Serologic Screening for Genital Herpes Infection
US Preventive Services Task Force
Reaffirmation Recommendation Statement

US Preventive Services Task Force

**Importance**
Genital herpes is a common sexually transmitted infection (STI) caused by 2 related viruses, herpes simplex type 1 (HSV-1) and herpes simplex type 2 (HSV-2). Infection is lifelong; currently, there is no cure for HSV infection. Antiviral medications may provide clinical benefits to symptomatic persons. Transmission of HSV from a pregnant person to their infant can occur, most commonly during delivery; when genital lesions or prodromal symptoms are present, cesarean delivery can reduce the risk of transmission. Neonatal herpes infection is uncommon yet can result in substantial morbidity and mortality.

**Objective**
To reaffirm its 2016 recommendation, the US Preventive Services Task Force (USPSTF) commissioned a reaffirmation evidence update on targeted key questions to systematically evaluate the evidence on accuracy, benefits, and harms of routine serologic screening for HSV-2 infection in asymptomatic adolescents, adults, and pregnant persons.

**Population**
Adolescents and adults, including pregnant persons, without known history, signs, or symptoms of genital HSV infection.

**Evidence Assessment**
The USPSTF concludes with moderate certainty that the harms outweigh the benefits for population-based screening for genital HSV infection in asymptomatic adolescents and adults, including pregnant persons.

**Recommendation**
The USPSTF recommends against routine serologic screening for genital HSV infection in asymptomatic adolescents and adults, including pregnant persons. (D recommendation)


See the Summary of Recommendation figure.

**Summary of Recommendation**

<table>
<thead>
<tr>
<th>Population</th>
<th>Recommendation</th>
<th>Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymptomatic adolescents and adults, including pregnant persons</td>
<td>The USPSTF recommends against routine serologic screening for genital herpes simplex virus infection in asymptomatic adolescents and adults, including pregnant persons.</td>
<td>D</td>
</tr>
</tbody>
</table>

USPSTF indicates US Preventive Services Task Force.

**Importance**
Genital herpes is a common sexually transmitted infection (STI) caused by 2 related viruses, herpes simplex type 1 (HSV-1) and herpes simplex type 2 (HSV-2). HSV-1 causes both orofacial and anogenital infection; HSV-2 rarely presents outside of the anogenital area. Infection is lifelong; currently, there is no cure for HSV infection. Antiviral medications may provide clinical benefits to symptomatic persons. Transmission of HSV from a pregnant person to their infant can occur, most commonly during delivery; when genital lesions or prodromal symptoms are present, cesarean delivery can reduce the risk of transmission. Neonatal herpes infection is uncommon yet can result in substantial morbidity and mortality. Currently, routine serologic screening for genital herpes is limited by the low predictive value of the widely available serologic screening tests and the expected high rate of false-positive results likely to occur with routine screening of asymptomatic persons in the US. Over the past 20 years, HSV-1 and HSV-2 estimated seroprevalence has steadily declined, yet specific populations remain at increased risk for HSV infection.
disproportionately affected by HSV infection. The precise prevalence of asymptomatic HSV-2 infection in the US is difficult to determine because prevalence estimates rely on serologic testing without confirmation with Western blot. The 2015-2016 National Health and Nutrition Examination Survey of persons aged 14 to 49 years estimates seroprevalence of HSV-1 to be highest in Mexican American (72%) and non-Hispanic Black (59%) persons compared with the general US population (48%). Estimated seroprevalence of HSV-2 in US non-Hispanic Black adolescents and adults (35%) is nearly 3 times that in the general US population (12%). In pregnant persons, an estimated 22% of the US population may be seropositive for HSV-2. HSV seroprevalence increases with deprivation and decreases with educational attainment, suggesting that HSV disparities may be influenced by social determinants of health.

**USPSTF Assessment of Magnitude of Net Benefit**

Using a reaffirmation process, the US Preventive Services Task Force (USPSTF) concludes with moderate certainty that the harms outweigh the benefits for population-based screening for genital HSV infection in asymptomatic adolescents and adults, including pregnant persons. See the Table for more information on the USPSTF recommendation rationale and assessment and the eFigure in the Supplement for information on the recommendation grade. See the Figure for a summary of the recommendation for clinicians. For more details on the methods the USPSTF uses to determine the net benefit, see the USPSTF Procedure Manual.

**Reaffirmation of Previous USPSTF Recommendation**

In 2016, the USPSTF reviewed the evidence for screening for genital herpes and issued a D recommendation. The USPSTF has decided to use a reaffirmation deliberation process to update this recommendation. The USPSTF uses the reaffirmation process for well-established, evidence-based standards of practice in current primary care practice for which only a very high level of evidence would justify a change in the grade of the recommendation. In its deliberation of the evidence, the USPSTF considers whether the new evidence is of sufficient strength and quality to change its previous conclusions about the evidence.

**Practice Considerations**

**Patient Population Under Consideration**

This recommendation statement applies to routine screening of adolescents and adults, including pregnant persons, without known history, signs, or symptoms of genital HSV infection. This recommendation statement does not apply to persons who present to clinicians requesting testing due to a history, signs, or symptoms suggestive of genital herpes or persons with HIV infection or other immunosuppressive disorders.

**Definitions**

In this recommendation statement, “asymptomatic” refers to persons without known past or current history of genital herpes and includes persons who may have unrecognized infection. Persons who are known to have genital herpes and are between outbreak occurrences are not considered to be asymptomatic for this recommendation. “Genital herpes” refers to a range of signs and symptoms related to HSV infection in the sacral nerve area. Many persons with genital herpes have intermittent, recurrent genital ulcers or vesicular lesions and may have local symptoms (eg, itching) or systemic signs (eg, fever).

**Treatment and Interventions**

Treatment of persons with symptoms of genital herpes often includes antiviral medications to provide symptomatic relief from painful outbreaks, prevent HSV recurrences, prevent transmission to sexual partners, and improve quality of life. In asymptomatic persons with serologic evidence of HSV, it is not clear whether antiviral...
Figure. Clinician Summary: Serologic Screening for Genital Herpes Infection

<table>
<thead>
<tr>
<th>What does the USPSTF recommend?</th>
<th>For asymptomatic adolescents and adults, including pregnant persons: Do not routinely screen for genital herpes simplex virus (HSV) infection. Grade: D</th>
</tr>
</thead>
</table>

To whom does this recommendation apply?

- This recommendation applies to routine screening of adolescents and adults, including pregnant persons, without known history, signs, or symptoms of genital HSV infection.
- "Asymptomatic" refers to persons without known past or current history of genital herpes.
- Includes persons who may have unrecognized infection.
- Persons who are known to have genital herpes and are between outbreak occurrences are not considered to be asymptomatic for this recommendation.
- This recommendation does not apply to persons who present to clinicians requesting testing due to a history, signs, or symptoms suggestive of genital herpes or persons with HIV infection or other immunosuppressive disorders.

What’s new?

This recommendation is consistent with the 2016 USPSTF recommendation.

What additional information should clinicians know about this recommendation?

- Currently, routine serologic screening for genital herpes is limited by the low predictive value of the widely available serologic screening tests and the expected high rate of false-positive results likely to occur with routine screening of asymptomatic persons in the US.
- Antiviral medications may provide clinical benefits to symptomatic persons. In asymptomatic persons with serologic evidence of HSV, the rationale for antiviral treatment is unclear.

Why is this recommendation and topic important?

- Genital herpes is a common sexually transmitted infection (STI).
- Over the past 20 years, HSV-1 and HSV-2 estimated seroprevalence has steadily declined, yet certain populations remain disproportionately affected by HSV infection.
- Infection is lifelong; currently, there is no cure for HSV infection.
- Neonatal herpes infection is uncommon yet can result in substantial morbidity and mortality.

What are other relevant USPSTF recommendations?

- The USPSTF recommends behavioral counseling interventions for all sexually active adolescents and adults who are at increased risk for STIs (https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/sexually-transmitted-infections-behavioral-counseling).
- The USPSTF has issued several related recommendations to prevent negative health outcomes related to sexual health (available at https://www.uspreventiveservicestaskforce.org/usps/f/).

What are additional tools and resources?

The following resources may assist clinicians in implementation of strategies to prevent STIs in the primary care setting.
- The Centers for Disease Control and Prevention provides detailed guidance for diagnosis and management of genital herpes, including counseling to prevent sexual and perinatal transmission.3,11
- Includes persons who may have unrecognized infection.
- Persons who are known to have genital herpes and are between outbreak occurrences are not considered to be asymptomatic for this recommendation.
- This recommendation does not apply to persons who present to clinicians requesting testing due to a history, signs, or symptoms suggestive of genital herpes or persons with HIV infection or other immunosuppressive disorders.

Additional Tools and Resources

The following resources may assist clinicians in implementation of strategies to prevent STIs in the primary care setting.
- The Centers for Disease Control and Prevention (CDC) provides detailed guidance for diagnosis and management of genital herpes, including counseling to prevent sexual and perinatal transmission.3,11
- 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.

Where to read the full recommendation statement?

Visit the USPSTF website (https://www.uspreventiveservicestaskforce.org/usps/f/) or JAMA website (https://jamanetwork.com/collections/44068/united-states-preventive-services-task-force) 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.
Other Related USPSTF Recommendations
The USPSTF has issued several related recommendations to prevent negative health outcomes related to STIs, including the following.
- Behavioral counseling interventions to prevent STIs
- Screening for chlamydia and gonorrhea
- Screening for HIV infection
- Screening for syphilis infection in nonpregnant adolescents and adults
- Screening for syphilis infection in pregnant persons

Supporting Evidence

Scope of Review
To reaffirm its recommendation, the USPSTF commissioned a reaffirmation update. The aim of the evidence update that supported the reaffirmation process was to identify new and substantial evidence that could be sufficient to change the prior recommendation. The reaffirmation update focused on targeted key questions to systematically evaluate the evidence on accuracy, benefits, and harms of routine serologic screening for HSV-2 infection in asymptomatic adolescents, adults, and pregnant persons. Additionally, evidence was sought on the effectiveness and harms of preventive medications and behavioral counseling interventions in asymptomatic populations to reduce future symptomatic episodes and transmission to susceptible sexual partners and infants.

The reaffirmation update that supports this recommendation found no new evidence since the 2016 review. In 2016, the USPSTF reviewed 17 studies (n = 9736) in 19 publications. The USPSTF reviewed evidence comparing accuracy of HerpeSelect (Focus Diagnostics) and the Biokit HSV-2 Rapid Test (American Screening LLC), 2 commercially available serologic tests approved by the US Food and Drug Administration, with the Western blot (the criterion standard). HerpeSelect and the Biokit HSV-2 Rapid Test are based on detection of HSV-specific glycoprotein G2. Serologic tests can detect antibodies to HSV infection typically 6 weeks to 3 months after infection.

Accuracy of Screening Tests
The USPSTF found no new studies assessing the accuracy of serologic screening for HSV-2 in asymptomatic adolescents, adults, and pregnant persons. Based on previous evidence from the 2016 review of 11 studies (n = 7129), accuracy estimates of HSV-2 serologic tests, which are largely derived from populations with higher prevalence of HSV-2 infection compared with the general US population, are of limited applicability to the general US primary care population. Most studies enrolled populations with seropositivity greater than 40% for HSV-2 based on Western blot. In 10 studies (n = 6537) using a cut point of 1.1, the HerpeSelect test had a pooled sensitivity estimate of 99% (95% CI, 97%-100%) and a pooled specificity estimate of 81% (95% CI, 68%-90%), compared with Western blot. In 4 studies (n = 1512), the Biokit test had a pooled sensitivity estimate of 84% (95% CI, 73%-91%) and pooled specificity estimate of 95% (95% CI, 93%-97%), compared with Western blot. Based on a previous review, in the US population, estimated positive predictive value for the Biokit test may be as low as 75% and as low as 50% for the HerpeSelect test for predicting true seropositivity. Estimated declines in HSV-2 seroprevalence in the US population (since the 2016 review) likely further limit test predictive value. Confirmatory testing with the highly specific Western blot is not widely available, complicating population-wide screening in the US. No studies have examined the screening accuracy of serologic tests for HSV-2 in pregnant persons.

Studies report that many new cases of genital herpes may be caused by HSV-1; while HSV-1 infection can be identified by serologic tests, it is highly prevalent (~48%), and serologic tests cannot determine the site of infection (oral or anogenital) in persons who have not previously experienced symptoms. Therefore, serologic tests are not useful for routine screening for asymptomatic genital herpes from HSV-1 infection.

Risk Assessment
The USPSTF found no evidence of externally validated, reliable risk stratification tools to identify individuals more or less likely to have genital herpes.

Benefits of Early Detection and Treatment
The USPSTF found no new studies evaluating effectiveness of antiviral medications to reduce genital HSV-2 viral shedding or effectiveness of antiviral medications or behavioral counseling interventions to reduce future symptomatic episodes or transmission of genital herpes in asymptomatic adolescents, adults, and pregnant persons. Based on evidence in the 2016 evidence review, the USPSTF found limited and heterogeneous evidence of benefit of early identification and early treatment of HSV-2 in asymptomatic adults, including pregnant persons. Genital herpes has no cure; the role of antiviral medications in asymptomatic persons is unclear. Pregnant persons with active genital lesions or prodromal symptoms can be managed with cesarean delivery to reduce the risk of neonatal transmission. Given these findings, the USPSTF concluded that routine screening for HSV-2 in asymptomatic persons would confer no more than a small population benefit.

Harms of Screening and Treatment
The USPSTF found no new studies reporting on the harms of screening for or treatment of genital herpes in asymptomatic adolescents, adults, and pregnant persons. Based on previous evidence, the USPSTF estimated that using the widely available serologic tests for HSV-2, nearly 1 of every 2 diagnoses in the general US primary care population could be false. A previous USPSTF review estimated that in a population of 10 000 persons with an HSV-2 prevalence of 15%, serologic screening could result in approximately 1585 true-positive and 1445 false-positive results. At the current US estimated prevalence of 12%, true-positive results would likely further decrease and false-positive results would likely further increase. Additionally, the USPSTF concluded that there may be potential social and emotional harms associated with a false-positive diagnosis and potential harms of unnecessary treatment with preventive antiviral medications in persons with a false-positive diagnosis.

Response to Public Comment
A draft version of this recommendation statement was posted for public comment on the USPSTF website from August 16, 2022, to September 12, 2022. The USPSTF reviewed and considered all comments received during this period. Comments expressed concern
that genital HSV infection is minimized and not taken seriously. Others expressed concern that persons with asymptomatic genital herpes infection can unknowingly transmit the infection to sexual partners. The USPSTF understands these concerns and recognizes the importance of sexual health. Several comments supported the USPSTF’s analysis and conclusions, noting that the recommendation is consistent with current clinical practice and guidelines from other organizations, including the CDC and the American College of Obstetricians and Gynecologists.

The USPSTF strongly calls for additional research into high-quality, accurate screening tests and effective interventions to prevent negative health outcomes of genital HSV in asymptomatic adolescents, adults, and pregnant persons. The USPSTF has several positive recommendations related to screening for and counseling to prevent STIs.

Research Needs and Gaps

The USPSTF recognizes the importance of improving screening for and treatment of genital herpes to prevent future symptomatic episodes and transmission. The USPSTF is calling for more studies to evaluate screening, detection, and management of asymptomatic genital HSV infection, including the following.

- Studies assessing screening test accuracy and predictive value in primary care settings in the US that include asymptomatic persons, validating against an accepted criterion standard, and clearly specifying practical methods for confirmation of initial serologic results.
- Studies that enroll enough participants from populations disproportionately affected by HSV (based on age, race, ethnicity, and sexual orientation) to understand screening accuracy and predictive value along with the benefits and harms of interventions in these specific populations.
- High-quality studies that provide consistent evidence about the effectiveness of behavioral counseling interventions, preventive medication interventions (eg, antiviral medications), or both to improve genital herpes outcomes in asymptomatic adolescents, adults, and pregnant persons who screen positive for HSV.
- Research to better clarify emerging associations of HSV infection with intermediate pregnancy outcomes (such as preterm labor and prolonged rupture of membranes) and potentially related neonatal morbidity and mortality.
- Continuing research to develop a cure for genital HSV infection and an effective vaccine to prevent genital HSV infection.

Recommendations of Others

The American Academy of Family Physicians supports the 2016 USPSTF recommendation against routine serologic screening for HSV infection in asymptomatic adolescents, adults, and pregnant persons.23 The American College of Obstetricians and Gynecologists does not recommend routine serologic screening for HSV in asymptomatic pregnant persons.4 For pregnant persons with a clinical history suggestive of HSV without laboratory confirmation, HSV screening may be helpful, and repeat serologic testing may be indicated.6 In symptomatic pregnant persons, antiviral therapy may be indicated; cesarean delivery is recommended for pregnant persons with active genital lesions or prodromal symptoms.6 The CDC does not recommend routine serologic screening for HSV-2 in asymptomatic persons, including pregnant persons.31 The CDC provides detailed guidelines for prevention and management of genital HSV in adolescents, adults, and pregnant persons, including consideration of HSV-2 serologic testing in certain scenarios.31 The CDC recommends counseling persons diagnosed with genital herpes to prevent sexual and perinatal transmission.31

ARTICLE INFORMATION

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Author Contributions: Dr Mangione had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. The USPSTF members contributed equally to the recommendation statement.

Conflict of Interest Disclosures: Authors followed the policy regarding conflicts of interest described at https://www.uspreventiveservicestaskforce.org/Page/Name/conflict-of-interest-disclosures. Dr Donahue reported that she is the vice chair of the University of North Carolina Evidence-based Practice Center, where faculty and primary care research fellows worked on the systematic evidence review for this topic. All members of the USPSTF received travel reimbursement and an honorarium for participating in USPSTF meetings.

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Disclaimer: Recommendations made by the USPSTF are independent of the US government. They should not be construed as an official position of AHRQ or the US Department of Health and Human Services.

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Additional Information: 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. Published by JAMA—Journal of the American Medical Association under arrangement with the Agency for Healthcare Research and Quality (AHRQ). ©2022 AMA and United States Government, as represented by the members of the United States Preventive Services Task Force (USPSTF). All rights reserved.

REFERENCES