation Categorization Table a, b, c, d, e, f

2018 CPG Recommendation #	2018 CPG Recommendation Text	2018 CPG Strength of Recommendation	2018 CPG Recommendation Category	2023 CPG Recommendation Category	2023 CPG Recommendation #
1.	We suggest offering a group model of prenatal care as an acceptable alternative to individual provider appointments.	Weak for	Not reviewed, Amended	Not reviewed, Deleted	NA
2.	We recommend that all healthy, pregnant women without known contraindications participate in regular mild to moderate exercise sessions, three or more times per week.	Strong for	Reviewed, Amended	Reviewed, Deleted	NA
3.	We suggest that women with uncomplicated pregnancies continue a standard work schedule throughout their pregnancy.	Weak for	Not reviewed, Amended	Not reviewed, Amended	8
4.	We recommend folic acid (at least 400 micrograms daily) to be taken starting one month before conception and continued throughout pregnancy and breastfeeding.	Strong for	Not reviewed, Amended	Not reviewed, Deleted	NA

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<sup>&</sup>lt;sup>a</sup> 2018 CPG Recommendation # column: This indicates the recommendation number of the recommendation in the 2018 VA/DoD Pregnancy CPG.

b 2018 CPG Recommendation Text column: This contains the wording of each recommendation from the 2018 VA/DoD Pregnancy CPG.

<sup>&</sup>lt;sup>c</sup> 2018 CPG Strength of Recommendation column: The 2018 VA/DoD Pregnancy CPG used the GRADE approach to determine the strength of each recommendation.

d 2018 CPG Recommendation Category column: This is the recommendation category assigned during the development of the 2018 VA/DoD Pregnancy CPG. Refer to the Recommendation Categorization section for more information on the description of the categorization process and the definition of each category.

e 2023 CPG Recommendation Category column: This is the recommendation category assigned during the development of the 2023 VA/DoD Pregnancy CPG. Refer to the Recommendation Categorization section for more information on the description of the categorization process and the definition of each category.

f 2023 CPG Recommendation # column: For recommendations that were carried forward to the 2018 VA/DoD Pregnancy CPG, this column indicates the new recommendation(s) to which they correspond.

2018 CPG Recommendation #	2018 CPG Recommendation Text	2018 CPG Strength of Recommendation	2018 CPG Recommendation Category	2023 CPG Recommendation Category	2023 CPG Recommendation #
5.	We recommend screening for use of tobacco, alcohol, illicit drugs, and unauthorized use of prescription medication because their use is common and can result in adverse outcomes. For women who screen positive, we recommend additional evaluations and treatment (see VA/DoD Clinical Practice Guidelines for the Management of Substance Use Disorders and the Management of Tobacco Use).	Strong for	Reviewed, New-replaced	Not reviewed, Amended	20
6.	We recommend screening for depression using a standardized tool such as the Edinburgh Postnatal Depression Scale or the 9-item Patient Health Questionnaire periodically during pregnancy and postpartum.	Strong for	Reviewed, New-replaced	Not reviewed, Not changed	21
7.	We recommend breastfeeding education, assessment, and support to all pregnant women and their families at the first visit and throughout the pregnancy and postpartum period using open-ended questions such as "What do you know about breastfeeding?"	Strong for	Reviewed, New-replaced	Reviewed, New-replaced	4
8.	We suggest making prenatal diagnostic testing for aneuploidy available to all pregnant women.	Weak for	Reviewed, New-replaced	Reviewed, Deleted	NA
9.	We recommend offering prenatal screening for aneuploidy and the most common clinically significant genetic disorders to all pregnant women. When aneuploidy screening is desired, cell free fetal DNA screening should be considered; however, screening test selection should be individualized and take into account the patient's age, baseline aneuploidy risk, and test performance for a given condition.	Strong for	Reviewed, New-replaced	Reviewed, Deleted	NA
10.	We suggest the two-step process (one-hour oral glucose challenge test followed by three-hour oral glucose tolerance test) to screen for gestational diabetes mellitus at 24-28 weeks gestation for all pregnant women.	Weak for	Reviewed, New-replaced	Reviewed, Deleted	NA

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2018 CPG Recommendation #	2018 CPG Recommendation Text	2018 CPG Strength of Recommendation	2018 CPG Recommendation Category	2023 CPG Recommendation Category	2023 CPG Recommendation #
11.	We recommend first-trimester ultrasound to establish or confirm the gestational age and estimated birth date, identify multiple pregnancies, and confirm the presence of cardiac activity. For pregnant women who present after the first trimester, we suggest performing a dating and anatomical ultrasound at the earliest opportunity, preferably prior to 22 weeks.	Strong for	Reviewed, New-replaced	Not reviewed, Deleted	NA
12.	We recommend offering scheduled delivery to women who reach 41 weeks and 0/7 days undelivered. Antepartum fetal testing should begin at 41 weeks and 0/7 days if not scheduled for delivery.	Strong for	Reviewed, Amended	Not reviewed, Not changed	7
13.	For pregnant women who have a past or current history of gestational diabetes mellitus, hypertension, or preeclampsia, we recommend documenting the reproductive history and making women aware of the increased lifetime risks of cardiovascular disease and/or diabetes.	Strong for	Reviewed, New-added	Not reviewed, Deleted	NA
14.	We suggest that pregnant women with an unexplained elevation of maternal serum alpha-fetoprotein be evaluated and counseled by a qualified obstetric provider due to increased risk for adverse perinatal outcomes.	Weak for	Not reviewed, Amended	Not reviewed, Deleted	NA
15.	We recommend against routine screening for preterm delivery using the fetal fibronectin test in asymptomatic women.	Strong against	Not reviewed, Amended	Not reviewed, Deleted	NA
16.	We recommend considering the use of fetal fibronectin testing as a part of the evaluation strategy in women between 24 and 34 6/7 weeks gestation with signs and symptoms of preterm labor, particularly in facilities where the result might affect management of delivery.	Strong for	Not reviewed, Amended	Not reviewed, Not changed	11
17.	In women at risk of preeclampsia, we recommend low dose (e.g., 100-150 mg daily) aspirin therapy initiated at or before 16 weeks gestation.	Strong for	Reviewed, New-added	Reviewed, New-replaced	14, 15

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2018 CPG Recommendation #	2018 CPG Recommendation Text	2018 CPG Strength of Recommendation	2018 CPG Recommendation Category	2023 CPG Recommendation Category	2023 CPG Recommendation #
18.	We recommend antenatal progesterone therapy in consultation with an advanced prenatal care provider (e.g., obstetrician or maternal-fetal medicine) for women at high risk for recurrent preterm delivery and who meet the generally accepted inclusion criteria.	Strong for	Not reviewed, Amended	Reviewed, Deleted	NA
19.	We suggest offering women greater than 44 years of age planned delivery at 38 weeks gestational age to reduce the risk of stillbirth.	Weak for	Reviewed, New-added	Not reviewed, Deleted	NA
20.	We suggest that women who have undergone bariatric surgery should be evaluated for nutritional deficiencies and need for nutritional supplementation where indicated (e.g., vitamin B12, folate, iron, calcium).	Weak for	Reviewed, New-replaced	Not reviewed, Amended	18
21.	For pregnant women who have undergone bariatric surgery, there is insufficient evidence to recommend for or against the routine supplementation of vitamins A, D, E, or K.	Neither for nor Against	Reviewed, New-replaced	Not reviewed, Amended	19
22.	We suggest that pregnant women with a history of gastric bypass surgery be evaluated by a surgeon with bariatric expertise.	Weak for	Reviewed, Amended	Not reviewed, Deleted	NA

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## **Appendix E. Participant List**

#### CDR Colleen C. Blosser, MSN, RN

Deputy Program Manager, Healthcare Delivery, Solutions Delivery Division, J6 Defense Health Agency Fairfax Station, Virginia

#### LTC Michael Bybel, DO, FAAFP

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Deputy Director Women's Reproductive Health Women's Health Office Veterans Health Administration Washington, DC

#### Michael E. Clark, MD, FACOG

Staff Physician, Madigan Army Medical Center Spanaway, Washington

#### LCDR Christine Higgins, DNP

Staff Certified Midwife NMRTC Twentynine Palms Twentynine Palms, California

#### Sophia Hill-Smith, MSN, RN

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#### Carrie Kairys, DNP, FNP-BC

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#### Adam Edward Lang, PharmD

Chief, Health Management
Deputy Chief, Department of Pharmacy
McDonald Army Health Center
Assistant Clinical Professor, Department of
Family Medicine and Population Health
Virginia Commonwealth University School
of Medicine
Fort Eustis, Virginia

#### Ashley Lauria, MA, RD, LDN, IBCLC

Memorandum of Understanding (MOU)
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## LTC Leigh Anne Lechanski, PT, DPT, OCS

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Veterans Affairs National Pharmacy
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#### Laura Miller, MD

Medical Director of Reproductive Mental Health VA Central Office Evanston, Illinois

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#### Amanda Owens, DO, FACOG

Staff Physician
Walter Reed National Military Medical
Center
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#### Lauren Pachl, LCSW, CLC

Maternity Care Coordinator and Lactation Counselor Robley Rex VA Medical Center Louisville, Kentucky

# Elizabeth Patton, MD, MPhil, MSc, FACOG

Division Director of Generalist OBGYN Boston University School of Medicine Boston, Massachusetts

#### Tammy Tenace, BSN, MS, ARNP-BC

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#### Kristi Shearer, PhD

Psychologist Madigan Army Medical Center Gig Harbor, Washington

#### Lt Col Dalia Wenckus, MFM MD, FACOG

Maternal Fetal Medicine Specialty
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Staff Physician, Department of OB/GYN, Maternal Fetal Medicine Division San Antonio, Texas

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## Appendix F: Literature Review Search Terms and Strategy

Table F-1. EMBASE and MEDLINE in EMBASE.com Syntax

Question	Set #	Concept	Strategy
	1.	Perinatal Depression/ Postnatal Depression	'perinatal depression'/exp OR 'postnatal depression'/exp
	2.	Pregnancy	'expectant mother'/exp OR 'parameters concerning the fetus, newborn and pregnancy'/exp OR 'perinatal care'/exp OR 'perinatal period'/exp OR 'pregnancy'/exp OR 'pregnant woman'/exp OR 'prenatal care'/exp OR 'prenatal period'/exp OR antenatal:ti,kw OR antepartum:ti,kw OR gestation*:ti,kw OR matern*:ti,kw OR obstet*:ti,kw OR 'peri natal':ti,kw OR perinatal:ti,kw OR 'pre natal':ti,kw OR prenatal:ti,kw OR pregnan*:ti,kw OR trimester*:ti,kw
	3.	Postpartum	'postnatal care'/exp OR 'pregnancy outcome'/exp OR 'puerperium'/exp OR 'after delivery':ti,kw OR 'following delivery':ti,kw OR 'post natal':ti,kw OR postnatal:ti,kw OR 'post neonatal':ti,kw OR postneonatal:ti,kw OR 'post partum':ti,kw OR postpartum:ti,kw OR puerperal:ti,kw OR puerperium:ti,kw
KQ 1	4.	Mental Health	'bipolar disorder'/exp OR 'depression'/exp OR 'infanticide'/de OR 'mental disease'/exp OR 'mental disease assessment'/exp OR 'mood disorder'/exp OR 'psychiatric diagnosis'/de OR 'psychological aspect'/de OR 'psychosis'/exp OR 'schizophrenia'/exp OR 'suicidal behavior'/exp OR bipolar:ti OR depress*:ti OR infanticid*:ti OR mania*:ti OR manic:ti OR 'mental health':ti OR mood*:ti OR neonaticid*:ti OR schiz*:ti OR psychotic*:ti OR psychos*:ti OR suicid*:ti OR ((behavior*:ti OR behaviour*:ti OR mental*:ti OR psychiatric*:ti OR psycho*:ti) AND (condition*:ti OR diagnos*:ti OR disorder*:ti OR distress*:ti OR health:ti OR ill*:ti OR issue*:ti OR problem*:ti OR well*:ti OR unwell:ti))
	5.	Mental Health Interventions	'cognitive behavioral therapy'/de OR 'cognitive therapy'/de OR 'mindfulness'/de OR 'mindfulness-based stress reduction'/de OR 'nutrition'/de OR 'peer'/de OR 'peer group'/de OR 'prevention and control'/de/mj OR 'psychotherapy'/de OR 'self care'/de OR 'self help'/de OR 'sleep hygiene'/de OR 'sleep therapy'/de OR 'social support'/de OR 'support group'/de OR cbt:ti OR cognitive:ti OR counsel*:ti OR diet:ti OR educat*:ti OR exercis*:ti OR group*:ti OR meditat*:ti OR mindful*:ti OR 'new mom*':ti OR 'new mother*':ti OR nutrition*:ti OR psychotherap*:ti OR peer*:ti OR rose:ti OR 'self care':ti OR 'self help':ti OR sleep:ti OR support*:ti OR 'survivor mom*' OR therapy:ti OR yoga:ti OR ('reach out' AND 'stay strong') OR ((ipt:ti OR iptp:ti) AND (interpersonal:ti OR psychotherap*:ti)) OR ('mothers and babies' AND (cbt OR cognitive)) OR ((childbirth:ti OR baby:ti OR babies:ti OR birthing:ti OR infant:ti OR infants:ti OR neonatal:ti OR newborn:ti) AND (class:ti OR classes:ti OR educat*:ti)) OR elimin*:ti OR avoid*:ti OR deterr*:ti OR precaution*:ti OR prevent*:ti OR prophyl*:ti OR protect*:ti OR safeguard*:ti
	6.	Combine Concepts	(#1 AND #5) OR ((#2 OR #3) AND #4 AND #5)

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Question	Set #	Concept	Strategy
KQ 1 (cont.)	7.	Remove Geographic Regions	#6 NOT (afghani*:ti OR africa:ti OR albania*:ti OR algeria*:ti OR angola*:ti OR antigua*:ti OR barbuda*:ti OR armenia*:ti OR azerbaijan*:ti OR bangladesh*:ti OR belize*:ti OR benin*:ti OR burundi*:ti OR bosnia*:ti OR botswan*:ti OR cameroon*:ti OR 'cape verde*':ti OR burundi*:ti OR cambodia*:ti OR cameroon*:ti OR cape verde*':ti OR comoros*:ti OR comgo*:ti OR cuba*:ti OR djibouti*:ti OR dominica*:ti OR comoros*:ti OR congo*:ti OR cuba*:ti OR djibouti*:ti OR dominica*:ti OR 'east timor*':ti OR ecuador*:ti OR egypt*:ti OR 'el salvador':ti OR 'equatorial guinea':ti OR eritrea*:ti OR eswatini*:ti OR grenada*:ti OR guatemala*:ti OR gabon*:ti OR gambia*:ti OR ghana*:ti OR goa:ti OR grenada*:ti OR guatemala*:ti OR guinea*:ti OR juinea bissau':ti OR guyan*:ti OR haiti*:ti OR hondura*:ti OR india:ti OR indonesia*:ti OR kerya*:ti OR kiribati*:ti OR kyrgyzstan*:ti OR laos:ti OR jordan*:ti OR leban*:ti OR kiribati*:ti OR kyrgyzstan*:ti OR laos:ti OR laotian:ti OR leban*:ti OR lesotho:ti OR liberia*:ti OR nation OR nations)):ti) OR macedonian:ti OR madagascar*:ti OR malawi*:ti OR maldives:ti OR mali*:ti OR marshall island*':ti OR mangolia*:ti OR mexico:ti OR morgama*:ti OR morgolia*:ti OR morgolia*:ti OR morgama*:ti OR norgama*:ti OR morgolia*:ti OR morgolia*:ti OR peal*:ti OR peal*:ti OR pleash*:ti OR nigeria*:ti OR north macedonia':ti OR peal*:ti OR peru*:ti OR pleash*:ti OR rajasthan*:ti OR republic of congo':ti OR rwanda*:ti OR salnt kitts and nevis':ti OR salnt lucia*':ti OR saint vincent and the grenadines':ti OR salvador*:ti OR saint lucia*':ti OR saint vincent and the grenadines':ti OR salvador*:ti OR saint lucia*':ti OR saint vincent and the grenadines':ti OR salvador*:ti OR saint lucia*':ti OR saint vincent and the grenadines':ti OR salvador*:ti OR saint lucia*':ti OR saint vincent and the grenadines':ti OR salvador*:ti OR sonoa*:ti OR saint vincent and the grenadines':ti OR salvador*:ti OR sonoa*:ti OR tonga*:ti OR tonga*:t
	8.	Remove Animal Studies	#7 NOT ([animals]/lim NOT [humans]/lim OR ((animal:ti OR animals:ti OR canine*:ti OR dog:ti OR dogs:ti OR feline:ti OR hamster*:ti OR lamb:ti OR lambs:ti OR mice:ti OR monkey:ti OR monkeys:ti OR mouse:ti OR murine:ti OR pig:ti OR piglet*:ti OR pigs:ti OR porcine:ti OR primate*:ti OR rabbit*:ti OR rat:ti OR rats:ti OR rodent*:ti OR sheep*:ti OR swine:ti OR veterinar*:ti OR (vitro:ti NOT vivo:ti)) NOT (fertilis*:ti OR fertiliz*:ti OR human*:ti OR ivf:ti OR patient*:ti OR woman:ti OR women:ti)))
	9.	Remove Unwanted Publication Types	#8 NOT (('book'/de OR 'case report'/de OR 'conference paper'/exp OR 'editorial'/de OR 'letter'/de OR book:it OR chapter:it OR conference:it OR editorial:it OR letter:it OR [conference abstract]/lim OR [conference paper]/lim OR [conference review]/lim OR [editorial]/lim OR [letter]/lim OR abstract:nc OR annual:nc OR conference:nc OR congress:nc OR meeting:nc OR proceedings:nc OR sessions:nc OR symposium:nc OR book:pt) NOT series:pt OR 'conference proceeding':pt OR 'case report':ti OR comment*:ti OR editorial:ti OR letter:ti OR news:ti OR (protocol:ti AND (study:ti OR trial:ti) NOT ('therapy protocol*':ti OR 'treatment protocol*':ti)))

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Question	Set #	Concept	Strategy
KQ 1	10.	Limit to Meta Analyses and Systematic Reviews	#9 AND ('meta analysis'/exp OR 'systematic review'/de OR cochrane:jt OR [cochrane review]/lim OR systematic*:ti OR cochrane*:ti,ab OR metaanaly*:ti,ab OR 'meta analy*':ti,ab OR (search*:ti,ab AND (cinahl*:ti,ab OR databases:ti,ab OR ebsco*:ti,ab OR embase*:ti,ab OR psychinfo*:ti,ab OR psycinfo*:ti,ab OR 'science direct*':ti,ab OR sciencedirect*:ti,ab OR sciencedirect*:ti,ab OR 'web of knowledge*':ti,ab OR 'web of science':ti,ab)) OR ((systematic* NEAR/3 review*):ti,ab)) NOT (((protocol NEXT/3 review):ti) OR 'review protocol':ti OR 'scoping review':ti)
(cont.)	11.	Limit to Randomized Controlled Trials	#9 AND ('random sample'/de OR 'randomization'/de OR 'randomized controlled trial'/exp OR 'phase 3':ti,ab OR 'phase iii':ti,ab OR random*:ti,ab OR rct:ti,ab)
	12.	Combine Concepts	#10 OR #11
	13.	Apply Date Limits	#12 AND [2017-2022]/py AND [04-02-2017]/sd NOT [01-06-2022]/sd
	14.	Limit to English	#13 AND [english]/lim
	15.	Pregnancy	'expectant mother'/exp OR 'parameters concerning the fetus, newborn and pregnancy'/exp OR 'perinatal care'/exp OR 'perinatal period'/exp OR 'pregnancy'/exp OR 'pregnancy disorder'/exp OR 'pregnant woman'/exp OR 'prenatal care'/exp OR 'prenatal period'/exp OR antenatal:ti,kw OR antepartum:ti,kw OR gestation*:ti,kw OR matern*:ti,kw OR obstet*:ti,kw OR 'peri natal':ti,kw OR perinatal:ti,kw OR 'pre natal':ti,kw OR pregnan*:ti,kw OR trimester*:ti,kw
KQ 2	16.	Labor/Delivery/ Childbirth	'birth setting'/exp OR 'cesarean section'/exp OR 'childbirth'/exp OR 'intrapartum care'/exp OR 'labor'/exp OR 'labor complication'/exp OR 'labor induction'/exp OR 'natural childbirth'/exp OR 'obstetric delivery'/exp OR 'vaginal delivery'/exp OR 'vaginal birth after cesarean'/exp OR birth*:ti,kw OR caesarean:ti,kw OR caesarian:ti,kw OR cesarean:ti,kw OR cesarian:ti,kw OR childbirth*:ti,kw OR hypnobirth*:ti,kw OR intrapartum:ti,kw OR labor:ti,kw OR 'vaginal delivery':ti,kw OR vbac:ti,kw
	17.	Postpartum	'postnatal care'/exp OR 'pregnancy outcome'/exp OR 'puerperium'/exp OR 'after delivery':ti,kw OR 'following delivery':ti,kw OR 'post natal':ti,kw OR postnatal:ti,kw OR 'post neonatal':ti,kw OR postneonatal:ti,kw OR 'post partum':ti,kw OR postpartum:ti,kw OR puerperal:ti,kw OR puerperium:ti,kw
	18.	Pelvic Floor Muscle Dysfunction	'pelvic floor disorder'/exp OR 'pelvic floor muscle training'/de OR 'pelvic floor prolapse'/exp OR 'pelvis floor'/exp OR 'pelvis floor muscle'/exp OR ((pelvic:ti OR pelvis:ti) AND floor:ti) OR ((biofeedback:ti,ab OR electrostimulation:ti,ab OR kegel:ti,ab OR exercise*:ti,ab OR neurofeedback:ti,ab OR 'physical therapy':ti,ab OR physiotherapy:ti,ab OR rehabilitation:ti,ab OR stimulation:ti,ab OR training:ti,ab) AND 'pelvic floor':ti,ab)
	19.	Combine Concepts	(#15 OR #16 OR #17) AND #18

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Question	Set #	Concept	Strategy
KQ 2 (cont.)	20.	Remove Geographic Regions	#19 NOT (afghani*:ti OR africa:ti OR albania*:ti OR algeria*:ti OR angola*:ti OR antigua*:ti OR barbuda*:ti OR armenia*:ti OR azerbaijan*:ti OR bangladesh*:ti OR belize*:ti OR benin*:ti OR bhutan*:ti OR bolivia*:ti OR bosnia*:ti OR botswan*:ti OR brazil*:ti OR 'burkina faso':ti OR burundi*:ti OR cambodia*:ti OR cameroon*:ti OR 'cape verde*':ti OR 'central african republic':ti OR chad:ti OR china:ti OR colombia*:ti OR comoros*:ti OR congo*:ti OR cuba*:ti OR dijbouti*:ti OR dominica*:ti OR 'east timor*:ti OR ecuador*:ti OR egypt*:ti OR 'el salvador':ti OR 'equatorial guinea':ti OR gambia*:ti OR eswatini*:ti OR ethiopia*:ti OR fiji*:ti OR gabon*:ti OR gambia*:ti OR ghana*:ti OR goa:ti OR grenada*:ti OR guatemala*:ti OR guinea*:ti OR lor grenada*:ti OR guatemala*:ti OR guinea*:ti OR hondura*:ti OR india:ti OR indonesia*:ti OR kenya*:ti OR kiribati*:ti OR kyrgyzstan*:ti OR india:ti OR laotian:ti OR leban*:ti OR lesotho:ti OR liberia*:ti OR laos:ti OR laotian:ti OR leban*:ti OR lesotho:ti OR liberia*:ti OR libya*:ti OR country OR countries OR nation OR nations)):ti) OR macedonian:ti OR madagascar*:ti OR malawi*:ti OR maldives:ti OR mali*:ti OR marshall island*':ti OR mangolia*:ti OR mexico:ti OR micronesia*:ti OR nigeria*:ti OR nongolia*:ti OR nepal*:ti OR nicaragua*:ti OR niger:ti OR nigeria*:ti OR north macedonia':ti OR pakistan*:ti OR palestin*:ti OR rajasthan*:ti OR republic of congo':ti OR rvanda*:ti OR 'saint kitts and nevis':ti OR salma*:ti OR samoa*:ti OR 'saint vincent and the grenadines':ti OR salvador*:ti OR samoa*:ti OR 'saint vincent and the grenadines':ti OR salvador*:ti OR samoa*:ti OR 'saint vincent and the grenadines':ti OR salvador*:ti OR samoa*:ti OR 'saint vincent and the grenadines':ti OR salvador*:ti OR samoa*:ti OR 'saint vincent and the grenadines':ti OR salvador*:ti OR samoa*:ti OR 'saint vincent and the grenadines':ti OR south sudan*:ti OR samoa*:ti OR south sudan*:ti OR tonja*:ti OR tonja
	21.	Remove Animal Studies	#20 NOT ([animals]/lim NOT [humans]/lim OR ((animal:ti OR animals:ti OR canine*:ti OR dog:ti OR dogs:ti OR feline:ti OR hamster*:ti OR lamb:ti OR lambs:ti OR mice:ti OR monkey:ti OR monkeys:ti OR mouse:ti OR murine:ti OR pig:ti OR piglet*:ti OR pigs:ti OR porcine:ti OR primate*:ti OR rabbit*:ti OR rat:ti OR rats:ti OR rodent*:ti OR sheep*:ti OR swine:ti OR veterinar*:ti OR (vitro:ti NOT vivo:ti)) NOT (fertilis*:ti OR fertiliz*:ti OR human*:ti OR ivf:ti OR patient*:ti OR woman:ti OR women:ti)))
	22.	Remove Unwanted Publication Types	#21 NOT (('book'/de OR 'case report'/de OR 'conference paper'/exp OR 'editorial'/de OR 'letter'/de OR book:it OR chapter:it OR conference:it OR editorial:it OR letter:it OR [conference abstract]/lim OR [conference paper]/lim OR [conference review]/lim OR [editorial]/lim OR [letter]/lim OR abstract:nc OR annual:nc OR conference:nc OR congress:nc OR meeting:nc OR proceedings:nc OR sessions:nc OR symposium:nc OR book:pt) NOT series:pt OR 'conference proceeding':pt OR 'case report':ti OR comment*:ti OR editorial:ti OR letter:ti OR news:ti OR (protocol:ti AND (study:ti OR trial:ti) NOT ('therapy protocol*':ti OR 'treatment protocol*':ti)))

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Question	Set #	Concept	Strategy
KQ 2 (cont.)	23.	Limit to Meta Analyses and Systematic Reviews	#22 AND ('meta analysis'/exp OR 'systematic review'/de OR cochrane:jt OR [cochrane review]/lim OR systematic*:ti OR cochrane*:ti,ab OR metaanaly*:ti,ab OR 'meta analy*':ti,ab OR (search*:ti,ab AND (cinahl*:ti,ab OR databases:ti,ab OR ebsco*:ti,ab OR embase*:ti,ab OR psychinfo*:ti,ab OR psychinfo*:ti,ab OR science direct*':ti,ab OR sciencedirect*:ti,ab OR sciencedirect*:ti,ab OR systematic*:ti,ab OR 'web of knowledge*':ti,ab OR 'web of science':ti,ab)) OR ((systematic* NEAR/3 review*):ti,ab)) NOT (((protocol NEXT/3 review):ti) OR 'review protocol':ti OR 'scoping review':ti)
(cont.)	24.	Limit to Randomized Controlled Trials	#22 AND ('random sample'/de OR 'randomization'/de OR 'randomized controlled trial'/exp OR 'phase 3':ti,ab OR 'phase iii':ti,ab OR random*:ti,ab OR rct:ti,ab)
	25.	Combine Concepts	#23 OR #24
	26.	Apply Date Limits	#25 AND [2017-2022]/py AND [04-02-2017]/sd NOT [01-06-2022]/sd
	27.	Limit to English	#26 AND [english]/lim
	28.	Pregnancy	'expectant mother'/exp OR 'parameters concerning the fetus, newborn and pregnancy'/exp OR 'perinatal care'/exp OR 'perinatal period'/exp OR 'pregnancy'/exp OR 'pregnancy disorder'/exp OR 'pregnant woman'/exp OR 'prenatal care'/exp OR 'prenatal period'/exp OR antenatal:ti,kw OR antepartum:ti,kw OR gestation*:ti,kw OR matern*:ti,kw OR obstet*:ti,kw OR 'peri natal':ti,kw OR perinatal:ti,kw OR 'pre natal':ti,kw OR pregnan*:ti,kw OR trimester*:ti,kw
KQ 3	29.	Postpartum	'postnatal care'/exp OR 'pregnancy outcome'/exp OR 'puerperium'/exp OR 'after delivery':ti,kw OR 'following delivery':ti,kw OR 'post natal':ti,kw OR postnatal:ti,kw OR 'post neonatal':ti,kw OR postneonatal:ti,kw OR 'post partum':ti,kw OR postpartum:ti,kw OR puerperal:ti,kw OR puerperium:ti,kw
	30.	Hypertension Monitoring	'blood pressure monitoring'/exp OR ((ambulatory:ti OR 'blood pressure':ti OR eclampsia:ti OR 'eclampsia and preeclampsia'/exp/mj OR 'elevated blood pressure'/mj OR ghtn:ti OR hellp:ti OR htn:ti OR hypertens*:ti OR 'hypertension'/mj OR 'maternal hypertension'/exp OR 'pre eclampsia:ti' OR preeclampsia:ti) AND (measur*:ti OR screen*:ti OR monitor*:ti OR 'non invasive procedure'/de OR 'screening'/mj)) OR ((bp:ti,kw OR 'blood pressure':ti,kw OR eclamps*:ti,kw OR hypertens*:ti,kw OR preeclampsia:ti,kw) AND (cloud:ti,kw OR bluetooth:ti,kw OR 'blue tooth':ti,kw OR home* OR remote:ti,kw OR wireless:ti,kw))
	31.	Combine Concepts	(#28 OR #29) AND #30

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Question	Set #	Concept	Strategy
KQ 3 (cont.)	32.	Remove Geographic Regions	#31 NOT (afghani*:ti OR africa:ti OR albania*:ti OR algeria*:ti OR angola*:ti OR antigua*:ti OR barbuda*:ti OR armenia*:ti OR azerbaijan*:ti OR bangladesh*:ti OR belize*:ti OR benin*:ti OR bhutan*:ti OR bolivia*:ti OR bosnia*:ti OR boswan*:ti OR cameroon*:ti OR 'burkina faso':ti OR burundi*:ti OR cambodia*:ti OR cameroon*:ti OR 'cape verde*':ti OR 'central african republic':ti OR chad:ti OR china:ti OR colombia*:ti OR comoros*:ti OR congo*:ti OR cuba*:ti OR djibouti*:ti OR dominica*:ti OR 'east timor*':ti OR ecuador*:ti OR egypt*:ti OR 'el salvador':ti OR 'equatorial guinea':ti OR gambia*:ti OR gypt*:ti OR 'el salvador':ti OR fiji*:ti OR gabon*:ti OR gambia*:ti OR gyana*:ti OR goa:ti OR grenada*:ti OR guatemala*:ti OR guinea*:ti OR lor guinea bissau':ti OR guyan*:ti OR haiti*:ti OR herzegovina*:ti OR 'lor y coast':ti OR india:ti OR indonesia*:ti OR kenya*:ti OR kiribati*:ti OR kyrgyzstan*:ti OR jamaica*:ti OR jordan*:ti OR kenya*:ti OR kiribati*:ti OR kyrgyzstan*:ti OR laos:ti OR (((low OR middle) NEXT/4 ((country OR countries OR nation OR nations)):ti) OR macedonian:ti OR madagascar*:ti OR malawi*:ti OR maldives:ti OR mali*:ti OR myanmar*:ti OR namibia*:ti OR mexico:ti OR micronesia*:ti OR nigeria*:ti OR nongolia*:ti OR nepal*:ti OR nicaragua*:ti OR nigeria*:ti OR nongolia*:ti OR parguay*:ti OR peru*:ti OR palestin*:ti OR rajasthan*:ti OR rajasthan*:ti OR samoa*:ti OR samoa*:ti OR saint kitts and nevis':ti OR samoa*:ti OR samoa*:ti OR saint kitts and nevis':ti OR samoa*:ti OR siant vincent and the grenadines':ti OR salvador*:ti OR samoa*:ti OR siant vincent and the grenadines':ti OR salvador*:ti OR senegal*:ti OR seychell*:ti OR siant vincent and the grenadines':ti OR salvador*:ti OR samoa*:ti OR siant vincent and the grenadines':ti OR salvador*:ti OR senegal*:ti OR south sudan*:ti OR seychell*:ti OR siant vincent and the grenadines':ti OR senegal*:ti OR seychell*:ti OR siant vincent and the grenadines':ti OR salvador*:ti OR senegal*:ti OR toga*:ti OR toga*:ti OR tunisia*:ti OR tunisia*:ti OR tobag*:ti OR toga
	33.	Remove Animal Studies	#32 NOT ([animals]/lim NOT [humans]/lim OR ((animal:ti OR animals:ti OR canine*:ti OR dog:ti OR dogs:ti OR feline:ti OR hamster*:ti OR lamb:ti OR lambs:ti OR mice:ti OR monkey:ti OR monkeys:ti OR mouse:ti OR murine:ti OR pig:ti OR piglet*:ti OR pigs:ti OR porcine:ti OR primate*:ti OR rabbit*:ti OR rat:ti OR rats:ti OR rodent*:ti OR sheep*:ti OR swine:ti OR veterinar*:ti OR (vitro:ti NOT vivo:ti)) NOT (fertilis*:ti OR fertiliz*:ti OR human*:ti OR ivf:ti OR patient*:ti OR woman:ti OR women:ti)))
	34.	Remove Unwanted Publication Types	#33 NOT (('book'/de OR 'case report'/de OR 'conference paper'/exp OR 'editorial'/de OR 'letter'/de OR book:it OR chapter:it OR conference:it OR editorial:it OR letter:it OR [conference abstract]/lim OR [conference paper]/lim OR [conference review]/lim OR [editorial]/lim OR [letter]/lim OR abstract:nc OR annual:nc OR conference:nc OR congress:nc OR meeting:nc OR proceedings:nc OR sessions:nc OR symposium:nc OR book:pt) NOT series:pt OR 'conference proceeding':pt OR 'case report':ti OR comment*:ti OR editorial:ti OR letter:ti OR news:ti OR (protocol:ti AND (study:ti OR trial:ti) NOT ('therapy protocol*':ti OR 'treatment protocol*':ti)))

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Question	Set #	Concept	Strategy
KQ 3 (cont.)	35.	Limit to Meta Analyses and Systematic Reviews	#34 AND ('meta analysis'/exp OR 'systematic review'/de OR cochrane:jt OR [cochrane review]/lim OR systematic*:ti OR cochrane*:ti,ab OR metaanaly*:ti,ab OR 'meta analy*':ti,ab OR (search*:ti,ab AND (cinahl*:ti,ab OR databases:ti,ab OR ebsco*:ti,ab OR embase*:ti,ab OR psychinfo*:ti,ab OR psychinfo*:ti,ab OR science direct*':ti,ab OR sciencedirect*:ti,ab OR sciencedirect*:ti,ab OR systematic*:ti,ab OR 'web of knowledge*':ti,ab OR 'web of science':ti,ab)) OR ((systematic* NEAR/3 review*):ti,ab)) NOT (((protocol NEXT/3 review):ti) OR 'review protocol':ti OR 'scoping review':ti)
	36.	Limit to Randomized Controlled Trials	#34 AND ('random sample'/de OR 'randomization'/de OR 'randomized controlled trial'/exp OR 'phase 3':ti,ab OR 'phase iii':ti,ab OR random*:ti,ab OR rct:ti,ab)
	37.	Combine Concepts	#35 OR #36
	38.	Apply Date Limits	#37 AND [2017-2022]/py AND [04-02-2017]/sd NOT [01-06-2022]/sd
	39.	Limit to English	#38 AND [english]/lim
KQ 4	40.	Pregnancy	'expectant mother'/exp OR 'parameters concerning the fetus, newborn and pregnancy'/exp OR 'perinatal care'/exp OR 'perinatal period'/exp OR 'pregnancy'/exp OR 'pregnancy disorder'/exp OR 'pregnant woman'/exp OR 'prenatal care'/exp OR 'prenatal period'/exp OR antenatal:ti,kw OR antepartum:ti,kw OR gestation*:ti,kw OR matern*:ti,kw OR obstet*:ti,kw OR 'peri natal':ti,kw OR perinatal:ti,kw OR 'pre natal':ti,kw OR prenatal:ti,kw OR pregnan*:ti,kw OR trimester*:ti,kw
	41.	Postpartum	'postnatal care'/exp OR 'pregnancy outcome'/exp OR 'puerperium'/exp OR 'after delivery':ti,kw OR 'following delivery':ti,kw OR 'post natal':ti,kw OR postnatal:ti,kw OR 'post neonatal':ti,kw OR postneonatal:ti,kw OR 'post partum':ti,kw OR postpartum:ti,kw OR puerperal:ti,kw OR puerperium:ti,kw

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Question	Set #	Concept	Strategy
KQ 4 (cont.)	42.	Telemedicine	'bluetooth'/mj OR 'cloud computing'/mj OR 'e therapy'/de OR 'internet'/mj OR 'mobile application'/de OR 'mobile phone'/de OR 'short message service'/de OR 'social media'/mj OR 'tablet computer'/de OR 'teleconsultation'/de OR 'telehealth'/de OR 'telemedicine'/de OR 'telemonitoring'/de OR 'telephone'/mj OR 'teletherapy'/de OR 'text messaging'/de OR 'video consultation'/de OR 'videoconferencing'/de OR 'web-based intervention'/de OR 'wireless communication'/mj OR (((distance OR mobil* OR remote OR tele* OR virtual OR remote OR wireless) NEAR/3 (care OR counsel* OR consult* OR health* OR med* OR monitor* OR therap* OR visit*)):ti) OR android*:ti OR app:ti OR apps:ti OR asynchronous*:ti OR 'blue tooth':ti OR bluetooth:ti OR 'care coordination home telehealth':ti OR ccht:ti OR cellphone*:ti OR cloud:ti OR 'computer based':ti OR cyber*:ti OR digital:ti OR 'e health*:ti OR ehealth*:ti OR facebook:ti OR facetime:ti OR internet:ti OR ipad:ti OR iphone:ti OR 'lap top*':ti OR laptop*:ti OR 'm health*:ti OR mhealth*:ti OR (((mobil* OR portab*) NEXT/1 (application OR based OR computer* OR device* OR health OR intervention* OR program* OR tablet* OR therap*)):ti) OR 'on line':ti OR online:ti OR phone:ti OR phones:ti OR samsung:ti OR 'short messag* service*':ti OR smartphone*:ti OR (((sms OR text) NEXT/2 messag*):ti) OR ((social NEXT/1 (media OR network* OR platform*)):ti) OR software:ti OR synchronous*:ti OR teleconsult*:ti OR teleconsult*:ti OR teleconsult*:ti OR teleconsult*:ti OR telephone*:ti OR telehealth*:ti OR telewoit:ti OR video*:ti OR virtual:ti OR video*:ti OR virtual:ti OR website*:ti OR website*:ti OR wireless:ti OR zoom*:ti
	43.	Combine Concepts	(#40 OR #41) AND #42

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Question	Set #	Concept	Strategy
KQ 4 (cont.)	44.	Remove Geographic Regions	#43 NOT (afghani*:ti OR africa:ti OR albania*:ti OR algeria*:ti OR angola*:ti OR antigua*:ti OR barbuda*:ti OR armenia*:ti OR azerbaijan*:ti OR bangladesh*:ti OR belize*:ti OR benin*:ti OR bhutan*:ti OR bolivia*:ti OR bosnia*:ti OR botswan*:ti OR brazil*:ti OR 'burkina faso':ti OR burundi*:ti OR cambodia*:ti OR cameroon*:ti OR 'cape verde*':ti OR 'central african republic':ti OR chad:ti OR djibouti*:ti OR colombia*:ti OR comoros*:ti OR congo*:ti OR cuba*:ti OR djibouti*:ti OR dominica*:ti OR 'east timor*':ti OR ecuador*:ti OR egypt*:ti OR 'el salvador':ti OR 'equatorial guinea':ti OR gambia*:ti OR ghana*:ti OR ethiopia*:ti OR fiji*:ti OR gabon*:ti OR gambia*:ti OR ghana*:ti OR goa:ti OR grenada*:ti OR guatemala*:ti OR guinea*:ti OR 'guinea bissau':ti OR guyan*:ti OR haiti*:ti OR herzegovina*:ti OR hondura*:ti OR india:ti OR indonesia*:ti OR kenya*:ti OR kiribati*:ti OR kyrgyzstan*:ti OR jamaica*:ti OR jordan*:ti OR kenya*:ti OR kiribati*:ti OR kyrgyzstan*:ti OR laos:ti OR laotian:ti OR leban*:ti OR lesotho:ti OR liberia*:ti OR madagascar*:ti OR malawi*:ti OR maldives:ti OR mali*:ti OR 'marshall island*':ti OR mauritania*:ti OR mexico:ti OR micronesia*:ti OR moldova*:ti OR mongolia*:ti OR nepal*:ti OR nicaragua*:ti OR nigeria*:ti OR nigeria*:ti OR namibia*:ti OR nepal*:ti OR nicaragua*:ti OR nigeria*:ti OR rajasthan*:ti OR paraguay*:ti OR peru*:ti OR palestin*:ti OR salvador*:ti OR saint lucia*:ti OR 'saint vincent and the grenadines':ti OR salvador*:ti OR seychell*:ti OR 'saint vincent and the grenadines':ti OR salvador*:ti OR samoa*:ti OR 'saint vincent and the grenadines':ti OR salvador*:ti OR samoa*:ti OR 'saint vincent and the grenadines':ti OR south sudan*:ti OR seychell*:ti OR siant vincent and the grenadines':ti OR solvador*:ti OR samoa*:ti OR 'saint vincent and the grenadines':ti OR solvador*:ti OR seychell*:ti OR 'saint vincent and the grenadines':ti OR solvador*:ti OR seychell*:ti OR 'saint vincent and the grenadines':ti OR turkmenistan*:ti OR tonga*:ti OR ukrain*:ti OR thaiti OR thailati:ti OR turkme
	45.	Remove Animal Studies	#44 NOT ([animals]/lim NOT [humans]/lim OR ((animal:ti OR animals:ti OR canine*:ti OR dogs:ti OR dogs:ti OR feline:ti OR hamster*:ti OR lamb:ti OR lambs:ti OR mice:ti OR monkey:ti OR monkeys:ti OR mouse:ti OR murine:ti OR pig:ti OR piglet*:ti OR pigs:ti OR porcine:ti OR primate*:ti OR rabbit*:ti OR rat:ti OR rats:ti OR rodent*:ti OR sheep*:ti OR swine:ti OR veterinar*:ti OR (vitro:ti NOT vivo:ti)) NOT (fertilis*:ti OR fertiliz*:ti OR human*:ti OR ivf:ti OR patient*:ti OR woman:ti OR women:ti)))
	46.	Remove Unwanted Publication Types	#45 NOT (('book'/de OR 'case report'/de OR 'conference paper'/exp OR 'editorial'/de OR 'letter'/de OR book:it OR chapter:it OR conference:it OR editorial:it OR letter:it OR [conference abstract]/lim OR [conference paper]/lim OR [conference review]/lim OR [editorial]/lim OR [letter]/lim OR abstract:nc OR annual:nc OR conference:nc OR congress:nc OR meeting:nc OR proceedings:nc OR sessions:nc OR symposium:nc OR book:pt) NOT series:pt OR 'conference proceeding':pt OR 'case report':ti OR comment*:ti OR editorial:ti OR letter:ti OR news:ti OR (protocol:ti AND (study:ti OR trial:ti) NOT ('therapy protocol*':ti OR 'treatment protocol*':ti)))

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Question	Set #	Concept	Strategy
KQ 4	47.	Limit to Meta Analyses and Systematic Reviews	#46 AND ('meta analysis'/exp OR 'systematic review'/de OR cochrane:jt OR [cochrane review]/lim OR systematic*:ti OR cochrane*:ti,ab OR metaanaly*:ti,ab OR 'meta analy*':ti,ab OR (search*:ti,ab AND (cinahl*:ti,ab OR databases:ti,ab OR ebsco*:ti,ab OR embase*:ti,ab OR psychinfo*:ti,ab OR psychinfo*:ti,ab OR science direct*':ti,ab OR sciencedirect*:ti,ab OR sciencedirect*:ti,ab OR systematic*:ti,ab OR 'web of knowledge*':ti,ab OR 'web of science':ti,ab)) OR ((systematic* NEAR/3 review*):ti,ab)) NOT (((protocol NEXT/3 review):ti) OR 'review protocol':ti OR 'scoping review':ti)
(cont.)	48.	Limit to Randomized Controlled Trials	#46 AND ('random sample'/de OR 'randomization'/de OR 'randomized controlled trial'/exp OR 'phase 3':ti,ab OR 'phase iii':ti,ab OR random*:ti,ab OR rct:ti,ab)
	49.	Combine Concepts	#47 OR #48
	50.	Apply Date Limits	#49 AND [2017-2022]/py AND [04-02-2017]/sd NOT [01-06-2022]/sd
	51.	Limit to English	#50 AND [english]/lim
KQ 5	52.	Pregnancy	'expectant mother'/exp OR 'parameters concerning the fetus, newborn and pregnancy'/exp OR 'perinatal care'/exp OR 'perinatal period'/exp OR 'pregnancy'/exp OR 'pregnancy disorder'/exp OR 'pregnant woman'/exp OR 'prenatal care'/exp OR 'prenatal period'/exp OR antenatal:ti,kw OR antepartum:ti,kw OR gestation*:ti,kw OR matern*:ti,kw OR obstet*:ti,kw OR 'peri natal':ti,kw OR perinatal:ti,kw OR 'pre natal':ti,kw OR pregnan*:ti,kw OR trimester*:ti,kw
	53.	Labor/Delivery/ Childbirth	'birth setting'/exp OR 'cesarean section'/exp OR 'childbirth'/exp OR 'intrapartum care'/exp OR 'labor'/exp OR 'labor complication'/exp OR 'labor induction'/exp OR 'natural childbirth'/exp OR 'obstetric delivery'/exp OR 'vaginal delivery'/exp OR 'vaginal birth after cesarean'/exp OR birth*:ti,kw OR caesarean:ti,kw OR caesarian:ti,kw OR cesarean:ti,kw OR cesarian:ti,kw OR childbirth*:ti,kw OR hypnobirth*:ti,kw OR intrapartum:ti,kw OR labor:ti,kw OR 'vaginal delivery':ti,kw OR vbac:ti,kw
	54.	Postpartum	'postnatal care'/exp OR 'pregnancy outcome'/exp OR 'puerperium'/exp OR 'after delivery':ti,kw OR 'following delivery':ti,kw OR 'post natal':ti,kw OR postnatal:ti,kw OR 'post neonatal':ti,kw OR postneonatal:ti,kw OR 'post partum':ti,kw OR postpartum:ti,kw OR puerperal:ti,kw OR puerperium:ti,kw
	55.	Anxiety/Distress/ Trauma/	('anxiety'/mj OR 'distress syndrome'/mj OR 'fear'/mj OR 'fear of childbirth'/de OR 'maternal stress'/de OR 'mental stress'/mj OR 'panic'/mj OR 'phobia'/mj OR 'psychotrauma'/mj OR 'posttraumatic stress disorder'/de OR afraid:ti OR anxiety:ti OR anxious*:ti OR distress*:ti OR fear*:ti OR panic*:ti OR ptsd:ti OR phobia*:ti OR phobic:ti OR 'post traumatic':ti OR posttraumatic:ti OR scare*:ti OR stress*:ti OR worry:ti OR worrie*:ti OR trauma*:ti) NOT (stress*:ti AND (heat* OR incontinen* OR oxidative:ti OR urin*:ti) OR 'respiratory distress':ti)
	56.	Combine Sets	(#52 OR #53 OR #54) AND #55

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Question	Set #	Concept	Strategy
KQ 5 (cont.)	57.	Remove Geographic Regions	#56 NOT (afghani*:ti OR africa:ti OR albania*:ti OR algeria*:ti OR angola*:ti OR antigua*:ti OR barbuda*:ti OR armenia*:ti OR azerbaijan*:ti OR bangladesh*:ti OR belize*:ti OR benin*:ti OR bhutan*:ti OR bolivia*:ti OR bosnia*:ti OR botswan*:ti OR brazil*:ti OR 'burkina faso':ti OR burundi*:ti OR cambodia*:ti OR cameroon*:ti OR 'cape verde*':ti OR 'central african republic':ti OR chad:ti OR china:ti OR colombia*:ti OR comoros*:ti OR congo*:ti OR cuba*:ti OR dijibouti*:ti OR dominica*:ti OR 'east timor*:ti OR ecuador*:ti OR egypt*:ti OR 'el salvador':ti OR 'equatorial guinea':ti OR gambia*:ti OR gyot*:ti OR ghana*:ti OR goa:ti OR grenada*:ti OR guatemala*:ti OR guinea*:ti OR 'guinea bissau':ti OR gyoyan*:ti OR haiti*:ti OR herzegovina*:ti OR 'or younea bissau':ti OR jordan*:ti OR kenya*:ti OR kiribati*:ti OR kyrgyzstan*:ti OR jamaica*:ti OR jordan*:ti OR kenya*:ti OR kiribati*:ti OR kyrgyzstan*:ti OR laos:ti OR laotian:ti OR leban*:ti OR lesotho:ti OR liberia*:ti OR imadagascar*:ti OR malawi*:ti OR macadonian:ti OR madagascar*:ti OR malawi*:ti OR maldives:ti OR mala*:ti OR malawi*:ti OR morcoc*:ti OR mala*:ti OR mala*:ti OR morcoc*:ti OR morconesia*:ti OR nigeria*:ti OR namibia*:ti OR nepal*:ti OR nicaragua*:ti OR niger:ti OR nigeria*:ti OR norcoc*:ti OR pakistan*:ti OR palestin*:ti OR rajasthan*:ti OR republic of congo':ti OR revanda*:ti OR saint lucia*':ti OR saint vincent and the grenadines':ti OR salvador*:ti OR samoa*:ti OR 'saint vincent and the grenadines':ti OR salvador*:ti OR samoa*:ti OR saint vincent and the grenadines':ti OR salvador*:ti OR samoa*:ti OR saint vincent and the grenadines':ti OR salvador*:ti OR samoa*:ti OR 'saint vincent and the grenadines':ti OR salvador*:ti OR samoa*:ti OR saint vincent and the grenadines':ti OR salvador*:ti OR samoa*:ti OR 'saint vincent and the grenadines':ti OR salvador*:ti OR samoa*:ti OR 'saint vincent and the grenadines':ti OR salvador*:ti OR samoa*:ti OR tanzania*:ti
	58.	Remove Animal Studies	#57 NOT ([animals]/lim NOT [humans]/lim OR ((animal:ti OR animals:ti OR canine*:ti OR dog:ti OR dogs:ti OR feline:ti OR hamster*:ti OR lamb:ti OR lambs:ti OR mice:ti OR monkey:ti OR monkeys:ti OR mouse:ti OR murine:ti OR pig:ti OR piglet*:ti OR pigs:ti OR porcine:ti OR primate*:ti OR rabbit*:ti OR rat:ti OR rats:ti OR rodent*:ti OR sheep*:ti OR swine:ti OR veterinar*:ti OR (vitro:ti NOT vivo:ti)) NOT (fertilis*:ti OR fertiliz*:ti OR human*:ti OR ivf:ti OR patient*:ti OR woman:ti OR women:ti)))
	59.	Remove Unwanted Publication Types	#58 NOT (('book'/de OR 'case report'/de OR 'conference paper'/exp OR 'editorial'/de OR 'letter'/de OR book:it OR chapter:it OR conference:it OR editorial:it OR letter:it OR [conference abstract]/lim OR [conference paper]/lim OR [conference review]/lim OR [editorial]/lim OR [letter]/lim OR abstract:nc OR annual:nc OR conference:nc OR congress:nc OR meeting:nc OR proceedings:nc OR sessions:nc OR symposium:nc OR book:pt) NOT series:pt OR 'conference proceeding':pt OR 'case report':ti OR comment*:ti OR editorial:ti OR letter:ti OR news:ti OR (protocol:ti AND (study:ti OR trial:ti) NOT ('therapy protocol*':ti OR 'treatment protocol*':ti)))

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Question	Set#	Concept	Strategy
	60.	Limit to Meta Analyses and Systematic Reviews	#59 AND ('meta analysis'/exp OR 'systematic review'/de OR cochrane:jt OR [cochrane review]/lim OR systematic*:ti OR cochrane*:ti,ab OR metaanaly*:ti,ab OR 'meta analy*':ti,ab OR (search*:ti,ab AND (cinahl*:ti,ab OR databases:ti,ab OR ebsco*:ti,ab OR embase*:ti,ab OR psychinfo*:ti,ab OR psycinfo*:ti,ab OR 'science direct*':ti,ab OR sciencedirect*:ti,ab OR sciencedirect*:ti,ab OR systematic*:ti,ab OR 'web of knowledge*':ti,ab OR 'web of science':ti,ab)) OR ((systematic* NEAR/3 review*):ti,ab)) NOT (((protocol NEXT/3 review):ti) OR 'review protocol':ti OR 'scoping review':ti)
KQ 5 (cont.)	61.	Limit to Randomized Controlled Trials	#59 AND ('random sample'/de OR 'randomization'/de OR 'randomized controlled trial'/exp OR 'phase 3':ti,ab OR 'phase iii':ti,ab OR random*:ti,ab OR rct:ti,ab)
	62.	Limit to Prognostic/ Cohort Studies	#59 AND ('cohort analysis'/mj OR 'cohort effect'/mj OR 'prognosis'/mj OR cohort*:ti OR death*:ti OR 'follow up':ti OR incidence:ti OR mortalit*:ti OR outcome*:ti OR predict*:ti OR prognos*:ti)
	63.	Combine Concepts	#60 OR #61 OR #62
	64.	Apply Date Limits	#63 AND [2017-2022]/py AND [04-02-2017]/sd NOT [01-06-2022]/sd
	65.	Limit to English	#64 AND [english]/lim
	66.	Maternal Hypertension	'eclampsia and preeclampsia'/exp OR 'maternal hypertension'/exp OR eclamps*:ti OR ghtn:ti OR preeclampsia:ti OR ((hypertens*:ti OR 'high blood pressure':ti) AND (gestation*:ti OR matern*:ti OR mother*:ti OR pregnan*:ti))
	67.	Hypertension (general)	'hypertension'/mj OR ((hypertens*:ti OR 'high blood pressure':ti OR htn:ti) NOT (gestation*:ti OR matern*:ti OR mother*:ti OR pregnan*))
KQ 6	68.	Pregnancy	'expectant mother'/exp OR 'parameters concerning the fetus, newborn and pregnancy'/exp OR 'perinatal care'/exp OR 'perinatal period'/exp OR 'pregnancy'/exp OR 'pregnancy disorder'/exp OR 'pregnant woman'/exp OR 'prenatal care'/exp OR 'prenatal period'/exp OR antenatal:ti,kw OR antepartum:ti,kw OR gestation*:ti,kw OR matern*:ti,kw OR obstet*:ti,kw OR 'peri natal':ti,kw OR perinatal:ti,kw OR 'pre natal':ti,kw OR pregnan*:ti,kw OR trimester*:ti,kw
	69.	Interventions for Hypertension	('acetylsalicylic acid'/exp OR 'antihypertensive agent'/exp OR 'body weight loss'/exp OR 'diet therapy'/exp OR 'exercise'/exp OR 'mindfulness'/exp OR 'mindfulness-based stress reduction'/exp OR 'weight loss program'/exp OR 'sleep hygiene'/exp OR antihypertens*:ti OR aspirin*:ti OR bmi:ti OR diet*:ti OR exercise*:ti OR obes*:ti OR meditat* OR mindful*.ti OR nutrition*:ti OR overweight:ti OR sleep* OR weigh*:ti OR yoga:ti) NOT (stress*:ti AND (heat* OR incontinen* OR oxidative:ti OR urin*:ti) OR 'respiratory distress':ti)
	70.	Combine Concepts	(#66 OR (#67 AND #68)) AND #69

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Question	Set #	Concept	Strategy
KQ 6 (cont.)	71.	Remove Geographic Regions	#70 NOT (afghani*:ti OR africa:ti OR albania*:ti OR algeria*:ti OR angola*:ti OR antigua*:ti OR barbuda*:ti OR armenia*:ti OR azerbaijan*:ti OR bangladesh*:ti OR belize*:ti OR benin*:ti OR bhutan*:ti OR bolivia*:ti OR bosnia*:ti OR botswan*:ti OR brazil*:ti OR 'burkina faso':ti OR burundi*:ti OR cambodia*:ti OR cameroon*:ti OR 'cape verde*':ti OR 'central african republic':ti OR chad:ti OR china:ti OR colombia*:ti OR comoros*:ti OR congo*:ti OR cuba*:ti OR djibouti*:ti OR colombia*:ti OR 'east timor*':ti OR ecuador*:ti OR egypt*:ti OR 'el salvador':ti OR 'equatorial guinea':ti OR gambia*:ti OR gastinia*:ti OR goa:ti OR grenada*:ti OR guatemala*:ti OR guinea*:ti OR 'guinea bissau':ti OR grenada*:ti OR guatemala*:ti OR guinea*:ti OR 'guinea bissau':ti OR guyan*:ti OR haiti*:ti OR herzegovina*:ti OR hondura*:ti OR india:ti OR india:ti OR kenya*:ti OR kenya*:ti OR kiribati*:ti OR kyrgyzstan*:ti OR laos:ti OR laotian:ti OR leban*:ti OR lesotho:ti OR liberia*:ti OR libya*:ti OR (((low OR middle) NEXT/4 (country OR countries OR nation OR nations)):ti) OR macedonian:ti OR madagascar*:ti OR malawi*:ti OR malavi*:ti OR micronesia*:ti OR mongolia*:ti OR morcoc*:ti OR mozambiq*:ti OR nigeria*:ti OR namibia*:ti OR nepal*:ti OR nicaragua*:ti OR nigeriti OR nigeria*:ti OR ronth macedonia':ti OR pakistan*:ti OR palestin*:ti OR rajasthan*:ti OR republic of congo':ti OR rwanda*:ti OR saint luica*:ti OR salvador*:ti OR saint luica*:ti OR saint vincent and the grenadines':ti OR salvador*:ti OR saint luica*:ti OR sierra leone*:ti OR solomon islands':ti OR senegal*:ti OR saint luica*:ti OR saint vincent and the grenadines':ti OR salvador*:ti OR solomon islands*:ti OR solomon islands':ti OR solomon*:ti OR topa*:ti OR topa*:ti OR topa*:ti OR thai:ti OR thai:ti OR thai:ti OR thai:ti OR thai:ti OR vanuatu*:ti OR venezuela*:ti OR vereda*:ti OR wereda*:ti OR
	72.	Remove Animal Studies	#71 NOT ([animals]/lim NOT [humans]/lim OR ((animal:ti OR animals:ti OR canine*:ti OR dog:ti OR dogs:ti OR feline:ti OR hamster*:ti OR lamb:ti OR lambs:ti OR mice:ti OR monkey:ti OR monkeys:ti OR mouse:ti OR murine:ti OR pig:ti OR piglet*:ti OR pigs:ti OR porcine:ti OR primate*:ti OR rabbit*:ti OR rat:ti OR rats:ti OR rodent*:ti OR sheep*:ti OR swine:ti OR veterinar*:ti OR (vitro:ti NOT vivo:ti)) NOT (fertilis*:ti OR fertiliz*:ti OR human*:ti OR patient*:ti OR woman:ti OR women:ti)))
	73.	Remove Unwanted Publication Types	#72 NOT (('book'/de OR 'case report'/de OR 'conference paper'/exp OR 'editorial'/de OR 'letter'/de OR book:it OR chapter:it OR conference:it OR editorial:it OR letter:it OR [conference abstract]/lim OR [conference paper]/lim OR [conference review]/lim OR [editorial]/lim OR [letter]/lim OR abstract:nc OR annual:nc OR conference:nc OR congress:nc OR meeting:nc OR proceedings:nc OR sessions:nc OR symposium:nc OR book:pt) NOT series:pt OR 'conference proceeding':pt OR 'case report':ti OR comment*:ti OR editorial:ti OR letter:ti OR news:ti OR (protocol:ti AND (study:ti OR trial:ti) NOT ('therapy protocol*':ti OR 'treatment protocol*':ti)))

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Question	Set #	Concept	Strategy
KQ 6 (cont.)	74.	Limit to Meta Analyses and Systematic Reviews	#73 AND ('meta analysis'/exp OR 'systematic review'/de OR cochrane:jt OR [cochrane review]/lim OR systematic*:ti OR cochrane*:ti,ab OR metaanaly*:ti,ab OR 'meta analy*:ti,ab OR (search*:ti,ab AND (cinahl*:ti,ab OR databases:ti,ab OR ebsco*:ti,ab OR embase*:ti,ab OR psychinfo*:ti,ab OR psycinfo*:ti,ab OR 'science direct*':ti,ab OR sciencedirect*:ti,ab OR scopus*:ti,ab OR systematic*:ti,ab OR 'web of knowledge*':ti,ab OR 'web of science':ti,ab)) OR ((systematic* NEAR/3 review*):ti,ab)) NOT (((protocol NEXT/3 review):ti) OR 'review protocol':ti OR 'scoping review':ti)
(Gont.)	75.	Limit to Randomized Controlled Trials	#73 AND ('random sample'/de OR 'randomization'/de OR 'randomized controlled trial'/exp OR 'phase 3':ti,ab OR 'phase iii':ti,ab OR random*:ti,ab OR rct:ti,ab)
	76.	Combine Concepts	#74 OR #75
	77.	Apply Date Limits	#76 AND [2017-2022]/py AND [04-02-2017]/sd NOT [01-06-2022]/sd
	78.	Limit to English	#77 AND [english]/lim
KQ 7	79.	Pregnancy	'expectant mother'/exp OR 'parameters concerning the fetus, newborn and pregnancy'/exp OR 'perinatal care'/exp OR 'perinatal period'/exp OR 'pregnancy'/exp OR 'pregnancy disorder'/exp OR 'pregnant woman'/exp OR 'prenatal care'/exp OR 'prenatal period'/exp OR antenatal:ti,kw OR antepartum:ti,kw OR gestation*:ti,kw OR matern*:ti,kw OR obstet*:ti,kw OR 'peri natal':ti,kw OR perinatal:ti,kw OR 'pre natal':ti,kw OR prenatal:ti,kw OR trimester*:ti,kw
	80.	Fetus	'embryonic and fetal functions'/exp OR 'fetal growth'/exp OR 'fetal malformation'/exp OR 'fetal monitoring'/exp OR 'fetal viability'/exp OR 'fetus'/exp OR 'fetus development'/exp OR 'fetus disease'/exp OR 'fetus distress'/exp OR 'fetus maturity'/exp OR 'fetus outcome'/exp OR 'fetus serum'/exp OR 'prenatal development'/exp OR fetal:ti OR fetus:ti OR foetal:ti OR foetus:ti
	81.	Aneuploidy	'aneuploidy'/exp OR 'down syndrome'/exp OR 'edwards syndrome'/exp OR 'monosomy'/exp OR 'klinefelter syndrome'/exp OR 'pentasomy'/exp OR 'tetrasomy'/exp OR 'trisomy'/exp OR 'turner syndrome'/exp OR aneuploid*:ti OR monosom*:ti OR nullisom*:ti OR pentasom*:ti OR tetrasom*:ti OR trisom*:ti OR (((down* OR edward* OR klinefelter* OR patau* OR turner* OR william* OR 'williams beuren') NEXT/1 syndrome):ti)
	82.	Screening (General)	'prenatal diagnosis'/exp OR 'prenatal screening'/exp OR (((perinatal OR prenatal) NEAR/2 (diagnos* OR screen* OR test*)):ti)
	83.	Non-invasive Screening	'fetus echography'/exp OR 'non invasive measurement'/exp OR 'preimplantation genetic screening'/exp OR nipt:ti OR 'noninvasive prenatal':ti OR 'non invasive prenatal:ti' OR ultraso*:ti OR ((dating:ti OR booking:ti) AND (scan*:ti OR ultraso*:ti))
	84.	Less-invasive Screening	'maternal serum screening'/exp OR 'uterine cervix mucus'/exp OR 'trophoblast'/exp OR 'cf dna':ti OR cfdna:ti OR cellfree:ti OR 'cell-free':ti OR 'serum screen*':ti OR trophoblast*:ti OR ((cervix:ti OR cervical:ti) AND (aspirat*:ti OR mucus:ti OR swab*:ti))

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Question	Set #	Concept	Strategy
	85.	Invasive Screening	'amniocentesis'/exp OR 'chorion villus sampling'/exp OR 'cordocentesis'/exp OR 'fetoscopy'/exp OR 'nuchal translucency measurement'/exp OR 'umbilical cord blood'/exp OR amniocentesis:ti OR cordocentesis:ti OR 'chorionic villus':ti OR embryoscop*:ti OR fetoscop*:ti OR 'nuchal fold':ti OR 'nuchal thickness':ti OR 'nuchal translucency':ti OR (pubs:ti AND umbilical:ti) OR 'umbilical cord blood':ti
	86.	Combine Concepts	(#79 OR #80) AND #81 AND (#82 OR #83 OR #84 OR #85)
KQ 7 (cont.)	87.	Remove Geographic Regions	#86 NOT (afghani*:ti OR africa:ti OR albania*:ti OR algeria*:ti OR angola*:ti OR antigua*:ti OR barbuda*:ti OR armenia*:ti OR azerbaijan*:ti OR bangladesh*:ti OR belize*:ti OR benin*:ti OR bhutan*:ti OR bolivia*:ti OR bosnia*:ti OR botswan*:ti OR cameroon*:ti OR 'cape verde*':ti OR burundi*:ti OR cambodia*:ti OR cameroon*:ti OR 'cape verde*':ti OR 'central african republic':ti OR chad:ti OR china:ti OR colombia*:ti OR comoros*:ti OR congo*:ti OR cuba*:ti OR djibouti*:ti OR dominica*:ti OR comoros*:ti OR congo*:ti OR cuba*:ti OR djibouti*:ti OR dominica*:ti OR 'east timor*':ti OR ecuador*:ti OR egypt*:ti OR 'el salvador':ti OR 'eaytatorial guinea':ti OR efitrea*:ti OR eswatini*:ti OR ethiopia*:ti OR fiji*:ti OR gabon*:ti OR gambia*:ti OR ghana*:ti OR goa:ti OR grenada*:ti OR guatemala*:ti OR guinea*:ti OR ly 'guinea bissau':ti OR guyan*:ti OR haiti*:ti OR herzegovina*:ti OR hondura*:ti OR india:ti OR indonesia*:ti OR kenya*:ti OR kiribati*:ti OR kyrgyzstan*:ti OR laos:ti OR laotian:ti OR leban*:ti OR lesotho:ti OR liberia*:ti OR libya*:ti OR (((low OR middle) NEXT/4 (country OR countries OR nation OR nations)):ti) OR macedonian:ti OR madagascar*:ti OR malawi*:ti OR malawi*:ti OR malawi*:ti OR malawi*:ti OR moroco*:ti OR moronesia*:ti OR moronesia*:ti OR moronesia*:ti OR moroco*:ti OR nonesia*:ti OR nonesia
	88.	Remove Animal Studies	#87 NOT ([animals]/lim NOT [humans]/lim OR ((animal:ti OR animals:ti OR canine*:ti OR dog:ti OR dogs:ti OR feline:ti OR hamster*:ti OR lamb:ti OR lambs:ti OR mice:ti OR monkey:ti OR monkeys:ti OR mouse:ti OR murine:ti OR pig:ti OR piglet*:ti OR pigs:ti OR porcine:ti OR primate*:ti OR rabbit*:ti OR rat:ti OR rats:ti OR rodent*:ti OR sheep*:ti OR swine:ti OR veterinar*:ti OR (vitro:ti NOT vivo:ti)) NOT (fertilis*:ti OR fertiliz*:ti OR human*:ti OR ivf:ti OR patient*:ti OR woman OR women)))

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Question	Set#	Concept	Strategy
	89.	Remove Unwanted Publication Types	#88 NOT (('book'/de OR 'case report'/de OR 'conference paper'/exp OR 'editorial'/de OR 'letter'/de OR book:it OR chapter:it OR conference:it OR editorial:it OR letter:it OR [conference abstract]/lim OR [conference paper]/lim OR [conference review]/lim OR [editorial]/lim OR [letter]/lim OR abstract:nc OR annual:nc OR conference:nc OR congress:nc OR meeting:nc OR proceedings:nc OR sessions:nc OR symposium:nc OR book:pt) NOT series:pt OR 'conference proceeding':pt OR 'case report':ti OR comment*:ti OR editorial:ti OR letter:ti OR news:ti OR (protocol:ti AND (study:ti OR trial:ti) NOT ('therapy protocol*':ti OR 'treatment protocol*':ti)))
KQ 7 (cont.)	90.	Limit to Meta Analyses and Systematic Reviews	#89 AND ('meta analysis'/exp OR 'systematic review'/de OR cochrane:jt OR [cochrane review]/lim OR systematic*:ti OR cochrane*:ti,ab OR metaanaly*:ti,ab OR 'meta analy*':ti,ab OR (search*:ti,ab AND (cinahl*:ti,ab OR databases:ti,ab OR ebsco*:ti,ab OR embase*:ti,ab OR psychinfo*:ti,ab OR psycinfo*:ti,ab OR science direct*':ti,ab OR sciencedirect*:ti,ab OR sciencedirect*:ti,ab OR 'web of knowledge*':ti,ab OR 'web of science':ti,ab)) OR ((systematic* NEAR/3 review*):ti,ab)) NOT (((protocol NEXT/3 review):ti) OR 'review protocol':ti OR 'scoping review':ti)
	91.	Limit to Randomized Controlled Trials	#89 AND ('random sample'/de OR 'randomization'/de OR 'randomized controlled trial'/exp OR 'phase 3':ti,ab OR 'phase iii':ti,ab OR random*:ti,ab OR rct:ti,ab)
	92.	Diagnostic Studies	#89 AND ('diagnostic accuracy'/exp OR 'diagnostic test accuracy study'/exp OR 'sensitivity and specificity'/de OR diagnos*:ti OR 'sensitivity and specificity':ti OR sensitiv*:ti)
	93.	Combine Concepts	#90 OR #91 OR #92
	94.	Apply Date Limits	#93 AND [2017-2022]/py AND [04-02-2017]/sd NOT [01-06-2022]/sd
	95.	Limit to English	#94 AND [english]/lim
	96.	Gestational Diabetes	'pregnancy diabetes mellitus'/exp
KQ 8	97.	Pregnancy	'expectant mother'/exp OR 'parameters concerning the fetus, newborn and pregnancy'/exp OR 'perinatal care'/exp OR 'perinatal period'/exp OR 'pregnancy'/exp OR 'pregnant woman'/exp OR 'prenatal care'/exp OR 'prenatal period'/exp OR antenatal:ti,kw OR antepartum:ti,kw OR gestation*:ti,kw OR matern*:ti,kw OR obstet*:ti,kw OR 'peri natal':ti,kw OR perinatal:ti,kw OR 'pre natal':ti,kw OR prenatal:ti,kw OR trimester*:ti,kw
	98.	Diabetes	'diabetes mellitus'/de OR diab*:ti
	99.	Screening	'screening'/exp OR detect*:ti OR diagnos*:ti OR identif*:ti OR screen*:ti OR test*:ti
	100.	Combine Sets	(#96 OR (#97 AND #98)) AND #99

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Question	Set #	Concept	Strategy
KQ 8 (cont.)	101.	Remove Geographic Areas	#100 NOT (afghani*:ti OR africa:ti OR albania*:ti OR algeria*:ti OR angola*:ti OR antigua*:ti OR barbuda*:ti OR armenia*:ti OR azerbaijan*:ti OR bangladesh*:ti OR belize*:ti OR benin*:ti OR bhutan*:ti OR bolivia*:ti OR bosnia*:ti OR botswan*:ti OR cameroon*:ti OR 'cape verde*':ti OR 'central african republic':ti OR chad:ti OR china:ti OR colombia*:ti OR comoros*:ti OR congo*:ti OR cuba*:ti OR djibouti*:ti OR dominica*:ti OR 'east timor*':ti OR ecuador*:ti OR egypt*:ti OR elsalvador':ti OR 'east timor*':ti OR ecuador*:ti OR egypt*:ti OR elsalvador':ti OR gipator*:ti OR gabon*:ti OR gambia*:ti OR ghana*:ti OR goa:ti OR grenada*:ti OR guatemala*:ti OR guinea*:ti OR 'guinea bissau':ti OR indonesia*:ti OR haiti*:ti OR horzegovina*:ti OR hondura*:ti OR lod india:ti OR indonesia*:ti OR kenya*:ti OR kiribati*:ti OR kyrgyzstan*:ti OR laos:ti OR laotian:ti OR leban*:ti OR lesotho:ti OR liberia*:ti OR libya*:ti OR (((low OR middle) NEXT/4 (country OR countries OR nation OR nations)):ti) OR macedonian:ti OR madagascar*:ti OR malawi*:ti OR malawi*:ti OR mongolia*:ti OR mongolia*:ti OR morcoc*:ti OR molamia*:ti OR mongolia*:ti OR nepal*:ti OR nicaragua*:ti OR nigeria*:ti OR north macedonia':ti OR peru*:ti OR plaesin*:ti OR nigeria*:ti OR north macedonia':ti OR peru*:ti OR plaesin*:ti OR nigeria*:ti OR north macedonia':ti OR peru*:ti OR plaesin*:ti OR nigeria*:ti OR north macedonia':ti OR peru*:ti OR plaesin*:ti OR nigeria*:ti OR north macedonia':ti OR peru*:ti OR plaesin*:ti OR nigeria*:ti OR north macedonia':ti OR peru*:ti OR plaesin*:ti OR salvador*:ti OR saint lucia*:ti OR saint vincent and the grenadines':ti OR salvador*:ti OR saint lucia*:ti OR saint vincent and the grenadines':ti OR salvador*:ti OR saint lucia*:ti OR saint vincent and the grenadines':ti OR salvador*:ti OR saint lucia*:ti OR saint vincent and the grenadines':ti OR salvador*:ti OR saint lucia*:ti OR sudan*:ti OR turnsania*:ti OR turnsani
	102.	Remove Animal Studies	#101 NOT ([animals]/lim NOT [humans]/lim OR ((animal:ti OR animals:ti OR canine*:ti OR dog:ti OR dogs:ti OR feline:ti OR hamster*:ti OR lamb:ti OR lambs:ti OR mice:ti OR monkey:ti OR monkeys:ti OR mouse:ti OR murine:ti OR pig:ti OR piglet*:ti OR pigs:ti OR porcine:ti OR primate*:ti OR rabbit*:ti OR rat:ti OR rats:ti OR rodent*:ti OR sheep*:ti OR swine:ti OR veterinar*:ti OR (vitro:ti NOT vivo:ti)) NOT (fertilis*:ti OR fertiliz*:ti OR human*:ti OR ivf:ti OR patient*:ti OR woman:ti OR women:ti)))
	103.	Remove Unwanted Publication Types	#102 NOT (('book'/de OR 'case report'/de OR 'conference paper'/exp OR 'editorial'/de OR 'letter'/de OR book:it OR chapter:it OR conference:it OR editorial:it OR letter:it OR [conference abstract]/lim OR [conference paper]/lim OR [conference review]/lim OR [editorial]/lim OR [letter]/lim OR abstract:nc OR annual:nc OR conference:nc OR congress:nc OR meeting:nc OR proceedings:nc OR sessions:nc OR symposium:nc OR book:pt) NOT series:pt OR 'conference proceeding':pt OR 'case report':ti OR comment*:ti OR editorial:ti OR letter:ti OR news:ti OR (protocol:ti AND (study:ti OR trial:ti) NOT ('therapy protocol*':ti OR 'treatment protocol*':ti)))

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Question	Set#	Concept	Strategy
	104.	Limit to Meta Analyses and Systematic Reviews	#103 AND ('meta analysis'/exp OR 'systematic review'/de OR cochrane:jt OR [cochrane review]/lim OR systematic*:ti OR cochrane*:ti,ab OR metaanaly*:ti,ab OR 'meta analy*':ti,ab OR (search*:ti,ab AND (cinahl*:ti,ab OR databases:ti,ab OR ebsco*:ti,ab OR embase*:ti,ab OR psychinfo*:ti,ab OR psycinfo*:ti,ab OR 'science direct*':ti,ab OR sciencedirect*:ti,ab OR sciencedirect*:ti,ab OR 'web of knowledge*':ti,ab OR 'web of science':ti,ab)) OR ((systematic* NEAR/3 review*):ti,ab)) NOT (((protocol NEXT/3 review):ti) OR 'review protocol':ti OR 'scoping review':ti)
KQ 8 (cont.)	105.	Limit to Randomized Controlled Trials	#103 AND ('random sample'/de OR 'randomization'/de OR 'randomized controlled trial'/exp OR 'phase 3':ti,ab OR 'phase iii':ti,ab OR random*:ti,ab OR rct:ti,ab)
	106.	Diagnostic Studies	#103 AND ('diagnostic accuracy'/mj OR 'diagnostic test accuracy study'/mj OR 'sensitivity and specificity'/mj OR diagnos*:ti OR 'sensitivity and specificity':ti OR sensitiv*:ti)
	107.	Combine Concepts	#104 OR #105 OR #106
	108.	Apply Date Limits	#107 AND [2017-2022]/py AND [04-02-2017]/sd NOT [01-06-2022]/sd
	109.	Limit to English	#108 AND [english]/lim
	110.	Preterm Delivery	'premature delivery'/exp
	111.	Pregnancy	'expectant mother'/exp OR 'parameters concerning the fetus, newborn and pregnancy'/exp OR 'perinatal care'/exp OR 'perinatal period'/exp OR 'pregnancy disorder'/exp OR 'pregnant woman'/exp OR 'prenatal care'/exp OR 'prenatal period'/exp OR antenatal:ti,kw OR antepartum:ti,kw OR gestation*:ti,kw OR matern*:ti,kw OR obstet*:ti,kw OR 'peri natal':ti,kw OR perinatal:ti,kw OR 'pre natal':ti,kw OR prenatal:ti,kw OR prenatal:ti,kw OR trimester*:ti,kw'
KQ 9	112.	Prematurity	(('pre term' OR preterm OR prematur*) NEAR/3 (babies OR baby OR bear* OR birth* OR born OR childb* OR deliver* OR neonat* OR infan* OR labor OR labour OR previous*)):ti
NQ 3	113.	Interventions to Reduce Preterm Delivery	'bed rest'/de OR 'biological marker'/de OR 'body weight loss'/de OR 'prevention and control'/de OR 'cerclage'/exp OR 'cervical length measurement'/exp OR 'progesterone'/exp OR 'bed rest':ti OR biomarker*:ti OR cerclage:ti OR 'fetal fibronectin':ti OR intervention*:ti OR pessar*:ti OR probiotic*:ti OR progestogen:ti OR progesterone:ti OR rest*:ti OR ((assess*:ti OR length*:ti OR long*:ti OR measur*:ti OR monitor*:ti OR screen*:ti OR ultraso*:ti) AND (cervical:ti OR cervix:ti)) OR (((assess* OR decreas* OR reduc*) NEAR/1 risk*):ti) OR elimin*:ti OR avoid*:ti OR deterr*:ti OR precaution*:ti OR prevent*:ti OR prophyl*:ti OR protect*:ti OR reduc*:ti OR safeguard*:ti
	114.	Combine Concepts	(#110 OR (#111 AND #112)) AND #113

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Question	Set #	Concept	Strategy
KQ 9 (cont.)	115.	Remove Geographic Areas	#114 NOT (afghani*:ti OR africa:ti OR albania*:ti OR algeria*:ti OR angola*:ti OR antigua*:ti OR barbuda*:ti OR armenia*:ti OR azerbaijan*:ti OR bangladesh*:ti OR belize*:ti OR benin*:ti OR bhutan*:ti OR bolivia*:ti OR bosnia*:ti OR botswan*:ti OR cameroon*:ti OR 'cape verde*':ti OR 'central african republic':ti OR chad:ti OR china:ti OR colombia*:ti OR comoros*:ti OR congo*:ti OR cuba*:ti OR djibouti*:ti OR dominica*:ti OR 'east timor*':ti OR ecuador*:ti OR egypt*:ti OR 'el salvador':ti OR 'east timor*':ti OR gambia*:ti OR gyth*:ti OR eswatini*:ti OR geranda*:ti OR guatemala*:ti OR gambia*:ti OR ghana*:ti OR goa:ti OR grenada*:ti OR guatemala*:ti OR guinea*:ti OR lor juinea bissau':ti OR guyan*:ti OR haiti*:ti OR horzegovina*:ti OR hondura*:ti OR india:ti OR indonesia*:ti OR kenya*:ti OR kiribati*:ti OR kyrgyzstan*:ti OR laos:ti OR laotian:ti OR leban*:ti OR lesotho:ti OR liberia*:ti OR libya*:ti OR (((low OR middle) NEXT/4 (country OR countries OR nation OR nations)):ti OR macedonian:ti OR madagascar*:ti OR malawi*:ti OR malawi*:ti OR morocc*:ti OR moramia*:ti OR moroca*:ti OR nation*:ti OR moroma*:ti OR nation*:ti OR moroca*:ti OR nation*:ti OR moroca*:ti OR noroca*:ti OR moroca*:ti OR noroca*:ti O
	116.	Remove Animal Studies	#115 NOT ([animals]/lim NOT [humans]/lim OR ((animal:ti OR animals:ti OR canine*:ti OR dog:ti OR dogs:ti OR feline:ti OR hamster*:ti OR lamb:ti OR lambs:ti OR mice:ti OR monkey:ti OR monkeys:ti OR mouse:ti OR murine:ti OR pig:ti OR piglet*:ti OR pigs:ti OR porcine:ti OR primate*:ti OR rabbit*:ti OR rat:ti OR rats:ti OR rodent*:ti OR sheep*:ti OR swine:ti OR veterinar*:ti OR (vitro:ti NOT vivo:ti)) NOT (fertilis*:ti OR fertiliz*:ti OR ivf:ti OR human*:ti OR patient*:ti OR woman:ti OR women:ti)))
	117.	Remove Unwanted Publication Types	#116 NOT (('book'/de OR 'case report'/de OR 'conference paper'/exp OR 'editorial'/de OR 'letter'/de OR book:it OR chapter:it OR conference:it OR editorial:it OR letter:it OR [conference abstract]/lim OR [conference paper]/lim OR [conference review]/lim OR [editorial]/lim OR [letter]/lim OR abstract:nc OR annual:nc OR conference:nc OR congress:nc OR meeting:nc OR proceedings:nc OR sessions:nc OR symposium:nc OR book:pt) NOT series:pt OR 'conference proceeding':pt OR 'case report':ti OR comment*:ti OR editorial:ti OR letter:ti OR news:ti OR (protocol:ti AND (study:ti OR trial:ti) NOT ('therapy protocol*':ti OR 'treatment protocol*':ti)))

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Question	Set #	Concept	Strategy
KQ 9	118.	Limit to Meta Analyses and Systematic Reviews	#117 AND ('meta analysis'/exp OR 'systematic review'/de OR cochrane:jt OR [cochrane review]/lim OR systematic*:ti OR cochrane*:ti,ab OR metaanaly*:ti,ab OR 'meta analy*:ti,ab OR (search*:ti,ab AND (cinahl*:ti,ab OR databases:ti,ab OR ebsco*:ti,ab OR embase*:ti,ab OR psychinfo*:ti,ab OR psycinfo*:ti,ab OR 'science direct*:ti,ab OR sciencedirect*:ti,ab OR sciencedirect*:ti,ab OR science':ti,ab OR systematic*:ti,ab OR 'web of knowledge*':ti,ab OR 'web of science':ti,ab)) OR ((systematic* NEAR/3 review*):ti,ab)) NOT (((protocol NEXT/3 review):ti) OR 'review protocol':ti OR 'scoping review':ti)
(cont.)	119.	Limit to Randomized Controlled Trials	#117 AND ('random sample'/de OR 'randomization'/de OR 'randomized controlled trial'/exp OR 'phase 3':ti,ab OR 'phase iii':ti,ab OR random*:ti,ab OR rct:ti,ab)
	120.	Combine Concepts	#118 OR #119
	121.	Apply Date Limits	#120 AND [2017-2022]/py AND [04-02-2017]/sd NOT [01-06-2022]/sd
	122.	Limit to English	#121 AND [english]/lim
KQs 10 and 11	123.	Breastfeeding/ Lactation	'attitude to breast feeding'/mj OR 'breast feeding'/mj OR 'breast feeding education'/mj OR 'breast milk expression'/mj OR 'lactation consultant'/mj OR 'breast feed':ti OR breastfeed:ti OR 'breast feed':ti OR breastfeed*:ti OR oR 'breast milk':ti OR breastmilk:ti OR lactation:ti OR ((lactat*:ti OR relactat*:ti) AND (allerg*:ti OR alcohol*:ti OR anaesthes*:ti OR anesthes*:ti OR ankyloglossia:ti OR common:ti OR consult*:ti OR dehydrat*:ti OR dermatitis:ti OR difficult*:ti OR duct*:ti OR eczema:ti OR encourage*:ti OR engorge*:ti OR express*:ti OR extract*:ti OR factor*:ti OR galactagogue:ti OR hypernatremia:ti OR latch*:ti OR ill:ti OR illness*:ti OR inadequate:ti OR infect*:ti OR intake:ti OR 'la leche':ti OR mastitis:ti OR medicine*:ti OR medicat*:ti OR nipple*:ti OR nutri*:ti OR position*:ti OR problem*:ti OR produce*:ti OR production:ti OR pump*:ti OR radiotherap*:ti OR radiat*:ti OR reposition*:ti OR retrognathia:ti OR sick*:ti OR solution*:ti OR suck*:ti OR suggest*:ti OR support*:ti OR surger*:ti OR thrush:ti OR 'tounge tie':ti OR weigh*:ti)) OR (('mother s' NEXT/1 milk):ti) OR ((mother* NEXT/1 milk):ti)

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Question	Set #	Concept	Strategy
KQs 10 and 11	124.	Remove Out of Scope Geographical Areas	#123 NOT (afghani*:ti OR africa:ti OR albania*:ti OR algeria*:ti OR angola*:ti OR antigua*:ti OR barbuda*:ti OR armenia*:ti OR azerbaijan*:ti OR bangladesh*:ti OR belize*:ti OR benin*:ti OR burundi*:ti OR bolivia*:ti OR bosnia*:ti OR botswan*:ti OR cameroon*:ti OR 'cape verde*':ti OR burundi*:ti OR cambodia*:ti OR cameroon*:ti OR cape verde*':ti OR 'central african republic':ti OR chad:ti OR china:ti OR colombia*:ti OR comoros*:ti OR congo*:ti OR cuba*:ti OR djibouti*:ti OR dominica*:ti OR 'east timor*':ti OR ecuador*:ti OR egypt*:ti OR el salvador':ti OR 'east timor*':ti OR gambia*:ti OR egypt*:ti OR el salvador':ti OR 'equatorial guinea':ti OR eritrea*:ti OR eswatini*:ti OR guyan*:ti OR fiji*:ti OR gabon*:ti OR gambia*:ti OR ghana*:ti OR goa:ti OR grenada*:ti OR guatemala*:ti OR guinea*:ti OR lor india:ti OR indonesia*:ti OR iran*:ti OR herzegovina*:ti OR hondura*:ti OR india:ti OR indonesia*:ti OR kenya*:ti OR kiribati*:ti OR kyrgyzstan*:ti OR laos:ti OR laotian:ti OR leban*:ti OR lesotho:ti OR liberia*:ti OR libya*:ti OR (((low OR middle) NEXT/4 (country OR countries OR nation OR nations)):ti) OR macedonian:ti OR madagascar*:ti OR malawi*:ti OR maldives:ti OR mali*:ti OR mongolia*:ti OR morocc*:ti OR mozambiq*:ti OR nigeria*:ti OR nomolia*:ti OR nongolia*:ti OR norocc*:ti OR mozambiq*:ti OR nigeria*:ti OR republic of congo':ti OR pakistan*:ti OR palestin*:ti OR rajasthan*:ti OR 'republic of congo':ti OR rwanda*:ti OR palestin*:ti OR salvador*:ti OR samoa*:ti OR 'saint vincent and the grenadines':ti OR salvador*:ti OR samoa*:ti OR saona*:ti OR solomon islands':ti OR senegal*:ti OR seychell*:ti OR 'saint lucia*':ti OR sudan*:ti OR ushada*:ti OR thai:ti OR thai:ti OR thailand:ti OR thai:ti OR vanuatu*:ti OR voreda*:ti OR vanuada*:ti OR uganda*:ti OR tongo*:ti OR tongo*:ti OR tongo*:ti OR tongo*:ti OR vanuatu*:ti OR venezuela*:ti OR vietnam*:ti OR uzbekistan*:ti OR vanuatu*:ti OR venezuela*:ti OR vietnam*:ti OR venezuela*:ti OR vietnam*:ti OR uzbekistan*:ti OR vanuatu*:ti OR venezuela*:ti OR vietnam*:ti OR viet
	125.	Remove Animal Studies	#124 NOT ([animals]/lim NOT [humans]/lim OR ((animal:ti OR animals:ti OR canine*:ti OR dogs:ti OR feline:ti OR hamster*:ti OR lamb:ti OR lambs:ti OR mice:ti OR monkey:ti OR monkeys:ti OR mouse:ti OR murine:ti OR pig:ti OR piglet*:ti OR pigs:ti OR porcine:ti OR primate*:ti OR rabbit*:ti OR rat:ti OR rats:ti OR rodent*:ti OR sheep*:ti OR swine:ti OR veterinar*:ti OR (vitro:ti NOT vivo:ti)) NOT (fertilis*:ti OR fertiliz*:ti OR human*:ti OR ivf:ti OR patient*:ti OR woman:ti OR women:ti)))
	126.	Remove Unwanted Publication Types	#125 NOT (('book'/de OR 'case report'/de OR 'conference paper'/exp OR 'editorial'/de OR 'letter'/de OR book:it OR chapter:it OR conference:it OR editorial:it OR letter:it OR [conference abstract]/lim OR [conference paper]/lim OR [conference review]/lim OR [editorial]/lim OR [letter]/lim OR abstract:nc OR annual:nc OR conference:nc OR congress:nc OR meeting:nc OR proceedings:nc OR sessions:nc OR symposium:nc OR book:pt) NOT series:pt OR 'conference proceeding':pt OR 'case report':ti OR comment*:ti OR editorial:ti OR letter:ti OR news:ti OR (protocol:ti AND (study:ti OR trial:ti) NOT ('therapy protocol*':ti OR 'treatment protocol*':ti)))

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Question	Set #	Concept	Strategy
KQs 10 and 11 (cont.)	127.	Limit to Meta Analyses and Systematic Reviews	#126 AND ('meta analysis'/exp OR 'systematic review'/de OR cochrane:jt OR [cochrane review]/lim OR systematic*:ti OR cochrane*:ti,ab OR metaanaly*:ti,ab OR 'meta analy*:ti,ab OR (search*:ti,ab AND (cinahl*:ti,ab OR databases:ti,ab OR ebsco*:ti,ab OR embase*:ti,ab OR psychinfo*:ti,ab OR psychinfo*:ti,ab OR science direct*:ti,ab OR sciencedirect*:ti,ab OR sciencedirect*:ti,ab OR science':ti,ab OR systematic*:ti,ab OR 'web of knowledge*':ti,ab OR 'web of science':ti,ab)) OR ((systematic* NEAR/3 review*):ti,ab)) NOT (((protocol NEXT/3 review):ti) OR 'review protocol':ti OR 'scoping review':ti)
	128.	Limit to Randomized Controlled Trials	#126 AND ('random sample'/de OR 'randomization'/de OR 'randomized controlled trial'/exp OR 'phase 3':ti,ab OR 'phase iii':ti,ab OR random*:ti,ab OR rct:ti,ab)
	129.	Combine Sets	#127 OR #128
	130.	Apply Date Limits	#129 AND [2017-2022]/py AND [04-02-2017]/sd NOT [01-06-2022]/sd
	131.	Limit to English	#130 AND [english]/lim
KQ 12	132.	Pregnancy	'expectant mother'/exp OR 'parameters concerning the fetus, newborn and pregnancy'/exp OR 'perinatal care'/exp OR 'perinatal period'/exp OR 'pregnancy disorder'/exp OR 'pregnant woman'/exp OR 'prenatal care'/exp OR 'prenatal period'/exp OR antenatal:ti,kw OR antepartum:ti,kw OR gestation*:ti,kw OR matern*:ti,kw OR obstet*:ti,kw OR 'peri natal':ti,kw OR perinatal:ti,kw OR 'pre natal':ti,kw OR pregnan*:ti,kw OR trimester*:ti,kw
	133.	Labor/Delivery/ Childbirth	'birth setting'/exp OR 'cesarean section'/exp OR 'childbirth'/exp OR 'intrapartum care'/exp OR 'labor'/exp OR 'labor complication'/exp OR 'labor induction'/exp OR 'natural childbirth'/exp OR 'obstetric delivery'/exp OR 'vaginal delivery'/exp OR 'vaginal birth after cesarean'/exp OR birth*:ti,kw OR caesarean:ti,kw OR caesarian:ti,kw OR cesarean:ti,kw OR cesarian:ti,kw OR childbirth*:ti,kw OR hypnobirth*:ti,kw OR intrapartum:ti,kw OR labor:ti,kw OR 'vaginal delivery':ti,kw OR vbac:ti,kw
	134.	Postpartum	'postnatal care'/exp OR 'pregnancy outcome'/exp OR 'puerperium'/exp OR 'after delivery':ti,kw OR 'following delivery':ti,kw OR 'post natal':ti,kw OR postnatal:ti,kw OR 'post neonatal':ti,kw OR postneonatal:ti,kw OR 'post partum':ti,kw OR postpartum:ti,kw OR puerperium:ti,kw
	135.	Specific Racial/ Ethnic groups	'african american'/mj OR 'alaska native'/mj OR 'american indian'/mj OR 'ancestry group'/mj OR 'asian american'/mj OR 'black person'/mj OR 'caucasian'/mj OR 'ethnic difference'/mj OR 'ethnic group'/mj OR 'ethnic or racial aspects'/mj OR 'ethnicity'/mj OR 'hispanic'/mj OR 'medically uninsured'/mj OR 'multiracial person'/mj OR 'pacific islander'/mj OR 'race'/mj OR 'race difference'/mj OR 'racism'/mj OR 'african american':ti OR 'alaska native*':ti OR 'alaskan native*':ti OR 'american indian*':ti OR ancestr*:ti OR bame:ti OR bipoc:ti OR 'bi racial*':ti OR biracial*:ti OR black:ti OR brown:ti OR caucasian:ti OR ethnic*:ti OR 'first nation':ti OR hispanic*:ti OR indigenous:ti OR latina*:ti OR latino*:ti OR latinx:ti OR minorit*:ti OR 'non caucasian*':ti OR noncaucasian*:ti OR 'non white*':ti OR nonwhite*:ti OR 'of colour':ti OR race:ti OR race*:ti OR racial*:ti OR uninsured:ti OR white:ti OR whites:ti OR (((asian OR mexican*) NEAR/5 (america* OR 'united states' OR us OR usa)):ti) OR (((mixed OR multi*) NEAR/2 (ancestr* OR ethnic* OR race* OR racial*)):ti) OR ((native NEAR/2 (american* OR alaskan*)):ti) OR ((pacific NEXT/2 islander*):ti) OR ((without NEXT/3 isurance):ti)

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Question	Set #	Concept	Strategy
	136.	Bias/Racism/ Disparities/ Inequities	'alcoholism'/mj OR 'bias'/exp/mj OR 'disadvantaged population'/mj OR 'disparity'/exp/mj OR 'drug dependence'/mj OR 'economic inequality'/mj OR 'educational status'/mj OR 'health care disparity'/mj OR 'health disparity'/mj OR 'health equity'/mj OR 'homelessness'/mj OR 'housing instability'/mj OR 'income inequality'/mj OR 'prejudice'/exp/mj OR 'rural area'/mj OR 'rural population'/mj OR 'social class'/mj OR 'social determinants of health'/exp/mj OR 'social status'/mj OR 'socioeconomic parameters'/mj OR 'poverty'/mj OR 'urban area'/mj OR 'urban rural difference'/mj OR 'vulnerable population'/mj OR 'wealth inequality'/de OR 'active duty':ti OR bias*:ti OR deploy*:ti OR disadvantage*:ti OR discriminat* OR disparit* OR enlist*:ti OR homeless*:ti OR incarcerat*:ti OR veteran*:ti OR 'social determinant*':ti OR rural*:ti OR urban:ti OR pollut*:ti OR prison*:ti
	137.	Combine Concepts	(#132 OR #133 OR #134) AND (#135 OR #136)
KQ 12 (cont.)	138.	Remove Out-of-Scope Geographical Areas	#137 NOT (afghani*:ti OR africa:ti OR albania*:ti OR algeria*:ti OR angola*:ti OR antigua*:ti OR barbuda*:ti OR armenia*:ti OR azerbaijan*:ti OR bangladesh*:ti OR belize*:ti OR benin*:ti OR bhutan*:ti OR bolivia*:ti OR bosnia*:ti OR botswan*:ti OR cameroon*:ti OR 'cape verde*:ti OR burundi*:ti OR cambodia*:ti OR cameroon*:ti OR 'cape verde*:ti OR central african republic':ti OR cameroon*:ti OR 'cape verde*:ti OR comoros*:ti OR congo*:ti OR cuba*:ti OR china:ti OR colombia*:ti OR comoros*:ti OR congo*:ti OR cuba*:ti OR dijbouti*:ti OR dominica*:ti OR 'east timor*:ti OR ecuador*:ti OR egypt*:ti OR 'el salvador':ti OR 'equatorial guinea':ti OR eritrea*:ti OR eswatini*:ti OR ethiopia*:ti OR jiji*:ti OR gabon*:ti OR gambia*:ti OR ghana*:ti OR goa:ti OR grenada*:ti OR guatemala*:ti OR guinea*:ti OR 'guinea bissau':ti OR guyan*:ti OR haiti*:ti OR herzegovina*:ti OR hondura*:ti OR india:ti OR indonesia*:ti OR kenya*:ti OR kiraya*:ti OR kiraya*:ti OR kiraya*:ti OR kiraya*:ti OR kiraya*:ti OR kiraya*:ti OR laos:ti OR laotian:ti OR leban*:ti OR lesotho:ti OR liberia*:ti OR libya*:ti OR (((low OR middle) NEXT/4 (country OR countries OR nation OR nations)):ti) OR macedonian:ti OR madagascar*:ti OR malawi*:ti OR maldives:ti OR mali*:ti OR moldova*:ti OR mongolia*:ti OR morocc*:ti OR mozambiq*:ti OR nigeria*:ti OR nondova*:ti OR nongolia*:ti OR nepal*:ti OR nicaragua*:ti OR nigeria*:ti OR namibia*:ti OR nepal*:ti OR pakistan*:ti OR palestin*:ti OR rajasthan*:ti OR 'republic of congo':ti OR rwanda*:ti OR salvador*:ti OR salvador*:ti OR samoa*:ti OR 'saint vincent and the grenadines':ti OR salvador*:ti OR saint lucia*:ti OR salvador*:ti OR sudan*:ti OR sudan*:ti OR sudan*:ti OR sudan*:ti OR solomon islands:ti OR south sudan*:ti OR seychell*:ti OR 'seri lanka*:ti OR sudan*:ti OR thai:ti OR thai:ti OR thai:ati OR thai:ati OR thai:ati OR thai:ati OR thai:ati OR thai:ati OR verneauela*:ti OR uganda*:ti OR ukrain*:ti OR uganda*:ti OR uganda*:ti OR ukrain*:ti OR uzbekistan*:ti OR vurkmenistan*:ti OR venezuela*:ti OR vietnam*:ti OR uk

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Question	Set#	Concept	Strategy
KQ 12 (cont.)	139.	Remove Animal Studies	#138 NOT ([animals]/lim NOT [humans]/lim OR ((animal:ti OR animals:ti OR canine*:ti OR dogs:ti OR feline:ti OR hamster*:ti OR lamb:ti OR lambs:ti OR mice:ti OR monkey:ti OR monkeys:ti OR mouse:ti OR murine:ti OR pig:ti OR piglet*:ti OR pigs:ti OR porcine:ti OR primate*:ti OR rabbit*:ti OR rats:ti OR rats:ti OR rodent*:ti OR sheep*:ti OR swine:ti OR veterinar*:ti OR (vitro:ti NOT vivo:ti)) NOT (fertilis*:ti OR fertiliz*:ti OR human*:ti OR ivf:ti OR patient*:ti OR woman:ti OR women:ti)))
	140.	Remove Unwanted Publication Types	#139 NOT (('book'/de OR 'case report'/de OR 'conference paper'/exp OR 'editorial'/de OR 'letter'/de OR book:it OR chapter:it OR conference:it OR editorial:it OR letter:it OR [conference abstract]/lim OR [conference paper]/lim OR [conference review]/lim OR [editorial]/lim OR [letter]/lim OR abstract:nc OR annual:nc OR conference:nc OR congress:nc OR meeting:nc OR proceedings:nc OR sessions:nc OR symposium:nc OR book:pt) NOT series:pt OR 'conference proceeding':pt OR 'case report':ti OR comment*:ti OR editorial:ti OR letter:ti OR news:ti OR (protocol:ti AND (study:ti OR trial:ti) NOT ('therapy protocol*':ti)))
	141.	Limit to Meta Analyses and Systematic Reviews	#140 AND ('meta analysis'/exp OR 'systematic review'/de OR cochrane:jt OR [cochrane review]/lim OR systematic*:ti OR cochrane*:ti,ab OR metaanaly*:ti,ab OR 'meta analy*:ti,ab OR (search*:ti,ab AND (cinahl*:ti,ab OR databases:ti,ab OR ebsco*:ti,ab OR embase*:ti,ab OR psychinfo*:ti,ab OR psychinfo*:ti,ab OR science direct*:ti,ab OR sciencedirect*:ti,ab OR scopus*:ti,ab OR systematic*:ti,ab OR 'web of knowledge*':ti,ab OR 'web of science':ti,ab)) OR ((systematic* NEAR/3 review*):ti,ab)) NOT (((protocol NEXT/3 review):ti) OR 'review protocol':ti OR 'scoping review':ti)
	142.	Limit to RCTs	#140 AND ('random sample'/de OR 'randomization'/de OR 'randomized controlled trial'/exp OR 'phase 3':ti,ab OR 'phase iii':ti,ab OR random*:ti,ab OR rct:ti,ab)
	143.	Combine Concepts	#141 OR #142
	144.	Apply Date Limits	#143 AND [2017-2022]/py AND [04-02-2017]/sd NOT [01-06-2022]/sd
	145.	Limit to English	#144 AND [english]/lim
	146.	Combine all KQ sets #1-12	#14 OR #27 OR #39 OR #51 OR #65 OR #78 OR #95 OR #109 OR #122 OR #131 OR #145
	147.	Remove retraction notices and retracted articles	#146 AND ('retraction notice'/de OR retracted:ti OR retraction:ti OR withdrawn:ti)
	148.	Run Unique ID numbers of retraction notices and retracted articles	I2013294090:id OR I2005929903:id OR I631887209:id OR I632485458:id OR I632077779:id OR I626643489:id OR I623714869:id OR I617629632:id OR I604771320:id OR I369610203:id
	149.	Remove retractions from cumulative results	TOTAL RESULTS – ALL KQs

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## **Appendix G: Abbreviations**

Abbreviation	Definition
17-OHPC	intramuscular progesterone
ACOG	American College of Obstetrics and Gynecologists
ADHD	attention-deficit/hyperactivity disorder
AHRQ	Agency for Healthcare Research and Quality
APLAS	antiphospholipid antibody syndrome
ASC	assessment + standard care
ВМІ	body mass index
СВТ	cognitive behavioral therapy
CDC	Centers for Disease Control and Prevention
CF	cystic fibrosis
cfDNA	prenatal cell-free DNA
cm	centimeter
COI	conflict of interest
CPG	clinical practice guideline
CVD	cardiovascular disease
DASH	Dietary Approaches to Stop Hypertension
DHA	Defense Health Agency
DM	diabetes mellitus
DoD	Department of Defense
DVT/PE	deep vein thrombosis and pulmonary embolism
EBPWG	Evidence-Based Practice Work Group
ECV	external cephalic version
EPDS	Edinburg Postnatal Depression Scale
FDA	Food and Drug Administration
FTF	face-to-face
g	gram
GBS	group B streptococcus
GCT	glucose challenge test
GDM	gestational diabetes mellitus
GHTN	gestational hypertension
GRADE	Grading of Recommendations Assessment, Development, and Evaluation
HDI	Human Development Index
HDP	hypertensive disorders of pregnancy

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Abbreviation	Definition
HELLP	hemolysis, elevated liver enzymes, low platelet count
HIV	human immunodeficiency virus
HPV	human papillomavirus
HSV	herpes simplex virus
HTN	hypertension
ICIQ-SF	International Consultation of Incontinence Questionnaire Short Form
ICU	intensive care unit
IPT	Interpersonal Psychotherapy
IPV	intimate partner violence
kg	kilogram
kg/m²	kilograms per square meter
KQ	key question
LARC	long-acting reversible contraceptive
lb	pound
LOI	list of obstetric indications
m	meter
MFM	maternal-fetal medicine
mg	milligram
MHS	Military Health System
MI	myocardial infarction
mm	millimeter
MMR	measles, mumps, and rubella
MSAFP	maternal serum alpha-fetoprotein
MST	military sexual trauma
MTF	Military Treatment Facility
NAS	neonatal abstinence syndrome
NICE	National Institute for Health and Care Excellence
NICU	neonatal intensive care unit
NIPT	non-invasive prenatal testing
NTD	neural tube defect
PFMT	pelvic floor muscle training
PHQ-9	Patient Health Questionnaire-9
PICOTS	population, intervention, comparison, outcome, timing, and setting
PNBI	patient navigation + behavioral incentives

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Abbreviation	Definition	
PTSD	posttraumatic stress disorder	
QoL	quality of life	
RCT	randomized controlled trial	
RDN	registered dietitian nutritionist	
Rh	Rhesus	
ROM	rupture of membranes	
R4U	Rotterdam reproduction risk reduction	
SIDS	sudden infant death syndrome	
SLE	systemic lupus erythematosus	
SMA	spinal muscular atrophy	
SMBP	self-monitoring blood pressure	
SMM	severe maternal morbidity	
SMS	short message service	
SPRM	severe pregnancy-related morbidity	
SR	systematic review	
TAU	treatment as usual	
Tdap	tetanus, diphtheria, and pertussis	
U.S.	United States	
USPSTF	United States Preventive Services Task Force	
VA	Department of Veterans Affairs	
VHA	Veterans Health Administration	
VZV	varicella zoster virus	

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