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Prevalence of *Neisseria gonorrhoeae* Among Persons 14 to 39 Years of Age, United States, 1999 to 2008

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Abstract

Background: Prevalence estimates from population-based surveys do not suffer from the same biases as case-report and clinic positivity data and may be better to monitor sexually transmitted disease morbidity over time.

Methods: We estimated the prevalence of *Neisseria gonorrhoeae* in a nationally representative sample of persons aged 14 to 39 years participating in the National Health and Nutrition Examination Survey.

Results: From 1999 to 2008, the overall prevalence of gonorrhea was 0.27% (95% confidence interval, 0.13%–0.47%). In the 2005 to 2006 and 2007 to 2008 cycles, prevalence approached 0% and was based on too few positive sample persons to obtain reliable estimates. In 2004, most infections were found in 1 survey location.

Discussion: Given the low prevalence and geographic clustering of disease, gonorrhea estimates from national probability surveys are often imprecise and unstable. In 2008, gonorrhea testing in National Health and Nutrition Examination Survey was discontinued. Continued surveillance of gonorrhea should include case reporting and prevalence estimates from local surveys and sentinel surveillance systems.

Infection with *Neisseria gonorrhoeae* can cause adverse reproductive health outcomes including infertility[1] and can facilitate HIV transmission.[2] Although gonorrhea burden has decreased significantly since the 1970s, it is still the second most common nationally notifiable disease in the United States, with 309,341 infections reported in 2010.[3] Gonorrhea has pronounced racial disparities, with the reported case rate in blacks in 2010 more than 18 times the case rate among whites.[3] However, using case-report data to monitor trends in morbidity has challenges. Gonorrhea may be asymptomatic, particularly in females.[1] Increasing use of dual-diagnostic tests for chlamydia and gonorrhea combined with expanded chlamydia screening programs has likely increased the number gonococcal infections identified and reported independent of changes in prevalence. Conversely, increased prevention and control strategies, such as expedited partner therapy where sexual

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partners of patients diagnosed as having gonorrhea are treated presumptively without clinical evaluation, may have led to a decrease in the number of infections identified and reported. Although poorly documented, rates of reporting detected infections likely vary by source of care and associated demographic factors, which change over time. Consequently, trends in case-report data are difficult to interpret.

To supplement national gonorrhea case-report data, trends in positivity data from patients tested for gonorrhea in sentinel sites including family planning, sexually transmitted disease (STD) and prenatal clinics are monitored.[3–6] Although clinic positivity may be a reasonable approximation of clinic prevalence,[7] it is likely an overestimate of prevalence in the general population because patients may be motivated to seek care because of symptoms or increased risk for gonorrhea (e.g., they have a partner with gonorrhea). In addition, trends in clinic positivity are influenced by changes in screening criteria, as well as changes in the population seeking care.[8] Prevalence estimates from special populations such as entrants to the National Job Training Program (NJTP) are also used to monitor morbidity,[3,9] but these estimates may not be representative of the general population. Thus, data from nationally representative surveys may be useful to better characterize the prevalence of gonorrhea in the US general population and to monitor trends in morbidity over time.

To provide nationally representative prevalence estimates, the National Health and Nutrition Examination Survey (NHANES) began testing participants for *N. gonorrhoeae* in 1999. An earlier report provided prevalence estimates from data collected from 1999 to 2002.[10] Here we report estimates of gonorrhea from 5 cycles of NHANES (1999–2008), examining temporal trends and reporting estimated prevalence by age, sex, and race/ethnicity.

METHODS

The NHANES is a series of cross-sectional, household surveys collected in 2-year cycles using a complex, multistage, probability sampling design to select participants representative of the US civilian, noninstitutionalized population. National Health and Nutrition Examination Survey samples from 12 to 15 geographic locations per year; locations may vary from cycle to cycle. Low-income persons, Mexican Americans, non-Hispanic blacks, and adolescents (oversampled from 1999 to 2006 only) were sampled at higher frequencies to improve stability of estimates for these subpopulations. Participants 18 years or older provided written informed consent. For participants younger than 18 years, parents provided written consent along with minor's assent. Data from participants collected during five 2-year cycles (1999–2008) were analyzed. The study protocol was reviewed and approved by an institutional review board at the Centers for Disease Control and Prevention.

Participants were interviewed and examined. Urine from participants aged 14 to 39 years was tested for *N. gonorrhoeae* by nucleic acid amplification tests.[11] From 1999 to 2002, Abbott Laboratories' (Abbott Park, IL) LCx assay and, thereafter, the Becton Dickinson's (Franklin Lakes, NJ) BDProbeTec assay were used according to the manufacturers' instructions. Protocols for specimen testing and test result notifications have been described in a previous report.[10]

We report the estimated prevalence of gonorrhea by age, race/ethnicity, and sex with corresponding 95% confidence intervals (CIs). Estimates were weighted to be nationally representative and to account for oversampling and nonresponse. Prevalence estimates with relative standard errors (RSEs) of more than 30%[12] or based on less than 10 positives persons are noted and are considered unstable and should be interpreted with caution. We anticipated low estimated prevalence and small sample sizes based on findings from an earlier report.[10] Given that we would likely be underpowered to detect statistical differences in subpopulations and in trends over time, we did not conduct statistical tests. Instead we provide 95% CIs as measures of precision of estimates.[13] SAS-callable SUDAAN v10.0 (RTI International, Research Triangle Park, NC) was used to account for the complex survey design when calculating standard errors.

RESULTS

Among the 20,836 participants aged 14 to 39 years selected to participate in NHANES from 1999 to 2008, 17,190 (83%) were interviewed and 15,885 (92% of those interviewed) were examined and tested for gonorrhea for an overall response rate of 76%.[14] In the 1999 to 2000 cycle, 21 infections were identified among the 3145 participants sampled, a weighted prevalence of 0.25% (95% CI, 0.10%–0.49%; RSE, 31%). Prevalence was similar in 2001 to 2002, with 15 infections found among 3487 participants (weighted prevalence, 0.20%; 95% CI, 0.08%–0.42%; RSE, 31%). Prevalence was highest in the 2003 to 2004 cycle (0.74%; 95% CI, 0.18%–1.99%; RSE, 49%) based on 27 infections among 3211 participants; however, 9 of the 13 infections detected in 2004 were found in 1 survey location, which resulted in an increased variance as indicated by the large 95% CI. In the 2005 to 2006 and 2007 to 2008 cycles, prevalence approached 0% and was based on too few positive sample persons (n = 7 and n = 2, respectively) to obtain reliable estimates. Although prevalence seemed to decrease over time, it was not possible to reliably estimate a percent decrease, given the instability of the estimates in the last 2 survey cycles.

Over the 10-year period, the overall weighted prevalence of gonorrhea among males and females aged 14 to 39 years was 0.27% (95% CI, 0.13%–0.47%; Fig. 1). Prevalence among females was 0.34% (95% CI, 0.16%–0.57%). Among persons aged 14 to 25 year, prevalence was 0.40% (95% CI, 0.20%–0.72%). Prevalence among non-Hispanic black males and females was 0.83% (95% CI, 0.56%%–01.20%) and was 0.18% (95% CI, 0.05%–0.44%; RSE, 44%) among males and females of other races/ethnicities. Among 14 to 25 year olds, prevalence was 1.82% (95% CI, 1.07%–2.89%) among non-Hispanic black females and was 0.31% (95% CI, 0.11%–0.70%; RSE, 42%) among females of other races/ethnicities.

DISCUSSION

Currently, NHANES is the only nationally representative data source for gonorrhea prevalence in adults and adolescents. Findings from the 1999 to 2008 surveys document low overall national prevalence of infection (<0.5%) and significant racial disparities. The racial disparity was especially pronounced among young females. These data supplement national case-report data, as well as positivity and prevalence estimates from screened populations.

Not surprisingly, the estimated national prevalence among females was lower than positivity found in STD clinics (state-specific median of 7% in 2000)[4] and in family planning clinics (state-specific median of 1.3% in 2005–2007).[5] The estimated prevalence in NHANES among 14- to 25-old-year males and females (0.40%; 95% CI, 0.20%–0.72%) is similar to the estimated 0.43% (95% CI, 0.29%–0.63%) prevalence among 18 to 26 year olds in the National Longitudinal Study of Adolescent Health in 2001 to 2002, a population-based survey of young adults.[15] Prevalence of gonorrhea among entrants to the NJTP, a vocational program for socioeconomically disadvantaged youth aged 16 to 24 years, is generally higher than estimates from population-based surveys. In 2004, the prevalence among male NJTP entrants was 1.3% and was 2.6% among female entrants.[9] However, the suggested decrease in prevalence over time in NHANES is similar to trends in prevalence among NJTP entrants. From 2004 to 2009, the odds of testing positive for gonorrhea decreased by 50% among female NJTP entrants and by 40% among male NJTP entrants.[9]

Using population data from the midpoint in the NHANES study period (2003/2004),[13] an overall prevalence of 0.27% (95% CI, 0.13%–0.47%) translates to approximately 275,000 prevalent infections (range, 135,000–489,000) among persons aged 14 to 39 years. Although symptom presence is not captured in NHANES, it is likely that most infections identified in NHANES were asymptomatic. From 1999 to 2008, there was an average of 314,000 cases of gonorrhea reported annually to Centers for Disease Control and Prevention among persons aged 15 to 39 years (range, 294,000–326,000).[3] However, estimated prevalence and reported case counts are not directly comparable because case reports include both incident and prevalent infections. As such, reported case counts are expected to be higher than estimated prevalence in population surveys.

The diagnostic tests used to test for *N. gonorrhoeae* in NHANES are not 100% sensitive or specific, which may result in biased prevalence estimates. In particular, a low positive predictive value could result in overestimation of prevalence. There was a change in assay used (LCx was used from 1999 to 2002 and ProbeTec from 2003 to 2008). Both assays were cleared by the Food and Drug Administration for identification of gonococcal infection and, as such, have some degree of equivalence. No published studies directly compare the test performance characteristics of these assays; however, one study compared each with a third standard.[16] In this study, ProbeTec had similar sensitivity and specificity to LCx. Although less pronounced than in case-report data, significant racial disparities exist with gonorrhea prevalence in non-Hispanic blacks higher than in other race/ethnic groups. Similar disparities have been noted in both the NJTP and clinic positivity data.[5,9] Continued, targeted prevention and control efforts including screening and partner services to ensure partners are appropriately treated are needed to reach those most at risk. Because NHANES data are not available at the local level, targeting may need to be based on local case-based surveillance.

Prevalence estimates in NHANES do not suffer from the same biases as case-report data, such as differential case ascertainment based on differences in health care–seeking behavior, screening, and reporting practices, and as such may be better to monitor disease burden over time.[8] However, we document that estimates from national probability surveys can be imprecise and may not reliably estimate low-prevalence diseases. In the last 2 survey cycles

of NHANES, very few infections were identified, and we were not able to reliably calculate prevalence estimates for those years. Consequently, we could not statistically examine temporal trends over the 5 cycles or quantify a change in prevalence. Although the low prevalence in the last 2 survey cycles suggests that prevalence may be declining, we are limited in our inference given the limits of the data. To provide age, sex, and race/ethnicity specific estimates, we assumed homogeneity across cycles and combined data from 10 years. Still, many estimates had wide CIs.

The NHANES data are not available by region or state. Because gonorrhea is a geographically clustered disease,[3] national estimates may fail to uncover important differences by region. In addition, clustering of disease can affect national prevalence estimates. The NHANES samples participants from different geographic locations each year independent of disease burden. Inadvertently sampling locations with high gonorrhea prevalence or finding a cluster can inflate national point estimates. Conversely, if only low-prevalence areas are sampled, national estimates may look misleadingly low.

The NHANES is nationally representative, but the sample size is not sufficient to adequately assess important differences among subpopulations. Given the continued emergence of antibiotic-resistance gonorrhea,[17] particularly among men who have sex with men (MSM), it is important to monitor trends in gonorrhea morbidity in MSM. Although sexual behavior and sexual identity data are captured in NHANES, we were not able to estimate prevalence among MSM, given the small sample size and low prevalence. Sentinel surveillance could be useful to provide this information. For example, the STD Surveillance Network (SSuN) provides enhanced data on gonorrhea positivity among MSM screened in selected STD clinics, as well as from enhanced data from a representative sample of reported cases.[3,6,18]

Although population prevalence estimates are valuable for monitoring gonorrhea, given the limitations of NHANES for monitoring low-prevalence diseases, testing for *N. gonorrhoeae* was halted at the end of 2008. Caution is needed when interpreting estimates based on existing data. National Health and Nutrition Examination Survey contains extensive data on the social and demographic characteristics of participants (e.g., health insurance status) and measures of self-reported sexual behaviors (e.g., number of sexual partners); however, given the small sample size and low prevalence of gonorrhea, subpopulation estimates would be unreliable and possibly misleading. Careful consideration must be given to the stability of the estimates when reporting prevalence estimates. Although NHANES is no longer used to monitor gonorrhea burden, it continues to be useful to population-based surveillance of other STDs such as Chlamydia trachomatis, human papillomavirus, and herpes simplex virus.[19–21]

Despite the limitations of the data, gonorrhea testing in NHANES from 1999 to 2008 document low estimated population prevalence and significant racial disparities. Currently, no other nationally representative survey contains testing for *N. gonorrhoeae*. Continued surveillance of gonorrhea morbidity is needed and should include case reporting, as well as prevalence estimates from local surveys and sentinel surveillance systems.

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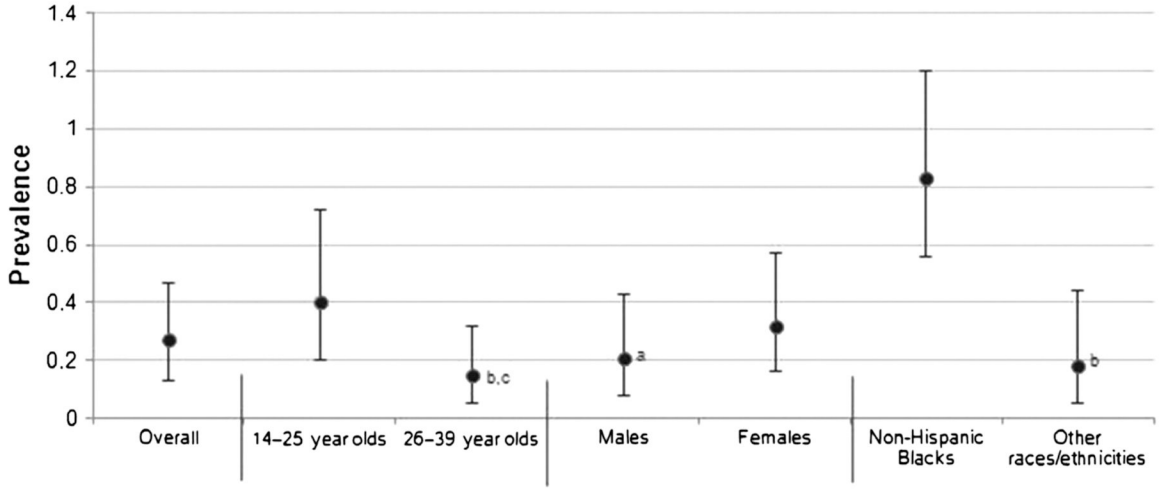

Figure 1.

Prevalence of *N. gonorrhoeae* among 14 to 39 year olds by age, sex, and race/ethnicity, NHANES, United States, 1999 to 2008. Estimates with RSEs more than 30% or based on less than 10 positive sampled persons are considered unstable and should be interpreted with caution. Bars are 95% CIs. A, RSE more than 30% but less than 40%. B, RSE of 40% or more but less than 50%. C, Numerator less than 10 positive sample persons.