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Idiopathic urethritis in young men in the United States: prevalence and comparison to infections with known sexually transmitted pathogens

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Abstract

Purpose—Urethritis is the most common male reproductive tract disease syndrome, yet 20–50% of diagnosed cases have no defined etiology and few population-level data exist on the prevalence or etiology of the syndrome. We estimated the prevalence of urethritis among young men in the United States and compared correlates of idiopathic cases to correlates of infections with STI pathogens.

Methods—Questionnaire data and urine specimens from 5,447 men ages 18–27 participating in Wave III of the National Longitudinal Study of Adolescent Health were analyzed. Symptomatic urethritis was defined as self-reported dysuria or urethral discharge in the past 24 hours. *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, *Trichomonas vaginalis*, and *Mycoplasma genitalium* were identified using nucleic acid amplification tests. Idiopathic urethritis (IU) was defined as urethral symptoms in the absence of these four pathogens. Stratified weighted analyses generated population-based estimates.

Results—Urethritis was reported by 1.2% (95% CI: 0.8–1.6%) of men, of whom 82.4% (61.1–93.3%) had IU. Men with previous STD diagnoses (aOR=9.3 [95% CI: 3.0–28.7]), or fewer (1–4) or no lifetime vaginal sex partners (aOR=7.5 [2.9–19.3] and aOR=7.2 [1.9–27.4]), were more likely to have IU compared to men without urethral symptoms or identified pathogens, whereas men of Native American or Asian/Pacific Islander descent (aOR=0.04 [0.01–0.2]) and heavy drinkers (aOR=0.08 [0.03–0.2]) were less likely to have IU. Unlike infection with known pathogens, IU was not associated with Black race, Hispanic ethnicity, or age at sexual debut.

Conclusions—Urethral symptoms were rarely associated with known pathogens. IU and known pathogens were associated with distinct characteristics.

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Keywords

Urethritis; sexually transmitted infection (STI); epidemiology

INTRODUCTION

Urethritis is the most common clinical syndrome affecting the male reproductive tract, and resulted in approximately 200,000 medical visits in the United States (US) in 2001 [1]. It has traditionally been associated with sexually transmitted organisms such as *Neisseria gonorrhoeae* and *Chlamydia trachomatis*, and less frequently, with *Trichomonas vaginalis* and herpes simplex virus (HSV) [2–5]. Recently it has also been associated with *Mycoplasma genitalium* and adenovirus [5–9]. However, there is poor correspondence between the clinical syndrome of urethritis and infection with known sexually transmitted infections (STI). In Wave III of the National Longitudinal Study of Adolescent Health (Add Health), *C. trachomatis* was detected in 3.7% of men ages 18–26, *N. gonorrhoeae* in 0.4% [10], *T. vaginalis* in 1.7% [11], and *M. genitalium* in 1.1% [12], yet only 2–4% of infected men had urethral symptoms [10–12]. Moreover, even in settings with comprehensive laboratory evaluations, many cases of urethritis are idiopathic; an estimated 20–50% have no definable etiology [6,9].

There are no accurate estimates of the current prevalence of urethritis, nor are there data on the proportion of cases that are idiopathic. Although idiopathic urethritis (IU) is a common and vexing source of morbidity in clinical settings, the extent to which idiopathic cases represent unidentified and potentially transmissible STI, and the significance, if any, of prevalent IU in the population, is uncertain. Therefore, we used the population-based sample of young men ages 18–27 in the US participating in Wave III of Add Health to estimate the prevalence of urethritis and identify factors that might explain idiopathic cases. We hypothesized that IU would be characterized by risk factors similar to those associated with recognized STI pathogens.

METHODS

Study population

The Add Health Study was designed to investigate the influence of social contexts on adolescent health and behaviors [13]. In Wave I (1994–1995), a nationally-representative sample of approximately 90,000 students in grades 7 through 12 completed a brief in-school questionnaire. Nearly 21,000 of these respondents, including a core sample from each participating community and members of oversampled sociodemographic groups, completed a more detailed in-home questionnaire. In Wave III (2001–2002), 7,167 male and 7,155 female participants of the Wave I in-home interview were located, received a visit by Add Health Study personnel, and provided informed consent.

Data Collection

Interviews were conducted primarily at study participants' homes. Trained interviewers asked questions about basic demographic and behavioral characteristics, while a Computer-Assisted Self Interview (CASI) was used for sensitive questions. In the CASI interview, participants were asked the following question to assess whether they had experienced symptoms of sexually transmitted disease (STD) syndromes in the past 24 hours and the past 12 months: "In the past 24 hours/12 months, have you had any of the following symptoms? Mark all that apply: [including] painful or very frequent urination (peeing) [or] dripping or oozing from your penis". We defined men as having urethral symptoms if they acknowledged either of the two symptom complexes potentially associated with urethritis. Participants who reported

romantic or sexual relationships within six years of the interview were asked to provide detailed partnership-specific information for each of the three most recent partnerships. Data on sexual behaviors other than vaginal intercourse (e.g., oral and anal sex), were available only for participants who completed this partnership-specific section. A total of 6,636 Wave III males (92.6%) provided a 15–20 mL first-catch urine specimen that was tested for *N. gonorrhoeae* and *C. trachomatis* by ligase chain reaction (LCR; Abbott LCx Probe System, Abbott Park, IL), and *T. vaginalis* by in-house polymerase chain reaction (PCR) assay [14,15]. *M. genitalium* testing by in-house PCR [16] was performed on 1,218 randomly-flagged specimens provided by men with valid questionnaire data and sampling weights. Given the low prevalence of *M. genitalium* in this study population (1.1% among men [12]) untested specimens were considered negative for the present analyses.

We classified men with at least one positive laboratory test as having a urethral infection with a recognized pathogen. We classified men with urethral symptoms in the 24 hours prior to the interview and no positive laboratory tests as having IU. Men with at least one urethral symptom and any positive laboratory test had pathogen-associated urethritis. Men who denied urethral symptoms and who had no urethral pathogens detected served as the referent group.

All study procedures and analyses were approved by the Institutional Review Boards at the University of North Carolina (Add Health Study) and the University of Washington (*M. genitalium* testing and epidemiologic analyses).

Statistical Analyses

To account for Add Health Study sampling design and non-response, we denoted school as the primary sampling unit and geographic region as the stratifying variable in our analyses and incorporated the post-stratification sampling weights developed for Wave I respondents who were interviewed at Wave III (accounting for differential response by gender, race, and original grade level). Our stratified weighted analyses produced unbiased population-level estimates of the prevalences of urethritis and infection with recognized pathogens overall, as well as two subgroups of urethritis (pathogen-associated and idiopathic) among young men in the US. Design-based Pearson's χ^2 -tests and adjusted Wald tests identified demographic and behavioral characteristics associated with these conditions. Proportional 95% confidence intervals (CI) were constructed using a logit transformation; 95% CIs for continuous variables were not transformed. Weighted multivariable logistic regression identified factors independently associated with IU and infection with recognized pathogens. Resultant odds ratios and 95% CIs closely approximate prevalence ratios in this sample because outcomes of interest were rare. Characteristics previously associated with urethritis in the published literature and/or marginally significant in bivariate analyses ($p \leq 0.1$) were entered into multivariable models. Terms with the largest non-significant p -values were removed one-by-one and models were re-fit. Covariates that remained significantly associated with the outcomes of interest ($p \leq 0.05$) and those whose removal resulted in meaningful changes to the remaining logit point estimates (*i.e.*, >10%) were retained in final multivariable models. We collapsed some racial categories in multivariable analyses to avoid sparse strata, and we categorized some continuous characteristics in order to assess non-linear relationships. Unweighted median values determined cutpoints for age of sexual debut and number of partners. To retain in multivariable analyses the 744 young men who reported never having vaginal intercourse and the 1,255 who did not provide partnership-specific data, we created separate strata for these men [17]. Due to extremely small numbers of men who reported a history of HSV diagnosis, we did not evaluate this individually, but included HSV in our composite variable representing history of any STD diagnosis. The few men with pathogen-associated symptoms ($n=7$) were largely similar to asymptotically infected men (data not shown). Therefore, we evaluated men with recognized pathogens detected irrespective of

reported symptoms on the day of the interview. Lastly, we performed sensitivity analyses to estimate the effect of misclassification of IU on prevalence estimates, by varying assumptions of sensitivity and specificity using the methods of Brookmeyer and Gail [18], as described by Miller et al. [10]. Sensitivity analyses of the effects of differential questionnaire non-response, refusal to provide specimens, and imperfect microbiologic test performance have been published elsewhere [10–12,19,20]. Assumptions of statistical tests were largely met and robust tests yielded valid inference when violations occurred (data not shown). All analyses were performed using STATA Version 10 (StataCorp, College Station, Texas).

RESULTS

Study population

Of the 7,167 male participants in Wave III of the Add Health Study 5,447 (76.0%) had self-reported symptom data, microbiologic data, and sampling weights available, and comprised our study population. Of these, 4,192 (77.0%) provided detailed partnership-specific information for each of the three most recent sexual partnerships. The mean age of participants was 22 years. The majority self-identified as White (76.6%), while 16.1% identified as Black and 7.3% as other races; 11.8% reported Hispanic ethnicity. Most (88.5%) had a high school diploma.

Urethritis

Among these men, 1.2% (95% CI: 0.8–1.6%) reported urethral symptoms on the day of the interview (*e.g.*, within the past 24 hours), and 3.7% (3.0–4.5%) reported having had symptoms in the preceding year. On the day of the interview, 0.3% (0.2–0.7%) reported urethral discharge only, 1.0% (0.7–1.4%) reported dysuria or frequency only, and 0.2% (0.05–0.5%) reported both symptoms. The distribution of symptoms in the past year was similar (data not shown). Of the men reporting symptoms on the day of the interview, 17.6% (6.7–38.9%) had known pathogens detected, leaving 82.4% (61.1%–93.3%) with IU. Men reporting both urethral symptoms were somewhat more likely than men with only one of these symptoms to have a known pathogen detected (48.9% vs. 12.8%, $p=0.12$).

Idiopathic urethritis

The prevalence of idiopathic urethral symptoms on the day of the interview was 1.0% (0.7–1.4%) and men with IU had a distinct sociodemographic and behavioral profile. In bivariate analyses, these men were less likely to report Asian/Pacific Islander or Native American descent, drink alcohol three or more days per week, or use marijuana than men with neither symptoms nor pathogens (Table 1). They were more likely to have accessed health care in the past three months (primarily due to “illness”), reported a prior diagnosis of depression, and experienced higher levels of depressive symptoms in the past week as measured by the modified Center for Epidemiologic Studies-Depression (CES-D) scale [21].

Although men with IU were more likely to have sought care for a suspected STD and report an STD diagnosis in the past year, they were less likely to report vaginal intercourse (ever or with their most recent sex partner) than men with neither symptoms nor pathogens detected (Table 1 and Table 2). Among those who reported vaginal intercourse, men with IU had fewer lifetime vaginal intercourse partners and were more likely to have used a condom during the most recent episode than pathogen-negative men without urethritis. Despite associations with some safer-sex behaviors, these men were also more likely to report having ever paid for sex and more likely to report their most recent sex partner had less than a high school education.

In multivariable analyses, men with IU were nearly 10-fold more likely to report a history of STD diagnosis, yet 7-fold more likely to report fewer or no vaginal intercourse partners than

men with neither symptoms nor pathogens detected. They were also dramatically less likely to report heavy drinking, or Native American or Asian/Pacific Islander ethnicity (Table 3). The association with previous depression diagnosis was marginal, and in a parallel model excluding this factor, depressive mood was also marginally associated with IU (aOR=1.1 [95% CI: 1.0–1.1] $p=0.066$; per one-point increase in CES-D score).

Comparison of idiopathic urethritis to urethral infection with known pathogens

Prevalent *N. gonorrhoeae*, *C. trachomatis*, *T. vaginalis*, and/or *M. genitalium* infections were detected in 5.9% (5.0–7.0%) of young men. Only 3.4% (1.4–8.3%) of these STI-positive men reported symptoms on the day of the interview (9.2% [5.4–15.2%] reported having had symptoms in the preceding year), thus the overall prevalence of pathogen-associated urethritis was 0.2% (0.08–0.5%).

Men from Southern states were more likely than those in other regions to test positive for at least one sexually transmitted pathogen, though this was not significant after controlling for age, race, ethnicity, and education (aOR=1.3 [0.9–1.9]; $p=0.1$). In bivariate analyses, compared to pathogen-negative men without symptoms, men infected with known STI pathogens were more likely to identify as Black, Native American, or Hispanic, have less than a high school education, no longer be enrolled in school, and use marijuana (Table 1). These men were more likely to report ever seeking care for an STD and histories of urethral symptoms and STD diagnoses within the past year, but less likely to report accessing health care within the past three months or any prescription drug use during the past year. They were more likely to report vaginal intercourse, a younger age at first vaginal sex, and slightly more lifetime vaginal sex partners ($p=0.07$), but similar numbers of vaginal sex partners in the past year (2.2 [1.9–2.6] partners vs. 2.0 [1.9–2.1]; $p=0.2$), and significantly fewer episodes of vaginal intercourse in the past year ($p=0.003$) compared to the referent group. Men with known pathogens who provided partner-specific information were more likely to report that their most recent partner was Black or Hispanic, and less likely to report having engaged in oral sex with this partner, compared to pathogen-negative men without symptoms (Table 2).

In contrast to characteristics independently associated with IU, Black race and Hispanic ethnicity remained independently associated with infection with recognized pathogens, as did a history of urethral symptoms and younger age at first vaginal sex in multivariable analyses (Table 3). Being in school at the time of the interview, recently accessing health care, and use of prescription drugs in the past year were inversely associated with detection of known pathogens.

Sensitivity analyses

The potential effect of IU misclassification on prevalence estimates was substantial (Table 4). The overall prevalence was >0% only when specificity was set at >0.99, although the true specificity in this population was likely lower.

DISCUSSION

A total of 1.2% of young men in Add Health reported symptoms consistent with urethritis, and over 80% of these men had no recognized pathogens detected, a percentage that is much higher than the 20–50% of IU cases reported from STD clinic populations [6,9]. We had hypothesized that IU would display an epidemiologic pattern consistent with STI, including associations with Black race and greater numbers of lifetime sex partners. However, the only observed association that suggested a sexually transmitted agent was history of STD diagnosis. Other correlates of IU, such as fewer vaginal sex partners and history of depression, have not consistently been associated with STI, suggesting that IU in this population may not represent

an STI. In contrast, men with known STI in this population were characterized by traditional STI risk factors such as race and young age at sexual debut, among others.

The high proportion of men with IU may be attributed, in part, to non-exhaustive biologic testing or false-negative results. The DNA amplification assays used to detect known pathogens may have reduced sensitivity in this largely asymptomatic study population due to lower organism burden. Further, we likely underestimated the prevalence of *M. genitalium* because specimens not flagged for *M. genitalium* testing were considered negative. Given the low overall prevalence of *M. genitalium* in Add Health [12], this effect was likely small. Perhaps more importantly, HSV and adenovirus have been associated with urethritis [3,5], although usually in a small proportion of men, yet testing for these viruses was not performed. Nor was Ureaplasma testing conducted. Recent studies reporting an association between nongonococcal urethritis (NGU) and the newly differentiated species *Ureaplasma urealyticum* [22,23] suggest this organism may also play a role in urethritis, although evidence has been inconsistent [5]. In light of the large proportion of men reporting symptoms consistent with urethritis in the absence of known pathogens, studies using broad range ribosomal DNA amplification techniques that can detect previously unidentified organisms [24] would be informative.

Notably, men with IU were less likely to report having had vaginal intercourse and had significantly fewer lifetime vaginal intercourse partners than pathogen-negative men without urethritis, consistent with previous investigations of NGU [25]. These associations may reflect priming of the immune system to undetected pathogens or commensal organisms. If first exposure to an organism results in a more exuberant immunologic response than re-exposure, men with fewer partners may be more likely to develop symptoms. This phenomenon is suggested by human challenge experiments, wherein repeated intraurethral inoculation with undifferentiated *Ureaplasma* spp. ceased to result in symptomatic infection after the fourth round [26]. Regrettably, we could not investigate associations with the number of oral or anal intercourse partners and frequency of these behaviors because these data were not collected in Add Health. Although men with IU were somewhat more likely to self-identify as homosexual or bisexual and to report that their most recent sexual partner was male, these differences were not significant, but could explain, in part, the lower prevalence of vaginal exposures in this group.

While some cases of IU may be explained by undetected pathogens, the marginal associations with previous diagnosis of depression and higher depressive mood score suggest alternate etiologies. Our findings are consistent with the well-documented association between clinical depression and markers of chronic inflammation or other inflammatory conditions [27–29], and with previous analyses of Waves I and II of Add Health demonstrating higher depressive symptoms among adolescents reporting more frequent physical symptoms, including urinary problems [30]. This may be attributable to underlying physiological abnormalities contributing to both depressive and urethral symptoms, or to somatic complaints related to depression (data on other somatic complaints were not available). Furthermore, relationships between the identified correlates of IU and underlying conditions of stress and inflammation may exist.

Some men were likely misclassified as having urethritis, without satisfying clinical diagnostic criteria [31], and our sensitivity analyses suggest potentially large impacts on IU prevalence estimates. Additionally, the cross-sectional nature of this study limits our ability to infer causality and potentially over-represents men with asymptomatic infections or chronic, low-grade symptomatic infections. Unfortunately, data regarding symptom duration and severity were not collected, and episodes of short duration may be characterized by different factors.

Post-stratification sampling weights were designed to partially offset non-response bias [32], and published sensitivity analyses suggest that pathogen-specific prevalence estimates and

associations are robust to differential response and imperfect test performance [10–12]. Although there may be additional bias if study participation or provision of the urine specimen was associated with other characteristics related to urethritis, investigations of non-response in Wave III of Add Health have found any such influence on study results to be negligible. Using Wave I data and the appropriate sampling weights, the bias remaining in population estimates of demographic and behavioral characteristics (the difference between the estimate among those who participated in Wave III and those who were eligible to participate in Wave III) was less than one percentage point for characteristics assessed in the present analysis [19]. This concern was also partially addressed in an analysis of HIV-related risk behaviors among Add Health participants which showed that those who provided an oral specimen for HIV testing (92.1% of Wave III participants) did not differ significantly with respect to sexual behavior data collected during Waves I and II from those who did not participate in Wave III or those who did not provide the specimen [20]. A related concern is missing questionnaire data from Wave III participants. For example, 15.3% (711 of 4,661) of those who reported ever having had vaginal intercourse on the main interview did not provide specific data regarding recent sexual partnerships, and because respondents were asked to provide information about sexual “relationships”, casual or transactional sexual encounters may not have been reported. However, failure to complete the partner-specific section was not associated with reported urethral symptoms or laboratory findings.

We sought to address some of the limitations of previous STD clinic-based investigations of urethritis by using population-based data. Although our findings may not be generalizable to individuals outside the target age range, and those who would not have been eligible for participation under the original school-based sampling design, the population-based nature of the Add Health study is a clear strength of our investigation. We also assessed a much broader range of individual-level and sex partner-specific correlates of infection and urethral symptoms than those investigated in previous analyses of Add Health data [10–12]. Consistent with previous investigations, Black race [6,33,34] and history of urethritis [6,33,34] were independently associated with urethral infection with recognized pathogens. The inverse relationship between oral sex and STI that has been demonstrated in some [6,33], but not all [5,35] studies, was observed in the present analysis, but was not statistically significant. Unlike previous studies [5,6,33,36,37], we found that neither age nor correct and consistent condom use were significantly associated with IU or detected STI. The lack of association with age may be due to the narrow age range in Add Health. The paradoxical lack of association with correct and consistent condom use with known STI has been previously reported [38], and may be due to selective and/or incorrect use of condoms with high risk partners. Data on circumcision status were not available.

Among young men in the US, symptomatic urethritis was rarely associated with a known pathogen and, contrary to our hypothesis that the epidemiologic pattern of IU would be similar to that seen in men with known STI pathogens, the constellation of correlates associated with idiopathic cases was distinct. Clinicians may need to conduct a thorough risk assessment to determine if treatment of persistent or recurrent IU as an STI is warranted. Some cases may be explained by unknown STI with unique epidemiologic profiles, while others may represent non-infectious causes of urethritis. Nonetheless, the observation that approximately half of men with idiopathic urethral symptoms reported accessing health care within the past three months suggests this condition places a burden on the health care system. Future research into the etiology and sequelae of IU should clarify how to manage these cases.

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Table 1

Characteristics of young adult men aged 18 to 27 in the US associated with idiopathic urethritis and urethral infections with recognized pathogens (2001–2002)

Characteristic [^]	Unweighted count or mean N=5,447	Weighted percentage or mean (95% CI) [‡]		
		No symptoms and no pathogens detected (referent group) n=5,030	Idiopathic urethritis [†] n=51	Urethral infection (NG, CT, TV, or MG) [†] n=366
Urethral discharge or dysuria symptoms, past 24 hours				
Either symptom	58	--	100%	3.4% (1.4–8.3%)
Discharge	15	--	19.8% (8.0–41.2%)	2.3% (0.6–7.6%)
Dysuria	50	--	89.1% (72.6–96.2%)	2.5% (0.8–7.5%)
Both symptoms	7	--	8.6% (2.9–22.4%)	1.3% (0.2–8.3%)
Sociodemographic characteristics				
Region				
West	1,396	16.1% (13.6–19.1%)	16.5% (7.1–33.8%)	13.1% (8.5–19.6%)
Midwest	1,321	30.3% (25.7–35.3%)	19.7% (8.2–40.3%)	23.8% (15.7–34.5%)
South	2,074	39.7% (36.0–43.5%)	50.8% (32.7–68.6%)	54.3% (44.9–63.4%) **
Northeast	656	13.9% (11.9–16.2%)	13.1% (4.3–33.4%)	8.8% (5.2–14.5%)
Race				
White	3,587	78.4% (73.4–82.8%)	79.6% (59.9–91.0%)	47.9% (37.8–58.1%) ***
Black	1,116	14.3% (10.9–18.6%)	20.1% (8.7–39.9%)	44.2% (33.8–55.3%) ***
Asian/Pacific Islander	471	4.5% (2.9–6.9%)	0.08% (0.1–0.6%) ***	2.8% (1.5–5.4%)
Native American	191	2.8% (1.8–4.3%)	0.2% (0.5–1.1%) ***	5.1% (2.5–10.0%) *
Hispanic ethnicity	915	11.2% (8.3–15.0%)	13.4% (5.2–30.4%)	20.3% (13.2–29.7%) ***
Age, years	22.0	21.8 (21.6–22.1)	22.4 (21.7–23.2)	22.0 (21.6–22.4)
No high school diploma or equivalent	557	11.0% (9.3–12.8%)	8.0% (1.8–28.6%)	20.1% (14.0–28.0%) ***
In school at the time of the interview [§]	1,884	34.8% (31.7–38.0%)	35.1% (18.2–56.7%)	22.3% (16.9–28.9%) ***
Alcohol and drug use				
Drinks alcohol ≥ 3 days per week	756	15.5% (13.9–17.3%)	1.0% (0.4–2.8%) ***	11.1% (7.6–15.8%)
Used marijuana, past 30 days	1,461	28.6% (26.5–30.8%)	18.8% (8.8–35.7%)	36.6% (29.1–44.9%) *
Health and health care seeking behaviors				
Accessed health care, past 3 months	1,572	30.4% (28.6–32.3%)	48.7% (30.9–66.8%) *	20.8% (15.5–27.4%) **
Main reason for accessing health care, past 3 months				
Illness	598	37.5% (33.5–41.7%)	53.0% (25.0–79.2%)	29.2% (18.0–43.7%)
Injury or accident	459	30.1% (26.8–33.6%)	30.4% (11.7–59.1%)	41.5% (27.3–57.4%)
Vaccine	59	4.3% (3.1–6.0%)	0.5% (0.06–3.7%) **	0.8% (0.1–5.8%)
Routine check-up or physical	452	28.1% (24.6–31.8%)	16.1% (3.5–50.2%)	28.5% (16.7–44.2%)
Used any prescription drugs, past year	2,671	52.1% (49.8–54.4%)	58.6% (38.6–76.2%)	35.1% (27.8–43.2%) ***
Depressive mood score, past 7 days	4.2	4.0 (3.9–4.2)	5.4 (4.2–6.6) *	4.5 (3.9–5.1)
Ever diagnosed with depression	372	7.9% (6.9–9.0%)	22.8% (9.7–44.7%) **	4.6% (2.5–8.3%)
Ever sought care for suspected STD	875	14.6% (13.1–16.2%)	29.3% (15.4–48.6%) *	25.3% (17.4–35.3%) **
History of STD diagnosis, past year ^{^^}	233	3.7% (3.0–4.5%)	26.3% (12.2–47.7%) ***	7.2% (3.9–13.0%) *
History of urethral symptoms (discharge or dysuria), past year ^{††}	186	2.6% (2.0–3.3%)	76.7% (55.8–89.5%) ***	9.2% (5.4–15.2%) ***
Sexual behaviors				
Ever had vaginal intercourse	4,661	86.6% (85.0–88.1%)	72.6% (52.4–86.4%) *	93.9% (90.2–96.2%) ***
Age of vaginal intercourse debut, years ^{‡‡}	16.5	16.5 (16.4–16.7)	17.6 (16.4–18.7)	15.7 (15.4–16.1) ***
Years since vaginal intercourse debut ^{‡‡}	5.6	5.4 (5.1–5.6)	4.6 (3.5–5.8)	6.3 (5.8–6.7) ***
Vaginal intercourse partners, lifetime ^{‡‡}	7.2	7.1 (6.7–7.6)	3.8 (2.2–5.3) ***	8.7 (7.1–10.4)
Vaginal intercourse episodes, past year ^{‡‡}	73.5	75.1 (70.2–80.1)	97.3 (31.0–163.5)	53.0 (38.9–67.1) **
Identifies as homosexual or bisexual	141	2.2% (1.8–2.8%)	6.9% (1.5–26.6%)	1.9% (0.7–5.0%)
Ever paid someone for sex	266	4.0% (3.3–5.0%)	16.0% (6.3–35.2%) *	6.3% (3.4–11.2%)

* $p \leq 0.05$ ** $p \leq 0.01$

*** $p \leq 0.001$ for the χ^2 -test or adjusted Wald test compared to the referent group (men with neither symptoms nor pathogens detected); statistical testing not performed for urethral discharge or dysuria symptoms in the past 24 hours

^ Other characteristics that were evaluated but were not significantly associated with IU or urethral infections with recognized pathogens were: household income; recent antibiotic use (past 30 days); smoking; psychological or emotional counseling in the past year; cocaine, crystal methamphetamine, injection drugs or other drug use (*i.e.*, LSD, PCP, ecstasy, mushrooms, inhalants, ice, heroin, or prescription medicines not prescribed for the study participant) in the past year; participation in a drug or alcohol treatment program in the past year, or ever being a member of a 12-step drug or alcohol addiction recovery program; prior arrest; having had sex with an injection drug user or ever having been paid for sex. Among men reporting ever having had vaginal sex, the following characteristics were evaluated, with no significant differences detected: number of recent vaginal sex partners (past year); condom use during all episodes of vaginal sex in the past year; correct consistent use of condoms for vaginal sex in the past year (*i.e.*, always using condoms for vaginal sex and reporting no breakage or slippage); condom use at the most recent vaginal sex; and having had a vaginal sex partner with an STD in the past year.

† Idiopathic urethritis was defined as urethral discharge and/or dysuria in the past 24 hours and no detection of *N. gonorrhoeae* (NG), *C. trachomatis* (CT), *T. vaginalis* (TV), and *M. genitalium* (MG).

‡ Weighted percentages, means and 95% confidence intervals (CI) reflect the representative values and proportions in the target US population.

§ Respondents who were enrolled in school but on school break or vacation at the time of the interview are considered to be “in school”.

|| The primary reasons for seeking care were estimated among those who accessed care in the past 3 months.

¶ Depressive mood score was measured using nine items from the Center for Epidemiologic Studies Depression Scale [21] with higher scores representing higher levels of depressive symptoms. Possible range of scores is 0 to 27.

^^ History of STD diagnosis includes a history of nongonococcal urethritis, *N. gonorrhoeae*, *C. trachomatis*, *M. genitalium*, *T. vaginalis*, syphilis, genital herpes simplex virus, genital warts, human papillomavirus, HIV/AIDS, or “other” STD.

†† The question regarding urethral symptoms in the past year preceded the question about urethral symptoms in the past 24 hours, but did not explicitly exclude the previous 24 hours.

‡‡ These behavioral characteristics pertaining to vaginal intercourse were estimated among men who reported ever having had vaginal intercourse.

Table 2

Recent partnership-specific characteristics of young adult men aged 18 to 27 in the US associated with idiopathic urethritis and urethral infection with recognized pathogens (2001–2002)

Characteristic [^]	Unweighted	Weighted percentage (95% CI) [§]		
	count	No symptoms and no pathogens detected (referent group)	Idiopathic urethritis [‡]	Urethral infection (NG, CT, TV, or MG) [‡]
	N=4,192 [†]	n=3,876	n=38	n=278
Sociodemographic characteristics of most recent partner				
Male partner	98	2.1% (1.6–2.8%)	8.5% (1.8–32.2%)	1.5% (0.6–3.8%)
Partner Race				
White	2,616	72.8% (67.7–77.3%)	63.7% (41.1–81.6%)	42.4% (32.7–2.7%) ***
Black	709	12.6% (9.4–16.7%)	12.9% (3.4–38.3%)	33.5% (23.8–44.8%) ***
Asian/Pacific Islander	288	4.0% (2.8–5.7%)	7.4% (0.2–28.9%)	2.9% (1.3–6.3%)
Native American	141	3.5% (2.5–5.0%)	2.6% (0.4–16.0%)	6.7% (3.2–13.6%)
Partner Hispanic ethnicity	614	11.7% (9.1–14.8%)	11.9% (3.8–31.5%)	19.3% (11.7–30.1%) *
Partner has no high school diploma or equivalent	423	12.0% (10.2–14.2%)	29.6% (12.5–55.4%) *	18.3% (12.1–26.8%)
Sexual behavior characteristics of most recent partnership				
Vaginal intercourse with partner	3,737	93.6% (92.3–94.7%)	81.9% (59.2–93.4%) *	92.7% (87.5–95.8%)
// Wore condom during last episode	1,729	46.5% (43.6–49.5%)	79.4% (53.6–92.8%) **	47.9% (39.6–56.4%)
Insertive anal intercourse with partner	757	19.4% (17.4–21.6%)	19.2% (6.7–44.1%)	18.5% (13.0–25.7%)
// Wore condom during last episode	160	22.5% (17.8–27.9%)	44.0% (6.5–89.8%)	31.7% (16.3–52.5%)
Received oral sex from partner	3,175	80.9% (78.6–82.9%)	80.5% (59.8–92.0%)	69.6% (62.2–76.1%) ***
// Wore condom during last episode	60	2.1% (1.5–3.0%)	11.3% (1.6–50.4%)	2.6% (0.7–9.8%)
Performed oral sex on partner	2,811	71.6% (69.1–74.0%)	68.0% (46.6–83.8%)	56.9% (48.6–64.8%) ***

*
 $p \leq 0.05$

**
 $p \leq 0.01$, and

***
 $p \leq 0.001$ for the χ^2 -test compared to the referent group (men with neither symptoms nor pathogens detected)

[^] Other partnership-specific characteristics that were evaluated but not significantly associated with IU or urethral infection with recognized pathogens were: age of partner, partnership was current, respondent lived with partner, respondent was married to partner, partnership was casual, respondent suspects partner had concurrent partners, and respondent used a condom the first he had vaginal intercourse with his current/most recent partner.

[†] Among the subset of the population-based sample (77.0% [4,192 of 5,447]) who reported detailed sexual behavior data from recent partnerships

[‡] Idiopathic urethritis was defined as urethral discharge and/or dysuria in the past 24 hours and no detection of *N. gonorrhoeae* (NG), *C. trachomatis* (CT), *T. vaginalis* (TV), and *M. genitalium* (MG).

[§] Weighted percentages and 95% confidence intervals (CI) reflect the representative proportions in the target US population.

// Estimated among men who reported engaging in that particular sexual behavior with their current or most recent partner, within the past year.

Table 3

Factors independently associated with idiopathic urethritis and urethral infection with recognized pathogens among young adult men aged 18 to 27 in the US, 2001–2002[^]

Idiopathic urethritis [†] N=4,749		
	aOR (95% CI)	p-value
Race		
White	ref	--
Black	1.37 (0.50–3.75)	0.538
Asian/Pacific Islander/Native American	0.04 (0.01–0.18)	<0.001
Drinks alcohol at least 3 days per week	0.08 (0.03–0.24)	<0.001
Ever diagnosed with depression	2.94 (0.88–9.81)	0.079
STD diagnosis, past year	9.29 (3.00–28.73)	<0.001
Number of lifetime vaginal intercourse partners		
≥ 5 partners	ref	--
1–4 partners	7.51 (2.92–19.35)	<0.001
Zero partners	7.24 (1.91–27.44)	0.004
Identifies as homosexual or bisexual	1.77 (0.25–12.68)	0.568
Ever paid someone for sex	2.90 (0.64–13.14)	0.167
Urethral infection (NG, CT, TV, or MG) [‡] N=5,192		
	aOR (95% CI)	p-value
Race		
White	ref	--
Black	4.41 (3.20–6.06)	<0.001
Asian/Pacific Islander/Native American	1.35 (0.71–2.57)	0.354
Hispanic ethnicity	3.06 (1.88–4.98)	<0.001
In school at the time of the interview	0.66 (0.45–0.94)	0.024
Accessed health care, past 3 months	0.67 (0.46–0.97)	0.035
Used any prescription drugs, past year	0.71 (0.50–1.00)	0.050
Urethral symptoms, past year	3.61 (1.85–7.06)	<0.001
Age of vaginal intercourse debut		
≥ 17 years old	ref	--
≤ 16 years old	1.81 (1.29–2.54)	0.001
Never had vaginal intercourse	0.72 (0.40–1.29)	0.262

[^] The sample sizes indicated for the multivariable models include all study participants with sampling weights and data on all included covariates. Men with neither symptoms nor pathogens detected served as the referent group for both multivariable models presented.

[†] Idiopathic urethritis was defined as urethral discharge and/or dysuria in the past 24 hours and no detection of *N. gonorrhoeae*, *C. trachomatis*, *T. vaginalis*, and *M. genitalium*.

[‡] *N. gonorrhoeae* (NG), *C. trachomatis* (CT), *T. vaginalis* (TV), *M. genitalium* (MG)

Table 4
Sensitivity analysis estimating the potential impact of misclassification on prevalence estimates of idiopathic urethritis among young adult men aged 18 to 27 in the US, 2001–2002

Subgroup	Corrected weighted idiopathic urethritis prevalence (95% CI) for assumed sensitivity and specificity of outcome classification			
	1.0 sensitivity 1.0 specificity	0.70 sensitivity [^] 0.991 specificity	0.70 sensitivity 0.995 specificity	0.95 sensitivity 0.995 specificity
Overall	1.0% (0.7–1.4%)	0.07% (0.0–0.7%)	0.7% (0.2–1.3%)	0.5% (0.2–0.9%)
Region				
West	1.0% (0.4–2.2%)	0.1% (0.0–1.9%)	0.7% (0.0–2.4%)	0.5% (0.0–1.8%)
Midwest	0.6% (0.3–1.6%)	†	0.2% (0.0–1.6%)	0.1% (0.0–1.2%)
South	1.2% (0.7–1.9%)	0.4% (0.0–1.5%)	1.0% (0.4–2.0%)	0.7% (0.3–1.5%)
Northeast	0.9% (0.3–3.0%)	0.03% (0.0–3.0%)	0.6% (0.0–3.5%)	0.4% (0.0–2.6%)
Race				
White	1.0% (0.7–1.5%)	0.1% (0.0–0.9%)	0.7% (0.2–1.5%)	0.5% (0.2–1.1%)
Black	1.2% (0.5–2.7%)	0.4% (0.0–2.6%)	1.0% (0.04–3.2%)	0.7% (0.03–2.3%)
Asian/Pacific Islander	0.02% (0.003–0.1%)	†	†	†
Native American	0.08% (0.02–0.4%)	†	†	†
Hispanic ethnicity	1.1% (0.5–2.6%)	0.3% (0.0–2.4%)	0.8% (0.0–3.0%)	0.6% (0.0–2.2%)
Drinks alcohol at least 3 days per week	0.7% (0.02–0.18%)	†	†	†
Ever diagnosed with depression	2.8% (1.2–6.5%)	2.7% (0.4–8.1%)	3.3% (1.0–8.7%)	2.4% (0.7–6.4%)
STD diagnosis, past year	6.0% (2.7–12.8%)	7.4% (2.6–17.2%)	7.8% (3.2–17.7%)	5.8% (2.3–13.0%)
Number of lifetime vaginal intercourse partners				
≥ 5 partners	0.2% (0.1–0.5%)	†	†	†
1–4 partners	1.3% (0.8–2.1%)	0.5% (0.0–1.7%)	1.1% (0.4–2.2%)	0.8% (0.3–1.6%)
Zero partners	2.0% (0.9–4.3%)	1.6% (0.1–4.9%)	2.2% (0.6–5.5%)	1.6% (0.5–4.0%)
Identifies as homosexual or bisexual	2.8% (0.6–11.8%)	2.7% (0.0–15.7%)	3.3% (0.2–16.2%)	2.4% (0.1–11.9%)
Ever paid someone for sex	3.6% (1.5–8.3%)	3.9% (0.9–10.7%)	4.4% (1.4–11.2%)	3.2% (1.1–8.3%)

[^] Overall prevalence was greater than zero only when specificity was set at >0.99.

† Estimated prevalence was less than zero in this stratum.