Screening for Gonorrhea and Chlamydia: A Systematic Review for the U.S. Preventive Services Task Force

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Background: Previous research has supported screening for gonorrhea and chlamydia in asymptomatic, sexually active women (including pregnant women) who are younger than 25 years or at increased risk but not in other patient populations.

Purpose: To update the 2005 and 2007 systematic reviews for the U.S. Preventive Services Task Force on screening for gonorrhea and chlamydia in men and women, including pregnant women and adolescents.

Data Sources: MEDLINE (1 January 2004 to 13 June 2014), Cochrane databases (May 2014), ClinicalTrials.gov, and reference lists.

Study Selection: English-language trials and observational studies about screening effectiveness, test accuracy, and screening harms.

Data Extraction: Extracted study data were confirmed by a second investigator, and study quality and applicability were dual-rated using prespecified criteria.

Data Synthesis: Screening a subset of asymptomatic young women for chlamydia in a good-quality trial did not significantly reduce the incidence of pelvic inflammatory disease over the following year (relative risk, 0.39 [95% CI, 0.14 to 1.08]); however, 1 previous trial reported a reduction. An observational study evaluating a risk prediction tool to identify persons with chlamydia in high-risk populations had low predictive ability and applicability. In 10 new studies of asymptomatic patients, nucleic acid amplification tests demonstrated sensitivity of 86% or greater and specificity of 97% or greater for diagnosing gonorrhea and chlamydia, regardless of specimen type or test.

Limitations: There were few relevant studies of screening benefits and harms. Only screening tests and methods cleared by the U.S. Food and Drug Administration for current clinical practice were included to determine diagnostic accuracy.

Conclusion: Chlamydia screening in young women may reduce the incidence of pelvic inflammatory disease. Nucleic acid amplification tests are accurate for diagnosing gonorrhea and chlamydia in asymptomatic persons.

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In 2005, on the basis of epidemiologic studies of screening and studies of the diagnostic accuracy of screening tests (1–3), the U.S. Preventive Services Task Force (USPSTF) recommended screening for gonorrhea in all sexually active or pregnant women at increased risk for infection (4). It recommended against routine screening in low-risk men and nonpregnant women and found insufficient evidence to recommend for or against routine screening in high-risk men and low-risk pregnant women.

In 2007, on the basis of studies of the effectiveness of screening, harms, and diagnostic accuracy of screening tests (1–3), the USPSTF recommended screening for chlamydia in all sexually active or pregnant women younger than 25 years and in older, high-risk women (5). It recommended against routine screening in low-risk women, regardless of pregnancy status, and found insufficient evidence to recommend for or against screening in men.

Gonorrhea and chlamydia are the 2 most commonly reported sexually transmitted infections (STIs) in the United States (6). In 2012, totals of 334 826 cases of gonorrhea and 1 422 976 cases of chlamydia were reported to the Centers for Disease Control and Prevention (6). However, the true incidence of gonorrhea and chlamydia is difficult to estimate because most infections are undetected.

In women, gonococcal and chlamydial infections are most often asymptomatic but can cause cervicitis and complications of pelvic inflammatory disease (PID), ectopic pregnancy, infertility, and chronic pelvic pain (6, 7). In men, these infections can cause urethritis and epididymitis (6, 8). Most men with gonococcal urethritis are symptomatic, prompting timely treatment that prevents serious complications (9). However, gonococcal infections at extragenital sites, including the pharynx and rectum, and genital chlamydial infections are typically asymptomatic. Gonorrhea and chlamydia can also facilitate HIV transmission in both men and women (6, 10, 11). Infection with either gonorrhea or chlamydia in pregnant women can lead to adverse neonatal outcomes, including preterm birth and transmission of infection to the newborn. Chlamydial infection also causes neonatal ophthalmia and pneumonia in infants.

Age is a strong predictor of risk for both gonorrhea and chlamydia, and infection rates are greatest among persons aged 15 to 24 years (6). Although rates are greater for women than men (108.7 cases of gonorrhea per 100 000 women vs. 105.8 per 100 000 men; 643.3 cases of chlamydia per 100 000 women vs. 262.6 per 100 000 men),

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rates have increased more rapidly among men in recent years (6). Other risk factors include having new or multiple sex partners or a partner with an STI, inconsistent condom use, and history of previous or coexisting STIs (1, 2). These risk factors are often used to define persons at increased risk in screening recommendations. Rates differ among population subgroups, and black and Hispanic persons generally have greater rates of infections compared with white persons (6, 12). Men who have sex with men who were tested in STD Surveillance Network clinics in 2012 had median prevalence rates of 16.4% for gonorrhea and 12.0% for chlamydia (6).

This systematic review is an update of previous reviews for the USPSTF (1–3). It focuses on new studies of the effectiveness and adverse effects of gonorrhea and chlamydia screening in asymptomatic men and women, including pregnant women and adolescents, as well as the diagnostic accuracy of screening tests.

Methods

Methods are further described in a technical report (13). We followed a standard protocol consistent with the Agency for Healthcare Research and Quality (AHRQ) methods for systematic reviews (14). On the basis of evidence gaps identified from previous reviews (1–3), the USPSTF and AHRQ determined the key questions for this update (15). The investigators created analytic frameworks incorporating the key questions and outlining the patient populations, interventions, outcomes, and potential adverse effects (**Supplements 1** and **2**, available at www.annals.org). A work plan was externally reviewed and modified but was not registered.

The target populations were asymptomatic, sexually active men and women, including pregnant women and adolescents. The key questions focused on the effectiveness of screening compared with not screening in preventing adverse health outcomes, effectiveness of different screening strategies, diagnostic accuracy of screening tests, and potential harms of screening. Screening strategies included selective screening of high-risk groups, sampling from various anatomical sites, cotesting for concurrent STIs (including HIV), and using different screening intervals, among others. Outcomes included reduction of complications of infection and transmission or acquisition of disease, including gonorrhea, chlamydia, and HIV. For pregnant women, outcomes also included reduction in maternal complications and adverse pregnancy and infant outcomes. Harms of screening included labeling, anxiety, false-positive and false-negative test results, and other consequences of testing. The efficacy and harms of antibiotic treatments were well-established and were not further evaluated.

Data Sources and Searches

We searched Ovid MEDLINE (1 January 2004 to 13 June 2014), the Cochrane Central Register of Controlled Trials (May 2014), the Cochrane Database of Systematic Reviews (May 2014), the Health Technology Assessment Database (May 2014), the Database of Abstracts of Reviews of Effects (May 2014), and ClinicalTrials.gov (May 2014) and reviewed reference lists for additional citations (13). Search terms are provided in **Supplement 3** (available at www.annals.org).

Study Selection

Abstracts were selected for full-text review if they included asymptomatic, sexually active men and women, including pregnant women and adolescents; were relevant to a key question; and met additional prespecified inclusion criteria for each key question (13). Although this update was intended to evaluate studies published since the previous USPSTF reviews, the scope, key questions, and inclusion criteria differ across reviews, resulting in the inclusion of older studies that have not been previously reviewed. We included only English-language articles and excluded studies that were published as abstracts only or did not report original data. The selection of studies is summarized in a literature flow diagram (**Supplement 4**, available at www.annals.org). Two reviewers independently evaluated each study to determine inclusion eligibility.

Only randomized, controlled trials (RCTs) and controlled observational studies were included to evaluate the effectiveness of screening, whereas uncontrolled observational studies were also included to determine adverse effects. Studies of screening strategies were included if they adequately described the study population and comparison groups, features of the screening program, and outcome measures. Inclusion criteria were less restrictive for effectiveness studies than diagnostic accuracy studies because the main comparison concerned outcomes related to the overall approach of screening compared with nonscreening rather than the characteristics of the individual tests.

Studies of the accuracy of diagnostic tests were included if they evaluated screening tests in asymptomatic participants using technologies and methods that have been cleared by the U.S. Food and Drug Administration (FDA) and are available for clinical practice in the United States. These inclusion criteria reflect the scope of the USPSTF recommendations about technologies and medications. On the basis of these criteria, rectal, pharyngeal, and self-collected vaginal specimens obtained in nonclinical settings and point-of-care or in-house tests were excluded. Tests that were previously cleared and subsequently removed from the U.S. market (such as the ligase chain reaction test) were also excluded (16). Included studies used credible reference standards, adequately described the study population, defined positive test results, and reported performance characteristics of tests (such as sensitivity and specificity) or provided data to calculate them.

Data Abstraction and Quality Rating

A single investigator abstracted details about study design, patient population, comparison groups, setting,

screening method, analysis, follow-up, and results. A second investigator reviewed data abstraction for accuracy. By using prespecified criteria for RCTs, cohort, and diagnostic accuracy studies developed by the USPSTF (14), 2 investigators independently rated the quality of studies (good, fair, or poor) and resolved discrepancies by consensus.

Data Synthesis and Analysis

Two independent reviewers assessed the internal validity (quality) of the body of evidence for the new studies for each key question using methods developed by the USPSTF, on the basis of the number, quality, and size of studies; consistency of results among studies; and directness of evidence (14, 15). Statistical meta-analysis was not done because of methodological limitations of the studies and heterogeneity in study designs, interventions, populations, and other factors. Studies included in previous reviews were reviewed for consistency with current results; however, lack of studies and differences in scope, key questions, and inclusion criteria limited aggregate synthesis with the updated evidence.

Role of the Funding Source

This research was funded by AHRQ under a contract to support the work of the USPSTF. The investigators worked with USPSTF members and AHRQ staff to develop and refine the scope, analytic frameworks, and key questions; resolve issues during the project; and finalize the report. AHRQ had no role in study selection, quality assessment, synthesis, or development of conclusions. AHRQ provided project oversight; reviewed the draft report; and distributed the draft for peer review, including to representatives of professional societies and federal agencies. AHRQ performed a final review of the manuscript to ensure that the analysis met methodological standards. The investigators are solely responsible for the content and the decision to submit the manuscript for publication.

Results

Effectiveness of Screening Asymptomatic Men and Nonpregnant Women, Including Adolescents

No studies of gonorrhea screening met inclusion criteria for the previous USPSTF reviews or this update. The 2001 (1) and 2007 (3) USPSTF reviews on chlamydia screening identified 2 trials of screening women at increased risk for chlamydia (17, 18) (**Table 1** and **Supplement 5**, available at www.annals.org). Incidence of PID was significantly reduced among women screened in a good-quality RCT of 2607 women aged 18 to 34 years who were recruited from an HMO in the United States (relative risk [RR], 0.44 [95% CI, 0.20 to 0.90]) (17, 18). Reductions were of borderline statistical significance in a poor-quality RCT of Danish students (RR, 0.50 [CI, 0.23 to 1.08]) (17, 18).

One new RCT of chlamydia screening in women (but none in men) met inclusion criteria for this update. The Prevention of Pelvic Infection trial was a good-quality RCT of 2529 sexually active young women recruited from universities in the United Kingdom (mean age, 21 years [range, 16 to 27 years]) (19) (**Table 1** and **Supplement 5**). Participants provided chlamydia tests using self-collected vaginal swabs. Specimens from participants randomly assigned to the screening group were immediately tested for chlamydia, whereas specimens from control participants were tested 1 year later. After 1 year, 94% of participants completed questionnaires about symptoms of PID and sexual behavior during the previous year. Medical records of women suspected of having PID on the basis of their questionnaire responses were reviewed by 3 blinded genitourinary physicians for diagnostic confirmation.

During follow-up, PID occurred in 1.3% of screened versus 1.9% of control participants (RR, 0.65 [CI, 0.34 to 1.22]) (19). Among a subgroup of participants who reported no symptoms during the 6 months before the study (that is, pelvic pain, dyspareunia, abnormal vaginal bleeding, or discharge), 0.6% (5 of 787) of screened participants versus 1.6% (14 of 861) of control participants developed PID during follow-up (RR, 0.39 [CI, 0.14 to 1.08]) (Kerry S. Personal communication.). In this trial, 79% (30 of 38) of PID cases occurred in women who tested negative at baseline. In addition, 22% of participants were tested for chlamydia outside of the study protocol during follow-up.

Effectiveness of Screening Strategies

Previous reviews did not directly address the effectiveness of different screening strategies but summarized risk factors associated with gonococcal and chlamydial infections (1, 2). An observational study comparing 9 sets of selective screening criteria for chlamydial infection among women attending family planning and STI clinics in the United States (20) indicated that age alone had similar or better sensitivity and specificity as more extensive criteria. In this study, nearly 80% of cases were identified while testing 50% of the population when using an age cutoff of 22 years or younger.

Only 1 new study of screening strategies met inclusion criteria. An observational study conducted in the Netherlands evaluated a risk prediction tool to identify persons infected with chlamydia in high-risk populations (21). Screening criteria were developed on the basis of questionnaire responses from sexually active participants who were subsequently tested for chlamydia and included items on age, education, ethnicity, lifetime sex partners, and condom use. When applied to high-risk populations, this risk tool was not an accurate predictor of infection (area under the receiver-operating characteristic curve, 0.66 to 0.68). The applicability of this study to U.S. populations is also limited.

Diagnostic Accuracy of Screening Tests for Gonorrhea and Chlamydia

The previous reviews reported high sensitivity and specificity in studies of the diagnostic accuracy of gonor-

Table 1. **Summary of Evidence**

Main Findings From Previous USPSTF Reviews	Studies in Update	Quality of Evidence	Limitations	Consistency	Applicability	Summary of Findings
Effectiveness of screening asymptomatic men and nonpregnant women, including adolescents						
Chlamydia screening reduced PID incidence in a good-quality RCT (RR, 0.44 [95% CI, 0.20–0.90]) but not in a poor-quality RCT (RR, 0.50 [CI, 0.23–1.08]).	1 good-quality RCT of chlamydia screening in women	Fair	Trial potentially underpowered; no studies of gonorrhea screening; no studies of chlamydia screening in other populations	Point estimates consistent with previous trials, although significance varies	Study conducted in the United Kingdom using self-collected samples	Screening a subset of asymptomatic young women for chlamydia did not significantly reduce PID incidence over the following year (RR, 0.39 [CI, 0.14–1.08]); 1 previous trial reported a reduction.
Effectiveness of different screening strategies						
9 sets of selective screening criteria for chlamydial infection indicated that age alone had sensitivity and specificity that were similar to or better than more extensive criteria.	1 observational study of chlamydia screening in women	Poor; studies are lacking	No studies of effectiveness or comparing cotesting or different screening intervals	NA	Study conducted in the Netherlands with limited applicability to the United States	A risk prediction tool to identify persons with chlamydia in high-risk populations was not an accurate predictor; a previous study indicated that an age cutoff of ≤22 y would identify 80% of cases while testing 50% of women.
Diagnostic accuracy of screening tests for detecting gonorrhea and chlamydia						
25 studies for gonorrhea and 33 for chlamydia indicated high accuracy, although studies included symptomatic participants and tests that are no longer used.	10 diagnostic accuracy studies of NAATs*	Good	Unclear sampling methods and interpretation of tests and inclusion of patients with uninterpretable results; some studies had technical shortcomings	Consistent	Studies included high-prevalence populations (>5%)	Gonorrhea: Sensitivity of 91%–100% and specificity of ≥97%† Chlamydia: Sensitivity of 86%–100% and specificity of ≥97%† Previous findings are similar but may not be clinically applicable.
Harms of screening asymptomatic men and nonpregnant women, including adolescents						
25 studies of tests for gonorrhea and 33 for chlamydia reported diagnostic accuracy. One qualitative interview study indicated anxiety with a positive test result.	10 diagnostic accuracy studies of NAATs*	Good for false-positive and false-negative result rates; lack other outcomes	No studies on other harms of screening met inclusion criteria	Consistent	Studies included high-prevalence populations (>5%)	Gonorrhea: False-positive results, ≤3%; false-negative results, 0% to 9%† Chlamydia: False-positive results, ≤3%; false-negative results, 0% to 14%† Previous findings are similar but may not be clinically applicable.
Effectiveness of screening asymptomatic pregnant women						
No studies; previous reviews cited descriptive studies predating the searches.	No studies	NA	NA	NA	NA	NA
Harms of screening asymptomatic pregnant women						
No studies met inclusion criteria.	No studies	NA	NA	NA	NA	NA

NA = not applicable; NAAT = nucleic acid amplification test; PID = pelvic inflammatory disease; RCT = randomized, controlled trial; RR = relative risk; USPSTF = U.S. Preventive Services Task Force.
* Specimens include endocervical, clinician-collected vaginal, self-collected vaginal, male urethral, and urine.
† For studies without major methodological limitations.

Table 2. **Diagnostic Accuracy Studies (2004–2013) of Nucleic Acid Amplification Tests for Gonorrhea and Chlamydia Screening**

Screening Test	Sensitivity/Specificity, by Specimen Type, %				
	Endocervical	Clinician-Collected Vaginal	Self-Collected Vaginal	Male Urethral	Urine
Gonorrhea					
Gen-Probe APTIMA Combo 2 Assay					
Van Der Pol et al, 2012 (24)	100/100	–	–	–	Female: 95.7/100
Van Der Pol et al, 2012 (25)	96.4/99.5	–	–	100/99.2	Female: 78.6/100 Male: 100/99.4
Stewart et al, 2012 (26)	90.0/100	–	98.0/100	–	–
Taylor et al, 2012 (23)	–	–	–	100/100	Male: 100/100
Gen-Probe APTIMA GC Assay					
Chernesky et al, 2005 (22)				100/97.1	Male: 90.9/99.5
BD ProbeTec ET System					
Van Der Pol et al, 2012 (25)	92.9/99.3	–	–	100/100	Female: 82.1/99.5 Male: 92.3/99.8
BD ProbeTec CT/GC Q^x Amplified DNA Assay					
Van Der Pol et al, 2012 (24)	91.3/99.8	–	–		Female: 100/99.9
Van Der Pol et al, 2012 (25)	96.3/99.5	–	–	100/99.2	Female: 100/99.5 Male: 100/99.2
Taylor et al, 2012 (23)		–	–	100/100	Male: 100/99.8
Roche Cobas 4800 CT/NG Test					
Van Der Pol et al, 2012 (24)	95.7/100	–	–	–	Female: 100/100
Taylor et al, 2012 (23)	–	–	–	–	Male: 100/100
Cepheid GeneXpert CT/NG Assay					
Gaydos et al, 2013 (27)	100/100	–	100/99.9	–	Female: 91.7/99.9 Male: 100/99.9
Chlamydia					
Roche Cobas Amplicor CT/NG Test					
Schachter et al, 2003 (28)	90.7/99.4	93.3/98.8	90.7/99.0	–	Female: 84.0/99.0
Shrier et al, 2004 (29)	51.9/100	55.6/100	51.9/99.0	–	Female: 44.4/100
Gen-Probe APTIMA Combo 2 Assay					
Schoeman et al, 2012 (31)	89.0/100	–	97.0/99.9	–	–
Taylor et al, 2012 (23)		–	–	94.1/98.9	Male: 98.0/99.0
Taylor et al, 2011 (30)	92.9/99.0	–	–	90.9/98.8	Female: 98.2/99.5 Male: 97.2/100
Van Der Pol et al, 2012 (24)	97.1/99.5	–	–	–	Female: 92.5/99.8
Gen-Probe APTIMA CT Assay					
Schachter et al, 2003 (28)	89.1/99.3	89.9/99.4	93.3/99.6	–	Female: 72.0/99.5
Chernesky et al, 2005 (22)	–			98.9/97.5	Male: 98.9/98.0
BD ProbeTec ET System					
Taylor et al, 2011 (30)	86.4/100	–	–	86.1/98.9	Female: 89.8/99.7 Male: 97.2/99.4
BD ProbeTec CT/GC Q^x Amplified DNA Assay					
Taylor et al, 2012 (23)	–	–	–	86.5/99.8	Male: 96.2/99.5
Taylor et al, 2011 (30)	93.0/98.0	–	–	88.6/98.9	Female: 94.7/99.5 Male: 100/98.9
Van Der Pol et al, 2012 (24)	96.2/99.7	–	–	–	Female: 96.2/99.7
Roche Cobas 4800 CT/NG Test					
Taylor et al, 2012 (23)	–	–	–	–	Male: 98.1/99.5
Van Der Pol et al, 2012 (24)	89.5/100	–		–	Female: 89.1/99.8
Cepheid GeneXpert CT/NG Assay					
Gaydos et al, 2013 (27)	95.8/99.4	–	98.0/99.4	–	Female: 96.1/99.8 Male: 100/99.9

rhea and chlamydia tests (1, 2). However, several studies included symptomatic persons and non–nucleic acid amplification tests (non-NAATs), including tests that are not currently available, diminishing their clinical applicability.

Ten new fair-quality studies reporting test characteristics of FDA-cleared NAATs met inclusion criteria (**Table 2** and **Supplements 6** and 7, available at www.annals.org): 6 for gonorrhea (22–27) and 8 for chlamydia (22–24, 27–31). Methodological limitations include unclear descriptions of sampling methods, whether interpretations of the screening test were independent of the reference standard (22–25, 28–30), and whether the analysis included participants with uninterpretable results (22, 24, 25, 28, 30). Three studies described additional methodological difficulties related to the reference standard (29) and technical approach (25, 28). Most studies reported more than 5% prevalence of infection among participants, although rates were lower in 3 studies (24, 26, 27). Although sensitivity

varied, specificity was high (≥97%) across all studies for gonorrhea and chlamydia in men and women, regardless of specimen or test.

Gonorrhea Tests

For women, 4 studies testing endocervical specimens using transcription-mediated amplification (TMA); polymerase chain reaction (PCR), including a new rapid test (27); or strand displacement amplification (SDA) reported sensitivities ranging from 90.0% to 100.0% (24–27) (**Figure 1**). Sensitivity using self-collected vaginal specimens obtained in a clinician's office was 98.0% by TMA (26) and 100% by PCR (27). Results of female urine specimens using TMA, PCR, or SDA ranged from 78.6% to 100% (24, 25, 27). However, the study reporting the lowest sensitivities for urine used urine volumes larger than recommended by the manufacturer of the screening test (25). When recommended urine volumes were used in a second study, the sensitivity of the same TMA test improved from 78.6% to 95.7% (24).

For men, testing urethral specimens with SDA and TMA and testing urine using TMA, SDA, or PCR resulted in similarly high sensitivities across tests in 4 studies (urethral specimen, 100%; urine, 90.0% to 100%) (22, 23, 25, 27) (**Figure 1**).

Chlamydia Tests

Among 5 studies of endocervical specimens, sensitivity of TMA was 89.0% to 97.1%, SDA was 86.4% to 96.2%, and PCR was 86.4% to 95.8% (24, 27, 28, 30, 31) (**Figure 2**). Clinician-collected vaginal swabs tested with TMA and PCR provided sensitivities of 89.9% and 98.8% (28), and self-collected vaginal swabs from clinical settings provided sensitivities of 97.0% with TMA (31) and 90.7% (28) and 98.0% (27) with PCR. Female urine samples tested with TMA, PCR, and SDA provided sensitivities of 72.0% to 98.2% (24, 27, 28, 30). Lower sensitivities for urine samples using TMA (72.0%) and PCR (84.0%) were reported in a study that experienced technical and specimen processing errors (28).

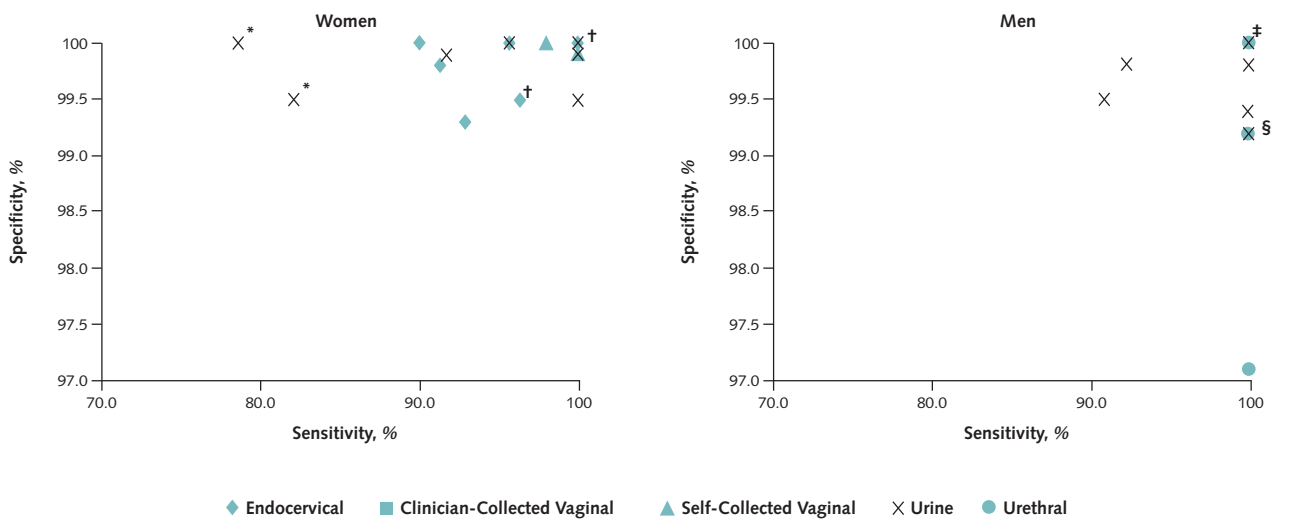
A single study of PCR reported sensitivities that were markedly lower than other studies (29), and results were not included in **Figure 2**. This study used a more conservative approach to analysis that required complete sets of results from 9 testing strategies. Also, the reference standard included positive NAAT results from 2 separate specimens. When a specimen-specific reference standard was used, sensitivities were similar to other studies (data were not provided).

Sensitivities for male urethral and urine specimens were consistently high, regardless of test, across 4 studies reporting sensitivities from 86.1% to 100% for TMA, SDA, or PCR (22, 23, 27, 30) (**Figure 2**).

Harms of Screening Asymptomatic Men and Nonpregnant Women, Including Adolescents

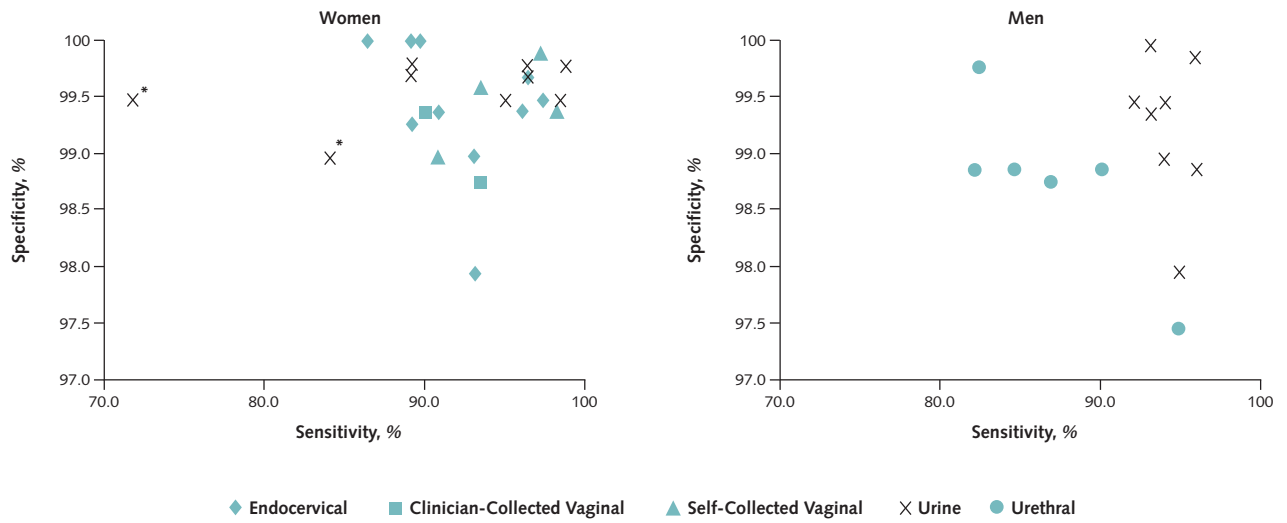
The previous reviews indicated low false-positive and false-negative results for screening tests (1–3) that were confirmed by the 10 new diagnostic accuracy studies described earlier. In the new studies without major methodological limitations, false-positive result rates for gonorrhea

Figure 1. **Diagnostic accuracy of nucleic acid amplification tests for gonorrhea screening in men and women.**



* The study reporting lower sensitivities for urine specimens in women (78.6% and 82.1%) used urine volumes that were larger than recommended (25), differing from the other studies.
† Two studies produced identical data points for tests of the endocervix.
‡ Three data points for urethral specimens and 3 data points for urine specimens.
§ Two data points for urethral specimens.

Figure 2. **Diagnostic accuracy of nucleic acid amplification tests for chlamydia screening in men and women.**



* The study reporting lower sensitivities for urine specimens in women (72.0% and 84.0%) experienced technical and specimen-processing errors (27), differing from the other studies.

and chlamydia were 3% or lower, and false-negative result rates ranged from 0% to 9% for gonorrhea and 0% to 14% for chlamydia across all NAATs and specimen types (22–31).

A previous review (3) included results of qualitative interviews about the experience of chlamydia testing from women having opportunistic screening (32). Although many women believed that screening was beneficial and important, common responses to a positive test result included feeling dirty, ashamed of passing on the infection, and suspicious about the origins of the infection.

Benefits and Harms of Screening Asymptomatic Pregnant Women

As in the previous reviews (2, 3), no studies reported the benefits or harms of screening pregnant women specifically.

Discussion

No studies were available to address several key questions, including the effectiveness of screening for gonorrhea in all population groups and screening for chlamydia in men, pregnant women, and adolescents specifically; the effectiveness of screening strategies; and harms of screening unrelated to the diagnostic accuracy of tests.

Only 1 new trial evaluated the effectiveness of screening for chlamydia in nonpregnant women (19) (key question 1). In the Prevention of Pelvic Infection trial, screening a subset of asymptomatic young women for chlamydia did not significantly reduce PID over the following year compared with no screening (RR, 0.39 [CI, 0.14 to 1.08]). Although it met the criteria for good quality, the trial was limited by inadequate recruitment, testing for chlamydia outside of the study protocol during follow-up in nearly one quarter of participants, and difficulties in ascertaining PID cases. These limitations imply that the study may have been underpowered and the intervention effects attenuated. In addition, most cases of PID occurred in women who tested negative at baseline, suggesting that frequent targeted screening of women at greater risk for infection, including those with new sexual partners or a recent history of chlamydia, may be more important than 1-time routine screening.

Two earlier trials also evaluated the incidence of PID after chlamydia screening of women at increased risk (17, 18). Although a good-quality trial in the United States reported a statistically significant reduction in PID incidence in the screened versus usual care group after 1 year of follow-up (RR, 0.44 [CI, 0.20 to 0.90]) (17, 18), reduction in PID incidence was not statistically significant in a poor-quality trial in Denmark comparing 1-time home-based screening with usual care (17, 18). Although all 3 trials reported point estimates suggesting reduced PID, only the U.S. trial showed a statistically significant reduction. This trial met criteria for good quality, is the largest trial, and is the most applicable to clinical practice in the United States.

Additional relevant studies of screening did not meet inclusion criteria because they did not provide results for asymptomatic participants or reported infection rates rather than health outcomes. These studies found no significant improvements in clinical outcomes among those screened for chlamydia, including a large Danish trial of more than 30 000 young men and women (33), a retrospective population-based cohort study of more than

40 000 Swedish women (34), and a register-based screening trial of more than 300 000 men and women in the Netherlands (35). A time trend analysis of a U.S. managed care population between 1997 and 2007 indicated increased cases of chlamydia for both men and women but decreased PID (36). It is not clear how screening influenced these outcomes.

The only new study addressing the effectiveness of different screening strategies (key question 2) was an observational study evaluating a risk prediction tool to identify persons with chlamydia in high-risk populations (21). However, the tool was not an accurate predictor and its relevance to current practice in the United States is uncertain. An older observational study comparing 9 sets of selective screening criteria for chlamydial infection among women (20) supported age-based screening in current guidelines but has not been updated by newer research. Future studies to address this key question would compare the effectiveness of screening versus not screening in populations with different levels of risk; include specimens from different anatomical sites; include cotesting for concurrent STIs, including HIV; and evaluate different screening intervals.

Ten studies of the diagnostic accuracy of screening tests met inclusion criteria (22–26, 28–31, 37) (key question 3). The current review differs from previous reviews (1, 2) by including only results from asymptomatic participants, a focus that is more clinically relevant to screening populations. Various types of NAATs are highly accurate in diagnosing gonorrhea and chlamydia in asymptomatic persons, regardless of specimen, site, or test (22–25, 28, 30, 37). Sensitivity was 85% or greater and specificity was 97% or greater in studies without major methodological limitations, resulting in generally low false-negative and false-positive results. The high accuracy of NAATs reported by these studies is consistent with previous reviews (1, 2) and is the basis for the Centers for Disease Control and Prevention's recommendation to use NAATs for gonorrhea and chlamydia testing (38).

Several studies of harms did not meet inclusion criteria for the update because they focused on the effects of receiving a positive test result, included symptomatic participants, and lacked comparison groups (39–42) (key question 4). In these studies, persons testing positive for chlamydia had greater anxiety (39, 40, 42) and more partner break-ups (39, 40) than those testing negative, who were generally relieved (40, 42).

No studies meeting inclusion criteria addressed screening in pregnant women despite the need for additional research in this population. For example, testing during the first trimester may not be sufficient, based on findings from an observational study suggesting that chlamydia test results during the first trimester may not predict chlamydia status during the third trimester (43). Although studies of repeated testing have been conducted in high-risk populations (44), more research is warranted to further evaluate the value of repeated testing during pregnancy to reduce potential complications, such as preterm delivery and premature rupture of membranes (45).

Limitations of this review include using only English-language articles, which could result in language bias, although we did not identify non–English-language studies that otherwise met inclusion criteria in our searches. We included only studies with asymptomatic participants and settings and tests applicable to current practice in the United States to improve clinical relevance for the USPSTF, excluding much research in the field. Studies were lacking for most key questions, and the number, quality, and applicability of studies varied widely. Also, the available screening trials evaluated only PID as the main outcome, and other outcomes are also important.

Nucleic acid amplification tests have been cleared by the FDA for use with male and female urine, endocervical, and male urethral specimens, and some NAATs are cleared for clinician- and self-collected vaginal specimens in clinical settings. Studies have also reported similar test characteristics for nurse- and patient-collected rectal swabs in men who have sex with men (26, 28, 29, 31, 46). Additional studies of NAATs using self-collected specimens could provide more evidence for FDA clearance of this technique and increase testing access and acceptability. This could potentially expand screening strategies to home-based, mail-in, or Internet-based screening and encourage the uptake of screening among persons at increased risk.

Limiting our review to FDA-cleared tests excluded studies of rectal and pharyngeal specimens that also demonstrate high accuracy in studies of NAATs (26, 28, 29, 31, 46) and are currently recommended by the Centers for Disease Control and Prevention (38). Expanding the range of specimen types for screening has the potential to increase identification of infected persons, especially asymptomatic men who have sex with men, for whom nearly 90% of all gonococcal infections are in nongenital sites (47). Among this population, NAATs have greater sensitivity at extragenital sites compared with culture, potentially because of lower bacterial loads at the pharynx and rectum (48, 49). In a study of men who have sex with men, 85% of rectal infections were asymptomatic and only detectable with routine screening (50). Urethral testing alone missed 84% of chlamydial and gonococcal infections compared with 9.8% missed by rectal and pharyngeal testing in another study (47).

In summary, screening for chlamydia may reduce the incidence of PID in young women. Risk prediction tools may be useful in identifying persons with infections but require validation in the populations of intended use. Nucleic acid amplification tests are accurate for diagnosing gonorrhea and chlamydia in asymptomatic persons, regardless of specimen, site, or test. Further research is needed to determine the effectiveness of screening in multiple populations and on various clinical outcomes, including but not

limited to PID; effective screening strategies; and harms of screening.

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