

**Data Inputs Supplement**  
**Estimates of the Prevalence and Incidence of**  
**Chlamydia and Gonorrhea Among US Men and Women, 2018**

**Description of the Parameters and Associated Inputs Included in Chlamydia and**  
**Gonorrhea Prevalence and Incidence Models**

***Population Size ( $N$ )***

For the population size estimates, we used data from the United States (US) Census Bureau's American Community Survey (ACS) representing the full resident population of the US in 2018. (1) Based on these data, there were 22.1 and 21.0 million male and female US residents aged 15–24 years and 33.8 and 33.2 million male and female US residents aged 25–39 years in 2018. The use of these population data incorporated two assumptions. First, we assumed the data are normally distributed and that there was no variability. Second, we assumed that the population size was constant and stable throughout the year and that these estimates reflected the population size at the midpoint of 2018.

***Number of Case Reports ( $\kappa$ )***

Based on national sexually transmitted infection (STI) case report data reported to the Centers for Disease Control and Prevention (CDC) in 2018, there were 306,110 and 779,367 chlamydia cases reported in men and women aged 15–24 years, respectively. (2) Among men and women aged 25–39 years, there were 246,601 and 318,246 cases reported, respectively. Likewise, there were 116,427 and 132,291 gonorrhea cases reported in men and women aged

15–24 years, respectively. Among men and women aged 25–39 years, there were 167,134 and 90,786 gonorrhea cases reported, respectively.

Various factors should be considered when interpreting chlamydia and gonorrhea case report data. These data reflect only those infections diagnosed and reported to the CDC. Also, given the current inability of case report data to adequately capture all anatomic sites of infection of a reported case, we assumed they represented urogenital infections only and excluded infections at extragenital sites, such as the rectum and oropharynx. As a result, the full burden of chlamydia and gonorrhea is underestimated due to the exclusion of infections at these anatomic sites. In addition, as these data represent case reports received, no uncertainty was assumed.

### ***Case Reporting Fraction ( $\rho$ )***

The case reporting fraction represents the proportion of all diagnosed cases that are reported to CDC. There is no system in place to measure case reporting completeness and no data were available to inform our estimates. Because chlamydia and gonorrhea are reportable conditions in all states and the District of Columbia (i.e., all positive laboratory results are sent to public health authorities), we felt it reasonable to assume reporting was high throughout the study period. Reporting has also improved in recent years as electronic laboratory reporting has expanded and STI surveillance systems have become increasingly automated. We acknowledged that reporting is less than 100% due to transmission and/or data entry errors, as some laboratories continue to report via paper and fax, but we assumed that the reporting fraction was likely near 100% due to the issues described above. We also assumed that the case

reporting fraction was uniformly distributed and did not vary by sex, age group, or disease. Therefore, we assumed a case reporting fraction of 95.0% (25<sup>th</sup> percentile [Q1]=93.7%, 75<sup>th</sup> percentile [Q3]=96.2%) for both chlamydia and gonorrhea. These estimates are consistent with the predominant assumptions being made in the literature. (3)

### ***Proportion of Cases that are Asymptomatic ( $\beta$ )***

Though infections due to chlamydia and gonorrhea can exist in one of two states, either symptomatic or asymptomatic, most infections are typically without symptoms and the proportion varies by sex. To quantify this for use in the models, we used data from one manuscript that estimated that 83.9% (Q1=80.6%, Q3=87.1%) of men and 74.5% (Q1=71.6%, Q3=77.5%) of women infected with chlamydia, and 41.3% (Q1=31.8%, Q3=51.1%) of men and 68.4% (Q1=61.8%, Q3=74.2%) of women infected with gonorrhea are asymptomatic. By using these data we assumed that the proportion of cases that are asymptomatic did not vary by age group and also that the subjects from the study from which these numbers were drawn, which was a convenience sample of people aged 18–29 years in New Orleans, were representative of all people infected with chlamydia and/or gonorrhea. (4)

### ***Annual Background Screening Rate ( $\sigma$ )***

We estimated the annual background screening rate for chlamydia and gonorrhea using data from the 2015–2017 cycle of the National Survey of Family Growth (NSFG). (5) Based on these data, we estimated that 14.4% (Q1=13.5%, Q3=15.3%) of men and 27.3% (Q1=26.1%, Q3=28.4%) of women aged 15–24 years were screened for chlamydia and gonorrhea in 2018.

Likewise, we estimated 17.6% (Q1=16.5%, Q3=18.7%) of men and 31.1% (Q1=30.0%, Q3=32.3%) of women aged 25–39 years were screened for chlamydia and gonorrhea in 2018.

The use of these data came with several assumptions. First, we assumed the data were normally distributed. Second, we assumed that background screening was constant and stable throughout the cycle, that these estimates reflected the background screening percent at the midpoint of the cycle, and that the estimates from NSFG 2015–2017 were applicable to 2018. Third, we assumed that if a person was screened for chlamydia, they were also screened for gonorrhea, and hence the annual background screening rate was equal for both. Lastly, these estimates are based on self-reported data, which are inherently subject to recall bias. The question asked of women was: “In the last 12 months, have you been tested for chlamydia?” This question assumed that the rate of testing (typically for diagnostic purposes among symptomatic persons) was reflective of the rate of background screening in (typically asymptomatic) women. The question asked of men was: “In the past 12 months, have you been tested for a sexually transmitted disease like gonorrhea, chlamydia, herpes, or syphilis?” This question assumed that the rate of background screening in men was equivalent to the rate of testing for all STIs in men.

#### ***Point Prevalence (P): Chlamydia***

Chlamydial point prevalence estimates were calculated using data from the 2015–2018 cycles of NHANES. (6, 7) NHANES is a cross-sectional, complex, multistage survey designed to be representative of the noninstitutionalized civilian population. Participants undergo a medical examination as part of their participation and voluntary chlamydia testing is a part of this

examination. During NHANES 2015–2018, a total of 4,896 persons aged 15–39 years were interviewed and had a medical examination (overall response rate: 58.0%) and 4,756 (97.1%) provided a urine specimen for chlamydia testing, the results of which were the focus of these analyses. Stratifying by age group, 2,246 and 2,650 persons aged 15–24 and 25–39, respectively, underwent the medical examination (response rates: 59.7% and 56.5%) and 2,178 (96.9%) and 2,578 (97.3%) provided a urine specimen for chlamydia testing, respectively.

We summarized age- and sex-specific point estimates by calculating the prevalence of chlamydia and associated relative standard error (RSE) for each subpopulation. The mobile examination center weights were combined across the 2015–2016 and 2017–2018 NHANES cycles to generate estimates of greater statistical reliability and we used the combined weights in addition to SAS-callable SUDAAN procedures to account for the complex survey sampling design. We then generated a probability distribution around the NHANES point prevalence estimates for each subpopulation to generate the median prevalence of chlamydia by sampling from a normal distribution with mean equal to the point estimate and standard deviation equal to the point estimate \* RSE. The use of NHANES data came with several assumptions. First, we assumed a normal distribution of the NHANES 2015–2018 data. Second, as chlamydia testing is performed on urine specimens in NHANES, these estimates represented urogenital infections only and excluded extragenital sites, such as the rectum or oropharynx. These estimates also did not account for infections in anyone younger than 15 and older than 39 years of age. Third, by applying the prevalence estimates from NHANES, which are representative of the US non-institutionalized civilian population, to the ACS full resident population estimates to calculate the number of prevalent infections, we assumed that the prevalence of chlamydia in the

institutionalized and military population was equivalent to the prevalence in the non-institutionalized population. Fourth, by combining the 2015–2016 and 2017–2018 NHANES cycles, we assumed that the prevalence was constant and stable across the cycles and that these estimates reflected the prevalence of chlamydia at the midpoint of the estimation period. Lastly, given the availability of chlamydia prevalence data from NHANES and the need to incorporate the prevalence data into the incidence model, the point prevalence of chlamydia was both an input and an output.

### ***Antimicrobial Resistant Gonorrhea***

We estimated the number of prevalent and incident AMR gonococcal infections using data from the Gonococcal Isolate Surveillance Program (GISP), which is the national sentinel surveillance system established in 1986 for AMR gonorrhea surveillance in the US. (8) This system collects gonococcal isolates from STI clinics around the US and performs susceptibility testing to evaluate resistance trends over time. (8)

In 2018, GISP performed susceptibility testing for ceftriaxone, cefixime, azithromycin, ciprofloxacin, penicillin, and tetracycline. When available, resistance breakpoints defined by the Clinical Laboratory and Standards Institute (CLSI) were used. When unavailable, isolates with elevated minimum inhibitory concentrations (MICs) were defined by GISP. (9) We used the following criteria to identify isolates as resistant or having elevated MICs:

- Ceftriaxone: MIC  $\geq 0.125$   $\mu\text{g/ml}$ , elevated MIC
- Cefixime: MIC  $\geq 0.25$   $\mu\text{g/ml}$ , elevated MIC
- Azithromycin: MIC  $\geq 2.0$   $\mu\text{g/ml}$ , elevated MIC

- Ciprofloxacin: MIC  $\geq 1.0$   $\mu\text{g/ml}$ , resistance
- Penicillin: MIC  $\geq 2.0$   $\mu\text{g/ml}$ , resistance
- Tetracycline: MIC  $\geq 2.0$   $\mu\text{g/ml}$ , resistance.

Using GISP data, it was estimated that 51.3% of all gonococcal infections in 2018 demonstrated resistance or elevated MICs to  $\geq 1$  antimicrobial tested. (2) We then multiplied the total number of prevalent and incident gonococcal infections by this proportion to calculate the number of prevalent and incident AMR gonococcal infections for 2018. Of note, the only currently recommended drug to treat gonorrhea is ceftriaxone; 0.2% of all gonococcal infections in GISP demonstrated elevated MICs to ceftriaxone in 2018. (2, 10)

### ***Rate of Natural Clearance ( $\psi$ )***

Informed by data from the literature, we calculated the rate of natural clearance of chlamydia and gonorrhea among asymptotically infected people as:

$$\frac{\text{\# of people with an asymptomatic chlamydial or gonococcal infection with natural clearance}}{\text{Total person-time contributed}}$$

For chlamydia, non-parametric bootstrapping techniques were used to resample data from the literature to generate distributions of the time to natural clearance (10,000 trials), and as a result, uncertainty estimates (25<sup>th</sup> and 75<sup>th</sup> percentiles) around that estimate. This yielded a sample of 131 men and 601 women, with a total person time of 19.8 person-years for men and 251.3 person-years for women. (11-19) For gonorrhea in women, data were based on nucleic acid amplification testing (NAATs) and only included a sample of 16 women with a total person-

time of 1.26 person-years. (20) We found gonococcal natural clearance data for men only in studies conducted in 1974 and both were based on culture, Gram stain, or fluorescent antibody tests. (21, 22) Given the use of outdated and less sensitive diagnostic test technology in these studies, we used the more recent study based on NAAT testing done solely in women and made the assumption (based on expert opinion) that men naturally clear gonorrhea twice as fast as women. Because of the small sample size, rather than bootstrapping, we sampled from a gamma distribution with resulting median similar to the study. (20) Specifically, we sampled from a gamma distribution with shape parameter=16 and rate=16/4.089 to generate a distribution of natural clearance in women; for men, we assumed the rate was twice as fast, also sampling from a gamma distribution. Based on these inputs, estimates of the rate of and days to natural clearance for chlamydia and gonorrhea, by sex, are presented in **Supplemental Table 1**.

**Supplemental Table 1.** Rate of and days to natural clearance of untreated *Chlamydia trachomatis* and *Neisseria gonorrhoeae*, by sex.

|           | Sex   | Median<br>(25 <sup>th</sup> –75 <sup>th</sup> percentile) |                           |
|-----------|-------|-----------------------------------------------------------|---------------------------|
|           |       | Rate                                                      | Days                      |
| Chlamydia | Men   | 1.01<br>(0.86–1.16)                                       | 361.35<br>(313.90–423.40) |
|           | Women | 0.92<br>(0.87–0.97)                                       | 397.85<br>(375.95–416.10) |
| Gonorrhea | Men   | 8.02<br>(6.71–9.47)                                       | 45.54<br>(38.56–54.44)    |
|           | Women | 4.00<br>(3.36–4.72)                                       | 91.25<br>(77.33–108.63)   |

There were a variety of assumptions that factored into these calculations. First, we assumed that the natural clearance of chlamydia or gonorrhea did not vary by age group or by anatomic



site of infection (urogenital vs. extragenital). Second, we assumed a constant exponential clearance rate from available data. Third, we assumed that the subjects in the studies from which these numbers were drawn were representative of all people infected with chlamydia and/or gonorrhea. Lastly, we assumed that the diagnostic tests used in different studies to identify chlamydial infections had equal sensitivity and specificity, eliminating the introduction of any possible diagnostic biases between studies.

### ***Rate of Symptomatic Treatment Seeking ( $\tau$ )***

Among symptomatic people, we estimated the rate of seeking treatment as a function of multiple inputs. These included the probability of a person never seeking treatment ( $\zeta$ ), the time from infection acquisition to symptom onset ( $d_1$ ), and time from symptom onset to testing due to symptoms ( $d_2$ ). These were combined as:  $\tau = (1 - \zeta) / (d_1 + d_2)$ . Note that  $\zeta$  does not represent the proportion of symptomatic infections that never receive treatment, as this would be given by  $(\sigma + \tau) / (\sigma + \tau + \psi)$ .

We used estimates from the literature for incubation period to estimate  $d_1$ . (23) For chlamydia, this was 13.8 days (Q1=9.7 days, Q3=17.9 days) in men and 25 days (Q1=17.4 days, Q3=32.2 days) in women. For gonorrhea, this was 6.2 days (Q1=4.3 days, Q3=8.1 days) in men and 11.2 days (Q1=7.9 days, Q3=14.6 days) in women. To estimate  $d_2$ , we used unpublished data from the STD Surveillance Network (PS13-1306, 2016–2018) summarizing time from symptoms to testing (among those who sought treatment); these data were specific to gonorrhea, but we assumed they also applied for chlamydia. In men, this was 6.5 days (Q1=6.4 days, Q3=6.6 days); in women, this was 13.9 days (Q1=13.7 days, Q3=14.1 days). To estimate

(1-  $\zeta$ ), we used data from Farley et al, which found that only a fraction of symptomatic people never sought treatment due to their urogenital symptoms: 20.8% (Q1=19.3%, Q3=22.3%). (4) Non-parametric bootstrapping techniques were used to resample data for  $d_2$ , while uniform and beta distributions were sampled from for  $d_1$  and  $\zeta$ . Based on these inputs and calculations, estimates of the rate ( $\text{year}^{-1}$ ) of and days to symptomatic treatment seeking for chlamydia and gonorrhea, by sex, are presented in **Supplemental Table 2**.

**Supplemental Table 2.** Rate of and days to symptomatic treatment seeking for infections due to *Chlamydia trachomatis* and *Neisseria gonorrhoeae*, by sex.

|           | Sex   | Median<br>(25 <sup>th</sup> –75 <sup>th</sup> percentile) |                     |
|-----------|-------|-----------------------------------------------------------|---------------------|
|           |       | Rate                                                      | Days                |
| Chlamydia | Men   | 14.3<br>(11.9–17.9)                                       | 25.5<br>(20.4–30.7) |
|           | Women | 7.4<br>(6.2–9.2)                                          | 49.4<br>(39.7–58.9) |
| Gonorrhea | Men   | 22.6<br>(19.8–26.4)                                       | 16.2<br>(13.8–18.4) |
|           | Women | 11.5<br>(10.1–13.3)                                       | 31.8<br>(27.5–36.2) |

## Criteria for Rating the Strength of Inputs for Model Parameters

The following describes the rating scale used to determine the strength of the inputs used for model parameters.

**Supplemental Table 3.** Criteria for Rating the Strength of Inputs for Model Parameters.\*

| Strength of Input | Criteria                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
|-------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| I (good)          | <p><b>Input estimate based on...</b><br/>           Consistent results from well-designed, well-conducted nationally representative studies<br/> <b>OR</b><br/>           Complete national reporting</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| II (fair)         | <p><b>Input estimate based on...</b><br/>           Consistent and geographically widespread data from convenience samples<br/> <b>OR</b><br/>           Consistent and geographically widespread, although incomplete, national reporting<br/> <b>OR</b><br/>           Extrapolations and assumptions based on representative national studies or consistent, although incomplete, national reporting</p> <p>Confidence in the input estimate may be constrained by such factors as: the number, size, or quality of individual studies; inconsistency of findings across individual studies; and limited generalizability of findings to general population.</p> |
| III (poor)        | <p><b>Input estimate based on...</b><br/>           Inconsistent or unstable estimates from nationally representative studies<br/> <b>OR</b><br/>           Incomplete national data<br/> <b>OR</b><br/>           Inconsistent data from small convenience samples<br/> <b>OR</b><br/>           Rough extrapolations, expert opinion</p> <p>Evidence is insufficient because of limited number or size of studies; important flaws in study design or methods; and findings that are not generalizable to general population.</p>                                                                                                                                 |

\* Rating scale adapted from (24, 25).

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