JAMA | US Preventive Services Task Force | RECOMMENDATION STATEMENT

Screening for Bacterial Vaginosis in Pregnant Persons to Prevent Preterm Delivery

US Preventive Services Task Force Recommendation Statement

US Preventive Services Task Force

IMPORTANCE Bacterial vaginosis is common and is caused by a disruption of the microbiological environment in the lower genital tract. In the US, reported prevalence of bacterial vaginosis among pregnant women ranges from 5.8% to 19.3% and is higher in some races/ethnicities. Bacterial vaginosis during pregnancy has been associated with adverse obstetrical outcomes including preterm delivery, early miscarriage, postpartum endometritis, and low birth weight.

OBJECTIVE To update its 2008 recommendation, the USPSTF commissioned a review of the evidence on the accuracy of screening and the benefits and harms of screening for and treatment of bacterial vaginosis in asymptomatic pregnant persons to prevent preterm delivery.

POPULATION This recommendation applies to pregnant persons without symptoms of bacterial vaginosis.

EVIDENCE ASSESSMENT The USPSTF concludes with moderate certainty that screening for asymptomatic bacterial vaginosis in pregnant persons not at increased risk for preterm delivery has no net benefit in preventing preterm delivery. The USPSTF concludes that for pregnant persons at increased risk for preterm delivery, the evidence is conflicting and insufficient, and the balance of benefits and harms cannot be determined.

CONCLUSIONS AND RECOMMENDATION The USPSTF recommends against screening for bacterial vaginosis in pregnant persons not at increased risk for preterm delivery. (D recommendation) The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for bacterial vaginosis in pregnant persons at increased risk for preterm delivery. (I statement)

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Group Information: The US Preventive Services Task Force (USPSTF) members are listed at the end of this article.

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Summary of Recommendations

The USPSTF recommends against screening for bacterial vaginosis in pregnant persons not at increased risk for preterm delivery.	D
The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for bacterial vaginosis in pregnant persons at increased risk for preterm delivery.	I

See the Figure for a more detailed summary of the recommendations for clinicians. See the Practice Considerations section for more information on risk assessment and suggestions for practice regarding the I statement. USPSTF indicates US Preventive Services Task Force.

Bacterial vaginosis is common and is caused by a disruption of the microbiological environment in the lower genital tract. In the US, reported prevalence of bacterial vaginosis among pregnant women ranges from 5.8% to 19.3% and is higher in some races/ethnicities.[1] Bacterial vaginosis during pregnancy has been associated with adverse obstetrical outcomes including preterm delivery,[2] early miscarriage,[3] postpartum endometritis,[4] and low birth weight.[5] Bacterial vaginosis is often asymptomatic, can resolve spontaneously, and recurs often, with or without treatment.[6] Most clinicians treat symptomatic bacterial vaginosis in pregnancy. The current recommendation statement focuses on screening for asymptomatic bacterial vaginosis in pregnancy.

In the US, approximately 10% of live births are preterm (born prior to 37 weeks' gestation).[7] Preterm birth is associated with serious complications, including major intraventricular hemorrhage, acute respiratory illnesses, and sepsis.[7-10] Approximately two-thirds of all infant deaths in the US occur among infants born

Figure. Clinician Summary: Screening for Bacterial Vaginosis in Pregnant Persons to Prevent Preterm Delivery

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What does the USPSTF recommend?	**For pregnant persons not at increased risk for preterm delivery: Grade D** Do not screen for bacterial vaginosis in pregnant persons who have no signs or symptoms of bacterial vaginosis.
	For pregnant persons at increased risk for preterm delivery: I statement The evidence is insufficient to assess the balance of benefits and harms of screening for bacterial vaginosis in pregnant persons who have no signs or symptoms of bacterial vaginosis.
To whom does this recommendation apply?	Pregnant persons without signs or symptoms of bacterial vaginosis.
What's new?	This recommendation is consistent with the 2008 USPSTF recommendation.
How to implement this recommendation?	1) **Assess risk for preterm delivery.** There are multiple factors that increase risk for preterm delivery; one of the strongest risk factors is prior preterm delivery. 2) Decide whether or not to screen for bacterial vaginosis: a) Do not screen pregnant persons not at increased risk for preterm delivery. b) Evidence is insufficient to recommend for or against screening pregnant persons at increased risk for preterm delivery.
What are other relevant USPSTF recommendations?	The USPSTF has also issued recommendations on screening for numerous other conditions in pregnant persons, including asymptomatic bacteriuria, syphilis, hepatitis B, and HIV.
Where to read the full recommendation statement?	Visit the USPSTF website (https://www.uspreventiveservicestaskforce.org) to read the full recommendation statement. This includes more details on the rationale of the recommendation, including benefits and harms; supporting evidence; and recommendations of others.

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.

USPSTF indicates US Preventive Services Task Force.

Table. Summary of USPSTF Rationale[a]

Rationale	Pregnant persons not at increased risk for preterm delivery	Pregnant persons at increased risk for preterm delivery
Detection	There is adequate evidence that currently available tests can accurately identify bacterial vaginosis in pregnant persons.	
Benefits of early detection and intervention and treatment	• There is inadequate direct evidence on the benefits of screening for asymptomatic bacterial vaginosis in pregnant persons to reduce adverse health outcomes. • There is adequate evidence that treatment of asymptomatic bacterial vaginosis with antibiotics in pregnant persons not at increased risk for preterm delivery does not provide a benefit in reducing adverse health outcomes.	• There is inadequate direct evidence on the benefits of screening for asymptomatic bacterial vaginosis in pregnant persons to reduce adverse health outcomes. • There is inadequate evidence to determine whether treatment of asymptomatic bacterial vaginosis in persons at increased risk for preterm delivery provides a benefit in reducing adverse health outcomes (because of the limited number of studies, conflicting and imprecise results, heterogeneity of studies, and other limitations of the study designs).
Harms of early detection and intervention and treatment	• There is inadequate direct evidence on the harms of screening for bacterial vaginosis in pregnant persons. • There is adequate evidence that treatment of bacterial vaginosis in pregnant persons results in small maternal harms, including vaginal candidiasis and gastrointestinal upset, and no harms to the fetus. • Overall, there is adequate evidence to bound the harms of screening for and treatment of bacterial vaginosis in pregnant persons as no greater than small, based on the false-positive results from screening and the reported minor adverse effects from treatment with antibiotics.	
USPSTF Assessment	The USPSTF concludes with moderate certainty that screening for asymptomatic bacterial vaginosis in pregnant persons not at increased risk for preterm delivery has no net benefit.	The USPSTF concludes that the evidence is insufficient and conflicting, and the balance of benefits and harms of screening for asymptomatic bacterial vaginosis in pregnant persons at increased risk for preterm delivery cannot be determined.

Abbreviation: USPSTF, US Preventive Services Task Force.

[a] See the eFigure in the Supplement for explanation of USPSTF grades and levels of evidence.

preterm.[8] The frequency and severity of adverse outcomes from preterm delivery are higher with earlier gestational age.

Assessment of Magnitude of Net Benefit

The US Preventive Services Task Force (USPSTF) concludes with moderate certainty that screening for asymptomatic bacterial vaginosis in pregnant persons not at increased risk for preterm delivery has **no net benefit** in preventing preterm delivery.

The USPSTF concludes that for pregnant persons at increased risk for preterm delivery, the **evidence is insufficient** and conflicting, and the balance of benefits and harms cannot be determined.

See the **Figure** and **Table** for more information on the USPSTF recommendation rationale and assessment. For more details on the

methods the USPSTF uses to determine the net benefit, see the USPSTF Procedure Manual.[11]

Practice Considerations

Patient Population Under Consideration

This recommendation statement applies to pregnant persons without symptoms of bacterial vaginosis.

Definition

Healthy vaginal flora is comprised of more than 90% lactobacilli. Bacterial vaginosis occurs when there is a shift in this flora to include a greater proportion of mixed anaerobic bacteria, such as the *Gardnerella*, *Prevotella*, and *Atopobium* species.[12,13] Most often, bacterial vaginosis is asymptomatic. When symptoms occur, they include off-white, thin, homogenous discharge, a vaginal "fishy" odor, or both.

Assessment of Risk

Persons who are not at increased risk for preterm delivery include pregnant persons with no history of previous preterm delivery or other risk factors for preterm delivery. While multiple factors increase risk for preterm delivery, one of the strongest risk factors is prior preterm delivery.

See the Potential Preventable Burden section for additional information on risk factors for preterm delivery.

Screening Tests

Screening tests for bacterial vaginosis are performed on vaginal secretions obtained during a pelvic examination in a primary care setting. Available screening tests include nucleic acid assays, sialidase assays, and clinical assessment (ie, using the Amsel criteria of pH, vaginal discharge, clue cells, and "whiff test").

Treatment

Oral metronidazole and oral clindamycin, as well as vaginal metronidazole gel or clindamycin cream, are the usual treatments for symptomatic bacterial vaginosis. The optimal treatment regimen for pregnant persons with bacterial vaginosis is unclear.

Additional Tools and Resources

The Centers for Disease Control and Prevention website provides current treatment recommendations.[14]

Suggestions for Practice Regarding the I Statement

Potential Preventable Burden

Bacterial vaginosis occurs in as many as 29% of women in the US[15] and in 5.8% to 19.3% of pregnant women, depending on the specific population being studied.[1,16] Reported factors that increase the likelihood of a diagnosis of bacterial vaginosis include African American race, poverty, smoking, increased body mass index, vaginal douching, low educational attainment, and certain sexual behaviors, including a high number of partners, lack of condom or contraceptive use, vaginal sex, sex with a female partner, and concurrent sexually transmitted infections.[6,15,17,18]

Causes of preterm delivery are likely multifactorial, and numerous risk factors are associated with an increased risk for preterm birth.[6] History of a prior preterm delivery is associated with a 2.5-fold higher odds for preterm delivery in subsequent pregnancies.[19] While bacterial vaginosis during pregnancy is associated with a 2-fold higher odds for preterm delivery,[2] it is not clear that bacterial vaginosis is a cause of preterm delivery. Other additional risk factors for preterm delivery include, but are not limited to, cervical insufficiency, multifetal gestation, young or advanced maternal age, low maternal body mass index (<20, calculated as weight in kilograms divided by height in meters squared), genitourinary infections, HIV infection, and other maternal medical conditions.[6,20-23] The association of these additional risk factors with preterm delivery is small to moderate, and factors can act in isolation or in combination. Preterm birth rates also vary by race/ethnicity in the US; recent data report preterm birth rates of 8.6% among Asian women, 11.8% among Native Hawaiian/Other Pacific Islander women, 9.7% among Hispanic women, 11.5% among American Indian/Alaska Native women, 14.1% among black women, and 9.1% among white women.[7] Among women with a prior preterm delivery, the rate of recurrent preterm delivery in African American women is 4 times higher than the rate of recurrent preterm delivery in white women.[20] Even when these risk factors are present, it is unclear whether screening and treating asymptomatic bacterial vaginosis in pregnant persons at increased risk for preterm delivery prevents preterm delivery.

African American race is both associated with bacterial vaginosis and strongly associated with preterm delivery. Other factors associated with both bacterial vaginosis and preterm delivery include young age, nulliparity, current tobacco use, low educational attainment, lower income, and concurrent sexually transmitted infections.

Five studies provided evidence on the benefit of treatment of bacterial vaginosis in women with a previous preterm delivery for reducing the incidence of preterm delivery. Four of these studies evaluated the treatment of bacterial vaginosis with oral metronidazole[6] and reported the incidence of preterm delivery at less than 37 weeks. Three of these studies reported statistically significant absolute reductions in preterm delivery after treatment (ranging from 18% to 29% absolute reductions in risk), and 1 study reported no significant difference. Limitations of the evidence, including imprecision, the fact that some of the results were from subgroup analyses, and the inconsistency of results, prevented a definitive conclusion about the benefit.[6] Two studies (1 evaluating oral metronidazole and the other evaluating vaginal clindamycin) presented results for preterm delivery at less than 34 weeks, and the results were mixed.[6]

Potential Harms

The harms of screening for bacterial vaginosis in pregnant persons and treatment with antibiotics generally involve adverse effects such as gastrointestinal upset and vaginal candidiasis.[6] Four observational studies and 2 large meta-analyses of observational studies on the use of metronidazole during pregnancy for any reason (not limited to bacterial vaginosis) reported no increase in congenital malformations or incident cancer in children exposed in utero.[24-29]

Current Practice

No data are available on how frequently pregnant persons at increased risk for preterm delivery are screened for bacterial vaginosis

during pregnancy, but screening in asymptomatic pregnant persons is not recommended by any large US professional organization. Clinicians routinely test and treat pregnant persons for symptomatic bacterial vaginosis.

Other Related USPSTF Recommendations

The USPSTF has also issued recommendations on screening for numerous conditions in pregnant persons, including asymptomatic bacteriuria,[30] syphilis,[31] hepatitis B,[32] and HIV.[33]

Update of Previous USPSTF Recommendation

The USPSTF last issued a recommendation on this topic in 2008. Although newer evidence was reviewed, the recommendations have essentially remained the same. The language used to describe a pregnant person's risk for preterm delivery has been updated to be more consistent with other current USPSTF recommendations.

Supporting Evidence

Scope of Review

To update its 2008 recommendation, the USPSTF commissioned a systematic review[6,34] to evaluate the accuracy of screening and the benefits and harms of screening for and treatment of bacterial vaginosis in asymptomatic pregnant persons.

Accuracy of Screening Tests

The USPSTF reviewed evidence from 25 cross-sectional studies that reported on test accuracy of the BD Affirm VPIII test (Becton, Dickinson), BD Max system, OSOM BVBLUE test (Sekisui Diagnostics), and the Amsel clinical criteria to diagnose bacterial vaginosis.[6,34] The vast majority of studies were conducted in nonpregnant and symptomatic women; only 2 studies were conducted exclusively in asymptomatic pregnant women, and 2 additional studies were conducted in symptomatic pregnant women. None of the available evidence indicated that accuracy would differ between pregnant and nonpregnant populations. Studies were conducted in a variety of settings, including academic, hospital-based outpatient, or community obstetrics-gynecology clinics; sexually transmitted infection and family planning clinics; local health department clinics; and longitudinal cohorts; most (13 studies) were conducted in the US.

Pooled sensitivity and specificity of the BD Affirm VPIII test was 0.87 (95% CI, 0.80-0.92) and 0.81 (95% CI, 0.73-0.88), respectively (5 studies; n = 2936).[6] Only 1 study (n = 1338) reported accuracy of the BD Max system; sensitivity was 0.93 (95% CI, 0.91-0.94) and specificity was 0.92 (95% CI, 0.90-0.94).[6] Three studies reported accuracy of the OSOM BVBLUE test (n = 864); sensitivity ranged from 0.61 to 0.92, and specificity ranged from 0.86 to 0.99.[6,34] Fifteen studies (n = 7171) reported on accuracy of complete Amsel criteria (having at least 3 of the following 4 criteria to detect bacterial vaginosis: vaginal pH >4.5, presence of clue cells, thin homogeneous discharge, and a positive whiff test result [an amine, "fishy" odor when potassium hydroxide is added to vaginal discharge]). Pooled sensitivity and specificity from 14 of those studies were 0.76 (95% CI, 0.63-0.85) and 0.95 (95% CI, 0.89-0.98), respectively.[6,34] Five studies (n = 2674) reported on the accuracy of using modified Amsel criteria (having at least 2 of the following 3 criteria to detect bacterial vaginosis: presence of clue cells, thin homogeneous discharge, and a positive whiff test result). Pooled sensitivity from 4 studies was 0.67 (95% CI, 0.54-0.78) and specificity was 0.96 (95% CI, 0.93-0.98).[6,34]

Benefits of Early Detection and Treatment

No studies were identified that directly evaluated the benefit of screening for bacterial vaginosis in asymptomatic pregnant persons on reducing preterm delivery and related morbidity and mortality.[6,34]

The USPSTF reviewed evidence from 13 randomized clinical trials that reported on the effect of treatment of asymptomatic bacterial vaginosis in pregnant women on preterm delivery and related morbidity.[6] Most studies enrolled pregnant women in their second trimester of pregnancy. Ten trials targeted a general obstetric population and enrolled participants without regard to risk for preterm delivery.[6,34-44] Zero percent to 10.9% of participants in these trials had a history of prior preterm delivery, and 2 of these trials reported results by subgroup of participants who had a history of prior preterm delivery. Three additional trials specifically targeted pregnant women who had a history of prior preterm delivery.[6,34,45-47] Of the 7 trials that reported information on race/ethnicity of participants, the percentage of participants who were nonwhite ranged from 2% to 85%. Four trials were conducted in the US; the others were conducted in Europe and Australia. Interventions evaluated included oral metronidazole (3 trials), oral metronidazole plus erythromycin (1 trial), oral clindamycin (2 trials), and intravaginal clindamycin (7 trials).

Findings from trials targeting a general obstetric population were largely consistent in reporting no benefit across a variety of preterm delivery outcomes. No statistically significant reduction was found in all-cause preterm delivery prior to 37 weeks (pooled relative risk [RR], 1.02 [95% CI, 0.86-1.20%]; 6 studies; n = 6307), spontaneous preterm delivery prior to 37 weeks (pooled RR, 0.78 [95% CI, 0.56-1.07]; 8 studies; n = 7571), preterm delivery prior to 32 weeks (pooled RR, 0.87 [95% CI, 0.54-1.42]; 3 studies; n = 5564), birth weight less than 2500 g (pooled RR, 1.03 [95% CI, 0.83-1.29]; 5 studies; n = 5377), birth weight less than 1500 g (pooled RR, 1.05 [95% CI, 0.50-2.18]; 3 studies; n = 5149), or premature rupture of membranes (PROM) or preterm PROM (pooled RR, 1.11 [95% CI, 0.72-1.72]; 4 studies; n = 3568).[6,34]

Findings from the 5 trials reporting outcomes for women with a history of prior preterm delivery were inconsistent. Four trials (n = 451) reported on preterm delivery prior to 37 weeks in women with a history of prior preterm delivery.[6] RRs ranged from 0.17 to 1.33; 3 of the studies had statistically significant findings favoring treatment, while 1 did not.[6,34] Two trials (n = 102) reported on preterm delivery prior to 34 weeks in women with a history of prior preterm delivery. RRs were 1.00 (95% CI, 0.07-14.05) in 1 study and 0.41 (95% CI, 0.08-2.11) in the other study.[6]

Harms of Screening and Treatment

No studies that directly evaluated the harms of screening for bacterial vaginosis in pregnancy were identified.

The USPSTF reviewed evidence on harms of treatment of bacterial vaginosis during pregnancy from 8 randomized clinical trials that reported on maternal harms and from 4 observational studies and 2 meta-analyses of observational studies that reported on harms to children from in utero exposure.

The 8 trials that reported on maternal harms of treatment of bacterial vaginosis during pregnancy also reported on benefits of treatment, so study characteristics are described above. Four trials[35,36,42,47] (n = 1718) reported on adverse events from intravaginal clindamycin. No serious adverse events were reported. Minor adverse effects such as vaginal candidiasis, troublesome discharge, and study withdrawal because of itching were reported infrequently and at similar rates between intervention and control groups. Maternal harms of oral clindamycin were reported in 2 trials[38,41] (n = 3345). Only 1 trial reported on serious adverse events and did not observe any in either treatment group. Both studies reported a higher incidence of stopping medication in the oral clindamycin group, although findings were statistically significant in only 1 study. Maternal harms of oral metronidazole were reported in 2 trials[39,40] (n = 2776). A higher incidence of adverse events was reported with oral metronidazole in both studies, although the finding was only statistically significant in 1 study.

Three observational studies[27,28] (n = 62 271) and 2 meta-analyses[24,25] (n >199 541) reported on congenital malformations among children exposed to metronidazole in utero for any clinical indication (not just bacterial vaginosis). The studies included in this body of evidence dated back to the 1960s to 1990s; the 3 observational studies were based on registry data from Denmark, Hungary, and Israel. None reported any significant increase in congenital malformations. A single observational study (n = 328 846) of the Tennessee Medicaid program reported on cancer incidence before age 5 years among children exposed to metronidazole in utero, and no significant increase with exposure was observed.[29]

Overall, the USPSTF found few reported maternal harms and no reported fetal harms in the literature. In addition, use of metronidazole and clindamycin to treat bacterial vaginosis during pregnancy has become the standard of care, with no signal of significant maternal or fetal adverse effects to date.

Is the Evidence Consistent With Biological Understanding?

Causes of preterm delivery are likely multifactorial, and the exact mechanism of how some risk factors may lead to preterm delivery is poorly understood. Epidemiologic data suggest that risk for preterm delivery may be higher when asymptomatic bacterial vaginosis is present (pooled odds ratio, 2.16 [95% CI, 1.56-3.00]; 32 studies; 30 518 participants).[2] However, the causal pathway of how bacterial vaginosis may lead to preterm delivery is unclear. Earlier theories postulated that bacterial vaginosis may lead to upper genital tract infections, which may in turn contribute to preterm PROM or preterm labor. More recently, it has been suggested that maternal vaginal mucosal immune response may play a role in preterm labor or preterm PROM, as well as acquisition of bacterial vaginosis. Although the evidence is clear that treating asymptomatic bacterial vaginosis in pregnant persons not at increased risk for preterm delivery does not prevent preterm delivery, it is still unclear whether treating asymptomatic pregnant persons at increased risk for preterm delivery may help prevent preterm delivery.

Response to Public Comment

A draft version of this recommendation statement was posted for public comment on the USPSTF website from October 8 to November 4, 2019. In response to public comments, language has been added clarifying that the current recommendation statement applies to screening for asymptomatic bacterial vaginosis. The current recommendation does not address treatment of symptomatic bacterial vaginosis, which is addressed by other treatment guidelines. Additionally, the need for studies that evaluate screening test accuracy in pregnant persons has been added to the Research Needs and Gaps section. Some comments requested additional information on subgroups and additional screening tests. Although this information was sought in the systematic evidence review that informed the recommendation, no additional evidence was identified.

Research Needs and Gaps

More studies are needed to evaluate screening for and treatment of asymptomatic bacterial vaginosis in pregnant persons at increased risk for preterm delivery. These studies should

- Include pregnant persons with a history of prior preterm delivery, as well as other risk factors for preterm delivery, such as cervical insufficiency, multifetal gestation, young or advanced maternal age, low maternal body mass index (<20), and African American, Native Hawaiian/Other Pacific Islander, or American Indian/Alaska Native race/ethnicity.
- Be adequately powered to detect a reduction of all-cause preterm delivery prior to 37 weeks' gestation.

If a reduction in preterm delivery is found with treatment of asymptomatic bacterial vaginosis in pregnant persons at increased risk for preterm delivery, then additional research is needed on ways to better identify persons at increased risk for preterm delivery. Additionally, given the biochemical and hormonal changes that occur during pregnancy, further studies of bacterial vaginosis screening tests in pregnant persons are needed to confirm test accuracy in this population.

Recommendations of Others

Most organizations in the US do not recommend screening for bacterial vaginosis in asymptomatic pregnant women. The American College of Obstetricians and Gynecologists states that several specific screening tests, including testing for bacterial vaginosis, have been proposed to assess a woman's risk of preterm delivery; however, intervention studies based on these screening tests in asymptomatic women (for preterm delivery) have not demonstrated improved perinatal outcomes, and the American College of Obstetricians and Gynecologists does not recommend the use of these tests as a screening strategy.[48] The Centers for Disease Control and Prevention states that "Evidence does not support routine screening for bacterial vaginosis in asymptomatic pregnant women at high risk for preterm delivery. Symptomatic women should be evaluated and treated."[49] The American Academy of Family Physicians endorses the 2008 USPSTF recommendation on screening for bacterial vaginosis.[50]

ARTICLE INFORMATION

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Additional Information: The 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.

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