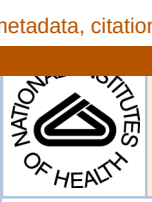

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Chlamydia trachomatis Infection in Minority Adolescent Women: A Public Health Challenge

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Abstract

Chlamydia trachomatis is the most common bacterial sexually-transmitted infection in the United States. This disease disproportionately affects adolescent minority women, and untreated infection can lead to lasting reproductive tract morbidity. Recommendations for primary prevention include patient counseling to decrease risky behavior and increase barrier protection use; secondary prevention recommendations include screening and treatment of affected individuals and their sexual partners, barrier contraception use, as well as counseling to decrease behaviors that lead to re-infection. Despite these strategies, both incidence and prevalence of Chlamydia have continued to escalate in this population. Interventions to decrease chlamydial infection should encompass all facets of primary and secondary prevention as well as address the fundamental barrier to prevention – lack of perception of risk in this young age group.

THE BURDEN OF DISEASE

Approximately 19 million new sexually-transmitted infections (STIs) occur each year in the United States; almost half are among young adults aged 15 to 24 years(1). The U.S. prevalence of *Chlamydia trachomatis* is 4.2% in young adults with the greatest number of cases (325,000) affecting women under 20 years of age (2). Given the treatable nature of the disease and the potential for reproductive health consequences of untreated infection, the Centers for Disease Control and Prevention (CDC), U.S. Preventive Services Task Force (USPSTF), American Congress of Obstetricians and Gynecologists (ACOG), and American Academy of Family Physicians (AAFP) recommend annual screening for all sexually active women younger than 26 years (Table 1) (3). Thus far, recommendations alone have not decreased the national burden of disease.

Ethnic minorities are disproportionately affected by chlamydial infection. African-Americans represent approximately 12% of the U.S. population, but account for nearly half of all infections. Hispanics comprise 15% of the U.S. population, but account for 19% of all reported chlamydial cases (1). Directed efforts to decrease the disease burden in these minority young women have not diminished this discrepancy.

Chlamydial infection rates increased from 87 to 370 cases per 100,000 persons between 1988 and 2007. Among women, the highest age-specific rates in 2007 were among those 15 to 19 years of age (3,000 cases per 100,000 females). Among sexually active youth aged 15

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to 29 years, the cost of STIs in the U.S. approximated $6.5 billion in 2000 (1). Chlamydial infections alone contributed $250 million in direct expenses, including treatment of infection and complications from undiagnosed and untreated infection. These estimates do not account for indirect nonmedical costs such as productivity loss, pain, and suffering. Given that many chlamydial infections are often unreported and the rate of STI acquisition in this age group is escalating, this underestimates the true cost to the U.S. health system (1).

The most significant effects on disease burden will result from efforts directed towards those most affected: urban minority female adolescents, aged 15–19 years. Successful prevention efforts to decrease disease prevalence among this subpopulation have the potential to lower national statistics. Both health care providers and young women may underestimate the scope and impact of this infection. Modification of individual and group adolescent behavior in conjunction with treatment of existing infection must occur if disease burden is to decrease. This review will address primary and secondary prevention of chlamydial infection as it pertains to this high-risk group, as well as innovative prevention strategies for this young population.

PREVENTION STRATEGIES

Strategies aimed at reducing the disease burden among adolescents include both primary and secondary prevention. Primary prevention efforts focus on decreasing disease acquisition through counseling and education to reduce sexual risk behavior, and increase use of barrier methods. In 1993, the CDC recommended that health care providers assess the risk of reproductive-aged female patients and provide patient education on delaying age at first intercourse, reducing the number of sexual partners, promoting use of condoms, choosing low-risk sexual partners, and encouraging mutually monogamous relationships (4). In 2006, the CDC outlined the use of open-ended questions when eliciting a sexual history and encouraged interactive individually-tailored counseling (3).

Secondary prevention efforts are intended to detect and treat existing disease as well as prevent re-infection. Efforts include counseling and barrier method use (to decrease re-infection) as well as screening and treatment of infected individuals and their sexual partners. In all 50 states and Washington D.C., minors aged 14 years and older may request STI screening without parental consent. Consent laws for minors' contraceptive services, however, vary from state to state (www.guttmacher.org). Promotion of counseling to decrease risk behavior, barrier method use, and screening for Chlamydia are almost universally recommended by national agencies. However, their utility and potential for decreasing disease burden are difficult to quantify.

PATIENT COUNSELING

Counseling of adolescents must occur in conjunction with screening tests, regardless of results, and the promotion of barrier condom use. These counseling efforts must be directed at obstacles that prevent teens from seeking screening and, more importantly, the multiple risk factors for STI acquisition. Adolescents may be less forthcoming with their sexual histories, and providers need to address sexual behavior with all young patients. The CDC recommends straightforward and nonjudgmental questioning when eliciting a sexual history and outlines a strategy for obtaining this history in the 2006 STD Treatment Guidelines (3). Providers must understand the sexual behavior of young women, and address barriers such as fear of social stigma, fear of abuse by a sexual partner, and the adolescent developmental mindset of invulnerability.

Choice of sexual partner, cultural and ethnic differences, and fear of potential abuse may decrease an adolescent's likelihood of seeking screening and impair ability to negotiate

condom use with sexual activity (5). Adolescent females with older male partners (compared to similar-aged partners) less often report consistent condom use; these women may have the highest risk of acquiring STIs (6–9). Among Latino adolescents, condom use is consistently lower than in African-American or Caucasian teens (10–12). Adolescents are more likely to use condoms with a partner they see as casual as compared to one they consider a long-term partner (13–15).

Data from the National Longitudinal Study of Adolescent health found that only 14% of all respondents and only 33% of those infected with an STI reported perceiving that they were at risk for STIs at time of diagnosis (16). Decreasing sexual risk behavior is perhaps the largest obstacle to overcome. **To reduce prevalence of *Chlamydia trachomatis* and other STIs in this population, efforts must be directed toward this fundamental barrier – an adolescent's lack of perception for disease risk** (17). Intervention programs designed to alter an individual's sexual risk perception are often founded on adolescent developmental theory and confront the mindset of invulnerability (18).

The NIH Consensus Development Statement (1997) supports the need to develop effective behavioral interventions for this population, with particular attention to language and cultural barriers (19, 20). One successful intervention program, "Sister to Sister", included an individual session between the client and nurse facilitator, showed brief videos, included condom-use demonstration, and used role-play to support behavioral change. The intervention was successful among African-Americans in decreasing sexual risk behaviors during the study period, including greater reported condom use 12 months later, and decreased acquisition of STIs (21, 22). Counseling, both individually tailored and designed for use in a busy clinical setting, are key areas for future investigation.

BARRIER METHODS

Consistent and correct use of male condoms is routinely recommended for preventing STI transmission (1). Latex condoms are effective mechanical barriers, virtually impermeable to sexually-transmitted pathogens (23, 24). When used by couples discordant for disease, condoms substantially decrease the transmission of *Chlamydia trachomatis* (25).

Although recognized as an effective prevention method, condom use remains inconsistent among adolescents and young adults. One study of African-American teens aged 14 to 18 years treated those diagnosed with *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, or trichomoniasis then retested them 6 months later if coitus was reported. In this sample of 380, 18% of those who reported consistent condom use with intercourse had at least one STI compared to 30% of those reporting inconsistent or no condom use (26). In contrast, two other prospective observational studies, one specific to adolescents and the other among an urban STI clinic population, did not find significantly different STI incidences between those who did and did not report consistent condom use (27, 28).

Surveys of patient behavior may be affected by social desirability bias - the tendency to report behavior that is viewed positively by others. Participants may over-report condom use or fail to report breakage, underestimating STI exposure (25, 29). Unknown partner infection status (and thus unknown exposure status) is difficult to quantitatively measure. Surrogate markers of exposure typically used – reported exposure, perceived high-risk partner, multiple partners, for example – may be invalid estimates of true exposure (30).

Limited information exists on the effectiveness of the female condom for STI prevention. A systematic review of the female condom reports that while acceptability in vulnerable populations has been demonstrated, use of the female condom may be lessened by increased cost and decreased availability as compared to the male condom (31). The female condom

has been shown to decrease the reported number of unprotected sex acts, but information on slippage and breakage is lacking. To date, randomized trials of STI prevention with use of the female condom have failed to demonstrate consistent benefit. The female condom is still recommended, however, as a method to decrease STI transmission and to prevent unplanned pregnancy as it augments a woman's choices for contraception and safe sexual practices (31).

SCREENING

Screening can be performed during routine physical exam visits, emergency room encounters, contraceptive counseling appointments, and primary care evaluations. The impetus for frequent screening in adolescents is derived from the high burden of disease and high re-infection rate among young females.

Screening rates for *Chlamydia trachomatis* among young women in the U.S. remain low despite recommendations by the CDC and USPSTF. In 2007, a review of nationwide insurance claims revealed that the annual screening rate was 42% for young females (32). Screening rates were lowest in the Southern United States (37%) and highest in the Northeast (46%). The true rate may be even lower than reported, as those without health insurance may be even less likely to access care (i.e., minority young women).

Provider adherence to *Chlamydia trachomatis* screening guidelines for adolescent and young adult women is inadequate. A review of the National Ambulatory Medical Care Survey in 2005 revealed that obstetricians-gynecologists did not perform screening at 69% of visits where pelvic exams were performed and 71% of visits with Papanicolaou smears for women aged 15 to 25 yr. (33). Primary care physicians did not perform urine screening tests at 99% of visits when urinalyses (for reasons other than *Chlamydia trachomatis* screening) were performed (33).

A 2009 systematic review specific to chlamydial and gonorrheal re-infection among adolescent women reported a median re-infection rate of almost 14%. Re-infection peaked at 13 months after initial diagnosis, and a consistent trend of higher re-infection rates was noted among younger ages (34). These findings suggest that young women diagnosed with chlamydial infection should be retested 3–6 months after initial infection and treatment (34). The CDC encourages re-screening 3–6 months after diagnosis and treatment – the impetus for re-screening is the high incidence of re-infection (35, 36). The USPSTF makes no recommendation as to early re-screening for those who test positive (37).

A recent analysis suggests frequent rescreening is cost effective (38). This analysis projected that annual screening prevents 864 cases of chronic pelvic pain, 967 cases of tubal infertility, and 435 cases of ectopic pregnancy per 100,000 women versus no annual testing. Rescreening 3–6 months after treatment of documented infection prevents an additional 64 cases of chronic pelvic pain, 72 cases of tubal infertility, and 32 cases of ectopic pregnancy per 100,000 women. **Annual screening with rescreening for those diagnosed with *Chlamydia trachomatis* within 3–6 months proved the most cost-effective strategy** (38).

Potential harms of screening include the risk of false-positive testing and stigma of diagnosis. While the risk for false-positive testing is low, given the high disease prevalence in this high-risk population, a false-positive screen could result in inappropriate antibiotic therapy. Endocervical culture and urine nucleic acid amplification tests are both highly specific, 98% and 95%, respectively; culture is slightly less sensitive than urine testing. Antibiotic therapy with single-dose azithromycin, 1 gm P.O., is well-tolerated in those without allergic sensitivity and is nearly 100% effective (39). Potential psychological harms, such as stigma associated with diagnosis and potential repercussions in a sexual relationship,

are difficult to quantify and likely under-reported. Overall, the benefits of screening appear to outweigh the potential harms, but screening remains only one part of the solution to a growing epidemic of STI infection among adolescents and young adults.

OPPORTUNITIES TO IMPROVE

Increasing the annual screening rate in this population to 50% - up from the current 42% - may decrease the missed diagnoses from 2543 to 2100 with a subsequent reduction in sequelae (32). While only a rough estimate, meeting current screening recommendations has important public health implications. Missing from these estimates, however, is the impact of individual behavior – from both providers and this high-risk population.

Pairing screening with Papanicolaou smears is a promising method for improving *Chlamydia trachomatis* surveillance

A retrospective cohort from a large group health plan showed rates of Chlamydia screening increased if providers performed testing during speculum examinations for Papanicolaou smears (40). The greatest rate of increase was in women aged 20 – 26 (24% increase), with a more modest increase in women aged 15 – 19 years (10% increase) (40). These findings underscore that increasing screening rates is feasible when paired with cervical cancer screening and a need for improvement persists in screening rates in young adolescents.

Pairing urine *Chlamydia trachomatis* screening with urine pregnancy tests for adolescents is a largely untapped opportunity

Risk factors for unplanned pregnancy mirror those of chlamydial infection, but few studies have evaluated frequency of STI screening at time of pregnancy testing. One recent study evaluated 1465 participants and found that 12% were diagnosed with *Chlamydia trachomatis* at the time of urine pregnancy testing, regardless of pregnancy diagnosis (41). In addition, those diagnosed with chlamydial infection were younger and of African-American ethnicity. Urine screening is simple and non-invasive as a urine sample is already collected for pregnancy testing.

Urine testing, rather than endocervical testing, may increase the acceptability of screening. A prospective cohort of adolescents in an urban emergency department indicated that urinary screening was acceptable to the majority of adolescents irrespective of the reason for emergency care. Of 1231 adolescents aged 14 to 20 years who were approached upon admission to the emergency department, 71% consented to undergo urine screening (42). Other opportunities, such as emergency room or provider visits for unrelated complaints, may increase screening in this population. Additional information, such as cost-effectiveness projections, is likely necessary before widespread implementation can be promoted.

While none of these studies was a randomized masked clinical trial, which is the gold standard study design, each offers compelling evidence to increase screening in ways that are easily adaptable to busy clinical settings. A summary of the evidence can be found in Table 2.

THE FUTURE

The USPSTF recognizes the lack of research regarding the negative outcomes of screening – the stigma of diagnosis and the impact of false-positive results. Consistent evidence for screening and treatment of adolescent males is lacking. As young women most frequently contract *Chlamydia trachomatis* through heterosexual behavior, primary prevention through disease identification in male partners is a potential area for improvement (15). To date,

widespread screening and treatment of adolescent males is not supported by cogent research (3).

Analysis of the evidence for screening, condom use, and counseling illustrates some of the uncertainties underlying both primary and secondary prevention. Strategies should be aimed at increasing adherence to national recommendations by providers and patients, as neither appears to fully appreciate the repercussions of untreated disease. Implementation of primary prevention strategies through behavioral change in partner selection, delaying first intercourse, and consistent condom use has proven difficult. Secondary prevention strategies, including screening and behavioral counseling at the time of clinical evaluation for both gynecologic and unrelated complaints, are also largely untapped opportunities. Developmentally appropriate interventions to improve an adolescent's perception of sexual risk, coupled with improving adherence to recommendations, may be keys to decreasing disease burden in this young, underserved, minority population.

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Table 1

Guidelines for Chlamydia Screening

Organization	Year	Recommendations for Screening	Interval
USPSTF [*] (AAFP) [+]	2007	• all sexually active women aged 24 and younger • all older women at increased risk • pregnant women at first prenatal visit if 24 and younger or at increased risk; third trimester screen for patients at risk in late pregnancy	Optimal interval unknown, annual testing recommended
CDC [↑] (Cites USPSTF 2001)	2006	• all sexually active women aged 25 and younger • all older women at increased risk	Annual; retest all patients with new infection at 3–12 months after treatment
ACOG [≠] (Cites USPSTF 2001, CDC 2006)	2006	• all sexually active women aged 25 and younger • all older women at increased risk	Annual

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Table 2

USPSTF Levels of Evidence for Opportunities to Improve

Author	Title	Study Design	Level of Evidence
Burstein GR, Snyder MH, Conley D, et al.	Chlamydia screening in a health plan before and after a national performance measure introduction	Retrospective cohort	II – 2 *
Geisler WM, James AB.	Chlamydial and gonococcal infections in women seeking pregnancy testing at family-planning clinics	Cross-sectional	II - 3 ≠
Monroe KW, Weiss HL, Jones M, et al.	Acceptability of urine screening for *Neisseria gonorrheae* and *Chlamydia trachomatis* in adolescents at an urban emergency department	Prospective cohort	II – 2 *

* Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one center or research group.

≠ Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments could also be regarded as this type of evidence.