Letters

RESEARCH LETTER

Serologic Screening for Genital Herpes: Updated Evidence Report and Systematic Review for the US Preventive Services Task Force

Genital herpes is a viral sexually transmitted infection (STI) caused by 1 of 2 herpes simplex virus (HSV) subtypes: HSV-1 or HSV-2. HSV-1 can cause infection at either the orofacial (eg, cold sores) or anogenital region, whereas HSV-2 infection is typically limited to the anogenital region.[1] In asymptomatic, seropositive persons who have never knowingly experienced an HSV outbreak, HSV-1 serology cannot predict the future outbreak site. Therefore, serologic screening for genital herpes is limited to HSV-2 only.

Editorial page 469

Multimedia

Related article page 502 and JAMA Patient Page page 520

Supplemental content

Genital herpes is one of the most prevalent STIs in the US and can lead to both acute and chronic morbidity in adolescents and adults, as well as significant morbidity and mortality in neonates.[1] In theory, early identification of unrecognized HSV-2 infection, followed by appropriate counseling or treatment, could reduce transmission to sexual partners and neonates as well as reduce morbidity from symptomatic recurrence.[1]

In 2016, the US Preventive Services Task Force (USPSTF) recommended against routine serologic screening for genital herpes infection in asymptomatic adolescents and adults, including those who are pregnant (D recommendation).[2] This limited evidence update aimed to identify studies published since the previous (2016) evidence review[3] conducted for the USPSTF to inform an updated recommendation.

Methods | A literature search of PubMed/MEDLINE, the Cochrane Library, EMBASE, and trial registries was conducted for studies from September 30, 2015, through January 16, 2022. Additional sources included reference lists of retrieved articles, outside experts, and public commenters, with ongoing surveillance of the literature through July 22, 2022. Two investigators independently evaluated the eligibility of all abstracts and articles and rated study quality using predefined criteria.[2] An analytic framework and 7 key questions (KQs) guided the evidence update (**Figure**). Detailed methods and results are available in the full evidence report.[1]

For purposes of this review, the term *asymptomatic* refers to individuals with no known past or current history of genital herpes, which may include individuals with unrecognized genital herpes because symptoms either were very mild or were attributed to other causes (eg, urinary tract infection). Studies of individuals previously diagnosed with genital herpes who are not currently experiencing symptoms (ie, an asymptomatic period following an outbreak of genital herpes) were not considered eligible for this review. Studies of persons with HIV or other immunosuppressive conditions were also not eligible for this review.

Results | We reviewed 3119 abstracts and 64 full-text articles. No new eligible studies were identified for any KQ. We identified 1 new diagnostic test accuracy study (KQ2), which was excluded because of poor study quality.

Discussion | This systematic review yielded no new eligible studies published since the 2016 recommendation against screening for genital herpes in asymptomatic persons. Therefore, the overall conclusions of this review are unchanged from those of the previous review. Foundational evidence for the prior recommendation against screening is based on psychosocial harms associated with false-positive test results due to poor screening test accuracy, especially in populations with low HSV-2 prevalence, and uncertain benefit of preventive viral medications for reducing viral shedding or improving health outcomes.

The Centers for Disease Control and Prevention recommends serologic screening for specific asymptomatic populations at higher risk for infection (eg, persons with HIV or other immunosuppressive conditions).[5] This current review, however, focused on the general population of asymptomatic adolescents and adults and therefore may not be applicable to populations at higher risk for infection.

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Author Contributions: Dr Asher had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Asher, Feltner, Harrison, Jonas.
Acquisition, analysis, or interpretation of data: Asher, Feltner, Harrison, Schwimmer, Rains, Jonas.
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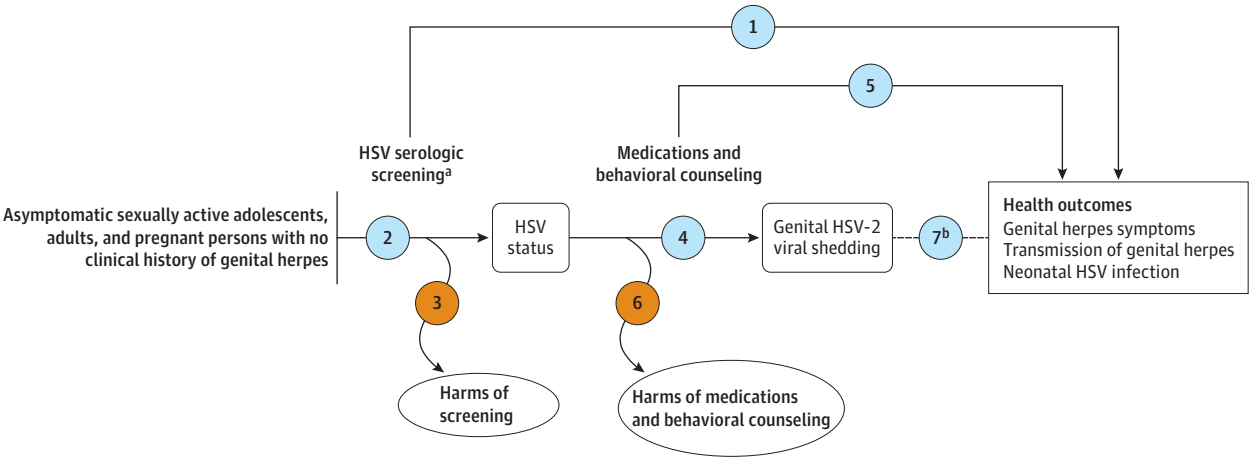
Figure. Analytic Framework: Serologic Screening for Genital Herpes



Key questions

1. Does serologic screening for HSV-2 or combined testing for HSV-1 and HSV-2 in asymptomatic adolescents and adults reduce future symptomatic episodes and transmission of genital herpes, including vertical transmission for pregnant persons?
2. What is the accuracy of serologic screening for HSV-2 in asymptomatic adolescents, adults, and pregnant persons?
3. What are the harms of serologic screening for HSV-2 or combined testing for HSV-1 and HSV-2 in asymptomatic adolescents, adults, and pregnant persons?
4. How effective are antiviral medications in reducing genital HSV-2 viral shedding in asymptomatic adolescents, adults, and pregnant persons?
5. How effective are antiviral medications and behavioral counseling interventions in reducing future symptomatic episodes and transmission of genital herpes in asymptomatic adolescents and adults, including vertical transmission for pregnant persons?
6. What are the harms of antiviral medications and behavioral counseling interventions for reducing future symptomatic episodes and transmission of genital herpes in asymptomatic adolescents and adults, including vertical transmission for pregnant persons?
7. What is the evidence supporting an association between subclinical genital HSV-2 viral shedding and health outcomes in asymptomatic adolescents, adults, and pregnant persons who are seropositive for HSV-2?

HSV-1 and HSV-2 indicate herpes simplex virus 1 and herpes simplex virus 2, respectively; KQ, key question.

[a] Studies that screened using an HSV-2 serologic test alone or a type-specific serologic test for both HSV-1 and HSV-2 simultaneously were included if they met other eligibility criteria; however, only the accuracy of test characteristics related to HSV-2 serologic tests was evaluated.

[b] KQ7 was only addressed if the literature for KQs 1 and 5 was insufficient, but the literature for KQ4 was sufficient. Evidence reviews for the US Preventive Services Task Force (USPSTF) use an analytic framework to visually display the KQs that the review will address to allow the USPSTF to evaluate the effectiveness and safety of a preventive service. The questions are depicted by linkages that relate to interventions and outcomes. Further details are available from the USPSTF procedure manual.[4]

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Role of the Funder/Sponsor: Investigators worked with USPSTF members and AHRQ staff to develop the scope, analytic framework, and key questions for this review. AHRQ had no role in study selection, quality assessment, or synthesis. AHRQ staff provided project oversight, reviewed the report to ensure the analysis met methodological standards, and distributed the draft for peer review. Otherwise, AHRQ had no role in the conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review, or approval of the manuscript findings. The opinions expressed in this document are those of the authors and do not represent the official position of AHRQ or the US Department of Health and Human Services.

Data Sharing Statement: See the Supplement.

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Additional Information: A draft version of the full evidence report underwent external peer review from 6 content experts (Barbara Van Der Pol, PhD, MPH, University of Alabama at Birmingham; David Grossman, MD, MPH, Kaiser Permanente Washington; 1 anonymous physician researcher; Laura E. Riley, MD, Weill Cornell Medicine; Christine Johnston, MD, MPH, University of Washington; and Terri Warren, RN, MSN, Westover Research Group) and 2 individuals from 2 federal partner reviewers (Centers for Disease Control and Prevention, National Institutes of Health). Comments from reviewers were presented to the USPSTF during its deliberation of the evidence and were considered in preparing the final evidence review.

Editorial Disclaimer: This evidence report is presented as a document in support of the accompanying USPSTF Recommendation Statement. It did not undergo additional peer review after submission to *JAMA*.

1. Asher G, Feltner C, Harrison W, Schwimmer M, Rains C, Jonas D. *Serologic Screening for Genital Herpes: An Evidence Report for the US Preventive Service Task Force. Evidence Synthesis No. 224*. Agency for Healthcare Research and Quality; 2023. AHRQ publication 22-05296-EF-1.

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