

Screening for Chlamydial and Gonococcal Infections

Updated Evidence Report and Systematic Review for the US Preventive Services Task Force

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IMPORTANCE The 2014 US Preventive Services Task Force (USPSTF) recommendation statement supported the effectiveness of screening for chlamydia and gonorrhea in asymptomatic, sexually active women 24 years or younger and in older women at increased risk for infection, although evidence for screening in men was insufficient.

OBJECTIVE To update the 2014 USPSTF review on screening for chlamydial and gonococcal infection in adults and adolescents, including those who are pregnant.

DATA SOURCES Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, and Ovid MEDLINE (January 1, 2014, through May 28, 2020) with surveillance through May 21, 2021.

STUDY SELECTION Randomized clinical trials and observational studies of screening effectiveness, accuracy of risk stratification and alternative screening methods, accuracy of tests, and screening harms.

DATA EXTRACTION AND SYNTHESIS One investigator abstracted data; a second checked accuracy. Two investigators independently assessed study quality.

MAIN OUTCOMES AND MEASURES Complications of infection; infection transmission or acquisition; diagnostic accuracy of anatomical site-specific testing and collection methods; screening harms.

RESULTS Twenty-seven studies were included (N = 179 515). Chlamydia screening compared with no screening was significantly associated with reduced risk of pelvic inflammatory disease (PID) in 2 of 4 trials and with reduced hospital-diagnosed PID (0.24% vs 0.38%); relative risk, 0.6 [95% CI, 0.4-1.0]), but not clinic-diagnosed PID or epididymitis, in the largest trial. In studies of risk prediction instruments in asymptomatic women, age younger than 22 years demonstrated comparable accuracy to extensive criteria. Sensitivity of chlamydial testing was similar at endocervical (89%-100%) and self- and clinician-collected vaginal (90%-100%) sites for women and at meatal (100%), urethral (99%), and rectal (92%) sites for men but lower at pharyngeal sites (69.2%) for men who have sex with men. Sensitivity of gonococcal testing was 89% or greater for all anatomical samples. False-positive and false-negative testing rates were low across anatomical sites and collection methods.

CONCLUSIONS AND RELEVANCE Screening for chlamydial infection was significantly associated with a lower risk of PID in young women. Risk prediction criteria demonstrated limited accuracy beyond age. Testing for asymptomatic chlamydial and gonococcal infections was highly accurate at most anatomical sites, including urine and self-collected specimens. Effectiveness of screening in men and during pregnancy, optimal screening intervals, and adverse effects of screening require further evaluation.

JAMA. 2021;326(10):957-966. doi:10.1001/jama.2021.10577

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Chlamydia is the most commonly reported sexually transmitted infection (STI) in the US, followed by gonorrhea. In 2019, 1 808 703 cases of chlamydia were reported to the Centers for Disease Control and Prevention (CDC), corresponding to a rate of 552.8 cases per 100 000 population.¹ Reported cases of chlamydial infections among US women vs men were 698.9 vs 399.9 cases per 100 000, respectively; however, rates among men increased 32.1% from 2015 to 2019. In 2019, there were 616 392 cases of gonococcal infections, corresponding to a rate of 188.4 cases per 100 000 persons. Both infections demonstrate differences in reported cases by geography, race and ethnicity, and HIV status.¹

In women, chlamydial infection is usually asymptomatic but can result in transmission.² Untreated chlamydial infections can progress to symptomatic pelvic inflammatory disease (PID) and can result in infertility, chronic pelvic pain, and ectopic pregnancy.^{2,3} In men, genital chlamydial infection is most often asymptomatic^{4,5} but can cause nongonococcal urethritis, epididymitis, and if symptomatic, may present as urethritis.² Chlamydial infection can facilitate HIV infection in both women and men and may potentiate the risk for cervical cancer.⁶ Gonococcal infections in women are often asymptomatic but in men can lead to symptomatic urethritis, epididymitis, and proctitis.^{7,8} In contrast, the majority of extragenital (eg, pharyngeal, rectal) infections in men are asymptomatic.^{9,10}

In 2014, the US Preventive Services Task Force (USPSTF) issued B recommendations for screening for chlamydia and gonorrhea in sexually active women 24 years or younger and in older women at increased risk for infection.¹¹ Evidence was insufficient to assess the balance of benefits and harms of screening for chlamydia and gonorrhea in men. This systematic review was conducted to update prior reviews on this topic for the USPSTF,¹²⁻¹⁴ to inform an updated recommendation.

Methods

Scope of the Review

Detailed methods and additional information about included studies are available in the full evidence report.¹⁵ **Figure 1** shows the analytic framework and key questions (KQs) that guided the review.

Data Sources and Searches

Searches included Ovid MEDLINE, the Cochrane Central Register of Controlled Trials, and the Cochrane Database of Systematic Reviews from January 1, 2014, through May 28, 2020 (eMethods 1 in the Supplement), with surveillance through May 21, 2021. Reference list review of relevant systematic reviews supplemented the searches.

Study Selection

Two investigators independently reviewed English-language titles, abstracts, and full-text articles for inclusion using predefined eligibility criteria (eMethods 2 in the Supplement). The screening population included asymptomatic, sexually active adults and adolescents, including those who are pregnant. This update primarily evaluated studies published since the prior USPSTF review.¹⁷ However, since the scope, KQs, and inclusion criteria differ from prior reviews, older studies that were not previously reviewed are also

included. Specifically, this review included new KQs focused on accuracy of risk stratification and screening strategies for identifying persons at increased risk, and a KQ evaluating the diagnostic accuracy of anatomical site-specific testing and collection methods. We did not rereview the diagnostic accuracy of specific assays or tests, which the prior review found to be highly accurate.¹⁷

For screening effectiveness and harms, randomized clinical trials (RCTs) and controlled observational studies of screening vs no screening in asymptomatic individuals that evaluated health outcomes were included. Outcomes for KQ1 included reduced complications of chlamydial or gonococcal infections and reduced transmission or acquisition of disease, including HIV and, for pregnant individuals, reduced adverse maternal, fetal, or infant outcomes. Studies of risk stratification methods and screening strategies (eg, selective screening of high-risk groups, sampling from various anatomical sites, cotesting for concurrent STIs including HIV, and using different screening intervals) for chlamydia and gonorrhea that reported measures of diagnostic accuracy or discrimination were included for KQ2.

For KQ3, studies of diagnostic accuracy that included measures of discrimination of testing at various anatomical sites or using different collection methods (self- vs clinician- collected) were included if studies used credible reference standards, adequately described the study population, defined positive test results, and reported performance characteristics of tests (eg, sensitivity, specificity) or provided data to calculate them. For KQ4 on harms of screening, uncontrolled observational studies were included in addition to RCTs and controlled observational studies. Harms include labeling, anxiety, false-positive and false-negative test results, and other consequences of testing.

Data Abstraction and Quality Rating

A single investigator abstracted details about study design, patient population, setting, interventions, analysis, follow-up, and results from each study. A second investigator reviewed abstracted data for accuracy. Two independent investigators assessed the quality of each study as good, fair, or poor using predefined criteria developed by the USPSTF (eMethods 3 in the Supplement).¹⁶ Discrepancies were resolved through consensus. In accordance with the USPSTF Procedure Manual,¹⁶ poor-quality studies were excluded due to methodological limitations.

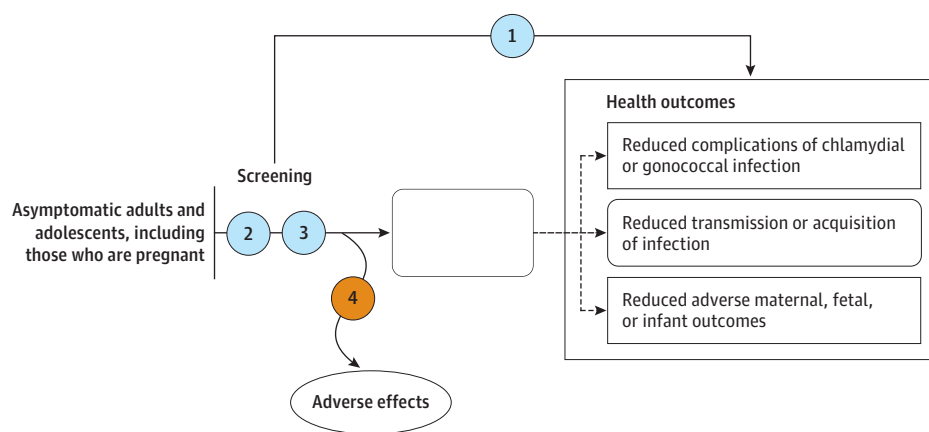
Data Synthesis

Two independent reviewers assessed the internal validity (quality) of the body of evidence for each KQ using methods developed by the USPSTF, based on the number, quality, and size of studies; consistency of results between studies; and directness of evidence.^{16,18} Statistical meta-analysis was not performed because of methodological limitations of the studies and heterogeneity in study designs, interventions, populations, and other factors.

Results

Of 2356 unique citations and 490 full-text articles reviewed, 20 studies (N = 179 515) met inclusion criteria, including 13 new studies¹⁹⁻³¹ and 7³²⁻³⁸ from the previous USPSTF report (**Figure 2**).

Figure 1. Analytic Framework: Screening for Chlamydial and Gonococcal Infections



Key questions

- 1 In asymptomatic, sexually active adults and adolescents, including those who are pregnant, what is the effectiveness of screening for chlamydial and gonococcal infections in reducing complications of infection and transmission or acquisition of disease, including gonorrhea, chlamydia, and HIV?
- 2 What is the accuracy of risk stratification methods or alternative screening strategies for identifying persons at increased risk of chlamydial and gonococcal infections (such as younger persons or men who have sex with men)? Screening strategies include testing for concurrent infections, including HIV, or using different screening intervals.
- 3 What is the diagnostic accuracy of anatomical site-specific testing and collection methods for identifying persons with chlamydial and gonococcal infections?
- 4 What are the harms of screening for chlamydial and gonococcal infections (such as labeling, anxiety, false-positive/false alarm results, false-negative results/reassurance, or change in risk behaviors or risk perception)?

Evidence reviews for the US Preventive Services Task Force (USPSTF) use an analytic framework to visually display the key questions 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 interventions and outcomes. A dashed line indicates a health outcome that immediately follows an intermediate outcome. For additional information see the USPSTF Procedure Manual.¹⁶

Screening Effectiveness

Key Question 1. In sexually active, asymptomatic adolescents and adults, including those who are pregnant, what is the effectiveness of screening for chlamydial or gonococcal infections in reducing complications of infection and transmission or acquisition of disease, including gonorrhea, chlamydia, and HIV?

Four randomized trials evaluated the effects of screening for chlamydial infection vs no screening on risk of complications of infection (Table 1),^{25,32,33,36} including 3 trials^{32,33,36} from the prior review.¹⁷ As in the previous reviews, no study evaluated the effectiveness of screening for gonorrhea.

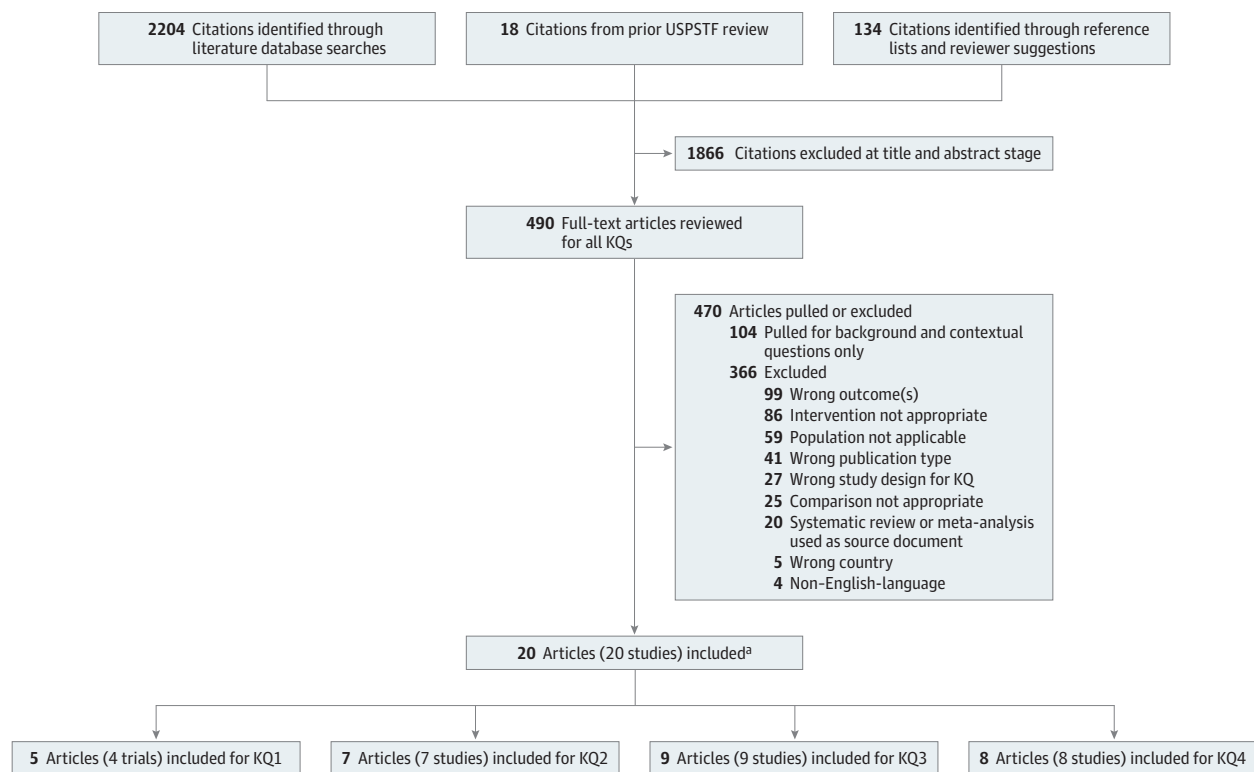
Sample sizes ranged from 1700 to 63 338 (total n = 70 174). Three trials enrolled exclusively women,^{32,33,36} 1 trial enrolled both women and men,²⁵ 1 trial enrolled exclusively adolescents,³³ and 3 enrolled a mix of adolescents and adults (16 to 34 years) from a rural primary care setting,²⁵ a university setting,³² and a population of higher-risk women.³⁶ Trials were conducted in the US,³⁶ Europe,^{32,33} and Australia²⁵ and compared screening vs usual care,²⁵ home sampling,³³ or clinic-based testing.³⁶ One trial compared immediate vs deferred screening.³² Three trials used self-collected vaginal^{25,32,33} or male urine testing.²⁵ Two trials were rated good-quality^{25,32} and 2 fair-quality (eTable 1 in the Supplement),^{33,36} because of unclear randomization methods and high loss to follow-up.

The Australian Chlamydia Control Effectiveness Pilot trial (ACCEPT), was a new, good-quality cluster randomized trial that

evaluated the effectiveness of screening for chlamydia compared with usual care in 180 355 men and women aged 16 to 29 years in 130 rural Australian primary care clinics.²⁵ While screening was significantly associated with reduced risk of hospital-diagnosed primary PID (relative risk [RR], 0.6 [95% CI, 0.4-1.0]), the absolute difference was small (0.24% [57/23 527] vs 0.38% [88/23 219]). Screening was not significantly associated with reduced repeat chlamydia infection within 6 weeks to 6 months of a positive test result (odds ratio [OR], 3.1 [95% CI, 0.7-13.8]), clinic-diagnosed PID (RR, 1.1 [95% CI, 0.7-1.8]; 0.45% [293/65 519] vs 0.39% [237/60 384]), or clinic-diagnosed epididymitis (RR, 1.1 [95% CI, 0.7-1.8]; 0.26% [106/41 168] vs 0.27% [106/38 717]).

Three trials included in the prior USPSTF review indicated an association between screening and decreased risk of PID, although results were statistically significant in only 1 trial.³² Chlamydia screening was significantly associated with reduced risk for PID in a fair-quality RCT of 2607 women aged 18 to 34 years at increased risk for chlamydia who were recruited from a health maintenance organization in the US (RR, 0.44 [95% CI, 0.20-0.90]).³⁶ In the Prevention of Pelvic Infection (POPI) trial, a good-quality RCT of 2529 sexually active symptomatic (35%) or asymptomatic (65%) young women in the UK, screening was not associated with a statistically significant reduced risk of PID (RR, 0.65 [95% CI, 0.34-1.22]).³² However, 79% (30/38) of PID cases occurred in women who had tested negative at baseline. A fair-quality RCT of 1761 Danish high school students indicated that risk of PID was not

Figure 2. Literature Search Flow Diagram: Screening for Chlamydial and Gonococcal Infections



KQ indicates key question; USPSTF, US Preventive Services Task Force.

^a Articles may be included for multiple key questions.

significantly associated with a reduction of PID for screening vs home sampling (RR, 0.50 [95% CI, 0.23-1.08]).³³

Risk Stratification

Key Question 2. What is the accuracy of risk stratification methods or alternative screening strategies for identifying persons at increased risk for chlamydial or gonococcal infections (such as younger persons or men who have sex with men)?

Seven fair-quality studies (n = 93 137) evaluated accuracy of strategies for identifying individuals at increased risk for chlamydial or gonococcal infections using different criteria to select patients for testing (eTables 2 and 3 in the Supplement).^{20-22,24,26-28} No study compared screening intervals or alternative screening strategies, such as testing for concurrent infection with HIV.

Two studies enrolled only women,^{27,28} and 5 included both men and women.^{20-22,24,26} Participants were asymptomatic in 3 studies,²⁰⁻²² symptom status was not reported in 3 studies,^{24,26,27} and 1 study included both asymptomatic (52%) and symptomatic (47%) participants.²⁸ Studies were conducted in Canada,²⁰⁻²² the US,^{24,26,28} and Europe²⁷ in family planning clinics,²⁸ STI or sexual health clinics,^{20-22,26,28} university or community clinics,²⁴ and a pregnancy termination clinic.²⁷ Six studies were cross-sectional,^{20-22,24,27,28} and 1 was a case-control study.²⁶ Key limitations included inadequate selection of patients and measurement of exposures or outcomes, including retro-

spective data collection,^{20-22,27} and baseline between-group differences between intervention and control groups.²⁸

In asymptomatic patients, 2 cross-sectional studies (n = 35 818) of the Vancouver risk estimation tool, an instrument for identifying asymptomatic women and heterosexual men at increased risk for chlamydial or gonococcal infection, demonstrated fair discrimination (area under the receiver operating characteristics curve [AUC], 0.64-0.73).^{20,21} Factors in the model included age, sex, race, number of partners, and other known STI risk factors. A cross-sectional study of a 3-item (age, indicators of risk, and injection drug use) risk score (n = 35 818) reported an AUC of 0.73 (95% CI, 0.71-0.74) in a population of asymptomatic men and women attending STI testing clinics in Canada.²²

A cross-sectional study of women attending family planning or STI clinics in the US (n = 6672) compared 9 sets of selective screening criteria for chlamydial infection.²⁸ In family planning clinics, 69% of women were asymptomatic, while nearly 80% of women in STI clinics reported genitourinary symptoms.²⁸ Age alone (≤ 22 years) performed nearly as well as multiple criteria in predicting chlamydial infection, demonstrating similar sensitivity (74%-77%), specificity (51%-56%), and AUC (0.69 [95% CI, 0.67-0.71]), compared with multi-item screening criteria (AUC, 0.72-0.73). Risk prediction tools evaluated in other settings, such as with intrauterine device insertion or surgical abortion, demonstrated poor accuracy in 2 other studies.^{24,27}

Table 1. Randomized Clinical Trials of Screening for Chlamydia to Reduce Adverse Outcomes

Source	Population	Interventions	Duration, y	Attrition, %	Outcomes, No./total (%)	Quality
Hocking et al, ²⁵ 2018	Sexually active males and females aged 16-29 y in 130 primary care clinics in Australia (n = 63 338)	Multifaceted screening program vs usual care (control)	3.1 (mean)	NR	Incidence of PID in clinic ^a : Screened: 293/65 519 (0.45) Control: 237/60 384 (0.39) RR, 1.1 (95% CI, 0.7-1.8) Incidence of PID in hospitals: Screened: 57/23 527 (0.24) Control: 88/23 219 (0.38) RR, 0.6 (95% CI, 0.4-1.0) Incidence of epididymitis ^b : Screened: 106/41 168 (0.26) Control: 106/38 717 (0.27) RR, 0.9 (95% CI, 0.6-1.4)	Good
Oakeshott et al, ³² 2010 ^c	Sexually active females aged ≤27 y recruited from universities and colleges in the UK (n = 2529)	Immediate screening vs deferred screening after 1 y (control)	1	Screened: 5 Control: 7	Incidence of PID in asymptomatic women (n = 1648): Screened: 5/787 (0.6) Control: 14/861 (1.6) RR, 0.39 (95% CI, 0.14-1.08) Incidence of PID in all women: Screened: 15/1191 (1.3) Control: 23/1186 (1.9) RR, 0.65 (95% CI, 0.34-1.22)	Good
Ostergaard et al, ³³ 2000 ^c	Female students recruited from high schools in 1 county in Denmark (n = 1700)	Home screening vs usual care opportunistic screening in a clinic (control)	1	Screened: 49 Control: 42	Incidence of new chlamydia infections in all females: Screened: 13/443 (2.9) Control: 32/487 (6.6) RR, 0.45 (95% CI, 0.24-0.84) P = .026 Incidence of PID in all females: Screened: 9/443 (2.1) Control: 20/487 (4.2) RR, 0.50 (95% CI, 0.23-1.08) P = .045	Fair
Scholes et al, ³⁶ 1996 ^c	Women aged 18 to 34 y recruited from a health maintenance organization in the US, selected by risk criteria (n = 2607)	Clinic screening vs usual care (control)	1	24 (did not return final questionnaire)	Incidence of PID in all women: Screened, 8 per 10 000 women-years (9 cases) Control, 18 per 10 000 women-years (33 cases) RR, 0.44 (95% CI, 0.20-0.90)	Fair

Abbreviations: NR, not reported; PID, pelvic inflammatory disease; RR, relative risk.

^a Denominator is the number of females aged 16 to 33 years with at least 1 consultation during the intervention period.

^b Denominator is the number of men aged 16 to 29 years with at least 1 consultation during the intervention period.

^c Included in prior US Preventive Services Task Force evidence review.

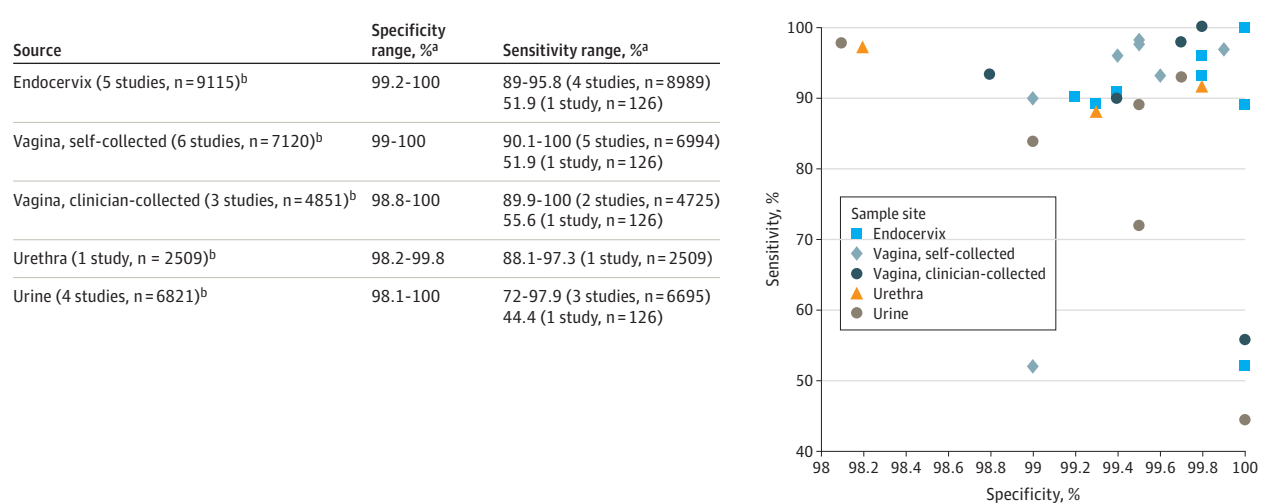
A case-control study conducted in 12 STI clinics in Los Angeles County (n = 245) evaluated the proportion of gonorrhea cases missed by limiting testing to urogenital gonorrhea in men or women aged 15 to 29 years reporting oral intercourse in the last 3 months with an opposite-sex partner.²⁶ The multivariable model demonstrated a strong association between higher number of oral sex partners in the last 3 months (adjusted OR, 5.7 [95% CI, 1.3-25.6]) and the presence of concurrent urogenital gonorrhea (adjusted OR, 6.2 [95% CI, 2.6-14.3]) and risk of pharyngeal gonorrhea, after adjusting for age, sex, and number of sex partners.²⁶

Diagnostic Accuracy of Tests

Key Question 3. What is the diagnostic accuracy of anatomical site-specific testing and collection methods for identifying persons with chlamydial or gonococcal infections?

Nine studies^{19,23,29-31,34,35,37,38} evaluated the diagnostic accuracy of anatomical site-specific testing, and 6 studies^{23,29,34,35,37,38} compared collection methods for identifying chlamydial or gonococcal infections (eTable 4 in the Supplement).^{19,23,29-31,34,35,37,38} Four studies were in the 2014 USPSTF review.^{34,35,37,38} All studies were conducted in the US,^{23,29,34,37} UK,^{19,30,31,35,38} or Canada and were fair quality (eTable 5 in the Supplement).³⁴ Sample sizes ranged from 133 to 3974 (total n = 16 204).^{19,23,29-31,34,35,37,38} Studies enrolled exclusively female participants^{23,30,34,35,37,38}; exclusively male participants,^{19,31} including 1 study that enrolled MSM³¹; or both male and female participants.²⁹ Infection prevalence ranged from 1.5% to 26.6% for chlamydial infection and 1.5% to 11.7% for gonococcal infection. Methodological limitations included unclear methods of enrollment^{19,23,29-31,34,35,37,38} and unclear description of

Figure 3. Diagnostic Accuracy of Site-Specific Testing for Female Chlamydial Infection



^a See eTable 6 in the Supplement for values from the individual studies.

^b One study (Schachter et al³⁴) reported sensitivity and specificity for 3 tests.

independent interpretation of index test results compared with a reference standard.^{19,23,29-31,34,35,37,38}

Anatomical Site-Specific Testing

The sensitivity of site-specific testing for chlamydial infection ranged from 89% to 100% for endocervical^{23,29,30,34,35} and 90% to 100% for vaginal testing,^{23,29,30,34,35} excluding 1 outlier study with lower sensitivities (Figure 3; eTable 6 in the Supplement).³⁷ Specificities were 99% to 100% for endocervical^{23,29,30,34,35,37} and 95% to 100% for vaginal^{23,29,30,34,35,37} testing. The sensitivity of urine testing was more variable than anatomical site testing in 5 studies (range, 44%-100%; median, 85%), with specificities ranging from 96% to 100%.^{23,29,30,34,37} Vaginal testing using patient and clinician-collected samples showed similar sensitivities (range, 90%-100%); specificity was also high (range, 95%-100%).^{23,29,30,34,35,37} Three studies of testing in males (eTable 7 in the Supplement)^{19,29,31} indicated high sensitivity for urine (89%-100%),^{19,29,31} meatal (92%),¹⁹ urethral (99%),³¹ and rectal (92%)³¹ samples. Pharyngeal testing had lower sensitivity (69%) in men who have sex with men (MSM).³¹ Specificity was not reported in studies of males.

Three studies of site-specific testing for gonorrhea in females (eTable 8 in the Supplement)^{23,29,38} indicated sensitivities of 90% to 98% for endocervical,^{23,29,38} 98% to 100% for vaginal (both self- and clinician-collected),^{23,29,38} and 91% to 100% for urine samples.²⁹ Specificity was also high for all sites (range, 99%-100%).^{23,29,38} Three studies of testing in males (eTable 9 in the Supplement)^{19,29,31} indicated high sensitivity (range, 93%-100%) and specificity (>99%) for urine^{19,31} and high sensitivity for meatal (100%),¹⁹ urethral (98%),³¹ rectal (93%),³¹ and pharyngeal (89%)³¹ samples.

Clinician and Self-Collected Testing

One new study²⁹ and 2 studies^{34,37} from the prior USPSTF review compared the accuracy of clinician- and self-collected vaginal samples for diagnosis of chlamydial infection in females (Figure 3; eTable 6 in the Supplement). In 2 studies, sensitivity was 90% to

100% for clinician-collected samples and 90% to 98% for self-collected samples.^{29,34} An additional study reported sensitivities of 56% for clinician-collected samples and 52% for self-collected samples using a different study methodology.³⁷ One study compared clinician- and self-collected vaginal samples for diagnosis of gonorrhea infection in females (eTable 8 in the Supplement).²⁹ In this study, sensitivities were 100% for both methods, and specificities were 100% for clinician-collected and 99.7% for self-collected samples. No study compared clinician- and self-collected testing for chlamydial or gonorrhea infections at other anatomical sites or in males.

Screening Harms

Key Question 4. What are the harms of screening for chlamydial or gonococcal infections (such as labeling, anxiety, false-positive/false alarm results, false-negative results/reassurance, or changes in risk behaviors or risk perception)?

Eight studies of diagnostic accuracy reported false-positive and false-negative rates for anatomical site-specific testing, and 6 studies reported rates for collection methods (eTables 10-13 in the Supplement).^{19,23,29,30,34,35,37,38} As in prior USPSTF reviews, no study evaluated psychosocial harms related to screening or evaluated effects of screening on changes in risk behaviors or risk perceptions.

For chlamydia testing in females, false-positive rates (1 - specificity) ranged from 0% to 2% across anatomical sites in 6 studies,^{23,29,30,34,35,37} including 0% to 0.7% for endocervical, 0% to 1.2% for vaginal, 0.2% to 1.7% for urethral, and 0% to 2% for urine testing. False-negative rates (1 - sensitivity) ranged from 0% to 28% in 5 studies^{23,29,30,34,35}; a sixth study³⁷ reported higher false-negative rates (44%-56%). False-positive rates in studies that compared self-collected and clinician-collected samples ranged from 0% to 1.2%.^{29,34,37} For chlamydia testing in males, false-positive rates were 0.4% for meatal testing¹⁹ and 0.3% to 0.7% for urine testing,^{19,29} while false-negative rates ranged from 0% to 8%.^{19,29}

For gonorrhea testing in females, false-positive rates were less than 1% and false-negative rates ranged from 0% to 10% across anatomical sites^{23,29,38} and were 0% for self-collected and 0.3% for clinician-collected samples²⁹ (eTables 10, 11, 12, and 13 in the Supplement). In males, false-positive rates were similarly low (<1% across sites).^{19,29} No study reported rates by collection method for chlamydia or gonorrhea in males.

Discussion

The evidence reviewed for this report on screening for chlamydial and gonococcal infection is summarized in Table 2. New data on screening were generally consistent with those from prior trials that found screening associated with decreased risk of PID. Evidence evaluating risk prediction tools indicated suboptimal accuracy and require validation in US primary care populations. Prior findings regarding high accuracy of diagnostic testing at various anatomical sites and home-based testing was largely confirmed by newer evidence that demonstrated low false-positive and false-negative rates. Important gaps include lack of studies on psychosocial or other harms related to screening, studies comparing screening intervals or alternative screening strategies, and studies evaluating changes in risk behaviors or risk perception.

Results of 4 screening trials demonstrated that screening for chlamydia was associated with decreased risk of PID, although effects were not statistically significant in most trials and the magnitude of benefit was relatively small. No studies reported on the effectiveness of screening in men, other than 1 study that reported rates of epididymitis,²⁵ and there were no studies conducted among pregnant individuals for any outcome. In contrast to screening trials from the prior review,^{32,33,36} the newest trial included young men and women in primary care settings at average risk and found a reduction in hospital-diagnosed PID associated with chlamydia screening, although absolute effects were small.²⁵

This report included studies on the accuracy of risk criteria, which was not addressed in prior USPSTF reviews. Three studies²⁰⁻²² in asymptomatic patients that found fair discrimination require further validation in diverse clinical and geographic settings. Age 22 years or younger alone vs multi-item risk criteria demonstrated similar discrimination in 1 study that included symptomatic and asymptomatic women.²⁸ A study reporting high rates of pharyngeal gonorrhea in a population of high-risk persons attending STI clinics, correlated increasing numbers of oral sex partners in the 3-month period with rates of pharyngeal gonorrhea.²⁶ Screening both urogenital and pharyngeal sites to increase sensitivity of case detection in certain populations may have implications for extragenital testing in other higher-risk populations.

Diagnostic testing for chlamydia was highly accurate across all genitourinary anatomical sites in both male and female anatomical samples, with vaginal and endocervical testing demonstrating the highest accuracy in females.^{23,29,30,34,35,37} Gonococcal testing was also highly accurate across anatomical sites for females, with endocervical and vaginal sites demonstrating the highest accuracy,^{23,29,38} and urine testing demonstrating the highest sensitivity in males compared with meatal testing.^{19,29} Extragenital (pharyngeal) testing in MSM demonstrated low sensitivity for chlamydial infection but higher sensitivity for gonococcal infection

based on 1 study.³¹ In females, self- and clinician-collected vaginal samples for chlamydia and gonorrhea diagnosis were both highly sensitive,^{29,34,37} but no studies meeting inclusion criteria compared collection methods in males. These results were largely based on asymptomatic patient populations, increasing relevance to screening populations in the US.

In addition to diagnostic accuracy, other factors that may inform testing at extragenital sites include higher prevalence of extragenital chlamydial and gonococcal infection in MSM and persons attending STI clinics, as well as persons engaging in sexual contact at extragenital sites. Recent data on the association between rectal STI and HIV acquisition in men may also inform decisions around extragenital testing.^{6,39} A small observational study of MSM in Australia demonstrated direct transmission of antibiotic-resistant strains of gonorrhea to partners of asymptomatic MSM in association with pharyngeal and rectal infection.⁴⁰ In the US, prevalence data indicate that MSM are disproportionately affected by STIs, including HIV.⁴¹ In a report of prevalence data from STI and HIV clinic attendees, approximately 1 in 8 men had an extragenital chlamydial or gonococcal infection.⁴¹ Given the reported rates of antibiotic resistant strains of gonococcal infection for MSM,⁴² expanding the range of specimen types for screening may increase identification of infected individuals, especially for asymptomatic MSM, in whom nearly 90% of all gonorrhea infections are in nongenital sites.⁴³

There are few harms of screening based on findings from this review, including low rates of false-positive or false-negative findings. However, no studies provided data about other potential adverse effects of screening for any population groups, including anxiety; changes in risk behaviors; or risk perception. Further research is needed to determine the effectiveness of screening in multiple populations and on various clinical outcomes; trials of gonorrhea screening, including screening high-risk groups; effective screening strategies and intervals; and harms of screening.

Despite many years of relatively consistent screening recommendations, rates of chlamydial and gonococcal infections continue to rise.¹ This trend is likely due in part to changes in risk behaviors, although there may be other contributors. Screening tests for chlamydial and gonococcal infections are accurate regardless of anatomical site or collection method. The clinical significance of asymptomatic extragenital infections and the effectiveness of screening at those sites warrants further evaluation. While most studies were primarily conducted in heterosexual populations, several groups continue to experience increased risk for sexually transmitted infections including MSM, gender minority populations, and transgender populations,^{44,45} but data are limited. Additional screening studies evaluating extragenital testing may also inform strategies for expanded screening in various settings and among target groups or those at increased risk.

Limitations

This review had several limitations. First, inclusion criteria considered settings and tests relevant to current US practice and did not reevaluate the accuracy of nucleic acid amplification testing, reducing the available evidence. However, this approach improved the relevance of the evidence to the USPSTF screening recommendation. Second, there was variation in the quality and applicability of studies. A number of studies were conducted in STI clinics or other high-risk clinical settings or in persons at higher risk for infection,

Table 2. Summary of Evidence

Population	Studies (No. of participants)	Summary of findings	Consistency and precision	Limitations	Strength of evidence	Applicability
KQ1: Effectiveness of screening vs no screening						
Young adults and adolescents	Prior review: 3 RCTs (n = 6836) Update: 1 RCT (n = 63 338)	One of 3 RCTs of screening women at increased risk for chlamydia indicated a statistically significant reduction in PID (RR, 0.44 [95% CI, 0.20-0.90]) Chlamydia screening compared with no screening reduced PID in 2 of 4 trials, with reduced hospital-diagnosed PID (RR, 0.6 [95% CI, 0.4-1.0]) but not clinic-diagnosed PID or epididymitis in the largest trial	Consistent; imprecise	Trials were underpowered to address health outcomes; no studies of gonorrhea screening or screening in pregnancy; limited studies of men	Moderate for chlamydial screening in women; insufficient for men, gonococcal infections in all populations	Moderate
KQ2: Accuracy of risk stratification methods for identifying persons at increased risk						
Young adults and adolescents	Prior review: 0 studies Update: 7 cross-sectional studies (n = 93 137)	Not addressed in prior review Seven studies evaluated accuracy of risk criteria and demonstrated low to moderate accuracy Age alone (≤22 y) performed nearly as well as multiple criteria in predicting chlamydial infection, demonstrating similar sensitivity (74%-77%), specificity (51%-56%), and AUC (0.69 [SD, 0.014]) compared with multi-item screening criteria (AUC, 0.72-0.73) No studies compared screening intervals or alternative screening strategies such as testing for concurrent infection, including HIV	Consistent; precise	Studies were retrospective and cross-sectional; models applied in 1 geographic location or population; unclear performance in other geographic locations or populations	Moderate	Moderate; most studies conducted in 1 geographic location or high-prevalence setting
KQ3: Diagnostic accuracy of anatomical site-specific testing and collection methods						
Men, women, MSM; adolescents	Prior review: 4 studies (n = 9474) Update: 5 studies (n = 6730)	Sensitivity of chlamydial testing was similar at endocervical (89%-100%) and self- and clinician-collected vaginal (90%-100%) sites for women and at meatal (100%), urethral (99%), and rectal (92%) sites for men but lower at pharyngeal sites (69.2%) for MSM Sensitivity of gonococcal testing was ≥89% for all anatomical samples	Consistent; precise, excluding 1 outlier study	Some studies included symptomatic participants; prevalence of chlamydial or gonococcal infection ranged up to 27%; limited evidence on collection methods	Moderate for accuracy of chlamydial and gonococcal testing; low for collection methods	High for accuracy of testing; moderate for collection methods
KQ4: Harms of screening vs no screening						
Men, women, MSM; adolescents	Prior review: 4 studies (n = 9474) Update: 4 studies (n = 5666)	False-positive (0%-1.2%) and false-negative (0%-28%) testing rates were low across anatomical sites and collection methods No studies reported harms of collection methods in males No studies of psychosocial harms, such as anxiety related to testing, or studies of risk behaviors or risk perception	Consistent for testing-related harms; precise for testing-related harms NA for psychosocial or risk behavior-related harms	Some studies included symptomatic participants; prevalence of chlamydial or gonococcal infection ranged up to 27%	Moderate for testing-related harms	Moderate for testing-related harms

Abbreviations: AUC, area under the receiving operating characteristic curve; KQ, key question; MSM, men who have sex with men; NA, not applicable; PID, pelvic inflammatory disease; RCT, randomized clinical trial; RR, relative risk.

reducing potential applicability to primary care settings or persons at lower risk. Third, evidence for men was limited and there were no studies of pregnant individuals, despite the need for additional research in these populations. Fourth, screening trials focused on PID and epididymitis as the main outcome; other health outcomes such as infertility, chronic pelvic pain, and ectopic pregnancy are also relevant but may be more challenging to correlate. Detection of PID and epididymitis in 1 trial may have been limited by relatively low screening rates (17%-25%).²⁵ Differences in assay sensitivity may have contributed to a differential effect on PID prevention, given that less sensitive assays may detect only patients with higher bacterial load, which has been linked in some studies to greater likelihood of developing PID. Fifth, there were no screening studies that reported disease acquisition or transmission. Sixth, meta-analysis was not performed due to relatively small numbers of studies and hetero-

geneity in populations, settings, comparisons, and outcomes. Formal graphical or statistical assessments for publication bias were not performed because of small numbers of studies.

Conclusions

Screening for chlamydial infection was significantly associated with a lower risk of PID in young women. Risk prediction criteria demonstrated limited accuracy beyond age. Testing for asymptomatic chlamydial and gonococcal infections was highly accurate at most anatomical sites, including urine and self-collected specimens. Effectiveness of screening in men and during pregnancy, optimal screening intervals, and adverse effects of screening require further evaluation.

ARTICLE INFORMATION

Accepted for Publication: June 11, 2021.

Author Contributions: Dr Cantor 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.

Concept and design: Cantor, Dana, Nelson, Winthrop, Chou.

Acquisition, analysis, or interpretation of data: Cantor, Dana, Griffin, Nelson, Weeks, Chou.

Drafting of the manuscript: Cantor, Dana, Griffin, Nelson, Weeks, Chou.

Critical revision of the manuscript for important intellectual content: Cantor, Griffin, Nelson, Winthrop, Chou.

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Obtained funding: Cantor, Chou.

Administrative, technical, or material support: Cantor, Dana, Griffin, Weeks, Winthrop.

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Conflict of Interest Disclosures: Dr Winthrop reported receiving personal fees from Insmmed, Paratek, RedHill, and Spero and receiving grants from Insmmed. No other disclosures were reported.

Funding/Support: This research was funded under contract HHS A290201500009-1, Prism No. HHS A29032014T, from the Agency for Healthcare Research and Quality (AHRQ), US Department of Health and Human Services, under a contract to support the US Preventive Services Task Force (USPSTF).

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 that 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 reflect the official position of AHRQ or the US Department of Health and Human Services.

Additional Contributions: We thank the following individuals for their contributions to this project: AHRQ Medical Officers Brandy Peaker, MD, MPH,

Tina Fan, MD, MPH, Kathleen Irwin, MD, MPH, and the USPSTF. We also acknowledge past and current USPSTF members who contributed to topic deliberations. The USPSTF members, external reviewers, and federal partner reviewers did not receive financial compensation for their contributions.

Additional Information: A draft version of this evidence report underwent external peer review from 4 federal partners representing the US Centers for Disease Control and Prevention, US Food and Drug Administration, and the National Institutes of Health and 3 content experts (Charlotte A. Gaydos, DrPH, MPH, MS; Katherine K. Hsu, MD, MPH; Susan Tuddenham, MD, MPH). 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*.

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