In 2016, the US Preventive Services Task Force (USPSTF) recommended, with an A recommendation, that asymptomatic, nonpregnant persons who are at increased risk for syphilis infection should be screened. Since that time, syphilis rates have continued to increase unabated, even with the barriers to testing and diagnoses imposed by the COVID-19 pandemic. In the new recommendation statement, USPSTF again provides an A recommendation to screen all asymptomatic, nonpregnant adults and adolescents persons at increased risk for syphilis, a well-timed reaffirmation to the current practices of sexual health clinicians. That said, wide gaps in syphilis testing and diagnoses remain, especially among clinicians who practice outside settings that emphasize sexually transmitted infection (STI) prevention services, including HIV care, sexual health, and prenatal clinics—even when screening is clearly indicated. Even at HIV clinics, many persons living with HIV do not receive the recommended screening despite their higher rates of syphilis and the unique factors associated with management and follow-up.

The USPSTF's updated 2022 recommendation cites new evidence in support of better outcomes with screening, improved risk identification, and identification of lower, manageable harms that screening might incur. In the evidence review, key points bolster the A recommendation: the effectiveness of screening asymptomatic persons to reduce syphilis complications and transmission of both syphilis and other STIs (including HIV), availability and ability of risk assessment instruments to identify persons needing screening, and the harms of screening for syphilis. While the new evidence is welcome and clearly bolsters the updated recommendations, each study cited has nuances that should inform the discussion of future syphilis control efforts.

First, to attest that screening asymptomatic persons for syphilis indeed improves outcomes, the USPSTF highlights a large, longitudinal Australian study demonstrating that screening asymptomatic men who have sex with men (MSM) was associated with increased detection of early latent syphilis and decreased incidence of secondary syphilis. In this case, both individual-level benefits (reduced likelihood of secondary syphilis) and population-level benefits (reduced transmission among MSM, a group with high syphilis incidence) were incurred. However, while syphilis testing increased considerably in both MSM living with HIV and those without HIV, at the end of the study, 91% of MSM without HIV received testing while only 77% of the MSM living with HIV did. Syphilis tests per individual increased from 1.3 to 1.6 among MSM without HIV and from 1.6 to 2.3 among MSM with HIV. Even though the mean number of tests increased more among MSM with HIV, a disparity remained among the proportion of MSM with HIV receiving syphilis testing compared with MSM without HIV. More recently, a stepped-wedge cluster-randomized clinical trial among men living with HIV in Canada (most of whom were MSM) showed that standing orders for syphilis screening at the time of routine HIV viral load measurements led to an increase in early syphilis detection. Many of these men did report at least 1 symptom, but an increase in syphilis detection was also observed among persons with no symptoms reported. The USPSTF expressly did not include studies among persons living with HIV, but with the increasing uptake of preexposure prophylaxis and better understanding of treatment as prevention, consideration of potential sex partners' HIV status may not be a major consideration in partner choice; thus, syphilis may be transmitted efficiently throughout these networks. These studies demonstrate that increased efforts to screen for syphilis will yield higher rates of disease detection, at least among men with increased risk. It may be challenging to generalize these data to other persons, particularly cisgender
women, since they were not included in these studies. Nevertheless, in the worsening STI climate, an approach that includes permissive, broadly applied screening to individuals at risk should be a pillar of the public health response, as endorsed by the USPSTF.3,4

Second, the USPSTF3,4 gives an A recommendation to screen asymptomatic persons at high risk, but the definition of high risk relies on clinicians understanding the complex sexual behaviors and networks of their patients as well as their socioeconomic, demographic, and other situational factors. Clinicians do not always take an adequate sexual history to determine the need for screening, which is the first step in prevention of any STI.13 The risk model cited by the USPSTF3,4 identifies significant factors associated with increased risk: number of male partners in the past 3 months, anal receptive intercourse, history of prior syphilis, and living with HIV.14 Essentially, this confirms factors already considered to be associated with high risk for syphilis. Moreover, the PICASSO cohort15 of that study did not include cisgender women, so the risk model cannot be generalized to use for cisgender women. Considerably less data are available to describe syphilis risk for cisgender women, which should be of paramount importance, considering the devastating congenital syphilis rates that are increasing rapidly in the US. Indeed, primary and secondary syphilis rates among women increased 21% from 2019 to 2020, despite the COVID-19 pandemic, and 147% from 2016 to 2020, with a concomitant increase in US congenital syphilis cases from 2016 to 2021.2 Interventions aimed primarily at the sexual networks that involve MSM and transgender persons may not have an appreciable impact on syphilis among nonpregnant cisgender women, given limited connectivity of these networks.16 Future research is critical to better determine how and when to screen this group. Syphilis screening during pregnancy is extraordinarily important, but identifying and treating syphilis before a woman becomes pregnant is also essential, especially for women who may be late to begin prenatal care or receive no prenatal care.

Third, harms associated with screening include the psychosocial stress associated with testing, as well as the stress associated with learning the results, as noted by Reynolds et al,17 who reported that stress associated with screening for syphilis was more common among Black persons, persons who inject drugs, and persons with less than high school education, while posttest stress related to learning the results was more common among persons with less than high school education and unmarried persons. The study did not determine if stress changed from before the test to after; however, it seems logical that psychological stress caused by testing could be mitigated with appropriate counseling. Other potential harms may include concerns related to incorrect results: false-positive results leading to undue stress or anxiety, unnecessary treatment, follow-up, or additional work-up, and false-negative results that inappropriately assure the patient, leading to disease progression or failure to interrupt transmission. Gaps remain in better understanding and mitigating these harms.

While the reiteration of the USPSTF recommendations3,4 for syphilis screening are crucial, we urgently need bold interventions to combat the sustained resurgence of this disease. These should be built on USPSTF’s recognition of the impact of such screening and could include prioritizing clinician awareness for proactive screening, making screening accessible and convenient, and ensuring prompt treatment. Notably, major barriers exist in laboratory capacity to screen for syphilis. Laboratory-based screening assays use a 2-step serologic test to reduce the rate of false positives; while these are the most accurate assays available, their interpretation can sometimes require skill. Point-of-care tests offer reasonable performance for screening assays and can identify previously undiagnosed cases in an office, community outreach setting, or even self-testing. Importantly, self-testing can be an easy avenue to identifying syphilis.18 It is prudent to remember that the point-of-care assays approved by the US Food and Drug Administration are qualitative treponemal antibody assays and thus do not provide the quantitative titer that can sometimes assist in distinguishing a new infection from latency. Syphilis diagnostics lag behind the nucleic acid amplification technologies that characterize assays used for screening chlamydia and gonorrhea. The challenge of developing accurate syphilis diagnostics remains formidable.
In summary, the reaffirmation of the USPSTF A recommendation to screen asymptomatic, nonpregnant persons with increased risk for syphilis is wholly justified and complements other STI and HIV care guidelines. The USPSTF reports on data showing improved outcomes with important, although relatively less severe, harms support this recommendation. As the USPSTF notes, more research needs to be done to better understand the effects of screening, especially to investigate screening in populations beyond those conventionally thought of as at risk. Syphilis screening must be expanded beyond the perceived niche of sexual health care and be emphasized in routine primary care and other settings where enhanced detection might ensue. Innovative approaches to increase awareness and convenient access to screening, which might be clinic-, community-, or home-based, coupled with quick and appropriate access to treatment are needed. This USPSTF A recommendation lays the essential foundation on which novel public health and patient care strategies should be developed to slow the spread of syphilis and should prime the field to expand and broaden its efforts.

ARTICLE INFORMATION
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