Screening for Preeclampsia

US Preventive Services Task Force Recommendation Statement

**IMPORTANCE** Preeclampsia affects approximately 4% of pregnancies in the United States. It is the second leading cause of maternal mortality worldwide and may lead to serious maternal complications, including stroke, eclampsia, and organ failure. Adverse perinatal outcomes for the fetus and newborn include intrauterine growth restriction, low birth weight, and stillbirth. Many of the complications associated with preeclampsia lead to early induction of labor or cesarean delivery and subsequent preterm birth.

**SUBPOPULATION CONSIDERATIONS** Preeclampsia is more prevalent among African American women than among white women. Differences in prevalence may be, in part, due to African American women being disproportionately affected by risk factors for preeclampsia. African American women also have case fatality rates related to preeclampsia 3 times higher than rates among white women. Inequalities in access to adequate prenatal care may contribute to poor outcomes associated with preeclampsia in African American women.

**OBJECTIVE** To update the 1996 US Preventive Services Task Force (USPSTF) recommendation on screening for preeclampsia.

**EVIDENCE REVIEW** The USPSTF reviewed the evidence on the accuracy of screening and diagnostic tests for preeclampsia, the potential benefits and harms of screening for preeclampsia, the effectiveness of risk prediction tools, and the benefits and harms of treatment of screen-detected preeclampsia.

**FINDINGS** Given the evidence that treatment can reduce maternal and perinatal morbidity and mortality, and the well-established accuracy of blood pressure measurements, the USPSTF found adequate evidence that screening for preeclampsia results in a substantial benefit for the mother and infant. In addition, there is adequate evidence to bound the harms of screening and treatment of preeclampsia as no greater than small. Therefore, the USPSTF concludes with moderate certainty that there is a substantial net benefit of screening for preeclampsia in pregnant women.

**CONCLUSIONS AND RECOMMENDATION** The USPSTF recommends screening for preeclampsia in pregnant women with blood pressure measurements throughout pregnancy. (B recommendation)
The US Preventive Services Task Force (USPSTF) makes recommendations about the effectiveness of specific preventive care services for patients without obvious related signs or symptoms.

It bases its recommendations on the evidence of both the benefits and harms of the service and an assessment of the balance. The USPSTF does not consider the costs of providing a service in this assessment.

The USPSTF recognizes that clinical decisions involve more considerations than evidence alone. Clinicians should understand the evidence but individualize decision making to the specific patient or situation. Similarly, the USPSTF notes that policy and coverage decisions involve considerations in addition to the evidence of clinical benefits and harms.

**Summary of Recommendation and Evidence**

The USPSTF recommends screening for preeclampsia in pregnant women with blood pressure measurements throughout pregnancy (B recommendation) (Figure 1).

**Rationale**

**Importance**

Preeclampsia, a relatively common hypertensive disorder occurring during pregnancy, affects approximately 4% of pregnancies in the United States. It has multiple subtypes and potentially serious, even fatal health outcomes. Although pregnant women can have other hypertensive conditions along with preeclampsia, preeclampsia is defined as new-onset hypertension (or, in patients with existing hypertension, worsening hypertension) occurring after 20 weeks of gestation, combined with either new-onset proteinuria (excess protein in the urine) or other signs or symptoms involving multiple organ systems. The specific etiology of preeclampsia is unclear. Preeclampsia can lead to poor health outcomes in both the mother and infant. It is the second leading cause of maternal mortality worldwide and may also lead to other serious maternal complications, including stroke, eclampsia, and organ failure. Adverse perinatal outcomes for the fetus and newborn include intrauterine growth restriction, low birth weight, and stillbirth. Many of the complications associated with preeclampsia lead to early induction of labor or cesarean delivery and subsequent preterm birth.

**Detection**

Obtaining blood pressure measurements to screen for preeclampsia could allow for early identification and diagnosis of the condition, resulting in close surveillance and effective treatment to prevent serious complications. The USPSTF has previously established that there is adequate evidence on the accuracy of blood pressure measurements to screen for preeclampsia.

The USPSTF found adequate evidence that testing for protein in the urine with a dipstick test has low diagnostic accuracy for detecting proteinuria in pregnancy.

**Benefits of Early Detection and Treatment**

Preeclampsia is a complex syndrome. It can quickly evolve into a severe disease that can result in serious, even fatal health outcomes for the mother and infant. The ability to screen for preeclampsia using blood pressure measurements is important to identify and effectively treat a potentially unpredictable and fatal condition. The USPSTF found adequate evidence that the well-established treatments of preeclampsia result in a substantial benefit for the mother and infant by reducing maternal and perinatal morbidity and mortality.

The USPSTF found inadequate evidence on the effectiveness of risk prediction tools (eg, clinical indicators, serum markers, or uterine artery pulsatility index) that would support different screening strategies for predicting preeclampsia.

**Harms of Early Detection and Treatment**

The USPSTF found adequate evidence to bound the potential harms of screening for and treatment of preeclampsia as no greater than small. This assessment was based on the known harms of treatment with antihypertension medications, induced labor, and magnesium sulfate; the likely few harms from screening with blood pressure measurements; and the potential poor maternal and perinatal outcomes resulting from severe untreated preeclampsia and eclampsia. The USPSTF found inadequate evidence on the harms of risk prediction.

**USPSTF Assessment**

The USPSTF concludes with moderate certainty that screening for preeclampsia in pregnant women with blood pressure measurements has a substantial net benefit.

**Clinical Considerations**

**Patient Population Under Consideration**

This recommendation applies to pregnant women without a known diagnosis of preeclampsia or hypertension (Figure 2).

**Assessment of Risk**

All pregnant women are at risk for preeclampsia and should be screened. Important clinical conditions associated with increased risk for preeclampsia include a history of eclampsia or preeclampsia (particularly early-onset preeclampsia), a previous adverse pregnancy outcome, maternal comorbid conditions (including type 1 or 2 diabetes prior to pregnancy, gestational diabetes, chronic hypertension, renal disease, and autoimmune diseases), and multifetal gestation. Other risk factors include nulliparity, obesity, African American race, low socioeconomic status, and advanced maternal age.

In the United States, preeclampsia is more prevalent among African American women than among white women. Differences in prevalence may be, in part, due to African American women being disproportionately affected by risk factors for preeclampsia. African American women have case fatality rates related to preeclampsia 3 times higher than rates among white women (73.5 vs 27.4 per 100 000 cases). Higher prevalence and case fatality rates factor into why African American women are 3 times more likely to die of preeclampsia than white women. Inequalities in access to adequate prenatal care may contribute to poor outcomes associated with preeclampsia in African American women.

**Screening Tests**

Blood pressure measurements are routinely used as a screening tool for preeclampsia. The accuracy of blood pressure measurements has
been well established. Sphygomanometry is the recommended method for blood pressure measurement during pregnancy. The patient should be relaxed prior to measurement. After 5 minutes has elapsed, the patient’s blood pressure should be read while she is in a sitting position, with her legs uncrossed and her back supported. The patient’s arm should be at the level of the right atrium of the heart. If the patient’s upper arm circumference is 33 cm or greater, a large blood pressure cuff should be used. Clinicians should avoid measuring blood pressure in the upper arm in the left lateral position because this position falsely lowers blood pressure readings. 

Recently revised criteria for the diagnosis of preeclampsia include elevated blood pressure (≥140/90 mm Hg on 2 occasions 4 hours apart, after 20 weeks of gestation) and either proteinuria (≥300 mg/dL on a 24-hour urine protein test, protein to creatinine ratio of ≥0.3 mg/mmol, or urine protein dipstick reading >1 if quantitative analysis is not available) or, in the absence of proteinuria, thrombocytopenia, renal insufficiency, impaired liver function, pulmonary edema, or cerebral or visual symptoms.

### Screening Interval

Blood pressure measurements should be obtained during each prenatal care visit throughout pregnancy. If a patient has an elevated blood pressure reading, the reading should be confirmed with repeated measurements. Further diagnostic evaluation and clinical
monitoring are indicated for patients with elevated blood pressure on multiple measurements.

**Treatment**
Management strategies for diagnosed preeclampsia include close fetal and maternal monitoring, antihypertension medications, and magnesium sulfate.4,5

**Additional Approaches to Prevention**
The USPSTF recommends the use of low-dose aspirin (81 mg/d) as preventive medication after 12 weeks of gestation in women at high risk for preeclampsia. This recommendation is available on the USPSTF website (https://www.uspreventiveservicestaskforce.org).

**Other Considerations**

**Research Needs and Gaps**
The USPSTF has identified several research gaps. More research on the complex pathophysiology of preeclampsia is needed to better understand and define its subtypes and their risks to maternal and perinatal health. Once preeclampsia is more clearly defined, screening tools targeting its various subtypes and different study populations may be necessary. Descriptive studies that characterize variations in current preeclampsia screening practices in various types of health care settings would be helpful for identifying alternative screening approaches to evaluate in clinical studies. Research examining screening algorithms and new markers for screening are needed. Studies are needed to further develop and validate tools for risk prediction using rigorous methodology, including appropriate calibration statistics and validated models that use parameters available in routine care (eg, clinical history and clinical testing). Large studies are needed to compare different approaches to screening and effects on maternal and perinatal health outcomes, as well as long-term health outcomes.

Further evaluation of the accuracy of the protein to creatinine ratio in point-of-care urine testing in general populations and repeat testing could better determine the optimal role of the ratio for detecting proteinuria. Research to evaluate the effects of changing diagnostic criteria on screening practices is also needed.

**Discussion**

**Burden of Disease**
Preeclampsia is a complex syndrome defined by new-onset hypertension after 20 weeks of gestation. Proteinuria is often but not always present. Recent guidance indicates that a preeclampsia diagnosis can be made without proteinuria when other clinical signs or symptoms are present.5

Preeclampsia is a multisystem inflammatory syndrome with an unclear etiology and natural history. Some have theorized that it may be composed of multiple subtypes.2-4 Preeclampsia is thought to
involve the abnormal formation of uterine arteries during placental development, possibly resulting in increased oxidative stress and a maternal inflammatory response. However, these 2 processes may occur alone or in combination.

Preeclampsia is a relatively common condition in pregnancy, affecting an estimated 2% to 8% of pregnancies worldwide. Approximately 9% of maternal deaths in the United States are directly attributed to preeclampsia and eclampsia, and more than one-third of severe obstetric complications are associated with preeclampsia. Maternal complications include cerebrovascular disease, placental abruption, disseminated coagulopathy, acute renal failure, cardiopulmonary arrest, and coma. Preterm infants (ie, those born before 37 weeks of gestation) are at increased risk of morbidity and mortality; the risk of poor outcomes increases with earlier delivery.

Fetal and neonatal complications of preeclampsia include intrauterine growth restriction, oligohydramnios, placental abruption, neonatal intensive care unit admission, stillbirth, and neonatal death. Delivery of the fetus is the definitive treatment of preeclampsia; as a result, preeclampsia is a leading cause of medically indicated induced preterm birth and low birth weight in the United States. Infants born to mothers with preeclampsia account for 6% of preterm births and 19% of medically indicated induced preterm births. Most cases of preeclampsia occur after 34 weeks of gestation. Preterm infants (ie, those born before 37 weeks of gestation) are at increased risk of morbidity and mortality; the risk of poor outcomes increases with earlier delivery.

Scope of Review
In 1996, the USPSTF recommended screening for preeclampsia using office-based blood pressure measurement for all pregnant women at the first prenatal visit and periodically throughout the remainder of the pregnancy (B recommendation). The USPSTF commissioned a systematic evidence review to appraise and update the evidence on screening for preeclampsia.

Accuracy of Screening Tests
The USPSTF has previously assessed the accuracy of blood pressure measurements to identify hypertension in adults as adequate.

Accuracy of Diagnostic Tests
There are several tests for proteinuria, including the protein to creatinine ratio urine test, albumin to creatinine ratio urine test, urine protein dipstick test, and 24-hour urine protein test. Although the 24-hour urine protein test is the gold standard, it is not practical for use in primary care. The USPSTF found variable and limited evidence on the accuracy of these tests.

Fourteen studies (n = 1888; 4 good quality and 10 fair quality) assessed the diagnostic accuracy of urine tests in detecting proteinuria compared with 24-hour urine collection (gold standard). Twelve studies assessed the protein to creatinine ratio urine test, 2 studies assessed the albumin to creatinine ratio urine test, and 4 studies assessed the urine protein dipstick test. Evidence on the accuracy of repeat testing was not found. All studies of urine protein test performance were conducted among pregnant women with suspected preeclampsia. Six studies took place in the United States, 4 in the United Kingdom, and 1 each in New Zealand, Canada, Chile, and the Netherlands. Meta-analysis was not performed due to clinical and statistical heterogeneity across the studies.

Sensitivity of the protein to creatinine ratio urine test ranged from 0.65 to 0.96 (I² = 80.5%; 11 studies), with most studies reporting sensitivity greater than 0.81; specificity ranged from 0.49 to 1.00 (I² = 91.8%; 11 studies). The albumin to creatinine ratio urine test (2 studies) had high sensitivity (0.94 and 1.00) and dissimilar specificity (0.94 and 0.68). The automated urine protein dipstick test (4 studies) had sensitivity ranging from 0.22 to 1.00 and specificity ranging from 0.36 to 1.00. One automated urine protein dipstick test had both specificity and sensitivity near 0.80. The remaining studies found either high sensitivity and low specificity or vice versa.

Performance of urine tests for protein varied widely. Issues such as limited information on the diversity of index tests used, study eligibility criteria, prevalence of proteinuria, spectrum bias, and heterogeneity limit the conclusions that can be made about the accuracy of urine tests for protein in routine clinical care. In addition, the studies were conducted among pregnant women with suspected preeclampsia and not in the general asymptomatic pregnant population typically found in primary care.

Evidence suggests that automated tests have better test performance than manually read tests. The time of day of testing is not predictive of performance for the protein to creatinine ratio test.

Effectiveness of Risk Prediction
The USPSTF identified 16 multivariable risk-prediction models evaluated in 4 external validation studies. The risk models had different outcomes: predicting any preeclampsia, early-onset preeclampsia requiring delivery prior to 34 weeks of gestation, or preeclampsia occurring or requiring delivery after 34 weeks of gestation. Five of the 16 externally validated multivariable risk prediction models had good or better discrimination (c statistic ≥0.80), but all had low positive predictive value (4%-39%). There was insufficient information on discrimination and no information on calibration from validation studies to comprehensively evaluate model performance.

In addition, the models used serum markers and Doppler ultrasonography, which are not always available in primary care and are not generally used in the first trimester of routine prenatal care. None of the risk models were based solely on patient history or clinical indicators that could be captured during prenatal visits.

Effectiveness of Early Detection and Treatment
No studies directly compared the effectiveness of screening for preeclampsia on health outcomes in a screened vs unscreened population. One randomized clinical trial examined the benefits and harms of a reduced prenatal visit schedule. This trial was an opportunity to evaluate a specific screening approach compared with the standard of care. This fair-quality trial (n = 2764) among low-risk pregnant women showed that fewer prenatal care visits (9 vs 14 visits) did not result in worse maternal or neonatal health outcomes at delivery. However, the mean difference in the number of visits between groups was smaller than intended (12.0 [SD, 4.2] vs 14.7 [SD, 4.2]; P < .001), and the study was underpowered to detect difference for some health outcomes. In addition, the trial was published nearly 20 years ago, and there have since been changes to clinical practice in the United States.
Although the USPSTF found no recent studies on the direct effectiveness of screening for preeclampsia in improving health outcomes, trial evidence and extensive clinical experience provide evidence of effective treatments for preeclampsia. Antihypertension medications, when indicated, and administration of magnesium sulfate reduce the risk of adverse events. The Magpie Trial (n = 10 141), an international randomized clinical trial of treatment with magnesium sulfate, showed a benefit for preventing eclampsia. Pregnant women diagnosed with severe preeclampsia who were given magnesium sulfate had a 58% lower risk of eclampsia (95% CI, 40%-71%) than women who received placebo.4,24 Incidence of placental abruption was significantly lower in the treatment group, and there was no evidence of short- or longer-term (≤2 years) harms from treatment for the mother or infant.5,24 A Cochrane review of anticonvulsant management of preeclampsia found that treatment with magnesium sulfate reduced the risk of eclampsia by more than half and also likely reduced maternal mortality.4,25

In studies of timing of delivery, trial evidence supports delivery of the fetus to reduce the risk of adverse maternal outcomes in women with preeclampsia after 37 weeks of gestation. The large multicenter HYPITAT (Hypertension and Preeclampsia Intervention Trial at Term) found that immediate delivery of the fetus reduced the risk of composite adverse maternal outcomes in women with preeclampsia after 37 weeks of gestation (relative risk, 0.71 [95% CI, 0.59-0.86]; P < .0001), with no difference in the cesarean delivery rate or neonatal outcomes.4,26

Potential Harms of Screening and Treatment
Previous evidence reviews commissioned by the USPSTF found good-quality evidence that measuring blood pressure has few major harms.13 The USPSTF found limited evidence on the harms of screening for and risk prediction of preeclampsia.

The USPSTF identified 2 fair-quality studies that reported on potential harms of alternative approaches to screening for preeclampsia. Neither study found evidence of harms, but both were underpowered to provide evidence on rare clinical outcomes. One was a fair-quality trial (n = 2764) that found no difference in birth outcomes (eg, low birth weight, preterm birth, or cesarean delivery) when the number of prenatal care visits was reduced from 14 to 9 visits.4,23 As noted earlier, this trial was not sufficiently powered to detect differences for rare outcomes related to preeclampsia such as progression to eclampsia, organ failure, stroke, and death.

The second study was a fair-quality, retrospective, before-after comparison cohort study (n = 1952) of low-income pregnant Hispanic women. The study did not identify any harms related to preeclampsia diagnosis and birth outcomes when targeted urine protein screening was used for specific indications only compared with routine use in prenatal care.4,27 One fair-quality prospective cohort study (n = 255) conducted in Spain found no difference in anxiety before and after counseling on preeclampsia risk and categorization as high or low risk based on results of a multivariable risk prediction model. High-risk women were subject to changes in their clinical care, and the low-risk group received usual care. Measures of anxiety over time did not change but were collected from less than half of the study participants.4,28

The potential harms of treating preeclampsia are well established and include preterm delivery, neonatal complications, cesarean delivery, and adverse effects from magnesium sulfate (eg, nausea, headache, blurry vision, and floppy infant) and antihypertension medications (eg, fatigue, headache, and nausea).29

Estimate of Magnitude of Net Benefit
Given the evidence that treatment can reduce maternal and perinatal morbidity and mortality, and the well-established accuracy of blood pressure measurements, the USPSTF found adequate evidence that screening for preeclampsia results in a substantial benefit for the mother and infant. In addition, there is adequate evidence to bound the harms of screening for and treatment of preeclampsia as no greater than small. Therefore, the USPSTF concludes with moderate certainty that there is a substantial net benefit of screening for preeclampsia in pregnant women.

How Does Evidence Fit With Biological Understanding?
Preeclampsia is a complex syndrome among a range of hypertension disorders occurring during pregnancy. Preeclampsia may involve abnormal formation of uterine arteries during placental development or increased oxidative stress and a maternal inflammatory response (or both).2,4 Although the condition may remain stable until delivery, it can rapidly and unpredictably result in serious, even fatal health outcomes for the mother and infant.4

Response to Public Comment
A draft version of this recommendation statement was posted for public comment on the USPSTF website from September 27 to October 24, 2016. Some comments requested elaboration on the urine protein dipstick test. In response, the USPSTF addressed testing for proteinuria in the Clinical Considerations and Rationale sections. Some comments requested more information on screening intervals, which is provided in the Clinical Considerations. Other comments requested clarification about risk prediction of preeclampsia. In response, the USPSTF added information about risk prediction models to the Rationale and Discussion sections.

Update of Previous USPSTF Recommendation
This recommendation updates the 1996 USPSTF recommendation statement on screening for preeclampsia with blood pressure measurements throughout pregnancy (B recommendation).38

Recommendations of Others
The Society of Obstetricians and Gynaecologists of Canada recommends that the diagnosis of hypertension be based on office or in-hospital blood pressure measurements and that all pregnant women should be assessed for proteinuria. It does not recommend screening with biomarkers or Doppler ultrasonography.30 The National Institute for Health and Care Excellence recommends screening for preeclampsia by obtaining blood pressure measurements and urinalysis for proteinuria at each antenatal visit.31 The American College of Obstetricians and Gynecologists recommends obtaining blood pressure measurements at every prenatal visit and using a detailed medical history to evaluate for risk factors for preeclampsia.32
USPSTF Recommendation: Screening for Preeclampsia

US Preventive Services Task Force

Clinical Review & Education

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REFERENCES