Screening for Chlamydial Infection: A Summary of the Evidence

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Epidemiology

In the United States, Chlamydia trachomatis is the most common sexually transmitted bacterial pathogen. There are estimated to be 3 million new infections each year.[1,2] Chlamydial genital tract infections are a major cause of urethritis, cervicitis, and pelvic inflammatory disease (PID) in women and are an important cause of ectopic pregnancy, infertility, and chronic pelvic pain. Chlamydial infections are responsible for 25% to 50% of the 2.5 million cases of PID that are reported annually in the United States.[3] Infections are also related to adverse pregnancy outcomes such as miscarriage, premature rupture of membranes,[4-6] preterm labor,[4] low birth weight infants,[4-7] infant mortality,[5,7] and postpartum infections. Perinatal transmission to infants can cause neonatal conjunctivitis and pneumonia.[8] Chlamydial infection in men is the cause of 30% to 40% of the 4 to 6 million visits each year for nongonococcal urethritis and 50% of more than 150,000 cases of acute epididymitis.[9] Rarely, men may experience chronic complications of chronic prostatitis, reactive anthritis,[10,11] urethral strictures[12] and possibly infertility.[13] Chlamydia is a cofactor in transmission of human immunodeficiency virus infection.[14,15] In the United States in 1994, the estimated cost of untreated chlamydial infections and their complications was $2 billion.[16]

70% to 90% of women and a large percentage of men are asymptomatic.[17-20] Because most men tested for chlamydia are those who present for care because they are symptomatic, or because they are a sexual contact of an infected woman, it is likely that a high proportion of infected men are asymptomatic. Untreated asymptomatic infections among women often persist for months[21] and have been associated with infertility and ectopic pregnancy. Complications of chlamydial infections may be due to immunopathologically mediated events related to predisposition of specific individuals as well as to the type of chlamydial strain.[22] Young women may be particularly susceptible because of increased cervical columnar epithelium in this age group.[19] Chlamydia is readily transmitted between sexual partners,[23] and infected men and women without symptoms serve as important reservoirs for new infections. Rates of hospitalization for ectopic pregnancy and PID increase with the number of recurrent chlamydial infections in women.[24]

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The USPSTF recommendations based on this evidence review can be found in Screening for Chlamydial Infection: Recommendations and Rationale (which precedes this chapter), available on the AHRQ Web site and through the AHRQ Publications Clearinghouse.

This chapter first appeared in *Am J Prev Med.* 2001;20(suppl 3):95-107.

The prevalence of chlamydial infection varies from less than 1% to nearly 40%, depending on the population. Chlamydia has the highest prevalence among groups who are least likely to regularly see a physician. Age is the strongest predictor of infection, with adolescent girls and young adult men recording the highest rates. Most screening programs target young women in sexually transmitted disease (STD) or family planning clinics to take advantage of the opportunity to obtain diagnostic tests in the context of other services. Young men have been much more difficult to study and screen, but their roles in transmitting initial and recurrent infections to women are important. Others considered at higher risk include those having multiple sexual partners,[25-32] a new sexual partner,[31,32] or an infected sex partner;[28,32-34] those who inconsistently use barrier contraceptives;[31,32,34] those with previous[31-33] or coexistent STDs;[35,36] and women with abnormalities on examination, such as vaginal discharge, cervicitis, cervical friability, and cervical ectopy.[25,27,28,30,32,35,37,38] Race is independently associated with chlamydial infection.[25,26,28,31-33,36] Even in populations without these risk factors, however, prevalence rates of more than 5% can occur.[9,32,39]

Screening Technology

Culture analysis of endocervical or urethral swab specimens was traditionally considered the diagnostic gold standard for chlamydial infection. Culture technology posed methodologic problems and is not widely available, however, and nonculture tests that use swab specimens were developed next to improve on some of the limitations of culture. These tests initially included antigen detection tests (direct fluorescent antibody [DFA] assay, enzyme immunoassay [EIA]) and nonamplified nucleic acid hybridization. Newer technologies are based on amplified DNA assays (polymerase chain reaction [PCR], ligase chain reaction [LCR], strand displacement assay [SDA], hybrid capture system [HCS]) and transcription-mediated amplification (TMA) of RNA. New tests using urine specimens provide a noninvasive method for both men and women.

Although culture is 100% specific for chlamydial infection (ie, no false positives), there is growing recognition that culture is not 100% sensitive and is, therefore, not an acceptable gold standard for assessing newer diagnostic technologies. Investigators have advocated the use of an expanded gold standard for the calculation of sensitivity and specificity of assays. In this case, a positive result is defined by a positive culture, or a negative culture with either a positive PCR or LCR test that has been confirmed positive by a DFA assay, or a PCR or LCR test directed against the major outer membrane protein. In these studies, however, the additional confirmation tests are usually performed only on specimens that had discrepant results from 2 or more other tests. These tests themselves often constitute part of the expanded gold standard, particularly when culture is not used in the study. Although use of "discrepant analysis" is very common in test performance studies, it is biased and can overestimate sensitivity and specificity results, depending on the reference test.[40]

Effective and low-cost treatment is available for chlamydial infections of the genital tract. Results of clinical trials indicate that a 7-day course of doxycycline or a single-dose of azithromycin are equally efficacious and lead to high cure rates (97%) in nonpregnant women and men.[9,41-44] A Cochrane review of 11 trials for treatment in pregnancy concluded that amoxicillin was as effective as erythromycin in achieving microbiologic cure (few trials are available for other drugs).[45] These drugs are orally administered and are generally well tolerated.

The purpose of this review is to update the evidence on the effectiveness of screening for chlamydial infection by a physician or other health care professional in a clinical setting since the second U.S. Preventive Services Task Force considered it in 1996. Specifically, we examine the evidence that early treatment of chlamydial infection improves health outcomes, as well as evidence of the effectiveness of screening strategies in nonpregnant women, pregnant women, and men, and the accuracy of tests used for screening.

Methods

Analytic Framework and Key Questions

We defined screening to include testing of asymptomatic persons, and "casefinding" testing of those found to have another sexually transmitted infections or symptoms. Universal screening means testing everyone regardless of symptoms or risk factors; selective screening indicates that only those who meet specific criteria are tested.

The analytic framework in Figure 1 indicates the strategy that we used to guide our literature search about screening nonpregnant women, pregnant women, and men. Key questions were identified as areas with unresolved issues pertinent to clinical practice that had new literature published since the last Task Force recommendations were published in 1996. These key questions correspond to selected arrows in the analytic framework and include:

- Arrow 1: Does screening reduce adverse health outcomes?
- Arrow 2: Does screening reduce the prevalence of infection?

  Are risk factors useful for selective screening?

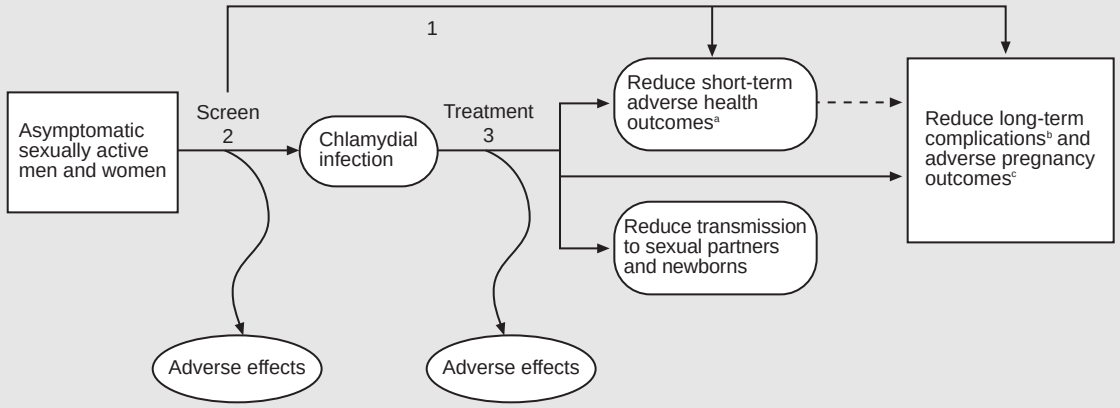
  What screening tests should be performed?
- Arrow 3: What are the implications of recurrent infection?

Literature Search and Synthesis

We searched the topic of chlamydia in the MEDLINE®, HealthSTAR, and Cochrane Library databases from January 1994 through July 2000. A single reader reviewed all English abstracts. Articles were selected for full review if they were about Chlamydia trachomatis genitourinary infections in nonpregnant women, pregnant women, or men and were relevant to key questions in the analytic framework. Reviewing reference lists of other relevant articles and consulting experts in the field identified additional studies. Articles published prior to 1994 and research abstracts were cited if particularly important to the key questions or to the interpretation of included articles.

For our review of diagnostic tests, we focused on the new DNA amplification tests using both swab and urine specimens. Studies comparing antigen detection tests that use swab specimens with culture

Figure 1. Screening for chlamydial infection: analytic framework



[a]Pelvic inflammatory disease in nonpregnant women; choriomnionitis, premature rupture membranes, preterm labor in pregnant women; epididymitis, urethritis, prostatis in men.

[b]Ectopic pregnancy, infertility, chronic pelvic pain in women, chronic prostatitis, reactive arthritis, urethral strictures in men.

[c]Spontaneous abortion, endometritis, preterm delivery/low birth weight.

Note: The analytic framework outlines the scope of the literature search. Numbered arrows correspond to key questions addressed in this report.

were not reviewed here because the performance of antigen detection tests has been previously acknowledged, and they are currently widely used in clinical practice. Antigen detection tests that use urine samples were also not reviewed because they have low sensitivity and are not recommended.

We assigned evidence codes and quality ratings to all studies based on criteria developed by the U.S. Preventive Services Task Force. To demonstrate screening strategy outcomes, we developed a balance sheet that compared three populations, including a low-risk health maintenance organization (HMO) population using a risk factor questionnaire and assumptions from a randomized, controlled trial of screening,[46] a theoretical high-risk population, and a theoretical low-risk population not using a risk factor questionnaire.

Nonpregnant Women

We systematically reviewed 3 types of studies about screening nonpregnant women: (1) studies about the effectiveness of screening programs in reducing prevalence rates of infection, (2) studies about risk factors for chlamydial infection in women, and (3) studies about chlamydia screening tests in women.

Studies about screening programs were included if they provided descriptions of the study population, features of the screening program, and prevalence rates at the beginning of the study period compared to those at a point in time several years later. Studies of risk factors for chlamydial infection were included if they reported descriptions of the study population, screening criteria (universal vs selective), type of chlamydia test, other forms of data collection (eg, questionnaire), and prevalence rate of the tested population. We also reviewed studies of new DNA amplification tests that used both swab and urine specimens. Studies of test performance were included only if they met quality criteria, including: (1) the test was appropriately performed in a standardized manner; (2) the index test, gold standard/expanded gold standard, and discrepant test were appropriately used; (3) the study population was adequately described; and (4) data were sufficient to determine the sensitivity and specificity of tests. We abstracted data about the test, study population, and outcome measures such as sensitivity, specificity, and positive and negative predictive values.

Pregnant Women

Our search found too few studies on pregnant women to apply review criteria. Individual studies related to key questions are described in this report.

Men

We reviewed 2 types of studies about screening men: (1) studies about risk factors for chlamydial infection in men and (2) studies about chlamydia screening tests in men. Studies about chlamydia risk factors in men were included if they described the study population, type of test used, prevalence, and significant associations of risk factors with infection. Studies of chlamydia screening tests for men were abstracted in a similar way as that described for women. We focused particularly on the performance of tests that used urine specimens because this type of testing would have the biggest effect on screening strategies for men.

Results

Does Screening Reduce Adverse Health Outcomes?

Nonpregnant Women

The best evidence to date about the effectiveness of screening for chlamydial infection in preventing PID is a good quality, randomized controlled trial conducted in a large HMO population in Seattle.[46] Screening and treatment of chlamydial infections in unmarried, asymptomatic women aged 18 to 34 years in this study were associated with a significantly reduced incidence of PID after 1 year of follow-up. Inclusion criteria for subjects were based on an earlier study of chlamydia prevalence and risk factors conducted in the primary care clinics of the same HMO.[47] On the basis of responses to a mailed questionnaire, women were assigned a risk score determined by age (24 years or less=1 point), race (black=2 points), nulligravidity (1 point), douching

(1 point), and having 2 or more sexual partners in the preceding 12 months (1 point). Those with a score of 3 or more were eligible for the screening trial and were randomly assigned to screening or usual care groups.

A total of 645 women in the screening group (64% of eligible subjects) were tested for chlamydia, and 7% had positive tests and were treated. The 1,598 women in the usual-care group were not tested. After 12 months, there were 9 confirmed cases of PID among women in the screening group (1.4%) and 33 among women in usual care (2.1%) (relative risk, 0.44; 95% confidence interval [CI], 0.20 to 0.90). Adjustment for various combinations of baseline characteristics did not alter the reduction in risk of PID associated with screening.

Long-term outcomes such as rates of recurrences, ectopic pregnancies, infertility, or chronic pelvic pain were not addressed in this study. Also, women younger than age 18 years, a group with generally higher prevalence rates than older women, were not included.

Two Swedish ecological analyses of chlamydia screening and reduction of PID and ectopic pregnancies support the findings of the screening trial.[48,49]

Pregnant Women

The previous Task Force recommendations for screening pregnant women were based on 2 studies that demonstrated improved pregnancy outcomes following treatment of chlamydial infection. In a time-series design study, untreated patients had a significantly higher incidence of premature rupture of membranes and low birth weight as well as a lower infant survival rate compared to treated patients and patients with negative cultures.[5] In a case-control study, the frequencies of premature rupture of membranes, premature contractions, and small-for-gestational-age infants were significantly lower among successfully treated patients compared to chlamydia-positive patients who were unresponsive to treatment, but they were not significantly different when compared to chlamydia-negative control patients. We identified no recent studies on this topic.

Men

No studies were found that described the effectiveness of screening or early treatment for men in reducing transmission to women or of preventing acute infections or complications in men. Many investigators advocate screening men as the essential next step to reduce infections, complications, and recurrences in women, as well as to improve the health of men themselves. However, these health outcomes have not yet been studied.

Does Screening Reduce the Prevalence of Infection?

No adequately controlled study has prospectively addressed this question, although several studies have been published that report declining prevalence rates in women after instituting chlamydia testing and treatment programs.[39,50-54] Changes in population prevalence rates have not been well documented because few studies have employed a representative population sample. Other unmeasured factors, such as condom use, changes in sexual behavior, and changes in testing methods,[55] could also be responsible for changes in prevalence rates.

Are Risk Factors Useful for Selective Screening?

Nonpregnant Women

Several studies describe risk factors for chlamydial infection among women tested in military, community, primary care, family planning, and STD clinics. Nearly all studies, representing a wide range of settings and prevalence rates (2.3% to 21.5%), report age as an important predictor (usually expressed as less than 25 years old). Current U.S. Preventive Services Task Force guidelines,[56] and those of the Centers for Disease Control and Prevention (CDC)[9], already use age as the primary determinant for screening. Sociodemographic factors such as black and other nonwhite race, marital status, urban location, and low income were also associated with infection in some studies.[25,26,28,31-33,36,37] Behavioral risk factors cited in these studies include multiple sexual partners, new partners, partner with symptoms of an STD, and inconsistent

or no barrier contraception use.[25-34,37] Personal history of PID, STD, pregnancy, douching, and oral contraceptive use were also noted as risk factors in some studies.[26,27,29,31-33,57] Most studies found that physical findings, symptoms, and co-existent gonorrheal infection were also predictive of chlamydial infection.[25,27,28,30,32,35-38] These factors, however, would necessitate chlamydial testing for reasons other than screening and would not be helpful in forming a selective screening strategy. Inconsistencies among studies are likely due to the different populations and risk factors examined.

One of the largest studies of risk factors universally screened 13,204 asymptomatic female U.S. Army recruits from 50 states with urine LCR and found a prevalence rate of 9.2%.[31] Independent predictors of infection included age younger than 25 years, black or other nonwhite race, more than one sexual partner or a new partner in the previous 90 days, not using a condom, and history of a previous STD. When the investigators tested the value of selective screening criteria in this population by using the risk factors of age younger than 25 years, more than 1 partner or a new partner in the previous 90 days, failure to use condoms in the previous 90 days, or history of a previous STD, they found that virtually all of the population would be eligible for screening. If they limited their screening to all women aged 25 years or younger, 87.9% of the population would need to be tested, and 95.3% of the positive subjects would be identified. Other studies found that use of age alone or in combination with 1 or 2 other variables (race, marital status, symptoms, or physical findings) as screening criteria could lead to the detection of 85% to 95% of infections.[25,36,37,58] Another study of 28,000 women aged 15 to 19 years seeking care in family planning clinics in the northwestern United States also identified several factors independently associated with chlamydia infection.[32,39] No single risk factor or combination of risk factors was particularly sensitive for selective screening. The lowest-risk group in this study, representing 21% of the total, accounted for 17% of all infections and had a 6% chlamydia prevalence rate (overall prevalence was 12.3%). Two other studies conducted in settings with greater than 20% prevalence rates also concluded that no risk factors could adequately select which women to screen in their populations.[34,38]

The usefulness of 3 sets of selective screening criteria was evaluated by using data from more than 37,000 female patients with risk factor information who were originally all universally tested in family planning and STD clinics.[59] Criteria based on age alone (younger than age 25 years) performed best among women from family planning clinics with lower prevalence rates (3.3%) than the STD clinics (6.6%), detecting 84% to 92% of cases by screening 59% to 71% of women.

A similar study[41] that tested sets of screening criteria, including age alone, in 6,672 women in public family planning and STD clinics in North Carolina found sensitivities of criteria, ranging from 0.50 to 0.97, and specificities from 0.05 to 0.66.[60] The best-performing criteria were age alone and those based on scores calculated from a set of risk factors determined from a study from an HMO population in Seattle.[47]

Pregnant Women

Previous studies reported prevalence rates for chlamydial infections in pregnant women, ranging from 2% to 31%. Very few studies describe risk factors for chlamydial infection in pregnant women, but, in general, they are similar to those for nonpregnant women with the addition of late onset of prenatal care.[61,62]

Men

Risk factors for chlamydial infections in men have been much less studied than for those in women. The most cited risk factor is age, with men younger than 25 years considered at higher risk than older men. Peak incidence occurs among older adolescents and younger adult men. A multiple-site study of adolescents in Seattle reported a prevalence rate of 5.4% by urine LCR and increased risk of infection for nonwhite race or ethnicity, 2 or more sexual partners in the previous 2 months, presence of symptoms, and increasing age within the cohort.[63] Using a condom was associated with a reduced risk of infection. Other studies concurred that age

groups younger than 25 years were at increased risk of infection.[29,38,54,64,65] One of these studies reported elevated odds ratios for chlamydial infection with early onset of sexual activity (younger than age 13 years) and with known STD in a partner.[38]

An abstract of findings from the 1995 National Survey of Adolescent Males indicated prevalence rates for chlamydia tested by urine PCR in a national household survey performed in the United States.[66] The prevalence among sexually active men aged 18 to 19 years was 4.2% (95% CI, 1.9 to 6.5), and among single, non-cohabiting sexually active men aged 22 to 26 years it was 8.3% (95% CI, 4.2 to 12.3). Rates varied by racial groups, with black men aged 18 to 19 years having rates of 15.4% (95% CI, 8.6 to 22.1) and white men having rates of 1.2% (95% CI, 0.0 to 2.9).

A research abstract from the CDC found that, among 4,797 asymptomatic men presenting to STD clinics in Ohio, those younger than 30 years, with more than 1 sexual partner in the past month, or with a sexual partner with syphilis, had higher risk for chlamydial infection.[67] Use of these risk factors as screening criteria in this low prevalence cohort (1.3%) would have resulted in screening 73% of men and detecting 93% of infections. No studies have been published, however, that prospectively test risk factor screening criteria in men.

What Screening Tests Should be Performed?

Nonpregnant Women

Thirty-three studies comparing 2 or more screening tests in the same study population were included in the systematic review.[68-101] These included 22 studies reporting culture results, 10 antigen detection tests, 14 LCR, 18 PCR, and 4 transcription-mediated amplification of RNA.

Culture specimens had 100% specificity (because most studies defined culture as the gold standard) and widely varying sensitivity, ranging from 42% to 100%. Antigen detection tests obtained by cervical swab (EIA, DFA) had improved sensitivity, with most results between 70% and 80% but with some decline in specificity (96% to 100%). New DNA amplification tests, PCR and LCR, had higher sensitivity and specificity than the antigen detection tests. PCR swab and urine specimens had similar sensitivities of 82% to 100% and specificities of 98% to 100%. LCR swab specimens had sensitivities of 81% to 98% and specificities of 96% to 100%; LCR urine tests had sensitivities of 70% to 96% and specificities of 99% to 100%. Only 4 studies of transcription-mediated amplification of RNA tests were identified from our search, and these performed comparably to the DNA amplification tests.

Endocervical swab specimens and first-void urine specimens had similar performance using DNA amplification tests. Urine tests allow noninvasive testing for women without the need for a pelvic examination, thereby expanding opportunities for screening.[102] No studies addressed the adverse effects of using these newer technologies.

Pregnant Women

Two studies compared urine LCR with endocervical culture in pregnant women and found LCR to be more sensitive and easier to use than culture.[68,103] Another study compared culture to DFA, EIA, and PCR (all obtained by endocervical swabs) and concluded that the nonculture techniques provided improved sensitivity compared to culture even in a population with a prevalence rate as low as 4.3%.[104] Another study reported 100% specificity and 97.2% sensitivity by using PCR on swab-obtained introital specimens compared to PCR endocervical specimens.[105]

Men

We reviewed 32 studies on test performance in men.[69,74-79,83-85,91-94,99,100,106-121] These included 15 studies reporting culture results, 18 antigen detection tests, 10 LCR, 14 PCR, and 3 transcription-mediated amplification of RNA. These studies compared 2 or more of these tests in the same study population.

Culture specimens had 100% specificity and widely varying sensitivity, ranging from 37% to 97%. Antigen detection tests (EIA, DFA) that used swab specimens had improved sensitivity compared to culture, averaging 80%, but with some decline in

specificity (96% to 100%). The new DNA amplification tests, PCR and LCR, had higher sensitivity and specificity than the antigen detection tests in ranges similar to the studies described above for women. Results of swab specimens compared to first-void urine specimens using DNA tests were similar. The 3 studies of transcription-mediated amplification of RNA reported results similar to the DNA amplification tests.

Most of these studies of men were conducted in STD clinics, and many were located outside the United States. The study population usually included both symptomatic and asymptomatic men, and few studies reported results separately. Very little demographic information was provided about the study population. The lack of test performance studies in community-based, lower-prevalence populations limits their generalizability.

Although studies indicate that urine techniques are capable of improved sensitivity compared to culture, the importance of detecting and treating culture-negative infections is not yet known. Asymptomatic, culture-negative infections may represent those with lower organism counts. The clinical importance and rate of transmission of these low-level infections have not yet been studied.

What are the Implications of Recurrent Infection?

Recurrent chlamydial infections in women have been associated with increased risks for PID and long-term complications. A recently published retrospective cohort study evaluated the risks of hospitalization for ectopic pregnancy or PID for 11,000 Wisconsin women with documented single and recurrent chlamydial infections.[24] Rates of hospitalization for ectopic pregnancy increased with the number of infections (13 of 10,000 for 1 infection, 49 of 10,000 for 2 infections, 140 of 10,000 for 3 or more infections). Similarly, rates of hospitalization for PID also increased with the number of infections (11 of 10,000 for 1 infection, 54 of 10,000 for 2 infections, 110 of 10,000 for 3 or more infections). Adjusted multivariable analyses indicated that women who had 2 and 3 or more chlamydial infections had elevated risks of ectopic pregnancy compared to those with 1 infection (2 infections: OR, 2.1; 95% CI, 1.3 to 3.4; 3 or more infections: OR, 4.5; 95% CI, 1.8 to 5.3), and elevated risks for PID (2 infections: OR, 4.0; 95% CI, 1.6 to 9.9; 3 or more infections: OR, 6.4; 95% CI, 2.2 to 18.4). Recurrent or persistent chlamydial infections were more likely to occur among women who were young, black, residents of Milwaukee County (large urban population), received care in STD clinics, or had documented gonorrhea infection.

Although the clinical importance of recurrent chlamydial infections in women is known, information about the effectiveness of screening for recurrence is limited. This type of information would be helpful in determining screening intervals for groups at risk of recurrences. We found 3 cohort studies that evaluated recurrence rates in high-risk teenage populations. These studies did not differentiate between recurrences because of reinfection and treatment failures. A prospective study of 3,202 high-risk, sexually active women aged 12 to 19 years found that the median time to the first positive chlamydia test result was 7.2 months and only 6.3 months to a repeat positive test among those with repeat visits.[34] A study of chlamydial infection among residents of Manitoba found that 13.4% of those initially infected had a subsequent recurrent infection.[122] In this study, recurrence was more common in women than men, in those aged 15 to 24 years, in registered Native American Indians, and in those with concomitant gonorrhea. Another study of sexually active urban adolescents in Birmingham, Alabama, detected an initial chlamydial infection rate of 23.2%. Of those initially infected, 20.8% presented with a positive test on follow-up.[123]

A research abstract from the CDC evaluated persistent and recurrent chlamydial infections in women presenting to STD, family planning, and adolescent clinics.[124] Six percent of participants had chlamydial infections detected at 1-month follow-up visits and 7.5% at 4 months. Factors related to persistence and recurrence were young age (14 to 21 years) and incomplete therapy.

Harms and Costs of Screening

We identified no studies of the adverse effects of screening for chlamydial infection. The inconvenience of testing, stigma of being diagnosed with an STD, and potential sexual partner discord were areas that we considered. The adverse effects of antibiotic treatment were reported in the treatment studies as mild-to-moderate gastrointestinal symptoms (nausea, diarrhea, abdominal pain).[41] Adverse effects of antibiotics were not specifically addressed in the context of screening.

Several economic evaluations of chlamydia screening have been published,[125-132] although they infrequently used the societal perspective and have methodologic limitations. Findings suggest that screening programs for detecting and treating chlamydia in nonpregnant women provide cost savings in populations with moderate-to-high prevalence of chlamydial infection.[125,126] Selective screening is more cost-effective than universal screening under most assumptions, although universal screening may be cost-effective in populations in which the prevalence of chlamydia is high or sensitivity of selective screening criteria is low.[125-128] Also, DNA amplification assays may improve the cost-effectiveness of chlamydial screening if estimates of its accuracy are correct.[129,130]

Discussion

Table 1 summarizes the evidence obtained for this systematic review by indicating the type of study design and quality of evidence for each key question, using criteria developed by the U.S. Preventive Services Task Force. The most compelling argument for screening in women is based on evidence for improvement of health outcomes. A randomized, controlled trial of selective screening and treatment indicated a significant reduction in rates of PID among screened women compared to non-screened women.[46] We found no new information on screening pregnant women, although previous studies indicated improved birth outcomes when pregnant women were screened and treated. The evidence for screening in men is limited, although the rationale for screening is reasonable because chlamydia is sexually transmitted.

The most difficult aspect of screening, however, is determining exactly who to screen and how frequently to do so. The most consistent evidence available supports age-based screening in women. These strategies appear to be effective even in settings with low-to-moderate prevalence rates (3% to 6%). Universal screening has been shown to be valuable in settings with higher prevalence rates (above 6%). Use of other selected risk factors may be helpful, but they vary between studies and may not translate to all clinical settings. Little information is available on how frequently to screen.

Chlamydia can be easily diagnosed by a number of new tests with relatively high sensitivity and specificity that outperform the traditional gold standard of culture. The DNA and RNA amplification tests that use urine specimens perform well in studies for both men and women and provide a quick, noninvasive method of screening.

Recurrent infections are associated with worse health outcomes, such as PID and ectopic pregnancies in women. Treating partners is important to prevent reinfection. Contract tracing and partner management, currently largely in the domain of public health programs not clinical practices, were not reviewed in this report. As the responsibility for these duties shifts to HMOs, clinicians may become more involved in these interventions.[133]

To demonstrate chlamydial screening outcomes based on assumptions from recent studies, we created a balance sheet for 10,000 women aged 18 to 34 years (Table 2). Three populations are represented, including a low-risk HMO population using a risk factor questionnaire and modeled after assumptions from a randomized, controlled trial of screening previously described,[46] a theoretical high-risk population, and a theoretical low-risk population not using a risk factor questionnaire. In the first scenario, a questionnaire is mailed to 10,000 women in a low-risk population with a prevalence rate of 3%. Of 5,701 women who respond to the questionnaire, 713 are identified as high-risk and offered chlamydia testing. Of these women, 457 (64%) are tested, and 32 are diagnosed with chlamydial infection and treated. By using this

Table 1. Summary of evidence

Key questions	Evidence codes[a]	Quality of evidence[b]
Arrow 1		
Does screening reduce adverse health outcomes?		
Nonpregnant women	I, II-3	Good: one randomized controlled trial indicates screening reduces pelvic inflammatory disease.
Pregnant women	II-2, II-3	Fair: no new studies; 2 studies used in prior recommendations indicate improved birth outcomes when pregnant women are screened and treated although the control group was based on temporal changes in treatment standards in one key study, differences between cases and controls were not different in another study.
Men	III	Poor: no studies of effectiveness of screening in preventing acute infections or complications.
Arrow 2		
Does screening reduce the prevalence of infection?	II-3	Poor-Fair: uncontrolled studies based on time trends after initiation of screening, studies from many populations and settings report declining rates.
Are risk factors useful for selective screening?		
Nonpregnant women	II-2	Fair: few studies in low prevalence, community populations, studies agree on age.
Pregnant women	III	Poor: very few studies based on small populations, descriptive.
Men	III	Poor: subjects mainly from sexually transmitted disease clinics, jail, etc, descriptive.
What screening tests should be performed?		
Nonpregnant women	II-1	Fair: many studies about test performance under study conditions, not well tested in large screening populations with low prevalence.
Pregnant women	II-1	Fair: few studies about test performance under study conditions, not tested in large screening populations.
Men	II-1	Fair: many studies about test performance under study conditions, not well tested in large screening populations with low prevalence.
Arrow 3		
What are the implications of recurrent infection?		
Nonpregnant women	II-2	Fair: studies include high-risk subjects, lack of internal control groups, report descriptive data.

[a]Study Design Categories (*Guide to Clinical Preventive Services,* 1996[56]). I: Randomized, controlled trials. II-1: Controlled trials without randomization. II-2: Cohort or case-control analytic studies. II-3: Multiple time series, dramatic uncontrolled experiments. III: Opinions of respected authorities, descriptive epidemiology.

[b]Quality of evidence ratings based on criteria developed by the U.S. Preventive Services Task Force.

Table 2. Balance sheet: screening for chlamydia in 10,000 women 18-34 years

Base case assumptions	Low risk (questionnaire)[a]	Low risk (no questionnaire)[b]	High risk[b]
Prevalence of chlamydia in population	0.03	0.03	0.094
Compliance with chlamydial testing	0.64	0.64	0.64
Sensitivity of test	100%	100%	100%
Results			
Mailed questionnaire	10,000		
Responded to questionnaire	5,701		
Identified as high-risk	713		
Prevalence in risk group	0.07	0.03	0.094
Tested for chlamydia	457	6,400	6,400
Cases of chlamydia diagnosed and treated	32	192	602
Cases of pelvic inflammatory disease prevented	9	53	167
Number needed to screen (using questionnaire) to prevent one case of pelvic inflammatory disease	1,130	not applicable	not applicable
Number needed to invite for screening (using chlamydial test) to prevent one case of pelvic inflammatory disease	81 (57)[c]	188 (120)	60 (39)

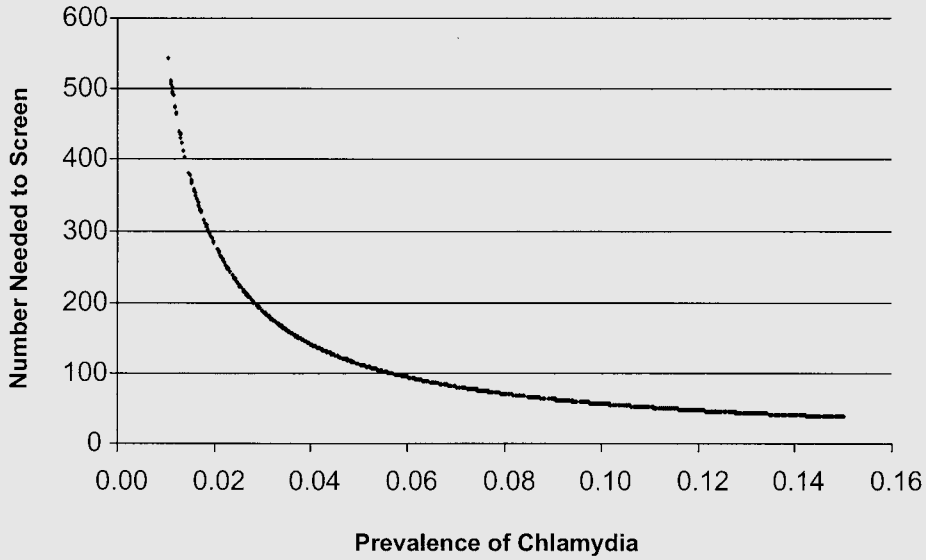
[a]Assumptions based on the results of a randomized controlled trial conducted at Group Health of Puget Sound[46] described in the text.
[b]Assumptions based on theoretical populations. The proportion of all patients who meet the criteria for "high risk" varies with practice setting, patient population, and the criteria used to define "high risk."
[c]Numbers in parentheses indicate number needed to screen based on actual number of women tested for chalmydia.

strategy, 9 cases of PID are prevented. The number needed to screen (NNS) with a questionnaire to prevent 1 case of PID is 1,130. Eighty-one women would need to be invited for screening and 57 tested to prevent 1 case of PID.

If, instead of using a questionnaire, all women in this population were offered screening, 53 cases of PID might be prevented, but the number needed to invite for screening would be 188 (120 tested). In a high-risk population with a prevalence of 9.4%, offering a chlamydial test to all women would prevent 167 cases of PID, and the number needed to invite for screening would be 60 (39 tested). For this strategy, the NNS depends heavily on the prevalence of the disease. Figure 2 shows the relationship between the NNS and prevalence of chlamydia based on the balance sheet assumptions. The NNS rises sharply at prevalence rates less than 3%.

There are important gaps in the evidence that limit support for routine screening of men, women, and pregnant women for chlamydial infection. Studies are needed that test screening criteria, diagnostic protocols, and testing intervals in community-based settings to determine the effectiveness of various screening strategies and their adverse effects. Research could include comparisons of universal, age-based, and risk factor-based criteria among populations with various prevalence rates. Studies of the effectiveness of screening in preventing infections and long-term complications, as well as in reducing rates of transmission and recurrence in both sexes, would improve screening programs. Research on the effectiveness of screening and treating asymptomatic men in preventing transmission to women is of potentially enormous benefit. Additional research is needed on the role of partner notification and presumptive treatment of partners to reduce transmission and reinfection.

Figure 2. Number needed to screen for chlamydial infection



Number needed to invite for screening to prevent one case of PID. The relationship between the number needed to screen and the prevalence of chlamydia in a population is based on the balance sheet assumptions in Table 2.

High-quality cost analyses of current clinical options such as screening criteria, treatment regimens, types of diagnostic tests, partner notification, and screening intervals could provide important information for health system program planning. Additional studies of the effectiveness of chlamydia tests, using urine specimens in community-based settings, are also needed to determine the clinical applications of this new technology.

This study was conducted by the Oregon Health & Science University Evidence-based Practice Center under contract to the Agency for Healthcare Research and Quality (Contract No. 290-97-0018), Rockville, MD.

This article is based on a more comprehensive Systematic Evidence Review, which is available on the AHRQ Web site (www.ahrq.gov/clinic/prevenix.htm). That document was reviewed by content experts, including Edward W. Hook, III, MD, University of Alabama at Birmingham, Jeanne Marrazzo, MD, MPH, University of Washington, and Felicia H. Stewart, MD, University of California, San Francisco; professional organizations, including American Academy of Family Physicians, the American Academy of Pediatrics, the American College of Obstetricians and Gynecologists, and the American College of Preventive Medicine; and public health organizations, including the Canadian Task Force on Preventive Health Care, the Indian Health Service, the National Institutes of Health, the Centers for Disease Control and Prevention, and the Veteran's Administration. Review by these individuals and groups does not necessarily imply endorsement of this article or of the accompanying recommendations of the U.S. Preventive Services Task Force.

Task Force members Carolyn Westhoff, MD, MSc, and Jeffrey F. Peipert, MD, MPH, Task Force chair Alfred O. Berg, MD, MPH, AHRQ senior health policy analyst, David Atkins, MD, MPH, as well as Somnath Saha MD, MPH, and Delia Scholes, PhD, also contributed to this project.

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AHRQ Pub. No. 02-504B
April 2001