Evidence Synthesis

Number 48

Screening for Chlamydial Infection:

A Focused Evidence Update

for the U.S. Preventive Services Task Force

Prepared for:
Agency for Healthcare Research and Quality
U.S. Department of Health and Human Services
540 Gaither Road
Rockville, MD 20850
www.ahrq.gov

Investigators
David S. Meyers, MD, FAAFP
Heather Halvorson MD, MPH
Sara Luckhaupt MD, MPH

AHRQ Publication No. 07-05101-EF-1

June 2007

The findings and conclusions in this document are those of the author(s), who are responsible for its content, and do not necessarily represent the views of AHRQ. No statement in this report should be construed as an official position of AHRQ or of the U.S. Department of Health and Human Services.

The information in this report is intended to help clinicians, employers, policymakers, and others make informed decisions about the provision of health care services. This report is intended as a reference and not as a substitute for clinical judgment.

Acknowledgement:
The authors thank Zhiping Mo and medical librarian Caryn McManus for their contributions to this review.

Suggested Citation:
Meyers D, Halvorson H, Luckhaupt S. Screening for chlamydial infection: A focused evidence update for the U.S.Preventive Services Task Force. Evidence Synthesis No. 48. Rockville, MD: Agency for Hea;thcare Research and Quality. June 2007. AHRQ Publication No. 07-15101-EF-1. Available at http://www.ahrq.gov/clinic/seriles.htm#chlamyd.

Introduction

In 2001, the United States Preventive Services Task Force (USPSTF) commissioned a systematic review of the evidence on screening for chlamydial infection [1]. Based on this review, the USPSTF found good evidence supporting screening for chlamydial infection among asymptomatic women at increased risk for infection, including women at risk due to young age. It found less evidence regarding screening for chlamydial infection in pregnant women and, based on estimates of benefits and harms, recommended screening for pregnant women at increased risk. At that time, the USPSTF found a major gap in the evidence on the effectiveness of screening men for chlamydial infection for the purposes of reducing the incidence of infection and improving health outcomes among women. (For more information about the USPSTF and its methodologies, please visit: www.preventiveservices.ahrq.gov)

Specifically, in 2001 the USPSTF stated the following [2]:

1) The U.S. Preventive Services Task Force (USPSTF) strongly recommends that clinicians routinely screen all sexually active women aged 25 years and younger, and other asymptomatic women at increased risk for infection, for chlamydial infection. **(A Recommendation)**
2) The USPSTF makes no recommendation for or against routinely screening asymptomatic low-risk women in the general population for chlamydial infection. **(C Recommendation)**
3) The USPSTF recommends that clinicians routinely screen all asymptomatic pregnant women aged 25 years and younger and others at increased risk for infection for chlamydial infection. (**B Recommendation)**
4) The USPSTF makes no recommendation for or against routine screening of asymptomatic, low-risk pregnant women aged 26 years and older for chlamydial infection. (**C Recommendation)**
5) The USPSTF concludes that the evidence is insufficient to recommend for or against routinely screening asymptomatic men for chlamydial infection. (**I Recommendation)**

In 2005, the USPSTF determined that a brief, focused evidence review was needed to update its 2001 recommendation on screening for chlamydial infection. Staff of the Agency for Healthcare Research and Quality (AHRQ) reviewed the literature published on this topic between July 2000 and July 2005 and prepared this evidence update. The review focused on a search for direct evidence on the effect of screening asymptomatic individuals on health outcomes. The USPSTF reviewed this evidence to update its recommendations.

Background

Chlamydia trachomatis is the most common sexually transmitted bacterial infection in the Untied States. In 2004, a total of 929,462 cases of chlamydial infection were reported to the Centers for Disease Control and Prevention (CDC) [3]. Because many cases are not reported, the actual number of new cases of chlamydial infection is thought to be more than 2.8 million per year [4].

Symptoms and Sequelae of Chlamydial infection

In women, *Chlamydia trachomatis* commonly results in cervicitis and urethritis. Up to 40% of untreated cases of *Chlamydia trachomatis* in women progress to pelvic inflammatory disease (PID) [5]. Of those with PID, it has been estimated that 20% become infertile, 18% experience chronic pelvic pain, and 9% may have a tubal pregnancy [6]. Chlamydial infection may also increase the risk for cervical cancer [7]. After the acute phase of infection, many women appear to experience a long duration of low-grade infection [8]. Seventy-five to 85%, of genital chlamydial infections in women are asymptomatic [9]. Women with low-grade PID may not experience significant enough symptoms to seek medical attention; yet, these low-grade infections may progress to infertility and chronic pelvic pain [10].

In men, genital chlamydial infection is also likely to be asymptomatic. In one large national sample, only 5% of infected men reported symptoms [11]. Chlamydial infection in men can cause nongonococcal urethritis, acute epididymitis, and, in rare instances, may result in uretheral strictures and Reiter Syndrome [5, 12].

As with other inflammatory sexually transmitted infections (STIs), Chlamydial infection facilitates the transmission of HIV infection in both men and women in both the HIV carrier and recipient [13, 14].

Chlamydial infections are also related to adverse pregnancy outcomes, including miscarriages, premature rupture of membranes, pre-term labor, low birth weight, infant mortality, neonatal chlamydial infection, and postpartum endometritis [1, 5, 15].

Epidemiology

Prevalence rates of chlamydial infection vary widely among populations. Age is the strongest predictor of risk. The CDC reports that 15- to 19-year-old women had the highest reported rates of chlamydial infection in 2004 (2,761.5 per 100,000 women, or 2.8%), followed by 20- to 24-year-old women (2,630.7 per 100,000 women, or 2.6%) [3]. Rates among older women, while steadily increasing in recent years, are lower: at 1,039.5 per 100,000 women aged 25-29 (1.0%) and 364.8 per 100,000 women aged 30-34 (0.36%) [3]. The highest rates among men were found in 20- to 24-year-olds (744.7 per 100,000 men, or 0.74%). [3]. The lower rates of infection in men reported to the CDC are largely due to decreased rates of testing. Datta and colleagues found a prevalence rate of 2.2% among 14- to 39-year-old women and men in a nationally representative study, with no statistically significant differences between the sexes [16]. This rate most likely

underestimates the true prevalence of chlamydial infection in adults, as non-sexually active adults were included in the sample. Miller and colleagues used a nationally representative sample of 14,322 young adults aged 18-26 to estimate the prevalence of chlamydial infection [11]. In this young age group, they found prevalence rates of 4.7% in women and 3.7% in men.

Race is independently associated with chlamydial infection in the United States [1]. In 2004, the rate of chlamydial infection among African American women reported to the CDC was more than seven and a half times the rate among white women (1,722.3 and 226.6 per 100,000, respectively); the rate of chlamydial infection among African American males was 11 times that among white males (645.2 and 57.3 per 100,000, respectively) [3]. While a significant portion of this disparity is likely due to variations in reporting, other nationally representative studies have also found higher prevalence rates among African Americans and Hispanic Americans than white Americans [11].

While there is some geographic variation in the rates of chlamydial infection in the United States, chlamydial infection is more uniformly prevalent than gonorrhea and syphilis infection, [3].

The prevalence of chlamydial infection in some vulnerable populations is much higher than in the general population. Prevalence rates of 10% to 20% have been found in studies of incarcerated populations, army recruits, and patients at public STI clinics [17-20].

Other risk factors associated with chlamydial infection include having multiple sexual partners, having a new sexual partner or an infected sexual partner, inconsistently using barrier contraceptives, and having a history of previous or coexistent STIs [1].

Screening for Chlamydial infection

In 2001, the USPSTF systematically reviewed the evidence regarding screening tests for chlamydial infection in non-pregnant women (33 studies), pregnant women (2 studies), and men (32 studies). They rated the overall body of evidence for all 3 populations as fair, noting that many studies were performed under study conditions rather than real-world conditions and that most studies did not utilize large screening populations with low prevalence rates. The review found that nucleic acid amplification tests (NAATs) had higher sensitivities and specificities than older antigen detection tests and higher sensitivities than culture. In 2001 the USPSTF did not provide clinical guidance as to which tests should be used, noting that the "choice of test will depend on issues of cost, convenience, and feasibility, which may vary in different settings."

In 2002, the CDC published recommendations for screening tests to detect chlamydial infection. Their recommendations were based on a review that utilized many of the same studies considered by the USPSTF, with the addition of a large, multicenter study on screening technologies. The CDC found results similar to those of the USPSTF. On the basis of these data, the CDC recommended that NAATs be used for screening both women and men [21].

In 2005, Cook and colleagues published a systematic review of non-invasive testing for chlamydial infection [22]. The pooled sensitivity for 14 tests of Polymerase Chain Reaction (PCR) was 83.3% for urine and 85.5% for cervical swabs when testing women. The specificity was 99.5% for urine and 99.6% for cervical samples. The team found similar results when pooling fewer studies of 2 other types of NAATs (transcription-mediated amplification and strand displacement amplification). Pooled sensitivity for the 2 studies with prevalence rates of less than 5% was 85.8%, slightly higher than that for the overall pool of studies. The team found, for 12 studies of PCR in men, a pooled sensitivity of 84.0% for urine and 87.5% for uretheral samples. The specificity was 99.3% for urine and 99.2% for uretheral samples. There were no studies evaluating PCR testing in men with infection prevalence rates of less than 5% [22].

Methodology

In preparing this review, the USPSTF began by considering what type of evidence would be necessary to require revision of the 2001 recommendation statement. For example, since the USPSTF in 2001 found insufficient evidence to conclude that screening men could lead to a decreased incidence of infection in women, new evidence concerning this question might lead to a revision of the USPSTF recommendation for screening men. Additionally, changes in the epidemiology of chlamydial infection might lead to a revision of the categorization of increased risk. After its preliminary evaluation, the USPSTF selected the targeted critical key questions, subsidiary questions, and search strategies listed below.

Critical key questions:

1. Does screening for chlamydial infection in non-pregnant women reduce adverse health outcomes?
2. Does screening for chlamydial infection in pregnant women reduce adverse health outcomes?
3. Does screening for chlamydial infection in men reduce adverse health outcomes in men, reduce adverse health outcomes in women, or reduce the incidence of infection in women?

Health outcomes of interest were defined as follows: pelvic inflammatory disease, ectopic pregnancy, infertility, and chronic pelvic pain in non-pregnant women; chorioamnionitis, premature rupture of membranes, pre-term labor, pre-term delivery, spontaneous abortion, endometritis, and low birth weight in pregnant women; and epididymitis, urethritis, prostatitis, chronic prostatitis, reactive arthritis, and urethral strictures in men.

Search strategy for critical key questions:

AHRQ staff conducted a systematic evidence review for each of the critical key questions. The search strategy included a review of English language articles identified

from PubMed between July 2000 and July 2005. Additional articles were found through bibliography reviews and discussion with experts. These searches identified 452 articles.

For key question 1, the review was limited to randomized controlled trials of non-pregnant women at increased risk for infection. For non-pregnant women not at increased risk, the search was expanded to include both randomized controlled trials and non-randomized, prospective, controlled studies. For key questions 2 and 3, the reviews were limited to randomized controlled trials and non-randomized, prospective, controlled studies. Abstracts were reviewed by two staff members. All abstracts that were clearly within the scope of this review and those with potential or ambiguous relevance were retained. Twenty-three articles were identified as potentially meeting these broad inclusion and exclusion criteria. (Figure)

Two reviewers independently reviewed the full articles of all identified studies to determine whether they met pre-determined inclusion criteria. Additional reviewers were consulted for consensus-building around 2 articles that were ultimately not included in this review. The 2 principal reviewers independently abstracted data from included articles to determine study quality.

Subsidiary key questions:

Members of the USPSTF determined several other questions for non-systematic review to assist them with updating their recommendations and supporting materials. These questions were as follows:

1. Has the epidemiology of chlamydial infection in the U.S. changed in significant ways since 2001, including within populations at increased risk?
2. What are the harms of screening for chlamydial infection?
3. Are screening tests for chlamydial infection accurate?
4. What is the optimal screening frequency?
5. Does chlamydial infection increase the risk for infection with HIV?
6. What is the cost-effectiveness of screening for chlamydial infection?

Search strategy for subsidiary questions:

Limited non-systematic reviews were conducted for the subsidiary questions. Literature reviews for subsidiary questions included review articles and topic-specific searches. Articles reviewed during the critical key question reviews were tagged if they addressed a subsidiary key question. Recommendations for sentinel articles were also sought from content experts. The purpose of these searches was to provide updated context for recommendations rather than to serve as evidence for changes in the recommendations.

Results

Critical Key Questions

1. Does screening for chlamydial infection reduce adverse health outcomes in non-pregnant women?

Women at increased risk

In 2001, based on a good quality randomized controlled trial by Scholes et al. published in 1996, the USPSTF was able to give an A rating to their recommendation that clinicians routinely screen all sexually active women at increased risk for chlamydial infection [23]. The study, conducted in a large Seattle managed care organization, concluded that screening and treating young women at increased risk for chlamydial infection resulted in a significant reduction in the incidence of pelvic inflammatory disease after 1 year of follow-up [23]. Based on the literature, the USPSTF in 2001 defined women at increased risk for chlamydial infection to be all women aged 25 and younger and older sexually active women who are unmarried, African American, have a history of a sexually transmitted infection, have new or multiple sexual partners, have cervical ectopy, or use barrier contraceptives inconsistently.

Only 1 study identified in the 2005 systematic review met the inclusion criteria and addressed the effectiveness of screening for chlamydial infection among non-pregnant women at increased risk [24]. In a cluster-randomized trail, Ostergaard and colleagues found that a one-time home-based screening intervention was associated with a lower prevalence of chlamydial infection and fewer reported cases of PID at 1-year of follow-up (See Table 1).

As part of a larger study, the team randomized 17 high schools in one Danish county to 1 of 2 groups. Students in schools selected to be in the intervention group were offered a single opportunity for home-based screening for chlamydial infection. Students in the control high schools were given the same educational information and encouraged to visit their physician for a free screening. Sexually active girls in both groups were offered the opportunity to receive follow-up in 1 year.

Ostergaard and colleagues found that the intervention was associated with a lower prevalence of chlamydial infection and fewer reported cases of PID at 1 year follow-up. Of 443 girls in the intervention group who participated in follow-up testing, 13 (2.9%) were found to have chlamydial infection and 9 (2.1%) reported receiving treatment for PID. Of 487 in the control group, 32 (6.6%) were found to have chlamydial infections and 20 (4.2%) reported receiving treatment for PID. Both of these differences were found to be statistically significant, with $p<0.05$. Given the differences in initial screening rates between the groups (93.4% versus 7.6%), the USPSTF chose to include this study as an example of a trial of screening versus not screening. The effect of baseline screening in the control group would be expected to decrease the ability of the intervention to demonstrate a difference between screening and not screening. This factor gives additional weight to the study's findings.

While offering universal screening, the study targeted high-school aged female adolescents, women defined by the USPSTF as being at increased risk for chlamydial infection due to their age alone. The overall initial prevalence rate of chlamydial infection among those screened was 5.0%. The USPSTF thus considered this a trial of screening women at increased risk, and not a trial of the effect of universal screening. The study was deemed to be of poor quality due to an unaccounted loss of women in both groups for follow-up screening. While 93.4% of those in the intervention group and 100% of those in the control group agreed to follow-up screening, only 51.1% in the intervention group and 58.5% in the control group actually participated in follow-up screening. The researchers did not provide sufficient information to assess the effects this loss may have had on the results of the study.

A study by Clark and colleagues was closely reviewed by the USPSTF [25]. While not meeting the criteria for the systematic review because it was a non-randomized trial of screening women at increased risk, it is presented here as a good quality study that contributes to our understanding of screening for chlamydial infection. Clark and colleagues conducted a non-randomized cohort study examining the hospitalization rates following screening for chlamydial infection in female military recruits [25]. A total of 7,053 women were screened and treated for chlamydial infection over a 2-year period upon arrival at basic training. A group of 21,021 women who were not screened upon their arrival were followed as a comparison group. Eighty percent of the women studied were younger than age 25 and the overall prevalence rate of chlamydial infection among the women screened was 9.1%. The average follow-up time for both cohorts was more than 1.5 years. Results were adjusted for age, race, education, and entrance aptitude score. The investigators found a slight decrease in the adjusted relative risk of hospitalization overall (0.94, 95%; CI, 0.90-0.99). While noting a lower adjusted relative risk of hospitalization for pelvic inflammatory disease, this difference was not statistically significant (0.94, 95%; CI, 0.69-1.29). The relative risk for hospitalizations for Chlamydia-related sequelae (PID, infertility, ectopic pregnancy) was non-statistically higher in the screened than in the unscreened group (1.10, 95% CI, 0.85-1.43).

The intervention and control groups differed significantly in terms of age, education, and entrance aptitude scores, with the screened group being slightly younger and with lower educational level and aptitude scores than the control group. Both groups were about 35% African American. The study examined military hospitalizations only and did not capture civilian hospital use by either group. In addition, the investigators were unable to include outpatient treatment for PID or other sequelae. While the research team did adjust for major known demographic confounders, the trial remains a non-randomized study in populations with significant differences. While the timeframe for this study may not have been adequate to detect the full consequences of the long-term effects of chlamydial infection, it serves to remind us that dramatic benefits from a single screening test may not be significant or may not be captured in a specific evaluation project.

Women not at increased risk

In 2001, the USPSTF did not find any direct trials of screening women not at increased risk that reported health outcomes. It was able to find fair evidence for each link in the analytic framework, noting that there was fair evidence that screening women not at increased at risk would find additional cases of chlamydial infection. The USPSTF found little evidence of the potential harms of screening. Given the low prevalence of chlamydial infection in this population, the USPSTF made no recommendation for or against routinely screening asymptomatic women not at increased risk for chlamydial infection; the USPSTF concluded that the potential benefits of screening women not at increased risk may be small and may not justify the potential harms.

The systematic review examining subsequent evidence found no new direct trials of screening for chlamydial infection among women not at increased risk.

2. Does screening for chlamydial infection reduce adverse health outcomes in pregnant women?

In 2001, the USPSTF found fair evidence that screening asymptomatic pregnant women can detect chlamydial infection, and that treatment of chlamydial infection during pregnancy improves health outcomes for both the mother and infant. The USPSTF concluded that the potential benefits outweighed the potential harms of screening pregnant women, and recommended that clinicians routinely screen all asymptomatic pregnant women aged 25 or younger, and other pregnant women at increased risk, for chlamydial infection. The USPSTF described pregnant women as being at increased risk for chlamydial infection using the same criteria as it did for non-pregnant women; that is, being age 25 or younger, of African American race, having a history of sexually transmitted infection, and having new or multiple sexual partners. The prevalence of chlamydial infection is lower in women who are not at increased risk than it is in women who are at increased risk. The USPSTF considered the potential net benefits of screening pregnant women who are not at increased risk to be small, leading it to make no recommendation for or against screening pregnant women not at increased risk for chlamydial infection.

Evidence reviewed for this report found no new randomized controlled studies or non-randomized cohort studies addressing this topic.

3. Does screening for chlamydial infection reduce adverse health outcomes in men, reduce adverse health outcomes in women, or decrease the prevalence of chlamydial infection in women?

In 2001, there was good evidence that screening men for chlamydial infection could accurately detect infection in men who had no symptoms and that treatment could result in cure. The USPSTF noted that the benefits to men of treating asymptomatic infection are small, since long-term sequelae are rare and treatment of symptomatic infection is

effective. The USPSTF looked for evidence that screening and treating asymptomatic infection in men could reduce the incidence of new infections in women. No direct evidence was found. The USPSTF, therefore, concluded that the evidence is insufficient to recommend for or against routinely screening asymptomatic men for chlamydial infection. However, the USPSTF noted the potential for significant benefit if screening in men can, in fact, decrease infection in women.

The 2005 systematic review identified no randomized controlled studies or non-randomized, prospective, controlled studies addressing this topic.

Results of review of subsidiary key questions

1. Has the epidemiology of chlamydial infection in the U.S. changed in significant ways since 2001, including within populations at increased risk?

The review found that the epidemiology of chlamydial infection in the United States has not changed in significant ways in recent years. A description of the current epidemiology of chlamydial infection has been incorporated into the Background section, above.

2. What are the harms associated with screening for chlamydial infection?

In 2001, the USPSTF was unable to identify any studies of the adverse effects of screening for chlamydial infection. However, Nelson and Helfand noted the potential for inconvenience, stigma associated with diagnosis, and discord between sexual partners. They further noted that treatment studies report adverse effects of mild to moderate gastrointestinal symptoms including nausea, diarrhea, and abdominal pain [1].

In our non-systematic review of the most recent evidence, we found several qualitative studies that examined the adverse effects associated with a diagnosis of chlamydial infection. No studies were identified that reported on the real or potential harms to screening program participants or to those with false-positive test results.

A 2003 paper addressed the psychosocial impact of the diagnosis of chlamydial infection through a qualitative study using semi-structured interviews with 17 Scottish women recently diagnosed with the infection. The researchers found that these women perceived that testing and diagnosis of chlamydial infection were associated with negative stereotypes, such as contamination and delinquency, and they perceived a social stigma attached to their diagnosis. The women expressed concern over the meaning of their diagnosis to their future fertility and had significant anxiety concerning the attitudes of their male partners. They also were concerned about notifying both current and past partners [26].

As part of a large trial of screening for chlamydial infection in England, Pimenta and colleagues conducted in-depth interviews with more than 400 women completing screening. Overall, participants were accepting of the screening program, and most found

screening beneficial. Participants with positive test results commonly reported "feeling dirty, feeling ashamed at passing on the infection, and [sensing others'] suspicion about where the infection originated." The authors report that for some women this led to "tension and suspicion within relationships," but this study identified no long-term repercussions within relationships [27].

A qualitative study with both heterosexual men and women recently diagnosed with chlamydial infection identified significant differences in the responses to diagnosis between the men and the women. The study of 12 men and 12 women found that the women reported feeling anxious about their future reproductive health, feared stigmatization, and blamed themselves for contracting chlamydial infection. The men generally reported less concern and were less willing to disclose their condition to sexual partners. Some of the men, according to the authors, blamed their partners for their infection and avoided accepting responsibility themselves. The female participants experienced blame and denial of the infection on the part of their male partners. The women also reported concern about potential threats to their relationships. The authors concluded that a culture of the "blameless male and stigmatized female" continues to persist around the issue of STIs. They note that avoidant attitudes and behaviors among men should be accounted for in STI screening and treatment programs [28].

3. Are screening tests for chlamydial infection accurate?

The 2001 USPSTF systematic review rated the body of evidence concerning screening tests as fair, noting that most trials were not conducted in the community and did not involve populations with low prevalence rates of chlamydial infection. The current review does not include a systematic updating of this body of evidence. Evidence describing the accuracy of screening tests for chlamydial infection, including evidence from recent studies conducted in community settings and with lower prevalence groups, has been incorporated into the background section, above.

4. What is the optimal screening frequency?

Non-pregnant women

No trials of different screening intervals for non-pregnant women were identified during the preparation of this update.

Researchers have begun to examine re-infection rates in non-pregnant women. During a two-year study of STI prevention through behavioral interventions, researchers worked with a control group of 249 African American and Hispanic women who, at baseline, had either chlamydial infection (74.7%) or gonorrhea infection (25.3%). Similar to the women in the intervention group, the control group participants were young (average age 21.6 years) and poor. During the first year of follow-up (retention rate: 92.0%), 26.8% of women in the control group experienced a new gonorrheal or chlamydial infection [29].

In a study published in 2001, Burstein and colleagues reported their findings after following a cohort of 3,860 sexually active women in Baltimore over 33 months. Among the 2,073 participants aged 25 or younger, chlamydial infection was diagnosed in 31.2%; the median time to repeat chlamydial infection was 7.0 months. Among 1,787 women older than 25, 9.6% were diagnosed with chlamydial infection, and the median time to re-infection was 13.8 months [30].

Rietmeijer and colleagues studied re-infection rates in men and women attending an STI clinic in Denver, Colorado. They found that among individuals tested more than once for chlamydial infection during the 30-month period, those who had an initial positive test result were more likely to have a positive result when tested again than those who had an initial negative test result. The team found that young age, African American race, a history of an STI, and inconsistent condom use were associated with new infections. In multivariate analysis, repeat infections were associated only with younger age, no use of condoms, and sexual contact with an infected partner. The authors noted that their findings can be used to support the theory that demographic variables associated with risk for chlamydial infection are proxies for sexual networks. They also noted that individuals who have a chlamydial infection are at risk for re-infection due to their involvement in such networks. They noted that their data support the theory that a large proportion of repeat infections are caused by re-exposure to untreated previous partners [20].

Others have also found evidence to support the idea that recurrent chlamydial infection among women is frequently not associated with new partners [31, 32]. The incidence of chlamydial infection among male partners of female patients who have chlamydial infection ranges from 23% to 57% [33-35]. In current clinical practice, patients who have chlamydial infection are often instructed to inform their sexual partners of their diagnosis and to refer them for testing (standard partner referral). With standard partner referral, follow-up is difficult to confirm. In fact, there is evidence that a large proportion of partners may never be evaluated or treated when standard partner referral is used [33, 36, 37]. This has led to the development and evaluation of more aggressive strategies for identifying and treating partners, broadly referred to as “expedited partner treatment.”

A 2001 Cochrane Review of strategies for partner notification of STIs concluded there was moderately strong evidence that, for HIV or any STI, provider referral, or a choice between patient or provider referral, increases the evaluation of partners compared with standard patient referral [38]. Three recent randomized controlled trials evaluated the strategy of patient-delivered partner treatment (PDPT). In these studies, patients who had STIs were given medication to give their partners, who did not have a medical evaluation. These studies showed that PDPT and other forms of expedited partner treatment can decrease bacterial STIs among index patients at follow-up, and can increase the proportion of partners treated [39-42]. Adoption of PDPT may be slow in the U.S. because of legal concerns and concern about potential adverse drug events. Nonetheless, a recent survey found that 50% to 56% of physicians in the U.S. have used PDPT for chlamydial infection or gonorrhea, and that 11% to 14% usually or always employed PDPT [43].

The CDC, in 2002, recommended that women recently infected with *Chlamydia trachomatis* be re-screened for infection 3-4 months after treatment [44].

Pregnant women

No trials of differing screening intervals for pregnant women were identified during the preparation of this update. One study conducted in 2001 examined risk-factor-based screening versus routine third-trimester screening for gonorrhea and chlamydial infection [45]. A prospective analysis was performed of women entering prenatal care over a 10-month period in an urban hospital. Magriples and colleagues found that for this sample of 542 women, the combination of being older than 19 and having a negative history of STIs and drug use had a negative predictive value of 99.1%.The researchers concluded that comprehensive risk factor screening may be an effective way to predict which women are at low risk for gonorrhea and chlamydial infection in their third trimester, after an initial test has proved to be negative.

Men

No trials that studied the optimal frequency of screening for chlamydial infection in men were found during the preparation of this update.

5. Does chlamydial infection increase the risk for infection with HIV?

There is broad consensus within the literature that, as with other inflammatory STIs, chlamydial infection facilitates the transmission of HIV infection in both men and women. Sexually transmitted infections increase both the infectivity of persons with HIV infection and the susceptibility of those with STIs to HIV infection [13, 14].

The prevalence of chlamydial infection outside of HIV care settings among men who have sex with men has not been studied widely. In addition, tests other than culture, which is not widely available, have not been cleared by the FDA for use with rectal or pharyngeal specimens.

6. What is the cost-effectiveness of screening for chlamydial infection?

This review identified no direct trials on the cost-effectiveness of screening for chlamydial infection. A number of reports of economic modeling of the cost-effectiveness of screening for chlamydial infection in non-pregnant women and men were found.

In 2002, Honey and colleagues published the results of a systematic review of economic modeling of the cost-effectiveness of screening for chlamydial infection in non-pregnant women [46]. They identified 10 studies that met their inclusion criteria (screening in primary care or family planning clinics, a primary focus on sexually active women under the age of 30, outcomes of cases of PID prevented or cases of chlamydial infection

detected) published between 1990 and 2000. Two studies were excluded from analysis due to poor quality. Six studies included a sensitivity analysis. All of the studies included found that screening asymptomatic women for chlamydial infection is cost-effective. The threshold population prevalence for chlamydial infection over which the models were cost-effective varied from 3.1% to 10.0% [46].

In 2004, Hu and colleagues developed a computer-based mathematical model to simulate screening, diagnosis, and treatment of chlamydial infection in a representative cohort of sexually active women in the U.S. Their robust model included assumptions about infection severity, treatment setting, and risk for long-term complications. The model also included estimates of transmissibility, sexual contacts, and assumptions concerning the effect of treating male partners to decrease the incidence of infection in women. The team performed extensive sensitivity analysis on their model. They also used their model to examine the effect of multiple screening strategies, including different age-based cut-offs (women under 20, under 25, and under 30) and different screening intervals. They concluded that annual screening of all sexually active women between the ages of 15 and 29, and screening all women with a history of chlamydial infection every 6 months, was the most cost-effective strategy examined – although all strategies were found to be more cost-effective than not screening. In addressing screening program costs, the team notes, "an annual screening strategy to the more restrictive age of 15 to 24 years may be reasonable" [47].

Several recent economic models explore the cost-effectiveness of screening men for chlamydial infection [48, 49]. While most models find screening men to be cost-effective, all such studies rely on the assumption that screening men will reduce the long-term sequelae of chlamydial infection in women, despite a lack of direct evidence to support this theory.

Emerging Issues

The systematic review uncovered no evidence on the effect of screening men to reduce the prevalence of infection in women, but our understanding of the ability of screening and treatment of a high-risk group to reduce community prevalence of an STI may be informed by a study in a South African mining community [50]. A research team conducted 2 cross-sectional samples of male miners in a mining town, where more than 90% of the miners live in single-sex hostels near the mines. The intervention consisted of the establishment of a mobile STI clinic for female sex workers and other local women with multiple sex partners. Women enrolled at the clinic were encouraged to return for monthly visits and were treated presumptively with azithromycin at each visit. For women who returned to the clinic, rates of gonorrheal and chlamydial infection decreased with each visit. At the end of the intervention, the rate of gonorrhea and/or chlamydial infection among miners decreased from 10.9% to 6.2% ($p<.001$), and for chalmydial infection from 6.6% to 3.5% ($p=.005$). Community records also showed that the miners significantly decreased their number of visits to local medical facilities for STI care.

Similar results were found in a study presented at a meeting of the International Society for Sexually Transmitted Disease Research in Ottawa, Canada, in 2003 [51]. Researchers reported that chlamydial infection among women declined by 50% at a health center serving a population in which men who had been screened and treated for chlamydial infection while incarcerated resided.

If this type of research continues, future recommendations regarding screening for chlamydial infection in men may have an evidence base.

Another area lacking research has been that of the potential harms associated with screening for chlamydial infection. The CDC has recently begun a study to examine the psychosocial impact of a positive diagnosis of chlamydial infection [C Walsh, personal communication, 2005].

Discussion

Table 2 summarizes the evidence obtained from the 2001 USPSTF systematic review and this update of the literature through 2005 . Only 2 studies were identified that examine the direct effect of screening for chlamydial infection on health outcomes. Both of these studies examined screening non-pregnant women at increased risk for infection. No studies were identified that examined the direct effect of screening women not at increased risk, pregnant women, or men. The effectiveness of screening men for chlamydial infection to reduce the incidence of infection and its sequelae in women remains a major gap in our current understanding of screening for chlamydial infection.

The epidemiology of chlamydial infection has not changed significantly since the USPSTF published its recommendations in 2001. Our understanding of the epidemiology of chlamydial infection has improved due to the publication of data from nationally representative samples of asymptomatic individuals, new studies of populations at increased risk, and continued surveillance by the CDC.

While this review did not include a systematic updating of the literature on the accuracy of screening tests, the review found many studies confirming the findings of the 2001 systematic review, along with a clear trend favoring the use of NAATs in screening programs.

This review found the beginnings of an evidence base for the harms of screening in qualitative studies examining the implications of a positive chlamydia test result. These studies find significant anxiety and concern for the future of intimate relationships following a positive diagnosis of chlamydial infection.

This review identified no studies investigating screening intervals for chlamydial infection. Therefore, there is no direct evidence to guide decisions about repeated screening in those who have already been screened, regardless of the outcome. Studies in this area will make a major contribution to improving the evidence base for screening programs.

Table 3 presents the outcomes of a screening program for chlamydial infection based on assumptions from recent studies. The table presents the results that might be expected from screening programs among populations of non-pregnant women with different underlying prevalence rates of chlamydial infection, including 0.1% (a group of women not at increased risk), 1.0% (a group of women aged 25 to 29 who are not otherwise at increased risk), 5.0% (a group of sexually active adolescent women), and 10.0% (a group of women at significant increased risk, such as military recruits). The positive predictive value increases from 8% to 91%, while the number needed to screen to prevent 1 case of PID decreases from 3800 to 38, between the groups with the lowest and highest prevalence rates.

Despite widespread recommendations strongly urging screening for chlamydial infection among women at increased risk for infection, including all sexually active women under the age of 25, many, if not most, women are not receiving this cost-effective preventive health service. The National Committee for Quality Assurance noted in their report, *State of Health Care Quality 2005*, that while there has been modest and steady improvement in the rates of screening women for chlamydial infection, in 2004 the screening rate among women aged 16-20 in commercial health plans was 32.6%; and among women enrolled in Medicaid managed care plans, it was 45.9%. For women aged 21 to 25, the rates were 31.7% in commercial plans and 49.0% in Medicaid plans [52]. In an editorial accompanying the article by Hu and colleagues [47] on the cost-effectiveness of screening for chlamydial infection, the editors of *Annals of Internal Medicine* acknowledge that "actual practice falls far short of recommended practice [53]." The editors suggest that before screening programs are expanded to men or to women with lower prevalence rates of Chlamydial infection, "sexually active women 15-24 years of age … should have the highest priority for screening [53]."

Figure 1: Stages of Article Review

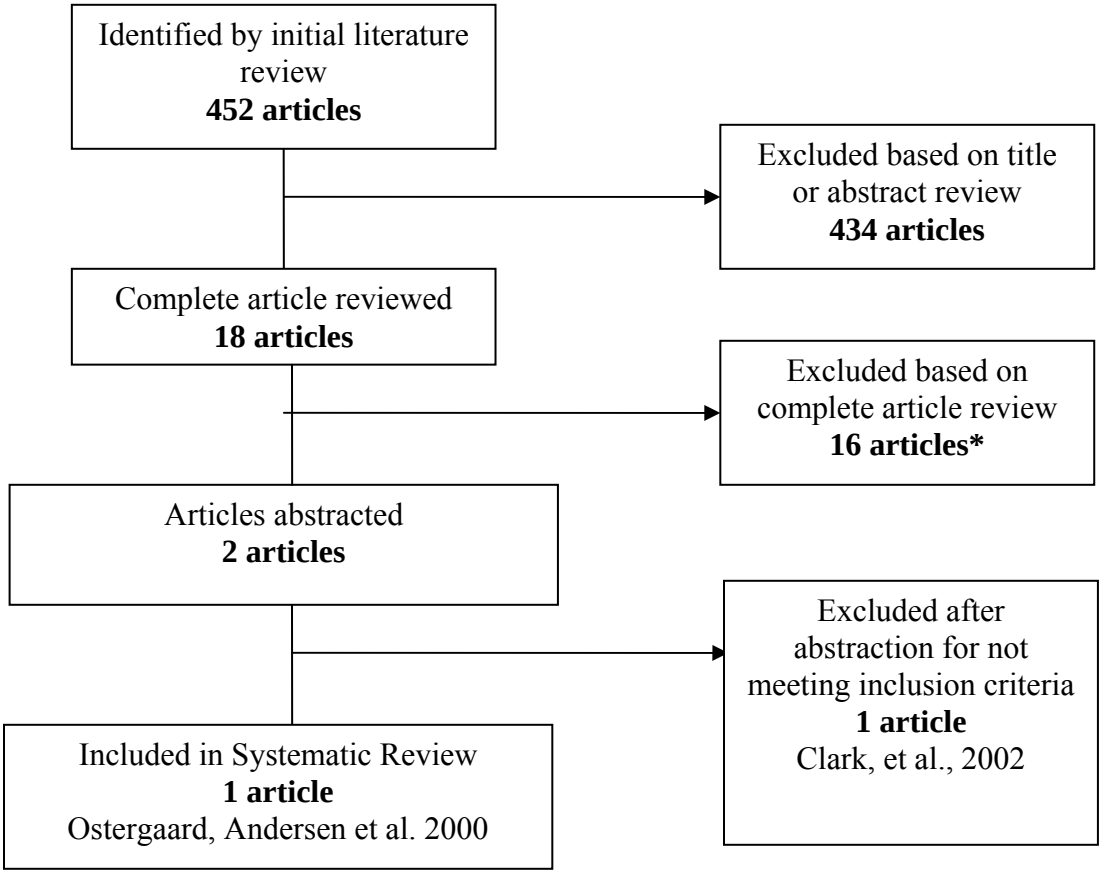

Table 1: Evidence Table of article abstracted for USPSTF update on screening for Chlamydial infection

Study Reference	Design Setting Source Population	Population Selection	N	Age Race Education	Data Sources Measures	Results	Threats to Internal Validity External Validity	Quality Rating
Ostergaard 2000	Randomized controlled trial to compare a home-based screening program to an office-based screening program. 17 high schools in Denmark randomly assigned to intervention/control by drawing lots. Study evaluated as a one-time screening versus no screening due to the fact that at baseline, 70% of girls in intervention completed screening (home-based) and only 6% of girls in control completed screening (office-based).	5,487 female students at baseline (2,603 intervention; 2,884 controls). A total of 1,254 intervention participants completed baseline. Of these, 928 were sexually active; 867 who were sexually active completed baseline. A total of 443 (51%) completed follow-up. Of 2,884 controls, 833 were sexually active. All completed baseline. A total of 487 (58%) completed follow-up. No significant differences found between intervention & control groups.	5,487 total: of which 2,603 were intervention and 2,884 control.	15-19 yr olds 95% White All current high school students	Self-administered questionnaire, laboratory testing, and medical record review All tests for chlamydia were conducted using the TMA* assay and confirmed with LCR**. Outcome measures included the prevalence of women at follow-up who were infected with Chlamydia after one year and the proportion of women reporting treatment for PID and hospitalization for PID.	Significantly more new infections in the control group than intervention (32, 6.6% vs. 13, 2.9%), p<.05). Significantly more girls in the control group were treated for PID than in the intervention group (20, 4.2% vs. 9, 2.1%, p< .05). There was not a statistically significant difference between the intervention & control groups in terms of hospitalization for PID***, although the trend is in the same direction (5 girls in control vs. 1 in intervention).	Internal Validity: Substantial. Considerable selection bias as almost half lost to follow-up. Measurement bias: minimal. Self-report data was confirmed using central Danish register for antimicrobial prescriptions. External validity: Generalizability as 95% white, all Protestant	Poor

*TMA assay: transcription-mediated amplification assay
**LCR: Ligase Chain Reaction
***PID: Pelvic Inflammatory Disease

Table 2: Summary of evidence reviewed for USPSTF update on Screening for Chlamydial Infection

	Non-pregnant women		Pregnant women		Men	
	At risk	Not at risk	At risk	Not at risk		
Direct evidence that screening reduces adverse health outcomes	Good*	Poor* (due to lack of data)	Poor* (due to lack of data)	Poor* (due to lack of data)	Poor* (due to lack of data)	
Ability of screening tests to identify infection in asymptomatic individuals	Fair**	Fair**	Fair**	Fair**	Fair**	
Ability of treatment to reduce adverse health outcomes	Not systematically reviewed♂	Not systematically reviewed♂	Fair**	Fair**	For health outcomes in men	Not systematically reviewed♂
					For health outcomes in women	Poor†
Harms of screening	Poor†	Poor†	Poor†	Poor†	Poor†	
Harms of treatment	Not systematically reviewed§	Not systematically reviewed§	Not systematically reviewed§	Not systematically reviewed§	Not systematically reviewed§	

* Based on systematic evidence review conducted in 2005.
** Based on a systematic evidence review conducted in 2001.
† Rated as poor due to lack of evidence.
♂ Assessed a priori to be established
§ Assessed a priori to be small.

Table 3: Outcomes Table: Screening 10,000 Asymptomatic Women for Chlamydial Infection

	Low	Moderate	Moderate-high	High
Prevalence	0.1%	1%	5%	10%
New cases	10	100	500	1000
Expected PID in untreated CT rate (1)	0.3	0.3	0.3	0.3
Expected cases of PID in untreated without screening	3	30	150	300
Screening				
Urine nucleic acid amplification test				
Sensitivity	0.90	0.90	0.90	0.90
Specificity	0.99	0.99	0.99	0.99
Screening results				
True positive	9	90	450	900
False negative	1	10	50	100
False positive	100	99	95	90
Total screening positive	109	189	545	990
Positive Predictive Value	8.25%	47.6%	82.3%	90.9%
Adherence to azithromycin*	0.80	0.80	0.80	0.80
CT treated (TPx0.8)	7.2	72	360	720
CT cured with Treatment*	0.96	0.96	0.96	0.96
CT cases cured	6.9	69	345.6	691.2
CT cases not cured	0.3	3	14.4	28.8
Total CT cases after screening and treatment (FN+Not cured)	1.3	13	64.4	128.8

Expected cases of PID with screening	0.39	4	19	39
Cases of PID avoided by screening	2.6	26	131	261
Number needed to screen to avoid 1 case PID	3846	384.6	76.3	38.3
Expected cases of infertility resulting from CT-related PID*	0.08	0.8	3.8	7.8
Cases of infertile avoided by screening	0.52	5.2	26.2	52.2
Number needed to screen to avoid 1 case of infertility due to CT	19,231	1,923	382	192

PID: Pelvic Inflammatory Disease / CT: Chlamydia trachomatis infection / TP: True Positive / FN: False Negative

* Assumptions made in this table, derived from a review of the literature by Hu and colleagues (47), include that 80% of women with a positive chlamydia test will be contacted, receive and take azithromycin, 96% of women treated with azithromycin will be cured of infection, and that 20% of women who experience pelvic inflammatory disease will become infertile.[47]

References

1. Nelson, H.D. and M. Helfand, *Screening for chlamydial infection.* Am J Prev Med, 2001. **20**(3 Suppl): p. 95-107.
2. USPSTF, *Screening for Chlamydial Infection: Recommendations and Rationale.* Am J Prev Med, 2001. **20**(3S): p. 90-4.
3. Centers for Disease Control and Prevention. *Sexually Transmitted Disease Surveillance, 2004*. Atlanta, GA: U.S. Department of Health and Human Services, September 2005.
4. Weinstock, H., S. Berman, and W. Cates, Jr., *Sexually transmitted diseases among American youth: incidence and prevalence estimates, 2000.* Perspect Sex Reprod Health, 2004. **36**(1): p. 6-10.
5. Hwang, L. and M.A. Shafer, *Chlamydia trachomatis infection in adolescents.* Adv Pediatr, 2004. **51**: p. 379-407.
6. Silins, I., et al., *Chlamydia trachomatis infection and persistence of human papillomavirus.* Int J Cancer, 2005. **116**(1): p. 110-5.
7. Wallin, K.L., et al., *A population-based prospective study of Chlamydia trachomatis infection and cervical carcinoma.* Int J Cancer, 2002. **101**(4): p. 371-4.
8. Miller, W.C. and J.M. Zenilman, *Epidemiology of chlamydial infection, gonorrhea, and trichomoniasis in the United States--2005.* Infect Dis Clin North Am, 2005. **19**(2): p. 281-96.
9. Risser, W.L., et al., *The epidemiology of sexually transmitted infections in adolescents.* Semin Pediatr Infect Dis, 2005. **16**(3): p. 160-7.
10. Wiesenfeld, H.C., et al., *Lower genital tract infection and endometritis: insight into subclinical pelvic inflammatory disease.* Obstet Gynecol, 2002. **100**(3): p. 456-63.
11. Miller, W.C., et al., *Prevalence of chlamydial and gonococcal infections among young adults in the United States.* Jama, 2004. **291**(18): p. 2229-36.
12. Arya, R., et al., *Incidence of genital Chlamydia trachomatis infection in the male partners attending an infertility clinic.* J Obstet Gynaecol, 2005. **25**(4): p. 364-7.
13. Rottingen, J.A., D.W. Cameron, and G.P. Garnett, *A systematic review of the epidemiologic interactions between classic sexually transmitted diseases and HIV: how much really is known?* Sex Transm Dis, 2001. **28**(10): p. 579-97.
14. Baeten, J.M. and J. Overbaugh, *Measuring the infectiousness of persons with HIV-1: opportunities for preventing sexual HIV-1 transmission.* Curr HIV Res, 2003. **1**(1): p. 69-86.
15. Mardh, P.A., *Influence of infection with Chlamydia trachomatis on pregnancy outcome, infant health and life-long sequelae in infected offspring.* Best Pract Res Clin Obstet Gynaecol, 2002. **16**(6): p. 847-64.
16. Datta SD , J.R., Papp J, McQuillan G, Weinstock H, *Prevalence Of Chlamydia And Gonorrhea In The United States Among Persons Aged 14-39 Years, 1999-*

2002 abstract (TP-078), 16th Biennial meeting of the International Society for Sexually Transmitted Diseases Research (ISSTDR). Amsterdam, July 10-13, 2005). 2005.
17. Mertz, K.J., et al., *Findings from STD screening of adolescents and adults entering corrections facilities: implications for STD control strategies.* Sex Transm Dis, 2002. **29**(12): p. 834-9.
18. Centers for Disease Control and Prevention, *Sexually Transmitted Disease Surveillance 2003 Supplement, Chlamydia Prevalence Monitoring Project.* 2004.
19. Gaydos, C.A., et al., *Sustained high prevalence of Chlamydia trachomatis infections in female army recruits.* Sex Transm Dis, 2003. **30**(7): p. 539-44.
20. Rietmeijer, C.A., et al., *Incidence and repeat infection rates of Chlamydia trachomatis among male and female patients in an STD clinic: implications for screening and rescreening.* Sex Transm Dis, 2002. **29**(2): p. 65-72.
21. Johnson, R.E., et al., *Screening tests to detect Chlamydia trachomatis and Neisseria gonorrhoeae infections--2002.* MMWR Recomm Rep, 2002. **51**(RR-15): p. 1-38; quiz CE1-4.
22. Cook, R.L., et al., *Systematic review: noninvasive testing for Chlamydia trachomatis and Neisseria gonorrhoeae.* Ann Intern Med, 2005. **142**(11): p. 914-25.
23. Scholes, D., et al., *Prevention of pelvic inflammatory disease by screening for cervical chlamydial infection.* N Engl J Med, 1996. **334**(21): p. 1362-6.
24. Ostergaard, L., et al., *Home sampling versus conventional swab sampling for screening of Chlamydia trachomatis in women: a cluster-randomized 1-year follow-up study.* Clin Infect Dis, 2000. **31**(4): p. 951-7.
25. Clark, K.L., et al., *Hospitalization rates in female US Army recruits associated with a screening program for Chlamydia trachomatis.* Sex Transm Dis, 2002. **29**(1): p. 1-5.
26. Duncan, B., et al., *Qualitative analysis of psychosocial impact of diagnosis of Chlamydia trachomatis: implications for screening.* Bmj, 2001. **322**(7280): p. 195-9.
27. Pimenta, J.M., et al., *Opportunistic screening for genital chlamydial infection. II: prevalence among healthcare attenders, outcome, and evaluation of positive cases.* Sex Transm Infect, 2003. **79**(1): p. 22-7.
28. Darroch, J., L. Myers, and J. Cassell, *Sex differences in the experience of testing positive for genital chlamydia infection: a qualitative study with implications for public health and for a national screening programme.* Sex Transm Infect, 2003. **79**(5): p. 372-3.
29. Shain, R.N., et al., *Prevention of gonorrhea and Chlamydia through behavioral intervention: results of a two-year controlled randomized trial in minority women.* Sex Transm Dis, 2004. **31**(7): p. 401-8.
30. Burstein, G.R., et al., *Predictors of repeat Chlamydia trachomatis infections diagnosed by DNA amplification testing among inner city females.* Sex Transm Infect, 2001. **77**(1): p. 26-32.
31. Fortenberry JD, B.E., Katz BP, Orr DP. , *Post-treatment sexual and prevention behaviours of adolescents with sexually transmitted infections* Sex Transm Infect, 2002 **78**(5): p. 365-8.

32. Whittington WLH, K.C., Kissinger P, Oh MK, Fortenberry JD, Hillis SE, et al. , *Determinants of persistant and recurrent Chlamydial trachomatis infection in young women: results of a multicenter cohort study.* Sex Transm Dis, 2001. **28**(2): p. 117-23.
33. van de Laar, M.J., F. Termorshuizen, and A. van den Hoek, *Partner referral by patients with gonorrhea and chlamydial infection. Case-finding observations.* Sex Transm Dis, 1997. **24**(6): p. 334-42.
34. Kamwendo, F., et al., *Gonorrhea, genital chlamydial infection, and nonspecific urethritis in male partners of women hospitalized and treated for acute pelvic inflammatory disease.* Sex Transm Dis, 1993. **20**(3): p. 143-6.
35. Khan, A., et al., *The prevalence of chlamydia, gonorrhea, and trichomonas in sexual partnerships: implications for partner notification and treatment.* Sex Transm Dis, 2005. **32**(4): p. 260-4.
36. Lim, S.W. and S.M. Coupey, *Are adolescent girls with Chlamydia infection notifying their partners?* J Pediatr Adolesc Gynecol, 2005. **18**(1): p. 33-8.
37. van Duynhoven, Y.T., et al., *Patient referral outcome in gonorrhoea and chlamydial infections.* Sex Transm Infect, 1998. **74**(5): p. 323-330.
38. Mathews, C., et al., *Strategies for partner notification for sexually transmitted diseases.* The Cochrane Database of Systematic Reviews, 2001. **Issue 4**: p. Art. No.: CD002843. DOI: 10.1002/14651858.CD002843.
39. Schillinger, J.A., et al., *Prevalence of Chlamydia trachomatis infection among men screened in 4 U.S. cities.* Sex Transm Dis, 2005. **32**(2): p. 74-7.
40. Golden, M.R., *Expedited partner therapy for sexually transmitted diseases.* Clin Infect Dis, 2005. **41**: p. 630-633.
41. Golden, M.R., et al., *Effect of expedited treatment of sex partners on recurrent or persistent gonorrhea or chlamydial infection.* N Engl J Med, 2005. **352**: p. 676-85.
42. Kissinger, P., et al., *Patient-delivered partner treatment for male urethritis: a randomized, controlled trial.* Clin Infect Dis, 2005. **41**: p. 623-9.
43. Hogben, M., D.H. McCree, and M.R. Golden, *Patient-delivered partner therapy for sexually transmitted diseases as practiced by U.S. physicians.* Sex Transm Dis, 2005. **32**(2): p. 101-5.
44. Centers for Disease Control and Prevention, *Sexually Transmitted Diseases Treatment Guidelines* MMWR, 2002. **51**: p. No. RR-6.
45. Magriples, U. and J.A. Copel, *Can risk factor assessment replace universal screening for gonorrhea and Chlamydia in the third trimester?* Am J Perinatol, 2001. **18**(8): p. 465-8.
46. Honey, E., et al., *Cost effectiveness of screening for Chlamydia trachomatis: a review of published studies.* Sex Transm Infect, 2002. **78**(6): p. 406-12.
47. Hu, D., E.W. Hook, 3rd, and S.J. Goldie, *Screening for Chlamydia trachomatis in women 15 to 29 years of age: a cost-effectiveness analysis.* Ann Intern Med, 2004. **141**(7): p. 501-13.
48. Blake, D.R., C.A. Gaydos, and T.C. Quinn, *Cost-effectiveness analysis of screening adolescent males for Chlamydia on admission to detention.* Sex Transm Dis, 2004. **31**(2): p. 85-95.

49. Ginocchio, R.H., et al., *The clinical and economic consequences of screening young men for genital chlamydial infection.* Sex Transm Dis, 2003. **30**(2): p. 99-106.
50. Steen, R., et al., *Evidence of declining STD prevalence in a South African mining community following a core-group intervention.* Sex Transm Dis, 2000. **27**(1): p. 1-8.
51. Steiner, K., et al., *Screening in Jails is Associated with a Decrease in Community Prevalence of Chlamydia: San Francisco, 1997-2002*[Abstract};. 15th Biennial Congress, International Society for STD Research Conference, Ottawa, Canada, 27-30 July 2003. Abstract 0146.
52. NCQA, *The State of Health Care Quality, 2005; Industry Trends and Analysis*, National Committee for Quality Assurance, Editor. 2005.
53. Stamm, WE. *Chlamydia Screening: Expanding the Scope.* Ann Intern Med, 2004. **141**(7): p. 570-2.