Chlamydial Infection among Young Adults: Selective Screening and Partner Age Difference an Investigation of the National Longitudinal Study of Adolescent Health

Cheryl R. Stein

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Approved by:

William C. Miller, MD, PhD, MPH

Paul J. Feldblum, PhD

Carol A. Ford, MD

Jay S. Kaufman, PhD

Peter A. Leone, MD

ABSTRACT

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(Under the direction of William C. Miller)

Among young adults, chlamydial infection is the most common bacterial sexually transmitted infection. Women and minorities are most affected. Screening rates are low despite recommendations for yearly testing. Programs to expand testing to community settings may increase screening rates. To examine this and other questions, we conducted a cross-sectional analysis of Wave III of the National Longitudinal Study of Adolescent Health (April 2, 2001 – May 9, 2002). *Chlamydia trachomatis* test results were available for 10,928 (88.6%) of the sexually experienced participants.

First, we developed selective screening guidelines for community settings. Separately for women and men, we developed three predictive models using unconditional multiple logistic regression. The initial models included predictor characteristics plus information on 1) respondent's race/ethnicity; or 2) respondent's most recent partner's race/ethnicity; or 3) no information on race/ethnicity. A combination of characteristics provides potentially useful screening tools. Applying these models to select ≤ 50 percent of the population for diagnostic testing identifies approximately 80 percent of infections in women and men. Using race/ethnicity in any screening algorithm is controversial and may have significant consequences. The model without race information, however, resulted in

many missed diagnoses in the minority group. Universal screening for chlamydial infection may be the only approach that reaches high prevalence populations while avoiding the stigma of screening guidelines incorporating race/ethnicity.

Second, we evaluated the association between partner age difference and chlamydial infection among young women. Adolescent girls with older male partners are at higher risk of STI compared to girls with partners their own age, but whether this association continues beyond adolescence is unclear. After multiple logistic regression, the odds of prevalent chlamydial infection among women with partners two to eight years younger were nearly two times greater (odds ratio (OR) 1.8, 95% confidence interval (CI) 0.9 – 3.5) than partners within one year's age. Among women with older partners, the adjusted odds of infection were similar for partners two to five years older (OR 1.4, 95% CI 0.9 – 2.3) and partners six to 36 years older (OR 1.6, 95% CI 0.9 – 2.8). Among young adult women, older partners are moderately associated with prevalent chlamydial infection.

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Add Health	National Longitudinal Study of Adolescent Health
AIDS	acquired immune deficiency syndrome
CASI	computer-assisted self-interview
CDC	Centers for Disease Control and Prevention
CI	confidence interval
HEDIS	Health Plan Employer Data and Information Set
HIV	human immunodeficiency virus
LCR	ligase chain reaction
ml	milliliter
NSAM	National Survey of Adolescent Males
OR	odds ratio
ROC	receiver operating characteristic
SE	standard error
STD	sexually transmitted disease
STI	sexually transmitted infection
US	United States

CHAPTER 1

OVERVIEW

Chlamydia trachomatis, with an estimated three million new infections each year, is the most common bacterial sexually transmitted infection (STI) in the United States (US), especially among adolescents and young adults (1). Black, Native American, and Latino women and men are disproportionately burdened with infection (2, 3). Chlamydial infection may cause pelvic inflammatory disease, ectopic pregnancy, and tubal infertility in women (4-6). In vitro studies suggest that *C. trachomatis* may affect sperm function in men (7). In both sexes, infection increases susceptibility to and transmission of HIV (8, 9). This STI causes substantial morbidity, yet it can be prevented using safer sex practices, detected with a urine-based nucleic acid amplification test, and cured by a single dose of oral antibiotics.

Testing for and treating STI may reduce potential complications, duration of infection, rates of transmission, and ultimately infection prevalence. However, identifying who, at a population level, is at risk of infection and would benefit from testing is challenging. The majority of men and women infected with chlamydia are asymptomatic (10). It is difficult to encourage people at risk of infection to seek care, as well as to encourage health care providers to view screening as a public health priority. For these and other reasons, screening rates for chlamydial infection remain low (11-13) and prevalence of chlamydial infection remains high (2, 3).

Urine-based diagnostic tests facilitate STI screening and make testing outside of traditional sexually transmitted disease (STD) and family planning clinics feasible. These tests can also be used in survey research to detect infection in the general population, including hard-to-reach segments like young people. With laboratory diagnostics linked to detailed demographic, personal history, and behavior data as it is in Wave III of the National Longitudinal Study of Adolescent Health (Add Health), we have the tools to develop population-based selective screening guidelines for prevalent chlamydial infection for both women and men. Additionally, these unique data provide information on sexual partnerships that can illuminate the association between partner age difference and prevalent chlamydial infection among young women.

Specific Aim One

Selective Screening Guidelines for Chlamydial Infection in US Young Adults

To develop criteria for screening young women and men in the US general population for prevalent chlamydial infection.

Hypothesis: The risk of prevalent chlamydial infection can be predicted with reasonable accuracy using a combination of demographic, behavioral, and clinical variables.

Overview: We will develop screening criteria separately for women and men using data collected in Add Health Wave III. Demographic, sexual behavior, self-perceived risk, medical, and health care factors will be analyzed as candidate predictor variables.

Rationale: Testing and treatment for chlamydial infection is challenging because infections are asymptomatic in approximately 70 percent of women and 50 percent of men (10). The

US Preventive Services Task Force "strongly recommends" that clinicians routinely screen all sexually active women aged 25 years or younger for chlamydial infection (14). However, screening rates are remarkably low (12, 13), despite the inclusion of chlamydial screening in the Health Plan Employer Data and Information Set (HEDIS) performance measures (11). Furthermore, chlamydial infection in men is not addressed by current recommendations. While this STI is a lesser problem among males compared to females (2, 3), a sizeable proportion of young men are consistently diagnosed with asymptomatic infection (15-17). Perhaps more importantly, these men may transmit chlamydial infection to their female partners. Programs to expand testing beyond clinic settings to locations such as community centers, health fairs, school campuses, and other locations frequented by young people may help screen more people. Community-based testing is a potentially valuable way to reach young adults in the general population with asymptomatic infection.

Specific Aim Two

Partner Age Difference and Chlamydial Infection among Young Adult Women

To assess the association between partner age difference and prevalent chlamydial infection among young adult women.

Hypothesis: Younger women in age-discordant partnerships have higher odds of chlamydial infection compared to older women in age-discordant partnerships.

Overview: We will describe the range of partner age difference within and across partnerships using data collected during Add Health Wave III. Partner age difference will be examined for association with prevalent chlamydial infection women.

Rationale: Sexual mixing between members of different groups facilitates the spread and maintenance of STI (18-21). Partner mixing by age is common among both adolescents and young adults (22, 23). Adolescent girls with older male partners are more likely to practice sexual behaviors such as young age at first sex and inconsistent condom use, which are risk factors for STI (24-31). Whether this relation between older partners and risky behavior continues beyond adolescence is uncertain. Two studies reporting the effect of partner age difference on STI among adults found little association, but one study diagnosed chlamydial infection by culture (18) and the other relied on self-report of STI test or treatment in the past year (23). The effect of another salient risk factor for STI, young age at first sex, does diminish with increasing age (32). These findings suggest that older male partners may play a lesser role in risk of STI as adolescent girls mature into adulthood. The knowledge that partner age difference has a heterogeneous effect on risk of chlamydial infection across age groups can contribute to an improved understanding of STI epidemiology and may inform clinical management, health education, and intervention programs.

CHAPTER TWO

BACKGROUND

Prevalence and Public Health Costs of Chlamydial Infection in the United States

Sexually transmitted infections constitute the overwhelming majority of nationally notifiable disease reporting in the US. In 2004, nearly 1.3 million STI, excluding HIV, herpes, hepatitis, and human papillomavirus, were reported to the Centers for Disease Control and Prevention (CDC) (2). These 1.3 million reported cases account only for a fraction of the 15 million estimated incident infections (33). Even with advancements in medical technology that permit more facile, less invasive diagnostic testing, and the availability of effective therapy, overall STI prevalence is rising in the US (2).

Infection with *Chlamydia trachomatis* is the most commonly reported notifiable condition in the US (2). The CDC recorded 929,462 chlamydial infections in 2004, but the true number is estimated to be three million (33, 34).

The long-term sequelae of chlamydial infection are significant. Among women, infection may cause pelvic inflammatory disease, ectopic pregnancy, tubal infertility, and chronic pelvic pain (4, 6). Infection may also be linked to cervical cancer (35). Among men, chlamydial infection may lead to chronic prostatitis, reactive arthritis, urethral strictures, and possible fertility problems (5, 7). In women and men, chlamydial infection increases susceptibility to and transmission of HIV (8, 9).

The direct, indirect, and intangible price of STI is also considerable. The yearly cost of a single prevalent chlamydial infection, adjusted to 1994 dollars, is $2,630 (36). Expenses total nearly eight billion dollars a year for the three million estimated annual incident infections. The estimated lifetime direct medical cost of a new chlamydial infection for Americans aged 15 to 24 years is 248.4 million dollars (37). This figure includes treating acute infection and sequelae of untreated or inadequately treated infection, but does not account for chlamydial infection's facilitative role in HIV transmission (37).

Prevalence of Chlamydial Infection Varies by Age, Gender, and Race/Ethnicity

The reported prevalence of chlamydial infection varies considerably across populations and testing situations (Appendix One). The prevalence of chlamydial infection ranges from a low of 2.1 percent in a convenience sample from a private pediatric practice in suburban North Carolina (38) to a high of 27.2 percent among females attending teen health clinics in Atlanta, Georgia (39).

Adolescents (ages 10 to 19 years) and young adults (ages 20 to 24 years) constitute a disproportionately large segment of the population with STI. While people aged 15 to 24 years comprise about 25 percent of the sexually active population, they account for nearly 50 percent of the STI (1). The highest reported rates of chlamydial infection occur among females aged 15 to 19 years and males aged 20 to 24 years (2). Minority youth have a higher reported rate of infection as compared to white youth. In 2004, black, non-Hispanic females aged 15 to 19 years were infected with chlamydia at a rate of 8,897.6 per 100,000 population, compared to 2,810.1 per 100,000 for similarly aged Hispanic and 1,408.8 per 100,000 for white, non-Hispanic females (2). These high rates of nationally reported infection in young

people, especially among minority young people, are consistently duplicated by population-based studies (3, 40, 41), and STI screening in high schools (42-44), the military (17, 45, 46), juvenile detention centers (15, 47, 48), the national job training program (49), and other non-clinic settings (50) (Appendix One). In the Add Health population, infection prevalence is highest in women, African Americans, and people from the southern region of the US (3).

Factors Contributing to Chlamydial Infection among Young People

The reasons for high STI prevalence among young people are numerous. Biologic, cognitive, behavioral, and social factors all contribute to the elevated prevalence. Adolescent vaginal physiology may increase susceptibility to STI through cervical ectopy, alkaline vaginal pH, and thin cervical mucous (51). The cognitive development of adolescents further puts them at risk of infection. Until middle or late adolescence, young people may have difficulty conceptualizing the long-term impact of current actions (51).

Behavior is often at the essence of STI risk. Adolescents and young adults engage in behaviors known to increase the rate of STI acquisition. Young age first sex may lead to a greater number of lifetime sexual partners, an important determinant of STI risk. Multiple sex partners within a short time period may increase risk behaviors like sequential and overlapping partners. Condom use is inconsistent and tends to diminish over the course of a relationship, making sequential partners a risk factor for infection if the gap between partners is shorter than the duration of infection (51).

Social issues are also intrinsic to the high STI rate among young people. The Institute of Medicine names the societal problems of poverty, lack of education, and social inequity as culpable in the STI epidemic (52). The “lack of openness and mixed messages regarding

sexuality" is an additional cited cause (52). Adults, be they parents, educators, or health care providers, often fail to share with children the information and tools needed to make timely, balanced, and informed choices regarding sexual activity (53). Procuring condoms may be logistically difficult for adolescents; yet making condoms readily available in schools and other locales frequented by young people remains controversial. Adolescents who want to access health services for STI counseling, testing, and treatment must know where to access care, be able to make an appointment, have transportation to the site, and pay for service, all potentially insurmountable barriers to a young person (53). Furthermore, maintaining patient confidentiality continues to be an issue when exercising benefits conferred by a parent's health insurance (51). These cognitive, behavioral, and social impediments all compound young people's innate biologic susceptibility to STI and significantly contribute to the epidemic spread of infection.

Using the Sexually Transmitted Disease Transmission Model to Reduce Prevalence

The May and Anderson model of STD transmission provides a useful framework for understanding the links among classical STI risk factors, risk markers, and health care (54, 55). Transmission or reproductive rate is a function of infectivity/transmissibility, the interaction between susceptibles and infectors, and the duration of infection. The traditional formula is $R_0 = \beta * c * D$ where R_0 is the reproductive rate or average number of secondary cases generated by a primary case; β is a measure of transmissibility; c is a measure of partner change; and D is duration of infectiousness. Condom use and sexual practices may affect transmissibility, β. Factors related to sexual partners, such as number of partners, rate of partner change, and concurrent partners affect parameter c. Duration of infection may be

influenced by immune factors and presence of symptoms. Reproductive rates greater than or equal to one will propagate or sustain the epidemic. Lowering disease prevalence requires reducing the reproductive rate by changing any or all of the model's parameters. Common interventions and known risk factors and markers can all be linked to specific parameters.

Testing and treatment for STI affect transmission primarily by reducing the duration of infectiousness, D and consequently the number of secondary cases infected by the index case (54, 55). Disease screening – testing for disease in the absence of symptoms – is particularly important for STI where asymptomatic infection is common and may have prolonged duration resulting in continued transmission over time.

Testing and treatment for chlamydial infection can reduce the overall prevalence of infection (56, 57) and the incidence of pelvic inflammatory disease (58). Rates of chlamydial infection dropped by up to 60 percent after the implementation of large-scale screening programs like the Department of Health and Human Services Region X program in family planning clinics in Alaska, Idaho, Oregon, and Washington (59). The lowest rates of chlamydial infection in a study of female military recruits were in women from states with active screening programs (46). Repeated STI screening through school-based programs also considerably lowered the prevalence of chlamydial infection among boys, with a lesser effect among girls (60). The CDC recently proclaimed that "increased screening by healthcare providers . . .will be necessary to reduce substantially the burden of chlamydial infection in the United States" (61). The National Commission on Prevention Priorities also named screening young women for chlamydial infection as an effective clinical preventive service, but with low implementation (62).

Screening for STI has proven cost effective in both minimizing disease burden and sequelae among women (63). Computer models also exhibit substantial cost savings – 1,086 dollars per major outcome averted during 10 years of screening a general population aged 15 to 64 years with a 4.1 percent baseline prevalence of chlamydial infection (64). Screening may be even more beneficial in populations with higher prevalence of infection. Shortening duration of infection through screening is a sensible approach to reducing the STI burden (10, 61).

Infection transmission is related to sexual partnership traits through all three parameters. While an individual's rate of partner change affects transmission through c, the actual characteristics of the partner exert influence through β, c, and D. To acquire a STI from a partner, the partner must be infected. The partner's risk of STI is shaped by his or her own sexual behaviors, partner change, and treatment practices.

Although elevated risk is a direct result of sexual behavior, health care, medical factors, and demographic characteristics such as age, race/ethnicity, and education status may crudely identify members of different subpopulations with disparate background risk of STI. An individual who selects a partner from a group with higher risk increases his or her own risk of STI. Consequently, an individual selecting a partner discordant with respect to age, race/ethnicity, or even educational attainment may be selecting a partner with a discordant risk of STI. These associations have been clearly established in small STD clinic populations (18). Assessing the existence of analogous relationships in the general population, particularly in a young population where discordant age may be more meaningful, has potential for shaping future efforts to minimize prevalence by targeting partner choice.

Asymptomatic Infection Hinders Management of Chlamydial Infection

Untreated infection is a driving force of the STI epidemic. Asymptomatic chlamydial infection contributes significantly to the complexity of controlling the spread of infection. In a cross-sectional survey of asymptomatic young adult, military personnel from four settings, the overall prevalence of chlamydial infection was 4.2 percent (65). Chlamydial infections are asymptomatic in approximately 70 percent of women and 50 percent of men (10). Men are more likely to have symptoms and experience a shorter duration of infection.

Getting people at risk of infection to present for screening is challenging in the absence of typical genitourinary symptoms like pain on urination or discharge. Focus groups of adolescents have revealed a lack of awareness of the importance of screening to detect asymptomatic STI as a barrier to screening (53). Health care providers outside of STD clinics may not evaluate asymptomatic, albeit at-risk patients for STI. Only 42 percent of primary care providers at a large, integrated health care delivery system reported annual chlamydial screening of sexually active adolescents (66). Systems-level change in commercial health plans has boosted screening rates (11). Non-traditional testing venues may also help improve screening rates, but the lack of screening guidelines applicable to the largely asymptomatic general population hinders public health efforts to control disease. Guidelines to be used in community settings should be based on data from the general population rather than algorithms derived from clinical settings.

Testing for Sexually Transmitted Infection

Sensitive and non-invasive tests can diagnose even asymptomatic sexually transmitted infection and facilitate testing outside of traditional clinic-base settings. Ligase chain reaction (LCR) for chlamydial infection can be applied to urine specimens and has excellent performance with sensitivities generally greater than 90 percent and specificities greater than 99 percent (67-78; Appendix Two). Performing tests on urine specimens is more acceptable than invasive testing methods, leading to higher rates of test taking, particularly among asymptomatic populations (79, 80). Identifying and treating disease in segments of the population broader than symptomatic persons or those attending STD clinics is crucial to reducing the overall prevalence of STI. Providers wishing to expand screening services into non-traditional settings, however, have little guidance since screening criteria developed in STD or family planning clinics may not be appropriate for the general population.

Current Selective Screening Guidelines are Unsuitable for the General Population

Screening is critical to the early detection and treatment of STI since seeking care only when symptoms occur will likely miss most infections (14). The CDC (81), American Medical Association (82), American Academy of Pediatrics (83), American College of Obstetrics and Gynecology (84), US Preventive Services Task Force (14), and American College of Preventive Medicine (85) all provide guidelines for chlamydial screening in women (Appendix Three). Numerous local American and international disease control programs have also developed selective screening criteria (86-97; Appendix Three). Many

of these guidelines are based just on age: any sexually active women younger than a specified age is to be screened for chlamydial infection. Some guidelines attempt to target specific populations by specifying young age alone or older age plus risk factors. Other guidelines include age as one of several risk factors. A few guidelines do not incorporate age at all. The age cutoffs for each of the guidelines are dependent on the study populations used to develop the guidelines. Unfortunately, when examined across diverse settings, selective screening criteria often fail to deliver the desired result of detecting most infections with a minimum number of false positives (46, 98-100). A primary reason for this failure is that criteria based on STD clinic populations perform poorly in non-clinic testing situations (90). These guidelines have diminished accuracy in lower prevalence settings with wider ranges of demographic characteristics and behavioral risk factors (101, 102).

Guidelines developed using data from STD and family planning clinics may not be applicable to the general population, which is the most suitable population to screen for asymptomatic disease. The higher infection prevalence in clinic compared to population settings can affect the scoring of risk assessment criteria. Additionally, demographic and behavioral characteristics differ between clinic attendees and the general population. A comparison of patients attending a STD clinic and community residents from the same town found that while both samples yielded similar estimates of the proportions using condoms and average age at first intercourse, risky behavior was more common in the clinic populations (103). The two populations also differed demographically. In another community there were differences between STD clinic and random digit dialed populations for all examined individual and partnership characteristics (104). STD clinic patients were younger at first sex and reported a greater number of lifetime partners, a higher rate of

partner change, more concurrent partnerships, and a more varied assortment of sexual activities (104).

Most STI screening criteria only address infection in women even though adverse outcomes are not limited to women. Men with untreated chlamydial infection can suffer from complications and continue to transmit infection to their partners. Limiting selective screening to women misses a sizable proportion of the at-risk population. Testing and treating men for infection is essential to reducing the spread of disease.

Most current screening criteria recommend STI testing for all sexually active young people up to age 24 and for anyone reporting risky behaviors. Information specific to young adults is sparse considering the different epidemiology and barriers to care among teens, younger, and older adults. As young adults age out of the interval with recommended universal screening, the more restrictive criteria suggested for older adults may miss a substantial at-risk population. When examining a representative sample of young people from the general population, markers of risk or infection status specific to them may be readily identifiable and incorporated into selective screening criteria directed at young adults.

Factors Associated with Chlamydial Infection among Young Adults

The number of infections identified and the number of tests used determines adequacy of screening performance (88, 101, 105, 106). To achieve successful selective screening there must be ways to discriminate between people at high risk and low risk of infection so that in settings with limited resources testing can be restricted to those at higher risk. Demographic, behavioral, perceived risk, medical, and health care characteristics can assist in differentiating across the risk spectrum.

The available research on asymptomatic young adults in the general population indicates that not all determinants of STI are consistently important from adolescence through young adulthood. The effect of young age at first sex on risk of STI diminishes with age (32). Neither is core group membership constant. Less than one percent of a cohort was a core group member, defined by number of sex partners, at age 18 and age 21 and age 26. Salient proportions, though, were core members at one of these ages (107). In the National Survey of Adolescents Males (NSAM), a greater proportion of participants aged 22 to 26 years, compared to 18 to19 years, tested positive for chlamydial infection (16). These numbers corroborate national surveillance data showing the highest rate of chlamydial infection among 20 to 24-year-olds (2). The prevalence of known risk factors also fluctuates over these ages. The older NSAM participants were more likely to have had unprotected sex, three or more female partners, or sex with a high-risk partner in the past year (16). Condom use (108) and STI knowledge also lag with age. A longitudinal assessment of young women's understanding of transmission, treatment, and sequelae showed increases between ages 16 and 18 but then a drop below baseline level at age 23 (109). Young adult men are less likely than adolescents to receive STI prevention information (110).

Adult risk factors for STI are not all strongly associated with infection in young people. There is an association between crack cocaine use and STI among adults, but not adolescents (111). In a cross-sectional study of emergency room patients, different predictors of gonorrhea or chlamydial infection emerged when analyzing patients aged 18 to 31 years rather than the full population, aged 18 to 44 years (112). Among women aged 18 to 44 years, the largest proportion reporting multiple partners were aged 20 to 29 years (113). The shifting of risk determinants between adolescence and adulthood may reflect differences

in high-risk sexual networks. If the early twenties is a period of transition from adolescent to adult behaviors and lifestyles, there may be a set of risk predictors unique to young adults.

Viable selective screening guidelines for young men and women are lacking for chlamydial infection, one of the most prevalent, costly, and curable STI. While screening criteria exist for adolescents and older adults, there are no comparable guidelines for young adults in the general population. Until now, the unique combination of data necessary to appropriately develop screening criteria for this population has not existed. Add Health combines the results of nucleic acid amplification tests for STI with comprehensive demographic, behavioral, and health care information for a large, representative sample of US young adults, all of which are essential to the development of usable, effective, and efficient screening criteria.

Partner Age Difference and Chlamydial Infection

Qualities of sexual partnerships may place one member at elevated risk of STI. Disparities in risk of chlamydial infection exist across categories of demographic, social, and behavioral factors. Higher STI rates are associated with specific mixing patterns – sexual links between members of distinct sexual networks and populations (18, 114). Discordant race/ethnicity (18), socioeconomic, employment or education status (18, 115), gap length between relationships (116), concurrency (115, 117-119), lack of monogamy (120), and partner behavior (18, 39, 121-123) facilitate the spread and maintenance of infection. Bridging across age also presents a prime opportunity for mixing low and high prevalence populations (18, 23, 124).

There is incomplete and conflicting information about the association between age discordancy and risk of STI. Partner mixing by age is common among both adolescents and young adults (22, 23). Among adolescents, females involved with older partners are more likely to have intercourse compared to females involved with partners their own age (28). When examining STI, rather than intercourse, older partners are not associated with repeat infection among adolescent females diagnosed with chlamydial infection (125). Among pregnant adolescents, however, those with older partners are four times more likely to test positive for chlamydial infection and twice as likely to report that their partner is not monogamous (24). Two studies reporting the effect of partner age difference on STI among adults found little association with older partners, but one study diagnosed chlamydial infection by culture (18) and the other relied on self-report of STI test or treatment in the past year (23). It is unclear whether age discordancy is truly a determinant of increased risk, and whether there is an age at which discordancy ceases to be an important factor. Methodological issues such as the magnitude of age difference, shifting importance of differences across ages, and choice of study population may account for some of the discrepant findings (126). An additional factor to consider is that most studies examine the association of STI and main partner only, when the age difference between non-main partners may be more suggestive of increased risk (126).

Conclusions

Sexually transmitted infections are an enormous public health burden, especially among young people. The long term effects of untreated or inadequately treated STI may reach beyond adolescence into adulthood, and the economic and personal costs may continue

over a lifetime. Screening is fundamental to reducing infection prevalence, yet population-based screening guidelines specific to young adults are lacking for both women and men. Analysis of the Add Health project can deliver these screening guidelines and fill this basic gap in STI prevention. Additionally, even though STI has been researched extensively, important questions about infection epidemiology, particularly among young adults, remain unanswered. A deeper understanding of the association of partner age difference with infection among young women may contribute greatly to reducing the incidence and prevalence of sexually transmitted infection.

CHAPTER 3

RESEARCH DESIGN AND METHODS

Overview of Study Design and Population

Wave I of the Add Health Study included questionnaires administered to individual participants, their parents, school peers, and school administrators. Wave II repeated similar questionnaires for the individual participants and updates from school administrators. Wave I and II field work was conducted by the National Opinion Research Center of the University of Chicago. The Wave I and II questionnaires administered to the individual participants were extensive. The questionnaires included 39 sections covering demographics, daily activities, romantic partnerships, sexual activity, contraceptive use, health care utilization, and risk taking behaviors. Wave III field work was conducted by the Research Triangle Institute. The Wave III questionnaire was updated to obtain relationship, marital, childbearing, educational, and employment histories as well as collecting biological specimens and interviewing a sample of heterosexual partners of respondents. An interviewer traveled to the participant's home or other suitable location identified by the potential participant. After obtaining written consent, interviewers conducted the approximately 90-minute session in as private an area as possible. For non-sensitive issues, the interviewer recorded responses directly into a laptop computer. For sensitive issues, computer-assisted self-interview (CASI) allowed the participant to enter responses

directly into the computer. The use of CASI tends to increase the frequency of responses for sensitive issues (127-131).

Add Health used a two-stage sampling scheme with over sampling of particular groups. The primary sampling frame for the original Add Health sample included all high schools in the US with an 11th grade and at least 30 students in the school. Feeder middle schools – schools that included a seventh grade and sent at least five graduates to a high school – were identified by the high school and selected with a probability proportional to the number of students continuing on to the high school. From this sampling frame, a systematic random sample of 80 high schools and 52 middle schools was chosen with unequal probability of selection. The sampling of schools was stratified into 80 clusters to ensure that the schools were representative of US schools with respect to key demographic features (Table 3.1). Over 70% of the originally sampled high schools participated.

Table 3.1 Add Health School Sampling Scheme

Characteristic	Categorizations			
region	northeast	midwest	south	west
urbanicity	urban	suburban	rural	
school size	125 or fewer	126 – 350	351 – 775	776 or greater
school type	public	private	parochial	
percent white	0	1 – 66	67 – 93	94 – 100
percent black	0	1 – 6	7 – 33	34 – 100
grade span	K – 12	7 – 12	9 – 12	10 – 12
curriculum	general	vocational	alternative	special education

The original study participants were identified from rosters of students in grades seven through 12 enrolled in the selected schools early in the 1994 to 1995 school year. 90,118 students and 164 school administrators completed self-administered, in-school questionnaires. Students in each school were stratified by grade and sex for selection into the in-home core sample. About 17 students were randomly chosen from each stratum so that a

total of approximately 200 adolescents were selected from each of the 80 school clusters. These 12,105 students comprised the core sample.

Special oversamples were also selected to complement the core sample. Oversample eligibility was determined by student response to the in-school questionnaire. Adolescents could qualify for more than one sample. Black students with a college-educated parent (n = 1,038), Chinese (n = 334), Cuban (n = 450), and Puerto Rican (n = 437) students were oversampled to increase the precision of the estimates for these groups. Other special subsamples included saturated schools, persons with disabilities, and genetic samples. In 16 schools, all enrolled students were selected for in-home interviews to facilitate social network analysis (n = 2,553). This saturation sample included two large schools – one predominantly white and located in a mid-sized town and the other ethnically heterogeneous and located in a major metropolitan area – and 14 small schools. The disability sample was for adolescents self-reporting a physical limb disability (n = 471). Lastly, various sibling pairs living in the same household (n = 4,527) were invited to participate to construct a genetic sample database. In total, 20,745 adolescents and 17,700 parents completed Wave I in-home interviews.

Wave II data collection included 128 follow-up school administrator questionnaires and 14,738 adolescent in-home interviews. The Wave II in-home interview sample was the same as the Wave I in-home interview sample except that 1) respondents who were in the 12^{th} grade at Wave I and who were not part of the genetic sample were not interviewed at Wave II; 2) respondents who were only in the Wave I disabled sample were not re-interviewed; and 3) 65 adolescents who were members of the genetic sample but had not been interviewed at Wave I were recruited at Wave II.

Wave III targeted all original Wave I participants currently living in the continental US, Alaska, or Hawaii, including military personnel stationed domestically and participants in detention facilities. Data collection covered 15,197 in-home interviews, 1,507 interviews with partners of respondents, and collection of biological specimens. Post-stratification sampling weights were calculated to account for persons who could not be located or refused to participate. With these sampling weights, accounting for the school as the primary sampling unit and using region of the country as a stratification variable, the Add Health Wave III cohort provides a representative sample of young adults aged 18 to 26 years living in the US. All participants with sample weights who reported at the Wave III interview ever having vaginal intercourse, and who had usable chlamydia test results, were included in the analyses.

Data Collection and Measurement

With the exception of laboratory-confirmed STI in Wave III and physical measurements for height and weight, all data collected throughout the Add Health project were self-reported. Certain family-level details from Wave I, such as family composition and socioeconomic status were gathered from both student and parent.

All Wave III original respondents and a sample of recruited partners aged 18 years or older were asked to provide a urine specimen to test for *Chlamydia trachomatis* (132). Before the start of each session, the interviewer described the Wave III interview, obtained consent for participation, and informed respondents that at the end of the interview they would be asked to provide urine specimens for STI testing. At the end of the interview, respondents were asked to consent to and provide a urine specimen for STI testing. Those

providing a urine specimen received $10. Respondents providing the specimen were given a toll-free telephone number and secure procedures to obtain counseling and their confidential test results, the toll-free telephone number for CDC's National STD and AIDS Hotline, and information about chlamydia and other sexually transmitted infections. Participants were also informed that they were not being tested for all STI and should not view their participation in Add Health as a substitute for health care. Results of these assays were not reported to local public health departments based on the terms of a Certificate of Confidentiality obtained from the US Department of Health and Human Services.

Urine specimens were tested for *Chlamydia trachomatis* per manufacturer instructions using ligase chain reaction (LCR™) amplification technology in the Abbott LCx® Probe System (Abbott Laboratories, Abbott Park, IL). Urine specimens were collected in a 30ml cup with a line marked at 15ml. Specimens were immediately cooled to 2 – 8 degrees Celsius inside a cooler with ice packs. The LCR assay required 15 – 20ml of first stream urine collected in a plastic, preservative-free, sterile urine specimen cup from respondents who had not urinated within one hour prior to collection. Respondents received instructions about collection procedures from interviewers who had extensive training, including training by Abbott Laboratory representatives. If respondents asked to be excused to urinate before the end of the interview, consent and specimen collection occurred at that time to avoid situations where the respondents would be ineligible to provide a specimen at the end of the interview because of voiding within the previous hour. Cooled urine specimens were packaged and overnight expressed to arrive for diagnostic testing at the University of North Carolina at Chapel Hill by the next morning. Samples were received in the laboratory within four days of collection. Upon arrival, urine specimens were inspected

for adherence to appropriate shipping conditions, including the presence of the appropriate bar code label, date and time of collection, temperature on arrival, and volume of urine. All urine samples were processed on the day of arrival by trained laboratory technologists.

C. trachomatis was identified in urine specimens by LCR assay. LCR assays were performed according to the manufacturer's instructions, except that specimens exceeding the recommended volume of 20ml were tested. The testing laboratory performed sample processing in a dedicated pre-amplification area that was monitored routinely for contamination by wipe testing. An open vial was maintained on the bench top and then carried through sample processing to monitor contamination. A laboratory-prepared positive control was also processed with each run as an external monitor of sample processing and detection. The post-amplification area, including instrumentation, was monitored by wipe testing in a fashion similar to the pre-amplification area. Routine instrumentation monitoring and preventive maintenance were performed per the manufacturer's recommendations. The LCR results were reviewed for acceptability by the responsible technologist as well as a second individual. Ligase chain reaction results were expressed as a signal to cutoff ratio determined by relating the sample rate for each specimen to the cutoff value of assay calibrator duplicates. The Abbott analyzer automatically performed these calculations. All samples with a signal to cutoff ratio of at least 0.80 were retested to reduce the potential for false-positive test results. Retested samples with a signal to cutoff ratio of at least 1.00 were considered positive.

All test results were entered into a database by an individual technologist who used a bar code scanner to ensure accurate result-sample identification. Two additional reviewers verified the computer entry.

Statistical Methods Aim One

Selective Screening Guidelines for Chlamydial Infection in US Young Adults

The Aim One objective was to develop criteria for screening young women and men in the US general population for prevalent chlamydial infection. The outcome of interest was a positive *C. trachomatis* test result. Analyses were performed separately by gender to accommodate sex-specific differences in predictors of STI and prevalence of chlamydial infection (111, 133-135). Candidate variables were identified from the literature and by their biologic or environmental plausibility of predicting infection with chlamydia. Numerous candidate predictor characteristics were derived from the self-reported demographic, behavior, perceived risk, and health care factors available from the in-home interview (Table 3.2). Variable derivation schemes are detailed in Appendix Two

Table 3.2 Candidate Variables for Screening Criteria

Demographic	Behavioral	Perceived Risk	Medical/Health Care
age, years	age at sexual debut	STD	STD-like symptoms
race/ethnicity	number of partners	HIV	tested for STD, past year
partner race/ethnicity	sexuality		prior STD
region	condom use		insurance status
marital status			recent health care use
shared housing			forgone care, past year
student status			antibiotic use, past 30 days
high school graduate			hormonal contraception
military history			pregnancy history
employment status			
functional poverty			

Initial analysis included frequency distributions of all covariates. The frequencies were tabulated for categorical and graphed for continuous variables. Candidate variables were eliminated if there were excessive missing data or the distribution was too narrow to be meaningfully predictive. We transformed continuous variables to quadratic or cubic splines

and assessed their fit. Continuous and multilevel categorical variables were evaluated for linearity in the logit by plotting the logits and examining the incremental odds ratios of the covariate–outcome association. Variables that did not meet this assumption were categorized using indicator variables. Collinearity was measured using standard techniques, including magnitude of the bivariate odds ratio, correlation coefficient, variable inflation factor, likelihood ratio tests, and Hosmer-Lemeshow goodness of fit statistics (136, 137). Highly correlated variables were recoded or only one variable was selected for use based on substantive meaning and the relation among variables.

Predictive models were developed using multiple logistic regression. Other modeling strategies, such as multiple additive regression tree models, can be beneficial for predicting outcomes, but logistic regression remains the preferred method for clinical use. The improvement in predictive power attained through alternative modeling methods is offset by logistic regression's ability to accommodate sample weighting from complex survey designs.

The reliability of a logistic predictive model is a function of the prevalence of the outcome in the study population, the total study population, the number of variables fitted in the model, and how well the variables have been measured. To estimate the maximum number of variables practical for a model, we used the formula $[(3*n_1*n_2)/N]/10$ where n_1 is the number of persons with the outcome, n_2 is the number of persons without the outcome, and N is the total population (138). In this community-based sample of approximately 5,800 women and 5,000 men with usable test results, the prevalence of chlamydial infection was five percent and four percent, respectively. Over 50 variables could be included in the regression models for women and men.

Analysis was performed using Stata Version 7.0 (Stata Corporation, College Station, TX). Evaluation of model fit and bootstrap estimates were obtained from unweighted data. All other analyses accounted for Add Health's complex survey design by using school as the primary sampling unit, region of the country as the stratification variable, and post-stratification weights. In preliminary analyses, we examined the frequency distribution of the potential predictor characteristics and calculated bivariate prevalence odds ratios (OR) and 95 percent confidence intervals (CI) to assess the association between each characteristic and chlamydial infection.

For each gender, we developed three separate predictive models using either 1) the respondent's race/ethnicity; or 2) the respondent's most recent partner's race/ethnicity; or 3) no information on race/ethnicity. The initial starting models included one of the race/ethnicity components and all variables with bivariate $p<0.25$. We used a high alpha level because bivariate analyses can lead to exclusion of important variables in the multivariate setting (139). Variables with excessive missing data, extreme collinearity, or uninformative distributions were excluded from the starting model regardless of p-value. Each model included only those respondents with complete information on all variables in that full model.

Predictive model development used unconditional multiple logistic regression for survey data with a backwards elimination strategy (138). Variables were removed one at a time from the model, beginning with the variable with the largest p-value. The model-based c-statistic, the area under the receiver operating characteristic (ROC) curve, was compared between each successive model to ensure that variable removal did not adversely affect model performance. A change in area under the ROC curve<0.01 was acceptable.

Backwards elimination stopped when all remaining variables had $p<0.05$. We examined the models for collinearity and overly influential covariate patterns (136).

We created three sets of clinical risk scores from each final model. The first was the predicted probability of infection based on the logistic model. The second was a weighted risk score calculated by multiplying the regression coefficients by two and rounding to the nearest integer. The third was an unweighted risk score that assigned each risk category a value of one, regardless of its strength of association with infection, and each reference category a value of zero. Sensitivity and specificity of each predictive model and its corresponding risk scores were assessed at three hypothetical program driven cutoffs based on a maximum percentage of the screened population (≤70%, ≤50%, ≤30%) to receive a diagnostic test. In settings with limited resources, the absolute number of tests (a function of the funds available) and the prevalence of infection in the population can aid cutoff selection (101). We validated risk score performance using 1,000 bootstrap samples with replacement (138), although this technique could not accommodate Add Health's complex survey design.

Statistical Methods Aim Two

Partner Age Difference and Chlamydial Infection among Young Adult Women

The Aim Two objective was to assess the association between partner age difference and prevalent chlamydial infection among young adult women. The outcome of interest was a positive *C. trachomatis* test result. The primary exposure measure was the difference in years between each female study participant and her most recent male sex partner. The woman reported her partner's age. A negative age difference meant the woman's partner

was younger. A positive age difference meant the woman's partner was older. Additionally, as a secondary exposure, we used the age difference of the most age-discordant partner in the past year. The exposure measures were categorized to reflect substantively meaningful age differences. Potential modifying or confounding variables were derived from the self-reported demographic, behavior, and health care factors available from the in-home interview (Table 3.3). Variable derivation schemes are detailed in Appendix Two.

Table 3.3 Candidate Effect Measure Modifiers or Confounders

Demographic	Behavioral	Medical/Health Care
age, years	age at first sex	antibiotic use, past 30 days
race/ethnicity	number of partners, past year	
marital status	condom use	
employment status	exchange sex for drugs or money	
functional poverty	regret sex, past year	
education		

Initial analysis included frequency distributions of all covariates. The frequencies were tabulated for categorical and graphed for continuous variables. Candidate variables were eliminated if there were excessive missing data. We transformed continuous variables to quadratic or cubic splines and assessed their fit. Continuous and multilevel categorical variables were evaluated for linearity in the logit by plotting the logits and examining the incremental odds ratios of the covariate–outcome association. Variables that did not meet this assumption were categorized using indicator variables. Collinearity was measured using standard techniques, including magnitude of bivariate odds ratio, correlation coefficient, variable inflation factor, likelihood ratio tests, and Hosmer-Lemeshow goodness of fit statistics (136, 137). Highly correlated variables were recoded or only one variable was selected for use based on substantive meaning and the relation among variables.

Interaction terms between the exposures and age, race/ethnicity, and number of sex partners in the past year were created to test for effect measure modification. If the modeled interaction term was significant ($p<0.15$) and the stratified odds ratios were substantively different from the unstratified measures, the interaction term was retained in the model.

Potential for confounding was appraised through modeled bivariate odds ratios to allow for sample weighting. The bivariate distribution of each covariate among all subjects and the outcome by each covariate conditional on non-exposure (partner age within one year of woman's age) was checked for strength of association to help identify which variables met the confounding criteria (140) and may be candidates for adjustment during the multiple regression modeling process.

Analysis was performed using Stata Version 7.0 (Stata Corporation, College Station, TX). Analyses accounted for Add Health's complex survey design by using school as the primary sampling unit, region of the country as the stratification variable, and post-stratification weights. In preliminary analyses, we examined the frequency distribution of the outcome, primary and secondary exposures, and other covariates. We calculated bivariate prevalence odds ratios and 95 percent confidence intervals to assess the relationship between the covariates and chlamydial infection.

Mixing by age within a partnership can be assortative (like-with-like), disassortative (like-with-unlike), or random. The Q statistic, defined as $(\Sigma_i w_i - 1)/(N - 1)$ where w_i is the matrix eigen value, uses an N*N mixing matrix to identify high or low within-group mixing (114, 141). For these analyses, the matrix rows were the categorized age of the woman and the matrix columns were the categorized age of the male partner, calculated for the two partner age difference measures. This assessment could not incorporate survey weighting.

Model development used unconditional multiple logistic regression for survey data with a backwards elimination strategy (142). Covariates that could potentially modify or confound the association between age difference and prevalent chlamydial infection were included in the full model. We tested the null hypothesis that interaction terms between the exposure and each potential modifier were equal to zero, and looked for substantive changes between unstratified and stratified effect estimates. After examination and removal of interaction terms, we eliminated potentially confounding covariates one at a time from the model beginning with the variable with the largest p-value. We evaluated confounding by comparing the crude, adjusted, and fully adjusted effect estimates. We retained the covariate if the change in estimates was greater than 10 percent (143). Otherwise, the covariate was dropped. Backwards elimination stopped when all covariates that neither modified nor confounded the association between age difference and chlamydial infection were eliminated. We examined the final model for collinearity and overly influential covariate patterns. Primary and secondary exposure measures were evaluated through separate but identical processes.

CHAPTER 4

RESULTS AIM ONE: COMMUNITY-BASED SELECTIVE SCREENING GUIDELINES FOR PREVALENT CHLAMYDIAL INFECTION IN US YOUNG ADULTS

Chlamydia trachomatis, with an estimated three million new infections each year, is the most common bacterial sexually transmitted infection (STI) in the United States (US), especially among adolescents and young adults (1). Black, Native American, and Latino women and men are disproportionately burdened with infection (2). Chlamydial infection may cause pelvic inflammatory disease, ectopic pregnancy, and tubal infertility in women (4-6). Infection increases susceptibility to and transmission of HIV in women and men (8, 9). This STI causes substantial morbidity, but it can be detected with a urine-based nucleic acid amplification test and cured by a single dose of oral antibiotics.

Testing and treatment for chlamydial infection is challenging because infections are asymptomatic in approximately 70 percent of women and 50 percent of men (10). The US Preventive Services Task Force "strongly recommends" that clinicians routinely screen all sexually active women aged 25 years or younger for chlamydial infection (14). However, screening rates remain remarkably low (12, 13), despite the inclusion of chlamydial screening in the Health Plan Employer Data and Information Set (HEDIS) performance measures (11). Furthermore, chlamydial infection in men is not addressed by current recommendations.

Programs to expand testing to community settings may increase screening rates. Community-based testing is a potentially valuable way to reach young adults in the general population with asymptomatic infection. Selective screening criteria to identify for testing individuals at greatest risk of infection may be necessary to make such programs logistically and economically feasible (144, 145). Guidelines to be used in community settings should be based on data from the general population, rather than algorithms derived from clinical settings. Wave III of the National Longitudinal Study of Adolescent Health (Add Health) was used to develop criteria for screening young women and men in the US general population for prevalent chlamydial infection.

MATERIALS AND METHODS

Study design and sample

Add Health is a prospective cohort study that has followed nearly 20,000 adolescents into adulthood over three waves of data collection (146). For this study, we conducted a cross-sectional analysis of Wave III (April 2, 2001 to May 9, 2002), which targeted all Wave I participants. Our study population was restricted to Wave III participants responding "Yes" when asked "Have you ever had vaginal intercourse?" The University of North Carolina institutional review board approved all study procedures.

The two-stage sampling of Add Health has been described in detail elsewhere (146, 147). Briefly, a systematic random sample of secondary schools was chosen with unequal probability of selection and stratified to ensure that the schools were representative of all US secondary schools with respect to key characteristics. The original participants were identified from students in grades seven through 12 enrolled in the schools. This core sample

was complemented by oversampling some black and Latino students to enhance the precision of estimates for these groups. Post-stratification sampling weights adjust for persons who did not participate in Wave III. After accounting for design effect, the Add Health Wave III cohort provides a representative sample of young adults aged 18 to 26 years living in the US.

Interview and specimen collection

For non-sensitive issues, the interviewer recorded responses into a computer. For sensitive issues like sexual behaviors, the participant used computer-assisted self-interview (CASI) to enter the responses directly into the computer.

Respondents were asked to provide a urine specimen to test for *Chlamydia trachomatis,* for which they received $10. A more detailed description of Add Health STI testing is available elsewhere (132). Specimens were tested for *C. trachomatis* per manufacturer instructions using ligase chain reaction (LCR™) amplification technology in the Abbott LCx® Probe System (Abbott Laboratories, Abbott Park, IL), except that specimens exceeding the recommended volume of 20ml were tested.

Measures

The outcome variable was a positive *C. trachomatis* test result. Possible predictor variables were derived from the self-reported demographic, behavior, perceived risk, and health care factors available from the in-home interview.

Statistical analyses

We conducted analyses using Stata Version 7.0 (Stata Corporation, College Station, TX). Evaluation of model fit and bootstrap estimates were obtained from unweighted data. All other analyses accounted for Add Health's complex survey design by using school as the primary sampling unit, region of the country as the stratification variable, and post-

stratification weights. Analyses were performed separately by gender to accommodate sex-specific differences in predictors of STI and prevalence of chlamydial infection (111, 133-135). In preliminary analyses, we examined the frequency distribution of potential predictor characteristics and calculated bivariate prevalence odds ratios (OR) and 95 percent confidence intervals (CI) to assess the association between each characteristic and chlamydial infection.

For each gender, we developed three separate predictive models using either 1) the respondent's race/ethnicity; or 2) the respondent's most recent partner's race/ethnicity; or 3) no information on respondent's or partner's race/ethnicity. The initial starting models included one of the race/ethnicity components and all variables with bivariate $p<0.25$. Variables with excessive missing data, extreme collinearity, or uninformative distributions were excluded from the starting models, regardless of p-value. Each model included only those respondents with complete information on all variables in that full model.

Predictive model development used unconditional multiple logistic regression for survey data with a backwards elimination strategy (138). Variables were removed one at a time from the model, beginning with the variable with the largest p-value. The model-based c-statistic, the area under the receiver operating characteristic (ROC) curve, was compared between each successive model to ensure that variable removal did not adversely affect model performance. A change in area under the ROC curve<0.01 was acceptable. Backwards elimination stopped when all remaining variables had $p<0.05$. We examined the models for collinearity and overly influential covariate patterns (136).

We created three sets of clinical risk scores from each final model. The first was based on the predicted probability of infection. The second was a weighted risk score

calculated by multiplying the regression coefficients by two and rounding to the nearest integer. The third was an unweighted risk score that assigned each risk category a value of one, regardless of its strength of association with infection, and each reference category a value of zero. Sensitivity and specificity of each predictive model and its risk scores were assessed at three hypothetical program driven cutoffs based on a maximum percentage of the population (≤70, ≤50, ≤30) to receive a diagnostic test. We validated model and risk score performance using 1,000 bootstrap samples with replacement (138), although this technique could not accommodate Add Health's complex survey design.

RESULTS

Study population

Of the 18,924 Add Health participants in the nationally representative Wave I sample, 1,109 (5.9%) refused participation, 3,493 (18.5%) could not be located or were unable to participate, and 14,322 (75.7%) were located and agreed to participate in Wave III. Of these, 12,334 (86.1%) reported ever having vaginal intercourse. *C. trachomatis* results were available for 10,928 (88.6%) of the sexually experienced participants. Reasons for unavailable test results included inability or refusal to provide a urine specimen, processing errors due to shipping, or laboratory problems.

Among participants with chlamydia test results, 50.0 percent of the study sample was women (Table 4.1). The majority (67.8%) was white, with representation of black (16.7%), Latino (11.5%), Asian American (3.2%), and Native American (0.8%) participants. The mean age of participants was 21.9 years (standard error (SE), 0.12 years). The mean age at sexual debut was 16.4 years (SE, 0.06 years) and the mean number of sex partners during the

past year was 1.8 partners (SE, 0.03 partners). On average, women had fewer partners (1.5 partners, SE 0.04) than men (2.0 partners, SE 0.06).

Females

*Bivariate analyses***.** The overall prevalence of chlamydial infection among sexually experienced women was 5.1 percent (95% CI 4.2%, 6.0%). Women who were black (OR 5.7, 95% CI 3.9, 8.5) or Native American (OR 6.1, 95% CI 2.3, 16.1) were more likely to have chlamydial infection as compared to whites (Table 4.2). Women reporting black partners (OR 6.9, 95% CI 4.5, 10.6) also were more likely to have chlamydial infection. When compared to women with no sex partners in the past year, the relation between number of partners and infection was nearly twice as strong for two or more sex partners (OR 7.4, 95% CI 2.8, 19.2) than for one partner (OR 3.4, 95% CI 1.4, 8.5). While a moderate or high perceived risk of STI (OR 5.5, 95% CI 3.1, 9.8) was indicative of infection, neither STI symptoms within the past 24 hours (OR 1.0, 95% CI 0.6, 1.8) nor STI symptoms (OR 1.0, 95% CI 0.7, 1.4), test (OR 1.1, 95% CI 0.8, 1.5), or diagnosis (OR 1.6, 95% CI 1.0, 2.4) within the past year, showed substantive association with prevalent chlamydial infection.

Multivariate analyses. We constructed three reference models for women that included the race/ethnicity component (respondent's race, partner's race, or no race) and 17 characteristics with bivariate $p<0.25$. After removing variables that minimally predicted chlamydial infection, number of partners, perceived risk of STI, and student status consistently remained important across the three final models (Table 4.3a). The final models with respondent race (area under ROC curve=0.77) and partner race (area under ROC curve=0.75) information performed comparably and both were substantially better than the model without race information (area under ROC curve=0.70; $p <0.001$; Figure 4.1a).

Risk Scores. The weighted risk scores for model with respondent race information ranged from zero for a white woman, with no sex partners in the past year, low perceived risk of STI, who was a student, aged 22 – 24 years, to a score of 13 for a Native American woman, with two or more sex partners in the past year, moderate or high perceived risk of STI, not a student, and was either younger than age 22 or older than age 24 years (Table 4.3a). Using the weighted risk score to identify no more than 50 percent of the population for testing, the sensitivity of the model with respondent race information (84.1%) was slightly higher than the model with partner race information (81.3%), but substantially higher than the model with no race information (60.1%; Table 4.4a).

While the sensitivity and specificity of the three models are comparable at several cutoffs, the models' performance is strikingly different when stratified by race (Table 4.5a). The most sensitive screening for white women uses the predicted probability from the model with no race information (72.5%). Among black women, however, the sensitivities of the models with respondent and partner race information are nearly all above 90 percent and the no race model performs poorly. Testing ≤50 percent using the weighted risk score for the model with no race information is 61.8 percent sensitive among black women, compared to 99.4 percent in the model with race and 94.7 percent in the model with partner race information. The situation for women of other races parallels that of black women.

To illustrate the impact of the differing sensitivities across the three models, we examined the estimated number of infections correctly identified in the general population of women aged 18 to 26 years (Table 4.6a). The race information model weighted risk score could correctly identify 142,350 out of 142,776 infections among black women. The no race information model would miss more than 50,000 of these infections. Among white women,

the number of missed infections between the models with and without race information is fewer than 10,000. The number of women without infection who were identified for testing (i.e. false positives) is substantial, regardless of the model.

Males

Bivariate analyses. The overall prevalence of chlamydial infection among sexually experienced men was 3.9 percent (95% CI 3.1%, 4.8%). Men who were black (OR 8.0, 95% CI 4.9, 13.1), Native American (OR 5.7, 95% CI 2.1, 15.6), or Latino (OR 5.3, 95% CI 2.9, 9.9) were more likely to have chlamydial infection as compared to whites. Men reporting black (OR 5.9, 95% CI 3.4, 10.4) or Latino (OR 3.5, 95% CI 1.6, 7.8) partners were also more likely to have chlamydial infection (Table 4.2). Similar to women, a moderate or high perceived risk of STI (OR 5.2, 95% CI 2.6, 10.4) was indicative of infection. Unlike women, STI symptoms (OR 2.4, 95% CI 1.5, 3.8) or diagnosis (OR 2.6, 95% CI 1.4, 5.0) within the past year as well as no recent antibiotic use (OR 2.9, 95% CI 1.4, 6.2) and shared housing (OR 2.3, 95% CI 1.5, 3.7) were linked to prevalent chlamydial infection.

Multivariate analyses. We constructed three reference models for men that included the race/ethnicity component and 16 characteristics with bivariate $p<0.25$. A core set of characteristics – perceived risk of STI, military history, shared housing, and high school degree – remained important in all three models (Table 4.3b). The final models with respondent race (area under ROC curve=0.74) and partner race (area under ROC curve=0.75) information were comparable, and superior to the model without race information (area under ROC curve=0.69; p=0.02; Figure 4.1b).

Risk scores. The weighted risk scores for the model with respondent race information ranged from zero for a white man, with low perceived risk of STI, no military history, lived

alone, had graduated from high school, and accessed health care within the past year, to 12 for a black man, with moderate or high perceived risk of STI, military experience, shared housing, who was not a high school graduate, and had not recently accessed health care (Table 4.3b). Using a weighted score to test ≤50 percent of those screened by the respondent race information model yielded a sensitivity of 82.5 percent and specificity of 55.3 percent (Table 4.4b).

The difference in model performance among white, black, and other respondents is again prominent (Table 4.5b). Testing ≤50 percent with a weighted risk score is 100 percent sensitive among black men with the respondent race information model, but only 71.4 percent sensitive with the no race information model. The models performed poorly for white men, with the no race information model yielding the highest sensitivity (58.7%) and the respondent race information model the lowest sensitivity (33.7%).

Using the survey weights to estimate the number of infections correctly identified in the general population of men aged 18 to 26 years, the weighted risk score for the model with race information would correctly identify all 80,756 infections among black men (Table 4.6b). The model with no race information would identify only 54,152 of these infections. Again, the number of men tested who do not have chlamydial infection is large.

Confidence intervals derived from bootstrap validation were consistent with all findings for women and men.

DISCUSSION

Testing and treatment for chlamydial infection can lower the prevalence of infection (56, 57, 59) and the incidence of pelvic inflammatory disease (58). Still, young people

remain unaware of asymptomatic STI and the need for screening (53). Current guidelines recommend annual universal testing of sexually active young women for chlamydial infection (14, 81), but only an estimated 55 – 66 percent of females aged 15 – 19 were screened in 2000 (12). Self-report of STI testing is even lower (13). One reason for low screening rates may be that these guidelines require women to visit health care providers. Community-based screening may expand screening coverage among young people, including men, who are often uninsured and unlikely to access health care regularly (148-150).

Our proposed screening criteria differ from earlier criteria because they were developed from a representative sample of the population they are designed to serve. Additionally, the guidelines are available for women and men. A combination of five characteristics for women (race/ethnicity, number of sex partners in the past year, perceived risk of STI, student status, and age) and six characteristics for men (race/ethnicity, perceived risk of STI, military history, shared housing, education level, and recent health care use) provide potentially useful screening tools, although implementation of these criteria may be problematic because of the inclusion of race-related information. Applying these criteria to select no more than 50 percent of the population for diagnostic testing would identify approximately 80 percent of infections in women and men. Many uninfected people would be tested, but there is no evidence of durable distress or harm after population screening for chlamydial infection (151). Also, the number of uninfected people tested would be lower than the number that would be tested under current universal screening guidelines.

Add Health provides the most comprehensive assessment to date of chlamydial infection and related risk factors in US young adults. It reinforces previous findings of marked differences in infection prevalence across racial/ethnic groups, with black and Native

American females and black, Latino, and Native American males, more likely to have a prevalent chlamydial infection than their white counterparts. The Add Health design ensured that estimated effects would be independent of reporting by clinicians and health care seeking behavior – common explanations for racial and ethnic differences evident in reported infection rates. Furthermore, the oversampling of black and Latino groups enhanced the precision of these estimates.

The two models developed with race/ethnicity information were similar in both constituent characteristics and overall performance because of the strong correlation between a respondent's and partner's race/ethnicity. In contrast, the performance of the model developed without information on race/ethnicity was greatly diminished for everyone except white women and men. Despite the inclusion of numerous covariates at the outset, no proxy for socioeconomic status or other connection to elevated prevalence remained in the final models. Detailed data on sexual networks or environmental characteristics that may address the disparity in infection prevalence were unavailable in these data and would not be typically available for use in routine screening settings.

Ideally, screening guidelines would identify individuals for testing based solely on risk behaviors. Risk stratification appears to differ by race/ethnicity (152). Chlamydial infection is increased among white young adults with traditional risk behaviors, but black young adults are at high risk of chlamydial infection even when practicing behaviors that are low risk for white youth (152). This observation may explain why the model without race/ethnicity information performed poorly among non-white subpopulations.

The use of race/ethnicity in any STI screening algorithm is undoubtedly controversial, and may have significant consequences. Stigmatization and perpetuation of inappropriate

and incorrect stereotypes may result. Using the model with a race/ethnicity criterion ignores both contemporary and historical context and may further marginalize minority communities.

It is essential, though, to recognize the potential damage from excluding race-related information. Exclusion of race-related information identified markedly fewer infections, especially among the minority populations with the highest prevalence. Consequently, if selective screening was implemented ignoring the race/ethnicity information, many minority young adults would go untested and untreated, thus perpetuating the high prevalence status quo. Although many would dismiss outright the inclusion of race-related information in STI screening guidelines, the true public health costs of this decision must be considered.

Universal screening, while financially expensive, is socially desirable. Ensuring truly universal screening for chlamydial infection would avoid the stigma of guidelines incorporating race/ethnicity, but must be considered in the prevailing context of unequal access to testing, treatment, and counseling.

Our study, like all studies using STI measures, is limited by the adequacy of the study sample and the characteristics of the diagnostic test used. The validity of our results depends on the representativeness of the original school-based sample, nonresponse to the Wave III follow-up survey, truthful reporting on sexual experience, and refusal or other problems that led to a missing outcome. The original sample included only students on school registers, but an evaluation of school dropouts suggests any resultant bias in Add Health is small (153). Poststratification sample weight adjustment accounted for the 24 percent of Wave I participants who could not be located for Wave III, a bias that was also small (154). Both the frequency and validity of responses to sensitive questions about sexual experiences were likely improved through the use of CASI (127-131). Additionally, participants who did and

did not provide urine specimens for STI testing were similar (155). Earlier analyses show prevalence estimates were robust to differences in characteristics of non-respondents and diagnostic test performance (3).

Undoubtedly messages about risky sexual behaviors and their link to STI are being communicated, given the strong association between some young adults' perceived risk of current STI and diagnosis with prevalent chlamydial infection. However, even with knowledge of what comprises risk behaviors, young adults in the US continue to be at high risk of chlamydial infection. Broadening screening programs beyond clinic settings, in conjunction with continued efforts focused on behavioral change, may reduce the STI burden among young people. The value of screening programs for men must also be considered carefully. Given the potential consequences of selectively screening, universal screening should be implemented where possible. Great care must be taken when addressing racial/ethnic disparities in infection prevalence. The performance of these selective screening guidelines, which require neither medical nor laboratory information to identify individuals for urine-based diagnostic testing, supports the practicality of community-based chlamydial screening for women and men. Local measures of infection prevalence and extent of resources can inform the choice of a testing cutoff specialized to each screening program. Locally relevant information will also be critical for determining whether the use of race/ethnicity is appropriate to improve the guidelines' performance. In time, if testing can be expanded to additional venues, screening rates may increase. With greater screening coverage, and treatment for the infected, the incidence and prevalence of chlamydial infection in young people, and the sequelae manifest throughout adulthood, will likely diminish.

Table 4.1 Characteristics of Sexually Experienced Respondents with *Chlamydia trachomatis* Test Results by Gender, National Longitudinal Study of Adolescent Health, 2001 – 2002

Characteristic	Females (n=5854)		Males (n=5074)	
	Number of Participants	Weighted Percent	Number of Participants	Weighted Percent
Chlamydial infection				
Positive	316	5.1	236	3.9
Negative	5538	94.9	4838	96.1
Race/ethnicity				
White	3178	68.2	2770	67.5
Black	1364	17.1	1033	16.3
Latino	909	11.0	864	11.9
Asian American	337	2.9	343	3.4
Native American	53	0.8	50	0.9
Partner race/ethnicity				
White	2534	62.0	2285	66.0
Black	1192	19.6	6387	13.0
Latino	739	11.1	595	12.3
Other	427	7.2	446	8.7
Region				
South	2216	38.8	1897	40.4
Outside South	3537	61.2	3101	59.6
Age, years				
18 – 21	2356	45.6	1775	42.5
22 – 24	3191	49.2	2942	49.4
25 – 26	307	5.2	357	8.1
Age at sexual debut, years				
10 – 16	3081	56.0	2623	53.6
17 – 25	2749	45.0	2420	46.4
Number of sex partners, past year				
0	459	6.9	489	9.3
1	3711	65.6	2604	51.6
2 – 50	1629	27.5	1914	39.1
Sexuality				
100% heterosexual	5600	96.1	5000	98.9
Not 100% heterosexual	227	3.9	58	1.1
Perceived risk of prevalent STI				
Low	5398	96.7	4659	96.1
Moderate or high	211	3.3	187	3.9
Perceived risk of lifetime HIV infection				
Low	5647	97.7	4844	96.6
Moderate or high	148	2.3	182	3.4
STI symptoms, past year				
Symptoms	1653	28.7	451	9.3
No Symptoms	4165	71.3	4580	90.7

Characteristic	Females (n=5854)		Males (n=5074)	
	Number of Participants	Weighted Percent	Number of Participants	Weighted Percent
STI test, past year				
Test	2172	36.9	902	18.2
No test	3631	63.1	4128	81.8
STI diagnosis, past year				
Diagnosis	840	14.1	228	4.3
No diagnosis	4919	85.8	4765	95.7
Insurance status				
Insurance	4612	77.1	3615	71.0
No insurance	1211	22.9	1431	29.0
Recent health care use				
Within past year	5473	93.9	3650	72.5
Longer than past year	375	6.1	1406	27.5
Forgone care, past year				
Forgone care	1422	23.3	1261	24.3
No forgone care	4428	76.7	3809	75.7
Antibiotic use, past 30 days				
Antibiotic	943	16.8	537	11.0
No antibiotic	4904	83.2	4531	89.0
Hormonal contraception use, current				
Contraception	3724	64.8	3057	62.2
No Contraception	2101	35.2	1977	37.8
Condom use, past year				
100% use	1440	23.6	1633	32.1
Not 100% use	4352	76.4	3379	67.9
Pregnancy history, females only				
Ever pregnant	2477	42.0		
Never pregnant	3331	58.0		
Marital status				
Married	1356	23.4	806	15.1
Not married	4498	76.6	4266	84.9
Housing				
Shared housing	2592	42.7	2712	52.7
Live alone	3262	57.3	2360	47.3
Student status				
Student	2224	37.2	1606	31.0
Not a student	3629	62.8	3465	69.0
High school graduate				
Graduate	5335	90.0	4529	88.0
Not a graduate	516	10.0	542	12.0
Military history				
Ever military	97	1.5	367	6.8
Never military	5752	98.5	4702	93.2

Characteristic	Females (n=5854)		Males (n=5074)	
	Number of Participants	Weighted Percent	Number of Participants	Weighted Percent
Employment status				
Job	3989	67.8	3764	74.4
No job	1865	32.2	1310	25.6
Functional poverty, past year				
Able to pay rent, utilities	5502	93.8	4841	95.9
Unable to pay rent, utilities	323	6.2	205	4.1

STI, sexually transmitted infection

Table 4.2 Bivariate Association of Prevalent Chlamydial Infection and Potential Predictor Characteristics among Sexually Experienced Respondents by Gender, National Longitudinal Study of Adolescent Health, 2001 – 2002

Characteristic	Females Prevalence Odds Ratio (95% CI)		Males Prevalence Odds Ratio (95% CI)	
Race/ethnicity				
White	1.0		1.0	
Black	5.7	(3.9 – 8.5)	8.0	(4.9 –13.1)
Latino	1.8	(1.1 – 2.9)	5.3	(2.9 – 9.9)
Asian American	1.2	(0.5 – 2.8)	1.0	(0.3 – 2.8)
Native American	6.1	(2.3 – 16.1)	5.7	(2.1 – 15.6)
		$p < 0.001$		$p < 0.001$
Partner's race/ethnicity				
White	1.0		1.0	
Black	6.9	(4.5 – 10.5)	5.9	(3.4 – 10.4)
Latino	2.3	(1.0 – 5.0)	3.5	(1.6 – 7.8)
Other	1.7	(0.8 – 3.8)	1.6	(0.5 – 5.1)
		$p < 0.001$		$p < 0.001$
Region				
South	1.4	(0.9 – 2.1)	1.7	(1.1 – 2.8)
Outside South	1.0		1.0	
		$p = 0.10$		$p = 0.03$
Age, years				
18 – 21	1.5	(1.1 – 2.2)	1.0	(0.6 – 1.5)
22 – 24	1.0		1.0	
25 – 26	2.1	(1.3 – 3.5)	0.8	(0.4 – 1.6)
		$p < 0.01$		$p = 0.82$
Age at sexual debut, years				
10 – 16	1.4	(1.0 – 2.0)	2.0	(1.3 –3.0)
17 – 25	1.0		1.0	
		$p = 0.04$		$p < 0.01$
Number of sex partners, past year				
0	1.0		1.0	
1	3.4	(1.4 – 8.5)	1.6	(0.7 – 3.3)
2 – 50	7.4	(2.8 –19.2)	2.3	(1.1 – 5.0)
		$p < 0.001$		$p = 0.04$
Sexuality				
100% heterosexual	1.0		1.0	
Not 100% heterosexual	0.6	(0.2 – 1.6)	2.6	(0.8 – 8.8)
		$p = 0.31$		$p = 0.11$
Perceived risk of prevalent STI				
Low	1.0		1.0	
Moderate or high	5.5	(3.1 – 9.8)	5.2	(2.6 –10.4)
		$p < 0.001$		$p < 0.001$

Characteristic	Females Prevalence Odds Ratio (95% CI)		Males Prevalence Odds Ratio (95% CI)	
Perceived risk of HIV infection				
Low	1.0		1.0	
Moderate or high	2.0	(0.9 – 4.5)	2.4	(1.1 – 5.1)
		p = 0.09		p = 0.03
STI symptoms, past year				
Symptoms	1.0	(0.7 – 1.4)	2.4	(1.5 – 3.8)
No Symptoms	1.0		1.0	
		p = 0.99		p < 0.001
STI test, past year				
Test	1.1	(0.8 – 1.5)	1.1	(0.8 – 1.9)
No test	1.0		1.0	
		p = 0.53		p = 0.68
STI diagnosis, past year				
Diagnosis	1.6	(1.0 – 2.4)	2.6	(1.4 – 5.0)
No diagnosis	1.0		1.0	
		p = 0.04		p < 0.01
Insurance status				
Insurance	1.0		1.0	
No insurance	1.4	(0.99 – 2.0)	1.9	(1.2 – 3.0)
		p = 0.08		p = 0.01
Recent health care use				
Within past year	1.0		1.0	
Longer than past year	0.8	(0.4 – 1.6)	1.4	(0.99 – 2.0)
		p = 0.60		p = 0.08
Forgone care, past year				
Forgone care	1.2	(0.8 – 1.6)	1.2	(0.8 – 1.8)
No forgone care	1.0		1.0	
		p = 0.32		p = 0.34
Antibiotic use, past 30 days				
Antibiotic	1.0		1.0	
No antibiotic	1.5	(0.99 – 2.3)	2.9	(1.4 – 6.2)
		p = 0.06		p = 0.01
Hormonal contraception use				
Contraception	1.0		1.0	
No Contraception	1.4	(0.9 – 2.0)	1.1	(0.8 – 1.6)
		p = 0.11		p = 0.43
Condom use, past year				
100% use	1.0		1.0	
Not 100% use	1.0	(0.7 – 1.5)	0.9	(0.6 – 1.4)
		p = 0.81		p = 0.65

Characteristic	Females Prevalence Odds Ratio (95% CI)		Males Prevalence Odds Ratio (95% CI)	
Pregnancy history, females only				
Never pregnant	1.0			
Ever pregnant	1.8	(1.2 – 2.5)		
		p < 0.01		
Marital status				
Married	1.0		1.0	
Not married	2.6	(1.5 – 4.4)	1.3	(0.8 – 3.0)
		p < 0.01		p = 0.30
Housing				
Shared housing	1.3	(0.9 – 1.9)	2.3	(1.5 – 3.7)
Live alone	1.0		1.0	
		p = 0.17		p < 0.001
Student status				
Student	1.0		1.0	
Not a student	1.8	(1.2 – 2.6)	1.6	(1.1 – 2.6)
		p < 0.01		p = 0.03
High school graduate				
Graduate	1.0		1.0	
Not a graduate	1.4	(0.9 – 2.1)	2.2	(1.3 – 3.6)
		p = 0.17		p < 0.01
Military history				
Never military	1.0		1.0	
Ever military	2.9	(1.2 – 5.5)	1.6	(0.9 – 3.0)
		p = 0.01		p = 0.13
Employment status				
Job	1.0		1.0	
No job	1.3	(0.9 – 1.8)	1.8	(1.2 – 2.8)
		p = 0.14		p = 0.01
Functional poverty, past year				
Able to pay rent, utilities	1.0		1.0	
Unable to pay rent, utilities	1.4	(0.8 – 2.5)	1.1	(0.5 – 2.5)
		p = 0.21		p = 0.81

CI, confidence interval; STI, sexually transmitted infection
p-value for adjusted Wald F-test

Table 4.3a Adjusted Odds Ratios and Risk Scores of Prevalent Chlamydial Infection by Predictor Characteristics among Sexually Experienced Females, National Longitudinal Study of Adolescent Health, 2001 – 2002

Characteristic	Model with Respondent Race Information (n=5239) area under ROC curve=0.7654				Model with Partner Race Information (n=4455) area under ROC curve=0.7519				Model with No Race Information (n=5252) area under ROC curve=0.6950			
	OR (95% CI)	β	W	U	OR (95% CI)	β	W	U	OR (95% CI)	β	W	U
Race/ethnicity												
White	1.0		0	0								
Black	5.6 (3.7–8.3)	1.72	3	1								
Latino	1.5 (0.9–2.8)	0.44	1	1								
Asian American	1.5 (0.6–3.7)	0.39	1	1								
Native American	6.5 (2.3–18.7)	1.88	4	1								
Partner race/ethnicity												
White					1.0		0	0				
Black					6.3 (4.1–9.8)	1.85	4	1				
Latino					2.0 (0.8–5.1)	0.72	1	1				
Other					1.9 (0.8–4.1)	0.62	1	1				
Number of partners, past year												
0	1.0		0	0	1.0		0	0	1.0		0	0
1	4.0 (1.5–10.7)	1.39	3	1	3.4 (1.1–10.9)	1.23	2	1	4.0 (1.5–10.9)	1.40	3	1
2 – 50	8.1 (3.0–21.8)	2.09	4	1	6.0 (1.9–19.2)	1.80	4	1	7.4 (2.7–20.5)	2.01	4	1
Perceived risk of prevalent STI												
Low	1.0		0	0	1.0		0	0	1.0		0	0
Moderate or high	3.5 (1.8–6.5)	1.24	2	1	3.3 (1.7–6.4)	1.21	2	1	3.7 (2.1–6.3)	1.30	3	1
Student status												
Student	1.0		0	0	1.0		0	0	1.0		0	0
Not a student	2.2 (1.4–3.3)	0.77	2	1	1.9 (1.2–2.9)	0.63	1	1	2.0 (1.3–3.0)	0.68	1	1
Age, years												
18 – 21	1.7 (1.2–2.3)	0.52	1	1					1.5 (1.1–2.2)	0.43	1	1
22 – 24	1.0		0	0					1.0		0	0
25 – 26	1.9 (1.0–3.4)	0.62	1	1					2.1 (1.2–3.7)	0.74	1	1

Characteristic	Model with Respondent Race Information (n=5239) area under ROC curve=0.7654				Model with Partner Race Information (n=4455) area under ROC curve=0.7519				Model with No Race Information (n=5252) area under ROC curve=0.6950			
	OR (95% CI)	β	W	U	OR (95% CI)	β	W	U	OR (95% CI)	β	W	U
Marital status												
Married									1.0		0	0
Not married									2.8 (1.5–5.2)	1.03	2	1
Pregnancy history												
Never pregnant									1.0		0	0
Ever pregnant									1.8 (1.2–2.6)	0.57	1	1
Hormonal contraception												
Contraception									1.0		0	0
No contraception									1.5 (1.0–2.4)	0.44	1	1
Constant		– 6.03				– 5.64				– 6.64		

ROC, receiver operating characteristic; OR, odds ratio; CI, confidence interval; β, regression coefficient; W, weighted score; U, unweighted score; STI, sexually transmitted infection

Table 4.3b Adjusted Odds Ratios and Risk Scores of Prevalent Chlamydial Infection by Predictor Characteristics among Sexually Experienced Males, National Longitudinal Study of Adolescent Health, 2001 – 2002

Characteristic	Model with Respondent Race Information (n=4529) area under ROC curve=0.7447				Model with Partner Race Information (n=3614) area under ROC curve=0.7481				Model with No Race Information (n=4541) area under ROC curve=0.6894			
	OR (95% CI)	β	W	U	OR (95% CI)	β	W	U	OR (95% CI)	β	W	U
Race/ethnicity												
White	1.0		0	0								
Black	7.0 (4.3–11.3)	1.94	4	1								
Latino	4.1 (2.2–7.3)	1.40	3	1								
Asian American	1.0 (0.4–2.9)	0.02	0	1								
Native American	5.4 (2.0–14.2)	1.68	3	1								
Partner race/ethnicity												
White					1.0		0	0				
Black					4.2 (2.3–7.8)	1.45	3	1				
Latino					2.7 (1.2–6.1)	1.01	2	1				
Other					1.6 (0.5–5.6)	0.49	1	1				
Perceived risk of prevalent STI												
Low	1.0		0	0	1.0		0	0	1.0		0	0
Moderate or high	3.5 (1.8–6.9)	1.26	3	1	3.5 (1.4–9.0)	1.27	3	1	4.1 (2.1–8.0)	1.42	3	1
Military history												
Never military	1.0		0	0	1.0		0	0	1.0		0	0
Ever military	2.4 (1.2–4.9)	0.89	2	1	2.2 (0.99–5.1)	0.80	2	1	1.9 (1.0–3.7)	0.66	1	1
Region												
Outside South					1.0		0	0	1.0		0	0
South					2.1 (1.3–3.5)	0.75	1	1	1.9 (1.2–3.0)	0.63	1	1
Housing												
Shared housing	2.0 (1.2–3.2)	0.68	1	1	1.9 (1.1–3.3)	0.66	1	1	2.3 (1.4–3.6)	0.82	2	1
Live alone	1.0		0	0	1.0		0	0	1.0		0	0
High school graduate												
Graduate	1.0		0	0	1.0		0	0	1.0		0	0
Not a graduate	1.7 (1.0–3.1)	0.56	1	1	2.2 (1.1–4.5)	0.80	2	1	1.8 (1.0–3.3)	0.60	1	1

Characteristic	Model with Respondent Race Information (n=4529) area under ROC curve=0.7447				Model with Partner Race Information (n=3614) area under ROC curve=0.7481				Model with No Race Information (n=4541) area under ROC curve=0.6894			
	OR (95% CI)	β	W	U	OR (95% CI)	β	W	U	OR (95% CI)	β	W	U
Recent health care use												
Within past year	1.0		0	0								
Longer than past year	1.5 (1.0–2.1)	0.39	1	1								
Antibiotic use, past 30 days												
Antibiotic									1.0		0	0
No antibiotic									2.9 (1.3–6.7)	1.07	2	1
STI diagnosis, past year												
Diagnosis									1.0		0	0
No diagnosis									1.9 (1.2–3.2)	0.66	1	1
Age at sexual debut, years												
10 – 16									1.0		0	0
17 – 25									1.7 (1.1–2.9)	0.56	1	1
Number of partners, past year												
0									1.0		0	0
1									1.4 (0.6–3.0)	0.33	1	1
2 – 50									1.5 (0.6–3.3)	0.39	1	1
Constant		– 4.87				– 4.97				– 6.03		

ROC, receiver operating characteristic; OR, odds ratio; CI, confidence interval; β, regression coefficient; W, weighted score; U, unweighted score; STI, sexually transmitted infection

Table 4.4a Performance of Selective Screening Criteria among Sexually Experienced Females, National Longitudinal Study of Adolescent Health, 2001 – 2002

Percent	Model with Respondent Race Information (n=5239)			Model with Partner Race Information (n=4455)			Model with No Race Information (n=5252)		
Tested	Cutoff	Sensitivity	Specificity	Cutoff	Sensitivity	Specificity	Cutoff	Sensitivity	Specificity
Predicted Probability									
≤ 70	0.02	87.6	45.0	0.02	82.0	58.7	0.02	90.9	31.7
≤ 50	0.03	81.7	56.5	0.02	82.0	58.7	0.04	76.6	52.4
≤ 30	0.05	69.9	73.8	0.04	64.6	74.0	0.05	62.1	71.9
Weighted Risk Score									
≤ 70	6	84.1	53.3	4	81.3	53.5	7	80.4	48.0
≤ 50	6	84.1	53.3	4	81.3	53.5	8	60.1	73.0
≤ 30	7	66.9	76.4	6	61.0	80.1	8	60.1	73.0
Unweighted Risk Score									
≤ 70	3	74.7	59.4	3	54.3	77.8	4	77.5	48.9
≤ 50	3	74.7	59.4	3	54.3	77.8	5	46.7	79.9
≤ 30	4	31.9	91.3	3	54.3	77.8	5	46.7	79.9

Table 4.4b Performance of Selective Screening Criteria among Sexually Experienced Males, National Longitudinal Study of Adolescent Health, 2001 – 2002

Percent	Model with Respondent Race Information (n=4529)			Model with Partner Race Information (n=3614)			Model with No Race Information (n=4541)		
Tested	Cutoff	Sensitivity	Specificity	Cutoff	Sensitivity	Specificity	Cutoff	Sensitivity	Specificity
Predicted Probability									
≤ 70	0.01	94.3	31.3	0.01	87.3	37.2	0.02	90.6	32.7
≤ 50	0.02	83.3	53.9	0.02	82.5	52.9	0.03	78.1	52.1
≤ 30	0.04	72.2	73.3	0.03	72.2	73.8	0.04	59.0	74.0
Weighted Risk Score									
≤ 70	2	82.5	55.3	2	84.7	49.7	5	87.3	39.8
≤ 50	2	82.5	55.3	3	74.5	68.0	6	67.7	64.0
≤ 30	4	70.2	74.9	4	63.0	81.0	7	46.8	84.2
Unweighted Risk Score									
≤ 70	2	71.7	61.7	2	80.3	57.6	4	79.2	51.4
≤ 50	2	71.7	61.7	2	80.3	57.6	4	79.2	51.4
≤ 30	3	42.8	89.1	3	46.6	86.2	5	50.4	81.6

Table 4.5a Performance of Selective Screening Criteria to Test ≤50% of Sexually Experienced Females by Respondent's Race, National Longitudinal Study of Adolescent Health, 2001 – 2002

Model with Respondent Race Information (n=5239)						Model with Partner Race Information (n=4455)						Model with No Race Information (n=5252)					
White		Black		Other		White		Black		Other		White		Black		Other	
SEN	SPE	SEN	SPE	SEN	SPE	SEN	SPE	SEN	SPE	SEN	SPE	SEN	SPE	SEN	SPE	SEN	SPE
Predicted Probability																	
61.9	66.9	99.4	4.9	77.1	55.2	60.2	73.9	99.4	6.4	90.8	29.0	72.5	56.1	79.0	39.9	80.5	46.5
Weighted Risk Score																	
61.9	67.2	99.4	4.9	94.7	31.4	64.5	66.1	94.7	3.7	88.9	34.9	55.6	75.5	61.8	63.4	68.1	70.2
Unweighted Risk Score																	
47.3	75.3	90.4	21.0	98.3	17.4	31.9	90.0	70.3	41.5	70.5	49.2	42.0	82.7	48.5	74.1	54.6	72.3

SEN, sensitivity; SPE, specificity

Table 4.5b Performance of Selective Screening Criteria to Test ≤50% of Sexually Experienced Males by Respondent's Race, National Longitudinal Study of Adolescent Health, 2001 – 2002

Model with Respondent Race Information (n=4529)						Model with Partner Race Information (n=3614)						Model with No Race Information (n=4541)					
White		Black		Other		White		Black		Other		White		Black		Other	
SEN	SPE	SEN	SPE	SEN	SPE	SEN	SPE	SEN	SPE	SEN	SPE	SEN	SPE	SEN	SPE	SEN	SPE
Predicted Probability																	
42.0	74.5	100	0	99.7	6.9	56.1	66.5	99.4	6.7	87.0	28.1	65.6	57.3	83.9	28.9	81.8	47.9
Weighted Risk Score																	
42.0	74.5	100	0	96.8	16.2	33.7	81.1	96.8	13.4	86.6	52.1	58.7	69.2	71.4	45.2	71.1	56.3
Unweighted Risk Score																	
31.2	78.1	86.2	25.5	90.9	18.6	56.1	68.9	94.1	20.6	86.8	35.8	65.6	56.4	83.4	28.4	86.6	48.0

SEN, sensitivity; SPE, specificity

Table 4.6a Performance of Selective Screening Criteria to Test ≤50% of Population of Sexually Experienced Females by Respondent's Race, National Longitudinal Study of Adolescent Health, 2001 – 2002

	Model with Respondent Race Information			Model with Partner Race Information			Model with No Race Information		
	White	Black	Other	White	Black	Other	White	Black	Other
Subpopulation	4,644,760	945,760	935,181	4,644,760	945,760	935,181	4,644,760	945,760	935,181
Number of infections	(130,771)	(142,776)	(40,995)	(130,771)	(142,776)	(40,995)	(130,771)	(142,776)	(40,995)
Predicted Probability									
Infections detected	80,476	142,350	30,467	78,744	141,957	37,209	94,241	110,927	32,207
Tests among uninfected	1,497,806	763,240	395,175	1,178,214	751,707	634,648	20,22,722	499,754	491,501
Weighted Risk Score									
Infections detected	80,476	142,350	38,249	84,299	135,240	36,463	71,189	90,716	27,114
Tests among uninfected	1,490,527	763,240	611,534	1,532,016	773,572	582,162	1,141,263	318,130	276,393
Unweighted Risk Score									
Infections detected	59,157	127,225	40,098	41,667	100,435	28,909	58,780	75,345	23,496
Tests among uninfected	1,105,094	634,370	742,951	449,814	469,847	454,571	824,402	226,904	264,591

Table 4.6b Performance of Selective Screening Criteria to Test ≤50% of Population of Sexually Experienced Males by Respondent's Race, National Longitudinal Study of Adolescent Health, 2001 – 2002

	Model with Respondent Race Information			Model with Partner Race Information			Model with No Race Information		
	White	Black	Other	White	Black	Other	White	Black	Other
Subpopulation	4,276,592	838,491	958,632	4,276,592	838,491	958,632	4,276,592	838,491	958,632
Number of infections	(60,848)	(80,756)	(55,640)	(60,848)	(80,756)	(55,640)	(60,848)	(80,756)	(55,640)
Predicted Probability									
Infections detected	24,964	80,756	55,508	34,142	80,287	48,383	40,114	66,179	45,025
Tests among uninfected	1,032,140	757,735	839,715	1,412,997	705,771	649,052	1,761,285	526,613	449,725
Weighted Risk Score									
Infections detected	24,964	80,756	55,508	20,529	78,202	48,186	36,750	54,152	39,023
Tests among uninfected	1,032,140	757,735	744,493	795,655	656,299	432,242	1,255,578	403,546	368,593
Unweighted Risk Score									
Infections detected	16,367	69,822	48,700	34,142	75,961	48,309	40,114	65,287	48,714
Tests among uninfected	879,713	552,387	724,975	1,310,123	601,589	579,504	1,797,801	538,094	450,062

Figure 4.1a Sensitivity of Predicted Probabilities by Percentage of Population Tested among Sexually Experienced Females, National Longitudinal Study of Adolescent Health, 2001 – 2002

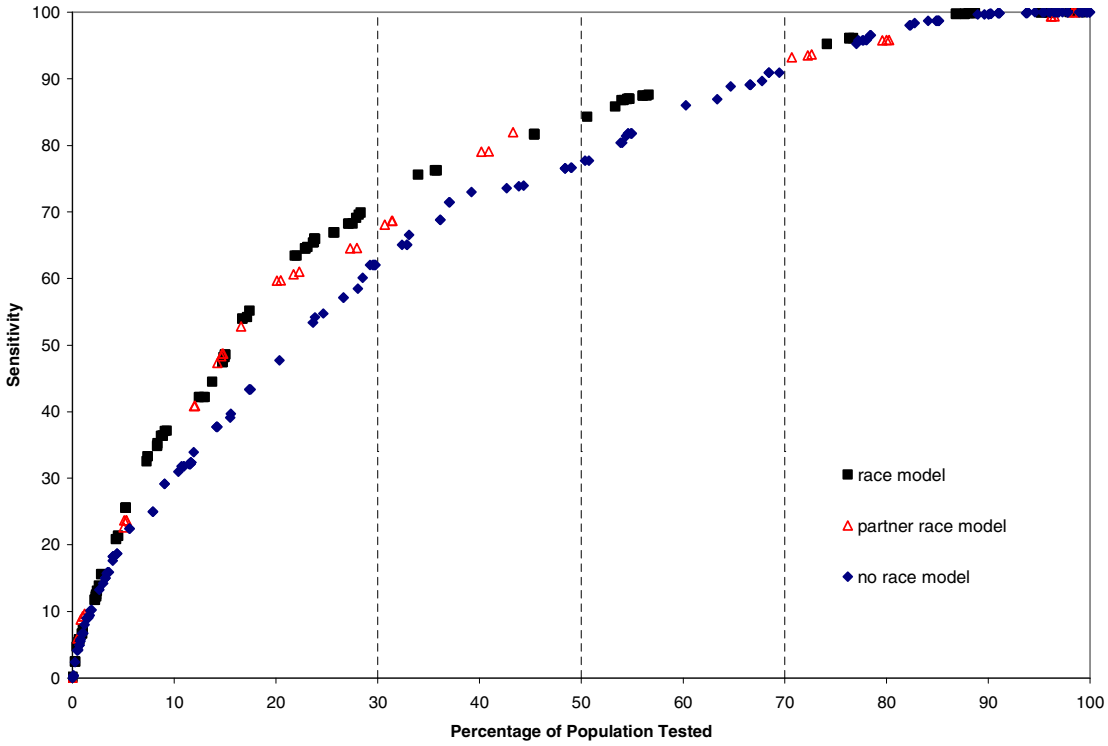
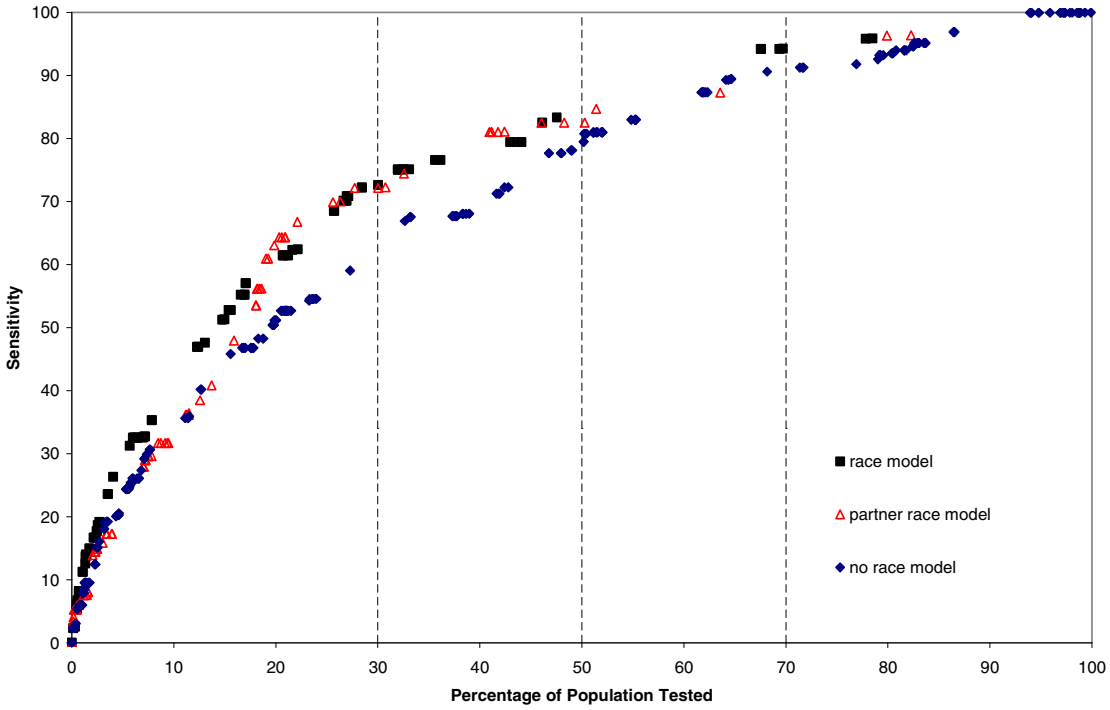


Figure 4.1b Sensitivity of Predicted Probabilities by Percentage of Population Tested among Sexually Experienced Males, National Longitudinal Study of Adolescent Health, 2001 – 2002



CHAPTER 5

RESULTS AIM TWO: PARTNER AGE DIFFERENCE AND CHLAMYDIAL INFECTION AMONG YOUNG ADULT WOMEN

Among adolescents and young adults, Chlamydia trachomatis is the most common bacterial sexually transmitted infection (STI) in the United States (US) (1). An estimated three million new infections occur each year. Chlamydial infection may cause pelvic inflammatory disease, ectopic pregnancy, and tubal infertility in women (4-6). Infection also increases susceptibility to and transmission of HIV in women and men (9, 156). Despite prevention and treatment measures, chlamydial infection continues to cause substantial morbidity.

Sexual mixing between members of different groups facilitates the spread of STI (18-21). Partner mixing by age is common among both adolescents and adults (22, 23). Adolescent girls with older male partners are more likely than girls with partners close in age to practice behaviors such as young age at first sex and inconsistent condom use, which are risk factors for STI (24-31). Whether this relation between older partners and risky behavior continues beyond adolescence is unclear. Two studies reporting the effect of partner age difference on STI among adults found little association with older partners, but both studies had major limitations. One study diagnosed chlamydial infection by culture (18), a diagnostic method that is no longer the gold standard (157). The other study relied on self-

report of STI test or treatment in the past year (23), which is again a sub-optimal method of determining infection status. These findings suggest that older male partners may play a lesser role in risk of STI as adolescent girls mature into adulthood.

The mechanism by which age difference affects risk of STI may be twofold. First, age discordant partnerships are purported to represent relationships with unequal distribution of power (30, 158). A younger woman may have more difficulty confronting sexual pressures, negotiating condom use or influencing her partner's sexual behavior with an older man rather than someone her own age. Second, partnerships between members of different sexual networks or populations have been linked to higher rates of chlamydial infection (18, 114). Age discordant partnerships among adolescents may facilitate mixing between populations with low and high STI prevalence (18, 39, 115, 124). Age-stratified rates of reported chlamydial infection differ across gender, with the highest reported rates among females aged 15 – 19 and males aged 20 – 24 (2).

Wave III of the National Longitudinal Study of Adolescent Health (Add Health) provides the necessary demographic, personal history, and behavior data together with laboratory-diagnosed STI results to examine the association between partner age difference and prevalent chlamydial infection among young adult women.

METHODS

Study Design and Sample

Add Health is a three-wave prospective cohort study that followed nearly 20,000 adolescents into adulthood from September 1994 to May 2002 (146). For this study, we conducted a cross-sectional analysis of Wave III (April 2, 2001 to May 9, 2002), which

targeted all Wave I participants. Our study population was restricted to female Wave III participants who answered "Yes" when asked "Have you ever had vaginal intercourse?" The University of North Carolina institutional review board approved all study procedures.

Add Health's two-stage sampling has been described in detail elsewhere (146, 147). In short, a systematic random sample of secondary schools was chosen with unequal probability of selection. The sample was stratified so that selected schools were representative of all US secondary schools with respect to region, urbanicity, and percent black and white. The original study participants were drawn from students in grades seven through 12 enrolled in the selected schools. Certain populations, including black students with a college-educated parent, Cubans, and Puerto Ricans, were oversampled to increase estimate precision for these groups. Post-stratification sampling weights account for persons who refused to participate or could not be located. The Add Health Wave III cohort, when incorporating design effect, provides a representative sample of young adults aged 18 to 26 years residing in the US.

Interview and Specimen Collection

Wave III sought participation from all original Wave I respondents who could be contacted. The in-home interviewer recorded responses into a laptop computer for non-sensitive issues. The participant used computer-assisted self-interview to enter responses directly into the computer for sensitive issues such as sexual experiences and behaviors.

Respondents who consented to provide a urine specimen for *Chlamydia trachomatis* testing received $10. A more detailed report of Add Health STI testing is available elsewhere (132). Cooled urine specimens were shipped by overnight express to the University of North Carolina at Chapel Hill for diagnostic testing.

Urine specimens were tested for *C. trachomatis* per manufacturer instructions using ligase chain reaction (LCR™) amplification technology in the Abbott LCx® Probe System (Abbott Laboratories, Abbott Park, IL). Specimens were tested even if they exceeded the recommended volume.

Measures

The outcome variable was a positive test result for *C. trachomatis*. The primary exposure was the difference in years between each female study participant and her most recent male sex partner. A negative age difference meant the woman's partner was younger; a positive age difference meant the woman's partner was older. Additionally, as a secondary exposure, we used the age difference of the most age discordant partner in the past year. The exposure measures were categorized to reflect substantively meaningful age differences. Potential modifying or confounding covariates were derived from the set of self-reported demographic, behavior, and health care factors available from the in-home interview.

Statistical Analyses

Analysis was performed using Stata Version 7.0 (Stata Corporation, College Station, TX). Analyses accounted for Add Health's complex survey design by using school as the primary sampling unit, region of the country as the stratification variable, and post-stratification weights. In preliminary analyses, we examined the frequency distribution of the outcome, primary and secondary exposures, and other covariates. We calculated bivariate prevalence odds ratios (OR) and 95 percent confidence intervals (CI) to assess the relation between the covariates and chlamydial infection.

Mixing by age within a partnership can be assortative (like-with-like), disassortative (like-with-unlike), or random. The Q statistic, defined as $(\Sigma_i w_i - 1)/(N - 1)$, where w_i is the

matrix eigen value, uses an N*N mixing matrix to identify high or low within-group mixing (18, 141). For our analyses, the matrix rows were the categorized age of the woman and the matrix columns were the categorized age of the male partner, calculated for the two partner age difference measures. This assessment could not incorporate survey weighting.

We used unconditional multiple logistic regression for survey data with a backwards elimination strategy (142). Covariates that could alter the association between age difference and prevalent chlamydial infection were included in the full model. We tested the null hypothesis that interaction terms between the exposure and each potential modifier were equal to zero, and looked for substantive changes between unstratified and stratified effect estimates. After examination and removal of interaction terms, we eliminated potentially confounding covariates one at a time from the model beginning with the variable with the largest p-value. We evaluated confounding by comparing the crude, adjusted, and fully adjusted effect estimates. We retained the covariate if the change in estimates was greater than 10 percent (143). Otherwise, the covariate was dropped. Backwards elimination stopped when all covariates that neither modified nor confounded the association between age difference and chlamydial infection were removed from the model. We examined the final model for collinearity and overly influential covariate patterns. Primary and secondary exposure measures were evaluated through separate but identical processes.

RESULTS

Study Population

Of the 18,924 Add Health participants in the nationally representative Wave I sample, 1,109 (5.9%) refused participation, 3,493 (18.5%) could not be located or were unable to

participate, and 14,322 (75.7%) were located and agreed to participate in Wave III. Of these, 6,594 were females who reported ever having vaginal intercourse (87.2% of all Wave III females). *C. trachomatis* test results were available for 5,854 (88.8%) of the sexually experienced females. Reasons for unavailable test results included inability or refusal to provide a urine specimen, processing errors due to shipping, or laboratory problems.

The overall prevalence of chlamydial infection among sexually experienced women was 5.1 percent (95% CI: 4.2%–6.0%; table 1). The majority of women with test results was white (68.2%), with representation of black (17.1%), Latino (11.0%), Asian American (2.9%), and Native American (0.8%) women. The mean age was 21.8 years (standard error (SE), 0.1 years), the mean age at first sex was 16.3 years (SE, 0.1 years) and the mean number of sex partners in the past year was 1.5 partners (SE, 0.04 partners). The mean age difference of the most recent partner was 2.9 years (SE, 0.1 years, figure 1) and mean age difference of the most age discordant partner in the past year was 3.4 years (SE, 0.1 years, figure 2).

Bivariate Analyses

There was little difference in chlamydial prevalence between women with a most recent partner two to eight years younger ("youngest"; OR 1.9, 95% CI: 1.0 – 3.7) and women with a most recent partner six or more years older ("oldest"; OR 1.6, 95% CI: 0.9 – 2.9) as compared to women with a most recent partner one year older or younger (the referent, "close in age"; table 2). The similarity of the effect estimates across age difference categories persisted when examining the secondary exposure measure, age difference of the most age discordant partner (youngest OR 2.4, 95% CI: 1.2 – 4.7; oldest OR 2.1, 95% CI: 1.2 – 3.4).

The *Q* statistics for the age difference with the most recent partner (*Q*=0.3) and the most age discordant partner (*Q*=0.2) indicated that mixing by age between women and their partners was random, with a tendency towards assortative (like-with-like) mixing.

Multivariate Analyses

Overall. In multiple logistic regression analyses, the odds of prevalent chlamydial infection among women with the youngest partners were approximately two times greater (most recent OR 1.8, 95% CI: 0.9 – 3.5; most discordant OR 2.1, 95% CI: 1.1 – 4.3) than among women with partners close in age, adjusting for number of partners in the past year (table 3). Among women with older partners, the adjusted odds of infection differ little between partners two to five years older (most recent OR 1.4, 95% CI: 0.9 – 2.3; most discordant OR 1.4, 95% CI: 0.8 – 2.3) and partners six or more years older (most recent OR 1.6, 95% CI: 0.9 – 2.8; most discordant OR 1.7, 95% CI: 1.0 – 2.8) as compared to partners within one year's age. The relation between partner age difference and chlamydial infection is consistent for the two exposure measures, although the estimates are imprecise. These associations did not vary by women's age or number of sex partners in the past year.

Stratified by Race. The relation between most discordant partner age difference and chlamydial infection did vary by women's race/ethnicity (interaction p=0.1). For white women, the greatest odds of infection are among those with the oldest partners (OR 2.8, 95% CI: 1.2 – 6.9) compared to partners close in age, adjusting for age, highest attained education, and number of partners in the past year (table 3). Youngest partners have little effect on adjusted odds of infection for this group (OR 1.2, 95% CI: 0.2 – 6.4). The associations are reversed, however, among black women. For black women, the adjusted odds ratio is greatest for the youngest partners (OR 3.2, 95% CI: 1.2 – 9.0) and shows little effect for the

oldest partners (OR 0.7, 95% CI: 0.3 – 1.4) as compared to partners close in age. The unstratified effect estimate showing the largest odds ratio for the youngest partners is clearly moderated by the experience of black women, who comprise only 17 percent of the study population.

Qualitatively similar results were seen for the stratified association between most recent partner age difference and chlamydial infection, although the variation across race/ethnicity was not statistically significant (interaction p=0.3; table 3). Only among Latino women is there a substantial difference between the two stratified exposure measures, with consistently stronger estimated effects for the most discordant, rather than most recent, partner age difference.

DISCUSSION

Among young adult women, older partners are moderately associated with prevalent chlamydial infection. A similar association was observed for younger partners as compared to partners within one year's age. These associations remain consistent when examining the age difference with the most recent partner and the most age discordant partner in the past year. This finding in young adults contrasts with previous studies of adolescent girls, for whom those with older partners were four times more likely to be infected with chlamydia (24).

The relation between most age discordant partner and chlamydial infection varies by women's race/ethnicity. The divergent effect on STI of older partners for white women and younger partners for black women may result from racial/ethnic differences in age-dependent

sexual behaviors or rates of chlamydial infection (2, 159). These results, however, should be interpreted cautiously because of the imprecision inherent in stratification.

It is unclear how the diminished overall association between partner age and chlamydial infection develops from adolescence to young adulthood, but several explanations are possible. Physical and emotional maturity may prepare a young woman to better protect herself by exercising more power in sexual decision-making. Older partners for young adults may also represent a different population than older partners for adolescents, both in terms of age-specific prevalence and social networks. Adolescents likely need to reach beyond their social setting to meet older partners. These partners may be links to networks with higher risk behaviors like multiple and overlapping partners, drug use, and transactional sex. Age is merely a marker for these risky behaviors. Alternatively, young adults may have more opportunities to meet older partners in their usual social network. Although the partners are older, they may be similar with respect to risk behaviors.

Few studies have rigorously assessed the association between partner age difference and prevalent chlamydial infection in young adult, rather than adolescent, females. Our study offers improvement over these earlier works by using nucleic acid amplification detection of chlamydial infection rather than culture (18) or self-report of recent or lifetime STI test, treatment, or diagnosis (23). Nucleic acid amplification testing is approximately 90 percent sensitive and 99 percent specific (69). Chlamydial culture is a considerably less sensitive diagnostic tool and is no longer the optimal diagnostic method (157). Results reliant on self-report of STI test are also subject to numerous biases. Moreover, evaluating chlamydial infection alone recognizes the distinct epidemiology and age distribution across the spectrum of STI.

Using the age difference with both the most recent and the most age discordant partner in the past year mitigates a limitation common to earlier investigations of partner age difference and STI. Since untreated chlamydial infection can persist for an extended period of time (160), the most recent partner may not be the source of a prevalent infection. Our findings show comparable estimated effects when examining either measure. Additionally, we assessed the applicability of calculating the exposure measure as the absolute difference in ages rather than subtracting the woman's age from that of her partner. The dose-response remained non-linear for the absolute difference, with the maximum observed effect at a difference of six to 10 years (p= 0.05).

Implicit in a difference between the age of the most recent partner and the age of the most age discordant partner is the existence of multiple partners. While we controlled for the number of partners, other unmeasured confounding behaviors that can only occur in the presence of multiple partners, like concurrency or shortened time between partners, might be important. Furthermore, type of partner may be of differential importance across the two exposure measures. Women with more than one partner in the past year may be more likely to have a main and a casual partner whereas women with a single partner may be more likely to have only a main partner. Type of partner may play a primary role in transmission of infection (161-163).

Our study findings are limited by the quality of both the study sample and the diagnostic test. The quality of our study sample depends on how well the original school-based sample represented all students attending US secondary schools, response to the Wave III follow-up survey, valid reporting of sexual experiences, and reason for missing diagnostic outcome. The original sample included only students on school registers, but bias in Add

Health caused by school dropouts is thought to be small (153). While 24 percent of Wave I participants could not be located for Wave III, the post-stratification sample weight adjustment ensured that this missing data bias is also small (154). Computer-assisted self-interview likely improved both the frequency and validity of answers to sensitive questions about sexual experiences (127-131). Additionally, respondents who participated in STI testing were similar to those who did not participate (164). Prevalence estimates also are robust to differences between survey responders and non-responders and to the performance of the diagnostic test for chlamydial infection (3). Unavailable information like accurate measures of partner concurrency or standard definitions of partner type would have enriched these analyses.

Understanding the role of partners in the social dynamics of chlamydial infection is central to developing successful public health interventions and treatment programs. Among young adults, older and younger partners convey essentially the same elevated risk of STI as compared to partners close in age. While other aspects of partnerships may be important, it is doubtful that partner age difference is a major cause behind the high rates of chlamydial infection common to young women. This finding is in clear juxtaposition to adolescent girls, for whom older partners are a strong risk factor for STI (24, 27) and likely facilitate maintenance of high infection rates in this group (165). This discrepancy in risk factor between adolescents and young adults may be exploited to better understand how adolescents in age discordant partnerships may be helped to protect themselves from STI. Programs to assist with self-esteem, relationship communication, condom negotiation, and partner notification may benefit by understanding why age difference is so important in STI risk among adolescents, but not when these women are just a few years older.

Young adults, unlike adolescents, are studied infrequently even though they continue to remain at high risk of chlamydial infection. This investigation and other recent work suggest that risk factors like partner age difference and age at first sex (32), which contribute to the spread of STI among adolescents, play distinctly lesser roles in the epidemiology of infection among young adults. Additional research focused on young adults is needed to understand the high STI rates in this age group and to identify how these rates may be reduced.

Table 5.1 Characteristics of Sexually Experienced Females with *Chlamydia trachomatis* Test Results (n=5854), National Longitudinal Study of Adolescent Health, 2001 – 2002

Characteristic	Number of Participants	Weighted Percent
Chlamydial infection		
Positive	316	5.1
Negative	5538	94.9
Partner age difference, most recent		
–8 to –2 years	254	5.1
–1 to 1 years	1964	39.1
2 to 5 years	1839	38.6
6 to 36 years	839	17.2
Partner age difference, most discordant, past year		
–8 to –2 years	254	5.8
–1 to 1 years	1484	33.1
2 to 5 years	1691	39.9
6 to 36 years	921	21.2
Age, years		
18 – 21	2356	45.6
22 – 23	2248	33.2
24 – 26	1250	21.2
Race/ethnicity		
White	3178	68.2
Black	1364	17.1
Latino	909	11.0
Asian American	337	2.9
Native American	53	0.8
Marital status		
Married	1356	23.5
Not married	4498	76.5
Employment status		
Job	3989	67.8
No job	1865	32.2
Functional poverty, past year		
Able to pay rent, utilities	5502	93.8
Unable to pay rent, utilities	323	6.2
Highest attained education		
High school	2621	46.3
College	3117	51.7
Graduate school	115	2.0
Antibiotic use, past 30 days		
Antibiotic	943	16.8
No antibiotic	4904	83.2

Characteristic	Number of Participants	Weighted Percent
Age at first sex, years		
10 – 15	1970	36.0
16 – 18	2975	50.3
19 – 25	885	13.7
Number of sex partners, past year		
0 – 1	4170	72.6
2 – 50	1629	27.4
Condom use, past year		
Never	1754	31.4
Sometimes	2598	45.0
Always/no sex	1440	23.6
Exchange sex for money/drugs, past year		
Exchange	75	1.3
No exchange/no sex	5779	98.7
Regret sex, past year		
Regret	747	13.4
No regret/no sex	5086	86.6

Table 5.2 Bivariate Association between Partner Age Difference and Prevalent Chlamydial Infection among Sexually Experienced Females, National Longitudinal Study of Adolescent Health, 2001 – 2002

Characteristic	Number of participants	Odds ratio (95% CI)
Partner age difference, most recent		
–8 to –2 years	254	1.9 (1.0 – 3.7)
–1 to 1 years	1964	1.0
2 to 5 years	1839	1.4 (0.9 – 2.1)
6 to 36 years	839	1.6 (0.9 – 2.9)
Partner age difference, most discordant, past year		
–8 to –2 years	254	2.4 (1.2 – 4.7)
–1 to 1 years	1484	1.0
2 to 5 years	1691	1.4 (0.9 – 2.3)
6 to 36 years	921	2.1 (1.2 – 3.4)

CI, confidence interval

Table 5.3 Unstratified and Stratified Adjusted Odds Ratios with 95% Confidence Intervals for the Estimated Effect of Partner Age Difference on Prevalent Chlamydial Infection among Sexually Experienced Females, National Longitudinal Study of Adolescent Health, 2001 – 2002

	Exposure Measure	
	Most Recent Partner	Most Age Discordant Partner, Past Year
Age Difference	Adjusted Odds Ratio (95% CI)	Adjusted Odds Ratio (95% CI)
Unstratified[1]		
–8 to –2 years	1.8 (0.9 – 3.5)	2.1 (1.1 – 4.3)
–1 to 1 years	1.0	1.0
2 to 5 years	1.4 (0.9 – 2.3)	1.4 (0.8 – 2.3)
6 to 36 years	1.6 (0.9 – 2.8)	1.7 (1.0 – 2.8)
Stratified by Race[2]		
White		
–8 to –2 years	1.0 (0.2 – 5.4)	1.2 (0.2 – 6.4)
–1 to 1 years	1.0	1.0
2 to 5 years	1.4 (0.7 – 3.8)	1.6 (0.6 – 4.3)
6 to 36 years	2.8 (1.0 – 7.3)	2.8 (1.2 – 6.9)
Black		
–8 to –2 years	2.8 (0.99 – 7.7)	3.2 (1.2 – 9.0)
–1 to 1 years	1.0	1.0
2 to 5 years	1.6 (0.7 – 2.4)	1.2 (0.7 – 2.2)
6 to 36 years	0.7 (0.3 – 1.3)	0.7 (0.3 – 1.4)
Latino		
–8 to –2 years	2.0 (0.3 – 13.7)	4.8 (0.7 – 35.6)
–1 to 1 years	1.0	1.0
2 to 5 years	1.9 (0.5 – 6.4)	2.9 (0.6 – 13.9)
6 to 36 years	2.4 (0.6 – 9.4)	4.5 (0.99 – 21.0)
Other		
–8 to –2 years	2.2 (0.2 – 25.9)	2.0 (0.2 – 25.4)
–1 to 1 years	1.0	1.0
2 to 5 years	1.0 (0.2 – 4.5)	0.6 (0.1 – 4.2)
6 to 36 years	0.7 (0.1 – 7.8)	1.0 (0.1 – 7.5)

CI, confidence interval

[1] adjusted for number of sex partners, past year

[2] adjusted for age, highest attained education, and number of sex partners, past year

Figure 5.1 Prevalence of chlamydial infection among sexually experienced females by age difference with the most recent partner, National Longitudinal Study of Adolescent Health, 2001 – 2002. The upper range of the age difference is grouped for women with partners 26 or more years older. The symbol size is proportional to the unweighted frequency in the data.

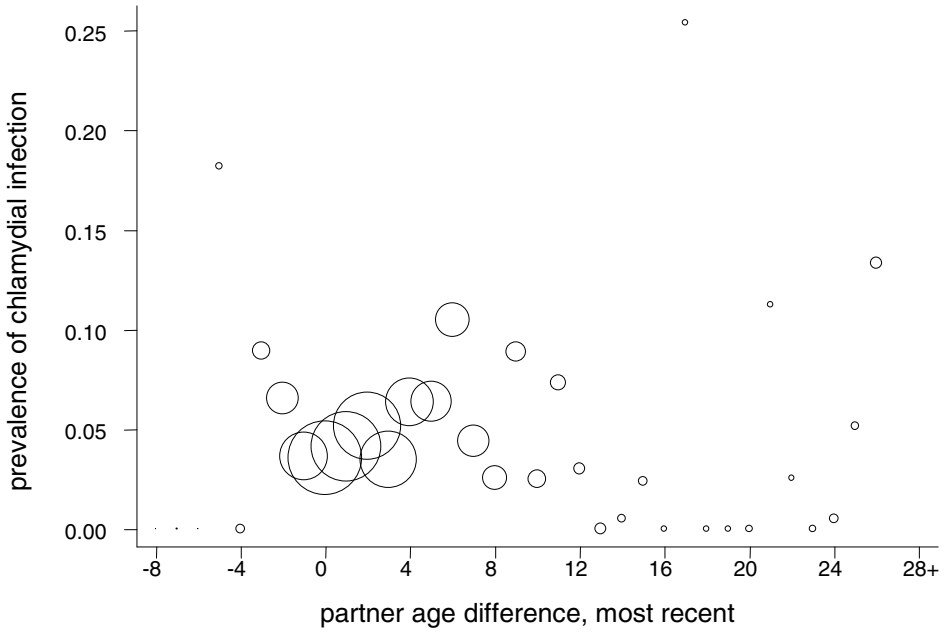
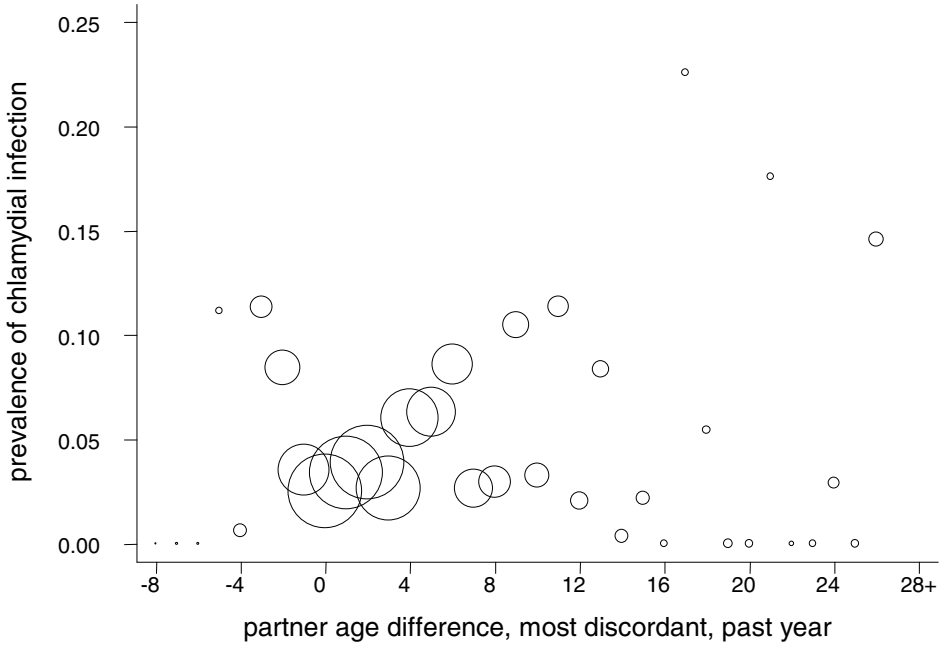


Figure 5.2 Prevalence of chlamydial infection among sexually experienced females by age difference with the most age discordant partner in the past year, National Longitudinal Study of Adolescent Health, 2001 – 2002. The upper range of the age difference is grouped for women with partners 26 or more years older. The symbol size is proportional to the unweighted frequency in the data.



CHAPTER 6

CONCLUSIONS

Chlamydial infection is the most common bacterial STI in the United States (2). Young adults are at high risk of infection. The racial/ethnic disparity in the prevalence of infection, even among youth, is extreme. Infection with chlamydia can lead to serious sequelae, particularly for women (4-6, 8, 9). The economic cost of infection is also great (36, 37). Screening for chlamydial infection is a cost-effective way to prevent additional infection and its harmful reproductive health outcomes (63, 64). Testing and treatment for infection can lower the prevalence of infection (56, 57) and the incidence of pelvic inflammatory disease (58).

The sexual mode of transmission makes controlling the spread of any STI difficult. Chlamydial infection is exceptionally difficult to address because infection is most often asymptomatic (10). Neither those individuals at risk nor health care providers can rely solely on medical signs and symptoms for knowing when infection occurs. For this reason, asymptomatic screening is essential to any chlamydial control program.

Current guidelines recommend annual universal testing of all sexually active women aged 25 years or younger (14). Even with this and similar recommendations by all major US health policy groups, screening rates remain abysmally low (11-13). Young adults are unaware of asymptomatic STI and the importance of screening (53). Many youth do not regularly access health care so they have limited opportunities to be tested (148-150). Many

health care providers do not follow screening guidelines (11, 62, 66). Guidelines provide limited information on screening men.

To expand screening coverage, testing programs must reach beyond traditional clinic settings. Community-based testing is an acceptable alternative (166). Because community programs may lack sufficient funds to test everyone, selective screening guidelines specific to the general population and appropriate for community-based testing may help make such programs feasible. Developing a rational approach for screening men is also important.

The Add Health project provided the information necessary to develop community-based selective screening guidelines for women and men. The detailed demographic, personal history, and behavior data, paired with laboratory-diagnosed chlamydial infection, led to the creation of potentially useful screening tools. Applying these criteria to select no more than 50 percent of the population for diagnostic testing could identify approximately 80 percent of infections in women and men. Implementation of these criteria, however, may be problematic because of the inclusion of race-related information. Additionally, these guidelines result in many unnecessary tests among persons without infection, but fewer people would be tested unnecessarily than with universal testing.

We created three sets of criteria separately for women and men, each beginning with identical potential predictor characteristics. We also included 1) the respondent's race/ethnicity; or 2) the respondent's most recent partner's race/ethnicity; or 3) no information on race/ethnicity. Ideally screening guidelines would identify individuals for testing based exclusively on behavior. In reality, the racial/ethnic disparity is so great that either the participant's or the partner's race/ethnicity often is the strongest marker for STI risk. Chlamydial infection is increased among white young adults with traditional risk

behaviors, but black young adults are at high risk of chlamydial infection even when practicing behaviors that are low risk for white youth (152). Given the potential problems and controversy of selective screening guidelines that incorporate race information, we attempted to find suitable alternative predictor characteristics. However, no other variable or combination of variables that could serve as a proxy for socioeconomic status or other connection to elevated prevalence remained in any of the final models. Information on concurrent relationships or partner type was of poor quality. Detailed data on sexual networks or environmental characteristics that may address the disparity in infection prevalence were unavailable in these data and would not typically be used in routine screening settings.

The presentation of these guidelines, which do include race-related information, is neither an endorsement of their value nor an encouragement for their general use. Rather, the purpose of presenting the selective screening criteria that include race-related information, in conjunction with the more inefficient criteria without race information, is to illustrate that implementation of either plan has significant and potentially harmful consequences. Perhaps the principal lesson learned from this exercise is that at present, on a national level universal screening is the best way to detect chlamydial infection. On a local level, programs may be able to develop suitable screening criteria without race information that include alternative data on geographical location or other markers of STI risk.

Institutional changes are also needed to improve screening practices among health care providers. Health communication programs must do a better job of assisting the public to understand the concepts of asymptomatic infection and screening. Policy changes are needed to address health disparities on a broader scale, of which STI is only one. Ensuring

truly universal screening for chlamydial infection would avoid the stigma of guidelines incorporating race/ethnicity, but must be considered in a framework that assures equal access to testing, treatment, and counseling.

In addition to the racial and ethnic disparity in the prevalence of chlamydial infection, there is also a disparate burden of infection by gender (2). Biologic and physiologic differences between women and men are a primary explanation for female's higher rates of infection (5). Social factors, though, also play an important – and modifiable – role. Conventional wisdom holds that it is "dangerous" for young girls to have older boyfriends. This belief is true in many respects among adolescents, for whom older partners are linked to young age at first sex and inconsistent condom use, both risk factors for STI (24-31). An unequal distribution of power and mixing between sexual networks with different background rates of STI contribute to this phenomenon (18, 30, 114, 158). It was unclear whether this relation between older partners and risky behavior continued beyond adolescence. Two methodologically limited studies reporting the effect of partner age difference on STI among adults found little association with older partners (18, 23).

Among young adult women in Wave III of Add Health, older partners are moderately associated with prevalent chlamydial infection. A similar association was observed for younger partners as compared to partners within one year's age. These associations remain consistent when examining the age difference with the most recent partner and the most age discordant partner in the past year. This finding in young adults contrasts with previous studies of adolescent girls, for whom those with older partners were four times more likely to be infected with chlamydia (24).

Our study mitigated several of the limitations common to earlier investigations of partner age difference and STI. We used the most sensitive diagnostic test available, examined partner age difference multiple ways, and assessed the importance of factors that could modify the exposure-outcome relationship, such as race/ethnicity, age, and number of partners. Unfortunately, good quality data on concurrent partnerships were unavailable. The cross-sectional design was an additional drawback. We examined prevalent infection so could not determine if the exposure partner was the partner transmitting infection.

Understanding the role of partners in the social dynamics of chlamydial infection is central to developing successful public health interventions and treatment programs. The incongruent risk of older partners for adolescents and young adults can inform future STI research. Programs to assist with self-esteem, relationship communication, condom negotiation, and partner notification may benefit from a better understanding of why age difference is so important in STI risk among adolescents, but not among young adults. Whatever changes occur during the intervening years reduces the impact of partner age difference from a major to a minor risk factor. Identifying these changes, and then incorporating them into prevention and counseling programs, may help adolescent girls sidestep a significant STI risk a few years earlier than would have occurred otherwise.

Young adults, unlike adolescents, are studied infrequently even though they continue to remain at high risk of chlamydial infection. This investigation and other recent work suggests that risk factors like partner age difference and age at first sex (32), which contribute to the spread of STI among adolescents, play distinctly lesser roles in the epidemiology of infection among young adults. Additional research focused on young adults

is needed to understand the high STI rates in this age group and to identify how these rates may be reduced.

Add Health is an excellent data source for the study of STI in young adults. The data are the most comprehensive assessment to date of chlamydial infection and related risk factors in US young adults. Few population-based studies provide such detailed information on this age group. Our study findings, though, are limited by the adequacy of the Add Health study sample and the characteristics of the diagnostic test used. The legitimacy of Add Health depends on the representativeness of the original school-based sample, nonresponse to the Wave III follow-up survey, truthful reporting on sexual experience, and refusal or other problems that led to a missing diagnostic outcome. The original sample included only students on school registers, but an evaluation of school dropouts suggests any resultant bias in Add Health is small (153). Post stratification sample weight adjustment accounted for the 24 percent of Wave I participants who could not be located for Wave III, a bias that was also small (154). Both the frequency and validity of responses to sensitive questions about sexual experiences were likely improved through the use of CASI (127-131). Additionally, participants who did and did not provide urine specimens for STI testing were similar (164). Earlier analyses show prevalence estimates were robust to differences in characteristics of non-respondents and diagnostic test performance (3).

This dissertation, complete with multiple limitations, was a worthy public health endeavor. The research addressed salient gaps in the epidemiology of chlamydial infection among US young adults, an understudied population. At the very least, the findings can initiate and inform new dialogue about how best to address racial and ethnic disparities in

sexual health. Furthermore, this work underscores that more remains to be uncovered about chlamydial infection and how it moves so effectively across populations.

APPENDIX ONE

PREVALENCE OF CHLAMYDIA TRACHOMATIS

Table A1.1 Prevalence of *Chlamydia trachomatis*

First Author (Reference)	Publication Year	Study Location	Source Population	Gender	Age Range (Mean)	Test Type	Sample Size	Infection Prevalence
Millstein SG (167)	1995	San Francisco, CA	FP clinics	female	13 – 19 (17)	culture	571	9.3
Gershman (168)	1996	Statewide, CO	FP clinics	female	NS	DNA probe	12,926	4.5
Stary A (72)	1996	National	military recruits	male	(27)	urine LCR and PCR	705	4.1
Marrazzo JM (44)	1997	Seattle, WA	non-traditional sites	male and female	(median=16)	urine LCR	10,118	6.9
Rietmeijer CA (50)	1997	Denver, CO	non-clinic sites	male and female	(17)	urine PCR	486	6.6
Schwebke JR (45)	1997	Birmingham, AL	STD clinic	male and female	NS	swab culture	14,162	10.9
Beck-Sague CM (169)	1998	Atlanta, GA	adolescent clinics	female	13 – 20 (17)	cervical PCR	451	20.7
Brodine SK (65)	1998	National and Okinawa, Japan	military personnel	male and female	NS	urine LCR	1,338	4.2
Burstein GR (42)	1998	Baltimore, MD	STD, FP, school-based clinics	female	12 – 19 (17)	cervical or urine PCR	3,202	24.1
Burstein GR (135)	1998	Baltimore, MD	school-based clinics	female	12 – 17 (14)	urine LCR	170	15.3
Cohen DA (156)	1998	Urban, LA	school-based screening	male and female	NS	urine PCR and LCR	1,933	6.5
Gaydos CA (43)	1998	Baltimore, MD	school-based clinics	female	13 – 21 (17)	urine PCR and LCR	408	15.7

First Author (Reference)	Publication Year	Study Location	Source Population	Gender	Age Range (Mean)	Test Type	Sample Size	Infection Prevalence
Gaydos CA (46)	1998	National	military recruits	female	17 – 39 (median=21)	urine LCR	13,204	9.2
Gunn RA (79)	1998	San Diego, CA	non-clinic sites	male	15 – 19	urine PCR	261	6.1
Mertz KJ (40)	1998	National	NHANES III sample	male and female	12 – 39	urine LCR	1,144	3.9
Oh MK (48)	1998	Birmingham, AL	juvenile jail	male and female	12 – 18	urine LCR	263	12.2
Bunnell RE (39)	1999	Atlanta, GA	teen health clinics	female	14 – 19 (median=16)	cervical PCR	635	27.2
Cohen DA (60)	1999	Urban, LA	school-based health centers	males	NS	urine LCR	2,308	6.2
Cohen DA (60)	1999	Urban, LA	school-based health centers	females	NS	urine LCR	2,497	11.5
Rosenberg MD (118)	1999	San Francisco, CA	STD clinic	male and female	14 – 19 (18)	urine LCR	283	17.0
Bachmann LH (170)	2000	Birmingham, AL	residential drug treatment	male and female	16 – 65 (median=36)	urine LCR	311	2.3
Joyner JL (171)	2000	Denver, CO	STD clinic	male	(32)	urine PCR	454	7.5
Pack RP (15)	2000	Birmingham, AL	juvenile jail	male	14 – 18 (16)	urine LCR	284	14.4
Best D (38)	2001	Suburban, NC	private pediatric practice	male and female	15 – 24 (17.1)	urine LCR	331	2.1
Harrington KF (172)	2001	Birmingham, AL	low income health clinics	female	14 – 18 (16)	vaginal LCR	522	17.1
Klausner JD (173)	2001	San Francisco, CA	population-based household survey	female	18 – 29 (24)	urine LCR	1,314	3.2
Mehta SD (112)	2001	Baltimore, MD	emergency department	male and female	18 – 44 (28)	urine LCR	655	6.7
Mertz KJ (49)	2001	National	job training program	female	16 – 24	cervical ELISA	141,336	12.5

First Author (Reference)	Publication Year	Study Location	Source Population	Gender	Age Range (Mean)	Test Type	Sample Size	Infection Prevalence
Bloomfield FP (174)	2002	San Francisco, CA	home-based mail-in testing	male and female	16 – 67 (41)	urine PCR	76	1.3
Ku L (16)	2002	National	NSAM	male	18 – 19	urine PCR	470	3.1
Ku L (16)	2002	National	NSAM	male	22 – 26	urine PCR	995	4.5
Turner CF (175)	2002	Baltimore, MD	household probability sample	male and female	18 – 35	urine LCR	579	3.0
Wingood GM (176)	2002	South, US	schools, health clinics	female	14 – 18 (16)	vaginal LCR	522	17.5
Farley TA (177)	2003	New Orleans, LA	non-traditional sites	male and female	18 – 29 (23)	urine LCR	1,610	10.2
Monroe KM (80)	2003	Birmingham, AL	emergency department	male and female	14 – 20 (16)	urine LCR	879	6.9
Schwebke JR (178)	2003	Birmingham, AL	STD clinic	male	NS	urine LCR	300	19.6
Sutton TL (17)	2003	Fort Lewis, WA	ROTC cadets	male	18 – 32 (23)	urine LCR	1,443	2.5
Bauer HM (179)	2004	24 CA health jurisdictions	non-clinic sites	male and female	NS	urine NAAT	16,279	6.6
Crosby RA (180)	2004	Atlanta, GA Providence, RI Miami, FL	primary care clinics and outreach	male and female	15 – 21 (18)	urine LCR	455	7.5
DiClemente RJ (181)	2004	Atlanta, GA	hospital prenatal clinic	female	14 – 20 (17)	urine LCR	170	13.0
Miller WC (3)	2004	National	Add Health	male and female	18 – 26 (22)	urine LCR	12,548	4.2
Nsuami M (182)	2004	Urban, LA	school-based screening	male and female	12 – 22 (16)	urine LCR	5,877	7.7

LCR = ligase chain reaction; PCR = polymerase chain reaction; NAAT = nucleic acid amplification test; NS = not stated; STD = sexually transmitted disease; FP = family planning; ROTC = reserve officer training corps; NHANES = National Health and Nutrition

Examination Survey; NSAM = National Survey of Adolescent Males; Add Health = National Longitudinal Study of Adolescent Health

APPENDIX TWO

NUCLEIC ACID AMPLIFICATION DIAGNOSTIC TEST CHARACTERISTICS

Table A2.1 Sensitivity and Specificity of Nucleic Acid Amplification Tests for *Chlamydia trachomatis*

First Author (Reference)	Publication Year	Source Population	Gender	Sample Size	Infection Prevalence	Sensitivity	Specificity	Sensitivity after DA	Specificity after DA
Chernesky MA (67)	1994	STD clinic Hamilton, ON	male	305	17.7	NC	NC	96.4	100
Chernesky MA (67)	1994	student health, abortion clinics Hamilton, ON	female	447	6.0	93.3	97.0	96.3	100
Bassiri M (68)	1995	FP clinic Västerås, Sweden	female	447	3.1	87.5 (by EIA)	100 (by EIA)	NS	NS
Lee HH (69)	1995	OB, STD, student health clinics Birmingham, AL Seattle, WA San Francisco, CA Hamilton, ON	female	1,937	7.7	93.8	99.9	NS	NS
van Doornum GJJ (70)	1995	STD clinic Amsterdam, The Netherlands	male	258	9.7	83.3	97.9	86.2	100
van Doornum GJJ (70)	1995	STD clinic Amsterdam, The Netherlands	female	237	10.5	86.7	94.6	78.1	100
Buimer M (71)	1996	STD clinic Amsterdam, The Netherlands	male	614	9.9	86.0	95.8	77.3	99.4
Buimer M (71)	1996	STD clinic Amsterdam, The Netherlands	female	602	9.1	83.3	94.8	78.8	99.4

First Author (Reference)	Publication Year	Source Population	Gender	Sample Size	Infection Prevalence	Sensitivity	Specificity	Sensitivity after DA	Specificity after DA
Stary A (72)	1996	military recruits, United Nations	male	705	3.8	45.8 (by EIA)	97.7 (by EIA)	93.1	100
Chernesky MA (73)	1997	STD clinic	male	287	11.5	NC	NC	94.3	99.6
Goessens WHF (74)	1997	STD clinic Rotterdam, The Netherlands	male, female	1,000	9.7	79.2	95.3	83.7	99.9
Pasternack R (75)	1997	STD, student health clinics Tampere, Finland	female	442	10.6	93.2	82.7	94.0	100
Schepetiuk S (76)	1997	STD clinic Adelaide, Australia	male, female	1,005	3.0	91.3	99.1	75.0	100
Morré, SA (77)	1999	general practice Amsterdam, The Netherlands	male, female	2,855	2.6	74.7 (by PCR)	99.6 (by PCR)	78.6	99.7
Black CM (78)	2002	STD clinics Birmingham, AL Indianapolis, IN New Orleans, LA San Francisco, CA Seattle, WA	female	3,551	11.4	82.6	96.6	NS	NS

Unless stated otherwise, infection prevalence is determined by LCR and sensitivity and specificity using culture as reference standard.

DA = discrepant analysis; NC = not calculable; NS = not stated; EIA = enzyme immunofluorescent assay; PCR = polymerase chain reaction; LCR = ligase chain reaction; STD = sexually transmitted disease; OB = obstetric.

APPENDIX THREE

SELECTIVE SCREENING CRITERIA FOR CHLAMYDIAL INFECTION

Table A3.1 Selective Screening Criteria for *Chlamydia trachomatis* in Women

Reference	(81)	(82)	(83)	(84)
Risk Assessment Criteria	any 1 # or age specific	any 1 #	any 1 #	any 1 #
Demographic Markers				
age < 20 years	#			
age ≤ 20 years				
age ≤ 21 years		#	#	
age ≤ 24 years	(with 1 º)			#
age > 24 years	(with 2 º)			
age ≤ 25 years				
age ≤ 30 years				
unmarried				
African American				
nulliparous				
Behavioral Markers				
barrier contraception use (none)	º			
barrier contraception use (inconsistent: < 100%)	º			
new sex partner (1 month)				
new sex partner (2-3 months)	º			
≥ 2 sex partners (2-3 months)	º			
new sex partner (1 year)				
≥ 2 sex partners (1 year)				
partner with STI				
partner with multiple partners				
douching (1 year)				
Symptoms				
frequent urination				
intermenstrual bleeding				
Physical Findings				
cervical friability				
cervical ectopy				
mucropurulent discharge	#			
Additional Diagnoses				
PID				
prior STI				
gonorrheal infection				
genital warts				

Reference Risk Assessment Criteria	(88) any 1 # or age specific	(89) any 1 # or age specific	(87) any 1 #	(14) any 1 #
Demographic Markers				
age < 20 years				
age ≤ 20 years				
age ≤ 21 years				
age ≤ 24 years	#	#		
age > 24 years	(with 1 º)	(with 1 º)		
age ≤ 25 years				#
age ≤ 30 years			#	
unmarried				
African American				
nulliparous				
Behavioral Markers				
barrier contraception use (none)				
barrier contraception use (inconsistent: < 100%)				
new sex partner (1 month)				
new sex partner (2-3 months)				
≥ 2 sex partners (2-3 months)				
new sex partner (1 year)		º		
≥ 2 sex partners (1 year)		º		
partner with STI	º			
partner with multiple partners				
douching (1 year)				
Symptoms				
frequent urination				
intermenstrual bleeding				
Physical Findings				
cervical friability	º			
cervical ecotopy	º			
mucropurulent discharge	º			
Additional Diagnoses				
PID				
prior STI				
gonorrheal infection				
genital warts				

Reference Risk Assessment Criteria	(90) any 1 #	(91) any 1 #	(92) any 1 #	(85) any 1 #
Demographic Markers				
age < 20 years				
age ≤ 20 years	#	#		
age ≤ 21 years				
age ≤ 24 years			#	
age > 24 years				
age ≤ 25 years				#
age ≤ 30 years				
unmarried			#	
African American				#
nulliparous				
Behavioral Markers				
barrier contraception use (none)				
barrier contraception use (inconsistent: < 100%)				#
new sex partner (1 month)	#			
new sex partner (2-3 months)				
≥ 2 sex partners (2-3 months)				
new sex partner (1 year)		#		#
≥ 2 sex partners (1 year)				#
partner with STI	#	#		
partner with multiple partners				
douching (1 year)				
Symptoms				
frequent urination		#		
intermenstrual bleeding		#		
Physical Findings				
cervical friability			#	
cervical ecotopy				#
mucropurulent discharge			#	#
Additional Diagnoses				
PID			#	
prior STI				#
gonorrheal infection				
genital warts				

Reference Risk Assessment Criteria	(93) any 2 #	(94) ≥2 # or ≥3 #	(95) – I ≥3 # or ≥4 #	(95) – II sum ≥ 4 or ≥5
Demographic Markers				
age < 20 years				
age ≤ 20 years				
age ≤ 21 years				
age ≤ 24 years	#	#	#	1
age > 24 years				
age ≤ 25 years				
age ≤ 30 years				
unmarried		#	#	2
African American			#	1
nulliparous			#	1
Behavioral Markers				
barrier contraception use (none)	#	#		
barrier contraception use (inconsistent: < 100%)				
new sex partner (1 month)				
new sex partner (2-3 months)	#	#		
≥ 2 sex partners (2-3 months)				
new sex partner (1 year)				
≥ 2 sex partners (1 year)			#	1
partner with STI				
partner with multiple partners				
douching (1 year)			#	1
Symptoms				
frequent urination				
intermenstrual bleeding				
Physical Findings				
cervical friability	#	#		
cervical ecotopy			#	2
mucropurulent discharge	#			
Additional Diagnoses				
PID				
prior STI				
gonorrheal infection				
genital warts				

Reference Risk Assessment Criteria	(58) sum ≥ 3	(96) any 1 #	(97) – I any 1 #	(97) – II any 1 #
Demographic Markers				
age < 20 years				
age ≤ 20 years				
age ≤ 21 years				
age ≤ 24 years	1			
age > 24 years				
age ≤ 25 years				
age ≤ 30 years				
unmarried				
African American	2			
nulliparous	1			
Behavioral Markers				
barrier contraception use (none)				
barrier contraception use (inconsistent: < 100%)				
new sex partner (1 month)				
new sex partner (2-3 months)		#		
≥ 2 sex partners (2-3 months)		#		
new sex partner (1 year)				#
≥ 2 sex partners (1 year)	1			
partner with STI		#		
partner with multiple partners				
douching (1 year)	1			
Symptoms				
frequent urination			#	#
intermenstrual bleeding			#	#
Physical Findings				
cervical friability		#	#	#
cervical ecotopy				
mucropurulent discharge		#	#	#
Additional Diagnoses				
PID		#	#	#
prior STI				
gonorrheal infection		#		
genital warts			#	#

APPENDIX FOUR

VARIABLE DERIVATION AND CODING SCHEMES

Individual Characteristics, Sociodemographic

Gender: Respondent's gender was confirmed by the interviewer [BIO_SEX3] and coded as 1 = male, 2 = female. This will be recoded as 0 = male, 1 = female.

Age: The respondent's age during the interview month will be calculated by subtracting the birth month and year from the interview month and year.

- Confirm birth date [H3OD1M, H3OD1Y].

Age will be examined as a continuous measure and categorized according to risk level observed in the data.

Race/Ethnicity: A five-level variable for participant's race/ethnicity will be coded through a multi-step process. A single race will first be identified for each participant. For participants reporting just one race, this is their race designation. The race designation for participants reporting multiple races will be their response to the one "best" racial background question. After identifying a single race for each subject, race and ethnicity will be examined in tandem. All participants responding affirmatively to the question of Hispanic or Latino origin will be coded as Latino. Participants not identifying as Hispanic or Latino will be coded according to their single best race designation: white, black, Asian American or Native American.

- Are you of Hispanic or Latino origin [H3OD2]?
- What is your race? You may give more than one answer [H3OD4A – D].
- Which one category best describes your racial background [H3OD6]?

Analyses will also be conducted on a subset of the population restricted to white, black, and Latino. All race/ethnicity variables will be coded with indicator coding.

Region: Participants were assigned one of the US census regions (northeast, Midwest, south, west) based on Wave III residence. This variable will be kept categorical and dichotomized to reflect disparate prevalence measures with 0 = outside southern US and 1 = southern US.

Marital status: Participants were asked

- How many times have you been married [H3MR1]?
- Are you still married [H3MR3_A-C]?

These two questions will be combined to create a dichotomous variable with 0 = not married and 1 = married.

Housing: Participants were asked

- Where do you live now? That is, where do you stay most often [H3HR2]?

Housing was dichotomized with 0 = no shared housing and 1 = shared housing.

Student status: Participants were asked

- Are you currently attending regular school? If you are enrolled but on a school break or vacation, count this as attending [H3ED23].

The coded response of 0 = no and 1 = yes will be retained.

Highest attained education: Participants were asked a series of questions about their education.

- What is the highest grade or year of regular school you have completed [H3ED1]?
- What degrees or diplomas have your received? Indicate all that apply.
    - GED or high school equivalency [H3ED2]
    - high school diploma [H3ED3]
    - associate or junior college degree – an AA [H3ED4]
    - bachelor's degree – a BA, AB, or BS [H3ED5]
    - master's degree – an MA or MS [H3ED6]
    - doctoral degree – a PhD, DrPH, and so on [H3ED7]
    - professional degree – a DDS, JD, MD, DVM, and so on [H3ED8]
- Is it correct that you have received no academic degree or diploma [H3ED9]?

The responses to these questions will be used to develop highest attained education as a categorical variable. The possibility of a linear relationship between education and STI will be examined to judge the validity of education as an ordered categorical variable using tertiles, quartiles or quintiles of highest education completed. More likely, education will be used a nominal categorical variable with indicator coding.

Employment status: Participants were asked

- Are you currently working for pay for at least 10 hours a week [H3LM7]?

The coded response of 0 = no and 1 = yes will be retained.

Military status: Participants were asked

- Are you currently serving in the full-time active-duty military [H3LM39]?
- Have you ever served in the active-duty military [H3LM43]?

Indicator variables will be used to account for a three-level categorization: never military, former military, and current military. This variable will also be dichotomized at 0 = never military and 1 = ever military.

Functional income: Participants were asked

- In the past 12 months, was there a time when you didn't pay the full amount of the rent or mortgage because you didn't have enough money [H3EC19]?
- In the past 12 months, was there a time when you didn't pay the full amount of a gas, electricity, or oil bill because you didn't have enough money [H3EC21]?

Functional income combined these two questions into 0 = no problem paying either and 1 = problem paying at least one.

Individual characteristics, Behavioral

Age at sexual debut: Participants were asked

- Have you ever had vaginal intercourse? (Vaginal intercourse is when a man inserts his penis into a woman's vagina) [H3SE1].
- How old were you the first time you had vaginal intercourse [H3SE2]?

Sexual debut will be used as a continuous variable and categorized to reflect patterns in the data.

Number of sex partners, lifetime: Participants were asked

- With how many partners have you ever had vaginal intercourse [H3SE3]?

This variable will be examined continuously and categorized to reflect the data distribution.

Number of sex partners, past 12 months: Participants were asked

- With how many different partners have you had vaginal intercourse in the past 12 months [H3SE4]?

This variable will be examined continuously and categorized to reflect the data distribution.

Current stable partnership: Participants were asked

- Are you currently involved in a sexual or romantic relationship with {initials}[H3TR1]?
- Has your relationship with {initials} lasted for at least three months in total [H3TR2]?

These dichotomous variables will be combined to create a new dichotomous variable with 0 = current partnership $\geq$ 3months duration, 1 = no current partnership $\geq$ 3 months duration.

Concurrent sex partners, past 12 months: Participants were asked to list all relationships since summer 1995 and asked

- Have you had sexual relations with {initials}? By "sexual relations" we mean vaginal intercourse, oral sex, or anal sex [H3TR8].

Participants answered detailed questions for each relationship identified as sexual, including the beginning and ending dates of the sexual relationship.

- In what month and year did your sexual relationship with <partner> begin [H3RD10M/Y]?
- In what month and year did your sexual relationship with <partner> end [H3RD20M/Y]?

Overlaps in sexual relationships can be identified through these responses. This variable will be dichotomized at 0 = no concurrent relationship and 1 = concurrent relationship.

Condom frequency, past 12 months: Participants were asked

- On how many of [the times you had vaginal intercourse] did you/your partner use a condom [H3SE8]?

Possible responses were 0 = none, 1 = some, 2 = half, 3 = most, or 4 = all. This variable will be examined as ordered categorical, as nominal categorical using four indicator variables, and dichotomized at 0 = 100% condom use and 1 = less than 100% condom use.

Paid or been paid for sex, past 12 months: This variable will be developed from responses to four questions.

- Have you ever paid someone to have sex with you [H3SE15]?
- In the past 12 months, how many times have you paid someone to have sex with you [H3SE16]?
- Have you ever had sex with someone who paid you to do so [H3SE17]?
- In the past 12 months, how many times have you had sex with someone who paid you to do so [H3SE18]?

A dichotomous variable with 0 = no payment for sex in past 12 months and 1 = payment for sex in past 12 months will be created.

Regrettable sex after drinking or drugs, past 12 months: Participants were asked

- Over the past 12 months, how many times did you get into a sexual situation that you later regretted because you had been drinking [H3TO48C]?
- During the past 12 months, how often did you get into a sexual situation that you later regretted because you had been using drugs [H3TO126]?

These questions will be combined to create a single dichotomous variable with 0 = no regrettable sexual situations after drinking or drugs in past 12 months and 1 = regrettable sexual situations after drinking or drugs in the past 12 months.

Sexuality: Participants were asked

- Please choose the description that best fits how you think about yourself [HSSE13].

Sexuality was dichotomized at 0 = 100% heterosexual and 1 = not 100% heterosexual.

Individual Characteristics, Risk Perception

Perceived risk of STD: Participants were asked on a five-point likert scale ranging from very high chance to very low chance

- What is the chance that right now you have either gonorrhea or chlamydia [H3SE32]?

The likert scale will be retained.

Perceived risk of HIV: Participants were asked on a five-point likert scale ranging from almost certain to almost no chance

- What do you think are the chances that you will get HIV or AIDS [H3EC61]?

The likert scale will be retained.

Individual Characteristics, Medical/Health Care

Recent health care utilization: Participants were asked about three separate events of health care utilization.

- How long ago did you last consult a doctor or nurse [H3HS11]?
- How long ago did you last have a routine check-up [H3HS14]?
- When was the last time you had a gynecological or pelvic exam [H3HS16]?

These are ordered categorical variables that range from within the past three months to two years ago or longer. The most recent of the three responses will be kept as an ordered variable if it is linear in the logit and more coarsely categorized based on the variable distribution.

Current insurance status: Participants were asked about if they have health insurance and through whom they have it.

- Which of the following best describes your current health insurance situation [H3HS5]?

This variable will be dichotomized to 0 = insurance and 1 = no insurance.

Forgone care, past 12 months: Participants were asked

- Has there been any time in the past 12 months when you thought you should get medical care, but you did not [H3HS6]?

The coded response of 0 = no and 1 = yes will be retained.

Antibiotic use, past 30 days: Participants were asked

- In the past 30 days, have you taken antibiotics, such as tetracycline, doxycycline, amoxicillin, or erythromycin [H3ID12]?

The coded response of 0 = no and 1 = yes will be retained.

Tested for STD, past 12 months: Participants were asked about testing for numerous STDs.

- Which, if any, of the following sexually transmitted diseases have you been tested for in the past 12 months?
    - chlamydia [H3SE22A]
    - gonorrhea [H3SE22B]
    - trichomoniasis [H3SE22C]
    - syphilis [H3SE22AD]
    - genital herpes [H3SE22E]
    - genital warts [H3SE22F]
    - human papilloma virus (HPV) [H3SE22G]
    - bacterial vaginosis [H3SE22H]
    - pelvic inflammatory disease (PID) [H3SE22I]
    - cervicitis or mucopurulent cervicitis (MPC) [H3SE22J]
    - urethritis (NGC) [H3SE22K]
    - vaginitis [H3SE22L]
    - HIV infection or AIDS [H3SE22M]
    - other [H3SE22N]

These variables will be grouped together to identify participants who had been tested for any STD in the past 12 months. The variable will be dichotomized at 0 = no STD testing and 1 = STD testing.

Prior STD: Participants were asked about diagnosis of numerous STDs.

- In the past 12 months, have you been told by a doctor or nurse that you had the following sexually transmitted disease?
    - chlamydia [H3SE21A]

- gonorrhea [H3SE21B]
- trichomoniasis [H3SE21C]
- syphilis [H3SE21AD]
- genital herpes [H3SE21E]
- genital warts [H3SE21F]
- human papilloma virus (HPV) [H3SE21G]
- bacterial vaginosis [H3SE21H]
- pelvic inflammatory disease (PID) [H3SE21I]
- cervicitis or mucopurulent cervicitis (MPC) [H3SE21J]
- urethritis (NGC) [H3SE21K]
- vaginitis [H3SE21L]
- HIV infection or AIDS [H3SE21M]
- other [H3SE21N]

These variables will be grouped together to identify participants who have been diagnosed with any STD in the past 12 months. The variable will be dichotomized at 0 = no prior STD and 1 = prior STD.

STD-like genitourinary symptoms: Participants were asked about STD-like symptoms in the past 12 months and in the past 24 hours.

- In the past 12 months/24 hours, have you had any of the following symptoms?
  - painful or very frequent urination (peeing) [H3SE23A, 24A]
  - painful sores or blisters on your genitals [H3SE23B, 24B]
  - warts on your genitals [H3SE23C, 24C]
  - dripping or oozing from your penis/vagina [H3SE23D, 24D]
  - bleeding after intercourse or between your periods [H3SE23E, 24E]
  - itching in the vagina or in the genital area [H3SE23F, 24F]

These variables will be examined for both past 12 months and past 24 hours. The variables will be dichotomized at 0 = no symptoms and 1 = symptoms.

Parity: Participants were asked about the number completed pregnancies with a separate response to indicate women who are currently pregnant.

- Please indicate how many babies were born alive [H3TP3].

This variable will be categorized several ways. It will be dichotomized at 0 = no current pregnancy and 1 = current pregnancy and at 0 = never pregnant and 1 = pregnant.

Hormonal contraception use: Participants were asked

- In the past 12 months, which of the following methods of birth control have you/has a female partner of yours used [H3SE29A – H3SE29C]?

Contraception was dichotomized with 0 = contraception and 1 = no contraception.

Partner Characteristics

Gender: All analyses will be restricted to heterosexual relationships. Participants were asked

- Please indicate whether your partner is male or female [H3TR3].

Responses were coded as 1 = male, 2 = female. This will be recoded as 0 = male, 1 = female.

Age: Partner's age is available as a constructed Add Health variable based on responses to questions the partner age difference [PAGE].

- Please indicate whether your partner is older or younger than you [H3TR4].
- How may years older/younger than you is your partner [H3TR5]?

Partner age will be examined continuously and categorized to best reflect data patterns and distributions.

Age difference: Age difference is available for all relationships since summer 1995 [H3TR5]. The age difference will be identified for the most recent partner and for the partner in the past year with the greatest age difference. Age difference will be assessed continuously and categorized based on the distribution of the variable in the data.

Race/ethnicity: Participants were asked

- Please indicate the race of your partner [H3TR6].
- Is your partner of Hispanic or Latino origin [H3TR7]?

Participants could place their partner in one of four categories: white, black, Asian American or Native American. A five-level variable for partner's race/ethnicity will be coded by examining race and ethnicity in tandem. All partners identified as Hispanic or Latino will be coded as Latino. Partners not identified as Hispanic or Latino will be coded according to their race designation: white, black, Asian American or Native American. Analyses will also be conducted on a subset of the population restricted to white, black, and Latino. All race/ethnicity variables will be coded with indicator coding.

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