2022 North Carolina STD Surveillance Report

HIV/STD/Hepatitis Surveillance Unit Division of Public Health North Carolina Department of Health and Human Services October 2023





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https://epi.publichealth.nc.gov/cd/stds/figures.html

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About the Contents of This Report

This document, the 2022 North Carolina STD Surveillance Report, includes summary tables of surveillance reports and other information for chlamydia, gonorrhea, and syphilis. In some instances, total numbers of reports may not agree between separate cross-tabulations due to missing values for some variables.

Detailed data tables of chlamydia, gonorrhea, and syphilis by county of diagnosis/residence and demographics can be found in the 2022 North Carolina STD Surveillance Data Tables excel file. This excel file can be downloaded from the Annual Reports page (https://epi.dph.ncdhhs.gov/cd/stds/annualrpts.html).

Rates are presented by age group, gender, race, and ethnicity for each disease and are expressed as cases per 100,000 population. Public health reporting data for chlamydia and gonorrhea cases primarily come from paper and electronic laboratory reports where transgender information is very incomplete. Therefore, we present only male/female gender for chlamydia and gonorrhea. Cases with a reported race of "other" were included in the unknown race category. Rates are also presented for counties across the state and are expressed as cases per 100,000 population. Rates are not available for unknown/unspecified categories (including age, gender, race, and ethnicity). Beginning with the 2021 Annual Report, rate denominators were estimated using the Census demographic population estimates for 2021 from the Census Bureau's Population Estimates Program (PEP). In this report, 2021 population estimates were used to calculate rates for both 2021 and 2022. More information about Census Population and Housing Estimates is available on the Census website (https://www.census.gov/programs-surveys/popest/data/special-tab/content.html). Use of these

population denominators enabled calculation of rates for the multiple race category.

Rates that are based on a small number of cases (fewer than 10) should be viewed with caution and are considered unreliable because these rates have large standard errors and can vary widely with small changes in case numbers. Data are suppressed in this document for table cells with a population denominator less than 500, according to the North Carolina Department of Health and Human Services, Division of Public Health Communicable Disease Branch data release guidelines.

*Please note that 2020 data should be treated with caution due to the impact of the COVID-19 pandemic on accessing STD testing, STD treatment, and surveillance activities in North Carolina.

Data Source: North Carolina Electronic Disease Surveillance System (NC EDSS) (data as of July 1, 2023) unless otherwise specified.

Bacterial and Other STDs in North Carolina Overview

Reportable Sexually Transmitted Diseases (STDs) in North Carolina

In North Carolina, eight bacterial sexually transmitted conditions (STDs) are reportable by law (10A NCAC 41A .0101) to the North Carolina Department of Health and Human Services (North Carolina DHHS).¹ Statewide surveillance information, such as patient demographics, diagnosis date, and treatment information, is collected by the local health departments and sent to the Communicable Disease Branch, within North Carolina DHHS. Local health departments are required to report bacterial STDs to the North Carolina DHHS according to the following schedule:

| Within 24 hours | Within seven days |
|---------------------|-----------------------------------|
| Chancroid* | Chlamydia* |
| Gonorrhea* | Lymphogranuloma venereum |
| Granuloma inguinale | Nongonococcal urethritis (NGU) |
| Syphilis* | Pelvic inflammatory disease (PID) |

*The conditions with asterisks are nationally notifiable to the Centers for Disease Control and Prevention.

Human papillomavirus (HPV), genital herpes, Mycoplasma genitalium, and trichomoniasis are non-reportable STDs in NC that impact North Carolinians.

| Bactorial STDs | G | Total* | |
|-----------------------------------|--------|--------|---------|
| Bacterial 31DS | Men | Women | Total |
| Chlamydia | 21,969 | 42,687 | 64,657 |
| Gonorrhea | 14,664 | 12,203 | 26,867 |
| Syphilis | | | |
| Primary Syphilis | 809 | 172 | 981 |
| Secondary Syphilis | 1,121 | 343 | 1,464 |
| Early Non-Primary, Non-Secondary | 1,304 | 374 | 1,678 |
| Late or Unknown duration Syphilis | 1,579 | 735 | 2,314 |
| Congenital Syphilis** | | | 57 |
| Nongonococcal urethritis (NGU) | 1,823 | 8 | 1,836 |
| Pelvic inflammatory disease (PID) | | 197 | 197 |
| Chancroid | 1 | 0 | 1 |
| Granuloma Inguinale | 0 | 0 | 0 |
| Lymphogranuloma venereum | 1 | 0 | 1 |
| Total | 43,271 | 56,719 | 100,054 |

Table A. NC Reportable Bacterial Sexually Transmitted Diseases (STDs) by Gender, 2022

*Total includes cases with missing gender.

**Congenital syphilis cases are not broken down by gender per the Communicable Disease Branch data confidentiality policy. Data Source: North Carolina Electronic Disease Surveillance System (data as of July 1, 2023).

¹North Carolina Office of Administrative Hearings (2019). Chapter 41: Epidemiology Health. Accessed July 2, 2019. Retrieved from <u>http://reports.oah.state.nc.us/ncac.asp?folderName=\Title%2010A%20-%20Health%20and%20Human%20Services\Chapter%2041%20-</u> %20Epidemiology%20Health.

Chlamydia

Chlamydia is the **most commonly reported sexually transmitted disease** in North Carolina and the United States.



Caused by the bacterium *Chlamydia trachomatis*.

| İ | |
|---|--|
| | |
| | |

Easily treated by antibiotics.



Most individuals are asymptomatic; symptoms include discharge and painful urination. Untreated chlamydial infection can cause severe damage to the female reproductive tract, including infertility and pelvic inflammatory disease in women.



Chlamydia and other STDs appear to increase susceptibility to human immunodeficiency virus (HIV) infection via inflammation, which increases the concentration of cells targeted by HIV in genital regions.



The CDC and NC DHHS recommend chlamydia screening for all sexually active women under 25 years of age, as well as all pregnant women and women \geq 25 years of age with risk factors (such as new or multiple sex partners).



No comparable screening programs exist for young men. As a result, chlamydia reporting is highly biased with respect to gender, with a higher number of cases detected and reported for women.

Chlamydia Disease Trends

| 2022 Summary | | |
|---|--|---|
| Number of cases | | 64,657 |
| Rate (per 100,000 population) | | 612.8 |
| Percent change from 2021 | | -0.8% |
| Mean age (in years) | | 25 |
| Gender | Number (%) | Rate |
| Male | 21,969 (34.0) | 426.1 |
| Female | 42,687 (66.0) | 791.2 |
| Unknown | 1 (<0.1) | - |
| Race | Number (%) | Rate |
| American Indian/Alaska Native | 817 (1 3) | 183 6 |
| , | 017 (1.5) | 405.0 |
| Asian/Pacific Islander | 608 (0.9) | 483.0 162.4 |
| Asian/Pacific Islander Black/African American | 608 (0.9) 29,247 (45.2) | 162.4 1244.7 |
| Asian/Pacific Islander Black/African American White | 608 (0.9) 29,247 (45.2) 16,624 (25.7) | 162.4 1244.7 224.9 |
| Asian/Pacific Islander Black/African American White Multiple Races | 608 (0.9) 29,247 (45.2) 16,624 (25.7) 449 (0.7) | 162.4 1244.7 224.9 168.9 |
| Asian/Pacific Islander Black/African American White Multiple Races Unknown | 608 (0.9) 29,247 (45.2) 16,624 (25.7) 449 (0.7) 16,912 (26.2) | 162.4 1244.7 224.9 168.9 |
| Asian/Pacific Islander Black/African American White Multiple Races Unknown Ethnicity | 608 (0.9) 29,247 (45.2) 16,624 (25.7) 449 (0.7) 16,912 (26.2) Number (%) | 162.4 1244.7 224.9 168.9 - Rate |
| Asian/Pacific Islander Black/African American White Multiple Races Unknown Ethnicity Hispanic/LatinX | 608 (0.9) 29,247 (45.2) 16,624 (25.7) 449 (0.7) 16,912 (26.2) Number (%) 6,829 (10.6) | 162.4 1244.7 224.9 168.9 - Rate 633.4 |
| Asian/Pacific Islander Black/African American White Multiple Races Unknown Ethnicity Hispanic/LatinX Non-Hispanic/Non-LatinX | 608 (0.9) 29,247 (45.2) 16,624 (25.7) 449 (0.7) 16,912 (26.2) Number (%) 6,829 (10.6) 35,095 (54.3) | 162.4 1244.7 224.9 168.9 - Rate 633.4 370.5 |

Two-thirds (66%) of

chlamydia cases were among **women** in 2022. Women are more likely to be screened for chlamydia (see page 12).



Chlamydia is increasing among Hispanic/LatinX

persons. Chlamydia cases increased 50% among Hispanic/LatinX in 2022 compared to 2018.



Chlamydia cases have remained **steady** since 2020; cases have not rebounded to prepandemic levels due in part to decreased testing.



80% of chlamydia cases in 2022 were among persons aged **15-29 years.**



Black/African American people were more affected by chlamydia; this group represents 45% of cases in 2022, while representing 22% of NC's population.



Gonorrhea

Antibiotic resistance is a growing concern for gonorrhea and is widely reported throughout the world.



Caused by the bacterium *Neisseria* gonorrhoeae.



Untreated urogenital gonorrhea can cause severe damage to the female reproductive tract, including infertility and pelvic inflammatory disease in women.



Cultures from all gonorrhea cases diagnosed through the Guilford County Health Department are screened for drug resistance. In 2020, a small number of organisms had partial resistance to drugs recommended for treatment, mainly to azithromycin.



Sexually transmitted disease that can most easily develop antibiotic resistance.



Gonorrhea and other STDs appear facilitate the acquisition of HIV in both men and women.



The majority of males with urethral gonorrhea experience symptoms, which include discharge and burning on urination; many women also experience symptoms, although they may be mild. Gonorrhea infections of the oropharynx and rectum are often asymptomatic.

Gonorrhea Disease Trends

| 2022 Summary | | |
|---|--|-------------------------------|
| Number of cases | | 26,867 |
| Rate (per 100,000 population) | | 254.6 |
| Percent change from 2021 | | -8.1% |
| Mean age (in years) | | 28 |
| Gender | Number (%) | Rate |
| Male | 14,664 (54.6) | 284.4 |
| Female | 12,203 (45.4) | 226.2 |
| Unknown | 0 (0.0) | - |
| Race | Number (%) | Rate |
| American Indian/Alaska Native | 415 (1.5) | 245.6 |
| Asian/Pacific Islander | 176 (0.7) | 47.0 |
| Black/African American | 15,889 (59.1) | 676.2 |
| White | 5,277 (19.6) | 71.4 |
| Multiple Races | 255 (0.9) | 95.9 |
| Unknown | 4,855 (18.1) | - |
| | | |
| Ethnicity | Number (%) | Rate |
| Ethnicity Hispanic/LatinX | Number (%) 1,505 (5.6) | Rate 139.6 |
| Ethnicity Hispanic/LatinX Non-Hispanic/Non-LatinX | Number (%) 1,505 (5.6) 17,633 (65.6) | Rate 139.6 186.1 |

55% of gonorrhea cases in 2022 were among men.



While disease incidence is **higher** among Non-Hispanic/Non-LatinX persons, there has been a **greater increase** in the rate among Hispanic/LatinX persons and cases among Hispanic/LatinX persons **doubled** from 2018 to 2022.



Gonorrhea cases slightly declined in 2022.



67% of gonorrhea cases in 2022 were among persons aged 15-29 years.



Black/African American persons were more affected by gonorrhea, with 59% of gonorrhea cases in 2022; Black/African American persons had 9.4 times the rate of White persons.



Syphilis

Syphilis is a complex disease with a natural history encompassing a number of different stages. **Early** stages are the most infectious and the focus of public health activity.



Caused by the spirochete bacterium *Treponema pallidum*.



Non-primary non-secondary early syphilis (formerly early latent) infections are asymptomatic but have evidence of having acquired the infection within the past 12 months.



Late or unknown duration syphilis are cases that have progressed past the early stage (greater than 12 months from initial infection). Individuals with late or unknown duration syphilis cannot transmit the infection to sex partners, so finding and treating this disease is still important as long-term consequences of untreated syphilis can be severe.



Most likely to have noticeable symptoms in primary or secondary stages of syphilis, such as a chancre or rash. Patients in these stages are more likely to have their disease diagnosed and reported because they go to a doctor for treatment.



Pregnant women with any stage of syphilis can pass the infection to their unborn child. Exposure to syphilis while in utero can result in stillbirth or infant death, especially when the pregnant woman is not treated during pregnancy.

Please note the case definition for syphilis changed in 2018. Therefore, data presented in this report before 2018 used the 2014 case definition, while data after 2018 uses the 2018 case definition. For more information on this, please refer to <u>Appendix A: STD Surveillance Notes and</u> <u>Case Definitions</u>.

Early Syphilis Disease Trends

| 2022 Summary | | |
|--|---|---|
| Number of cases | | 4,123 |
| Rate (per 100,000 population) | | 39.1 |
| Percent change from 2021 | | +30.0 |
| Mean age (in years) | | 35 |
| Gender | Number (%) | Rate |
| Male | 3,185 (77.2) | 61.8 |
| Female | 876 (21.2) | 16.2 |
| Transgender | 62 (1.5) | - |
| Unknown | 0 (0.0) | - |
| Race | Number (%) | Pate |
| nace | Number (70) | Nate |
| American Indian/Alaska Native | 41 (1.0) | 24.3 |
| American Indian/Alaska Native Asian/Pacific Islander | 41 (1.0) 39 (0.9) | 24.3 10.4 |
| American Indian/Alaska Native Asian/Pacific Islander Black/African American | 41 (1.0) 39 (0.9) 2,316 (56.2) | 24.3 10.4 98.6 |
| American Indian/Alaska Native Asian/Pacific Islander Black/African American White | 41 (1.0) 39 (0.9) 2,316 (56.2) 1,398 (33.9) | 24.3 10.4 98.6 18.9 |
| American Indian/Alaska Native Asian/Pacific Islander Black/African American White Multiple Races | 41 (1.0) 39 (0.9) 2,316 (56.2) 1,398 (33.9) 304 (7.4) | 24.3 10.4 98.6 18.9 114.3 |
| American Indian/Alaska Native Asian/Pacific Islander Black/African American White Multiple Races Unknown/Unspecified | 41 (1.0) 39 (0.9) 2,316 (56.2) 1,398 (33.9) 304 (7.4) 25 (0.6) | 24.3 10.4 98.6 18.9 114.3 |
| American Indian/Alaska Native Asian/Pacific Islander Black/African American White Multiple Races Unknown/Unspecified Ethnicity | 41 (1.0) 39 (0.9) 2,316 (56.2) 1,398 (33.9) 304 (7.4) 25 (0.6) Number (%) | 24.3 10.4 98.6 18.9 114.3 - Rate |
| American Indian/Alaska Native Asian/Pacific Islander Black/African American White Multiple Races Unknown/Unspecified Ethnicity Hispanic/LatinX | 41 (1.0) 39 (0.9) 2,316 (56.2) 1,398 (33.9) 304 (7.4) 25 (0.6) Number (%) 429 (10.4) | 24.3 10.4 98.6 18.9 114.3 - Rate 39.8 |
| American Indian/Alaska Native Asian/Pacific Islander Black/African American White Multiple Races Unknown/Unspecified Ethnicity Hispanic/LatinX Non-Hispanic/Non-LatinX | 41 (1.0) 39 (0.9) 2,316 (56.2) 1,398 (33.9) 304 (7.4) 25 (0.6) Number (%) 429 (10.4) 3,548 (86.1) | 24.3 10.4 98.6 18.9 114.3 - Rate 39.8 37.5 |

Nearly **8 of 10** people with early syphilis were **men**; however, the increase is **higher** among **women**.



Most people with early syphilis did not identify as Hispanic; however, cases among Hispanic/LatinX people increased more **rapidly** since 2018 (186%) compared to non-Hispanic/LatinX (109%).



Early syphilis cases increased **631%** compared to 2012. Cases have more than **doubled** since 2018.



38% of early syphilis cases were among persons aged **25-34 years** in 2022.



More than half of early syphilis cases in 2022 were diagnosed among Black/African American people. Black/African American people had 5.2 times the rate of White persons in 2022.



North Carolina DHHS

6

Communicable Disease

Congenital Syphilis

Congenital syphilis is increasing. Compared to 2018, congenital syphilis cases increased 200% in 2022.



Pregnant women with any stage of syphilis can pass the infection to their unborn child. Exposure to syphilis while in utero can result in stillbirth or infant death, especially when the pregnant woman is not treated during pregnancy.



Congenital syphilis is preventable; pregnant women who receive consistent and timely prenatal care can prevent passing the infection to their unborn child.



Up to 40% of babies born to women with untreated syphilis may be stillborn or die from the infection as a newborn.



Infants that are born with congenital syphilis can have a skin rash, low birth weight, jaundice, bone and joint deformities, and eye and ear nerve damage.



The North Carolina Administrative Code requires that all pregnant women be tested for syphilis at first prenatal visit, between 28-30 weeks of gestation, and at delivery. Failure to detect maternal syphilis infection during pregnancy or at delivery can result in delayed identification of infection in children who can have ongoing infection for months to years before being diagnosed.

Table 1. Number of Infants Diagnosed with Congenital Syphilis in North Carolina byYear of Birth, 2012-2022*

| Classification | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 | 2019 | 2020* | 2021 | 2022 |
|-----------------------|------|------|------|------|------|------|------|------|-------|------|------|
| Presumptive/Probable | 1 | 3 | 5 | 11 | 16 | 23 | 18 | 26 | 32 | 40 | 57 |
| Confirmed-Live birth | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| Confirmed-Still birth | 0 | 2 | 2 | 0 | 1 | 0 | 1 | 1 | 0 | 2 | 0 |
| Total | 1 | 5 | 7 | 11 | 18 | 23 | 19 | 27 | 32 | 42 | 57 |

*2020 data should be treated with caution due to the impact of the COVID-19 pandemic on accessing STD testing, STD treatment, and surveillance activities in North Carolina. 2020 data is italicized for this reason. Data Source: North Carolina Electronic Disease Surveillance System (NC EDSS) (data as of July 1, 2023).

Chlamydia, Gonorrhea, and Syphilis Annual Rate Maps by County of Residence at Diagnosis, 2022

Figure 1. Newly Diagnosed Chlamydia Rates in North Carolina by County of Residence at Diagnosis, 2022



Data Source: North Carolina Electronic Disease Surveillance System (NC EDSS) (data as of July 1, 2023).





Data Source: North Carolina Electronic Disease Surveillance System (NC EDSS) (data as of July 1, 2023).

Figure 3. Newly Diagnosed Early Syphilis (Primary, Secondary, and Early Non-Primary Non-Secondary) Rates in North Carolina by County of Residence at Diagnosis, 2022



Data Source: North Carolina Electronic Disease Surveillance System (NC EDSS) (data as of July 1, 2023).

Poverty and STDs

While the North Carolina surveillance data shows higher STD rates in some racial and ethnic groups, factors such as poverty and large gaps in wealth distribution may be driving these differences.² People who cannot afford basic needs may also have trouble accessing quality sexual health services, and may have had experiences with the health system that discourage the accessing of testing and care.²⁹ For each person diagnosed with a STD in North Carolina in 2022, we calculated the proportion of the population living below the poverty line in their census tract of residence at the time of their diagnosis using 5-year (2016-2020) estimates from the American Community Survey. This calculation estimated the neighborhood poverty level experienced for people newly diagnosed with STDs in North Carolina. Figures 4 and 5 show the rate of newly diagnosed STDs in 2022 by census tract poverty rate. Figures 4 and 5 demonstrate that although people living at all levels of poverty get STDs, those living in census tracts with a higher proportion of residents residing below the federal poverty line are more likely to be diagnosed with STDs.

Figure 4. People Newly Diagnosed with Chlamydia and Gonorrhea in North Carolina by Poverty Indicator*



*Estimates of people living below the poverty line within a census tract and all population estimates obtained from the American Community Survey, 2016-2020, five-year estimate.

Data Sources: North Carolina Electronic Disease Surveillance System (NC EDSS) (data as of July 1, 2023), and 2016-2020 American Community Survey (ACS) five-year estimates (accessed from https://data.census.gov/).

²Centers for Disease Control and Prevention. (2020). STD health equity. Updated March 2, 2020. Accessed September 2, 2022. Retrieved from <u>https://www.cdc.gov/std/health-disparities/default.htm#ftn5</u>.

Figure 5. People Newly Diagnosed with Early Syphilis (Primary, Secondary, and Early Non-Primary Non-Secondary) in North Carolina by Poverty Indicator*



Proportion of Census Tract Living in Poverty

*Estimates of people living below the poverty line within a census tract and all population estimates obtained from the American Community Survey, 2016-2020, five-year estimate.

Data Sources: North Carolina Electronic Disease Surveillance System (NC EDSS) (data as of July 1, 2023), and 2016-2020 American Community Survey (ACS) five-year estimates (accessed from https://data.census.gov/).

Sexually Transmitted Disease Information

Reportable Sexually Transmitted Diseases in North Carolina

Chlamydia

Chlamydia is caused by the bacterium *Chlamydia trachomatis* and is the most frequently reported bacterial STD both nationally and in North Carolina. Although symptoms from infections caused by *C. trachomatis* include discharge and painful urination, most individuals with chlamydia have no symptoms at all.³ Chlamydia is easily treated with antibiotics. Chlamydia and other STDs appear to increase susceptibility to human immunodeficiency virus (HIV) infection via inflammation, which increases the concentration of cells targeted by HIV in genital regions.⁴ In addition, the infection can cause severe damage to the female reproductive tract, including infertility and PID.² Chlamydia in untreated pregnant women can result in problems during pregnancy, including preterm labor, premature rupture of the membranes surrounding the baby in the uterus, and low birth weight. The newborn may also become infected during delivery as the baby passes through the birth canal, leading primarily to eye and lung infections.⁵ For this reason, the Centers for Disease Control and Prevention (CDC) and North Carolina DHHS recommend that all sexually active females age 25 years and younger, as well as all pregnant women and older women with risk factors, such as new or multiple sex partners, be screened for chlamydia. No comparable screening programs exist for young men. As a result, chlamydia reporting is highly biased with respect to gender, with a higher number of cases detected and reported among women.

Gonorrhea

Gonorrhea is caused by the bacterium *Neisseria gonorrhoeae*. Nearly all infected males experience symptoms of a gonorrheal infection, including discharge and burning on urination.⁶ Many women also experience symptoms, although they may be mild. Like chlamydia, untreated gonorrhea can cause severe damage to the female reproductive tract, including PID and infertility, and facilitates the acquisition of HIV in both men and women.⁷

Gonorrhea is the most likely of the bacterial STDs to develop antibiotic resistance. Antibiotic resistance is widely reported throughout the world.⁸ North Carolina contributes to CDC's gonorrhea resistance screening project, Strengthening the United States to Respond to Resistant Gonorrhea (SURRG).⁹ Cultures from all gonorrhea cases diagnosed in Guilford County are screened for drug resistance. In 2018, a small number of organisms had partial resistance to drugs used for treatment. Resistance was mainly to azithromycin, with a very small number of

³Centers for Disease Control and Prevention (2014). Chlamydia CDC detailed fact sheet. Updated January 23, 2014. Accessed April 9, 2019. Retrieved from https://www.cdc.gov/std/chlamydia/stdfact-chlamydia.htm.

⁴Centers for Disease Control and Prevention (2014). STDs and HIV-CDC detailed fact sheet. Updated December 16, 2014. Accessed April 9, 2019. Retrieved from <u>https://www.cdc.gov/std/hiv/stdfact-std-hiv.htm.</u>

⁵Centers for Disease Control and Prevention (2016). STDs during Pregnancy-CDC detailed fact sheet. Updated March 28, 2016. Accessed Retrieved April 9, 2019. Retrieved from <u>https://www.cdc.gov/std/pregnancy/stdfact-pregnancy.htm.</u>

⁶Centers for Disease Control and Prevention (2014). Gonorrhea-CDC detailed fact sheet. Updated January 29, 2014. Retrieved April 9, 2019. <u>https://www.cdc.gov/std/gonorrhea/stdfact-gonorrhea.htm</u>.

⁷Hook, E. & Handsfield, H. (1999). Chapter 32: Gonococcal infections in the adult. In K.K. Holmes, P.F. Sparling, P.A. Mårdh, S.M. Lemon, W.E. Stamm, P. Piot & J.N. Wasserheit (eds.), *Sexually Transmitted Diseases, 3rd Edition* (pp. 1165-1189). New York: McGraw-Hill.

⁸Hook, E & Kirkcaldy, R. (2018). A Brief History of Evolving Diagnostics and Therapy for Gonorrhea: Lessons Learned. Clinical Infectious Diseases. 67(8): pp 1294-9.

⁹Centers for Disease Control and Prevention (2017). Combating the Threat of Antibiotic-Resistant Gonorrhea. Updated August 9, 2017. Accessed July 2, 2019. Retrieved from <u>https://www.cdc.gov/std/gonorrhea/arg/CARB_FACTSHEET-2018.pdf</u>.

gonorrhea isolates resistant to cefixime or ceftriaxone. Resistance is North Carolina is more limited than in other parts of the country.¹⁰ Surveillance for resistance is very important and will continue.

Ophthalmia Neonatorum

Ophthalmic infection (also known as neonatal conjunctivitis) with *N. gonorrhoeae* or *C. trachomatis* can occur in infants when a pregnant woman has an untreated case of gonorrhea or chlamydia. During delivery, the infant's eyes can become infected with either bacterium.¹¹ In the past, ophthalmia neonatorum was reportable by law in North Carolina, but it is no longer a reportable disease in the state. However, cases may be reported because positive lab tests for *N. gonorrhoeae* and *C. trachomatis* are reportable. Cases are reviewed to detect repeated ophthalmia neonatorum in a delivery hospital, which may indicate imperfect practice.

Syphilis

Please note the case definition for syphilis changed in 2018. Therefore, data presented in this report before 2018 used the 2014 case definition, while data after 2018 uses the 2018 case definition. For more information on this, please refer to <u>Appendix A: STD Surveillance Notes and Case Definitions</u>.

Syphilis is a complex disease with a natural history encompassing a number of different stages, caused by the spirochete bacterium *Treponema pallidium*.¹² Early stages are the most infectious and the focus of public health activity.

Patients in the primary or secondary stages of syphilis are most likely to have noticeable symptoms, such as a chancre or rash, and to have their disease diagnosed and reported because they go to a doctor for treatment. These stages are also the most infectious and, therefore, of the greatest public health concern. Non-primary non-secondary early syphilis (formerly early latent) does not have symptoms. Patients in the asymptomatic stage are also infectious to their sexual partners, although less so than in the primary or secondary stages of disease.¹¹ Such cases are less likely to be diagnosed and are generally identified through screening or partner notification. Primary, secondary, and early (non-primary non-secondary) stages all occur within the first year of infection.¹³ These stages are often grouped together when discussing infectious syphilis and are called "early syphilis."

If a case progresses past the early stage (greater than 12 months from initial infection), the infection moves into a stage known as late or unknown duration syphilis. These syphilis cases are detected and reported in several different ways. Some patients with late syphilis develop symptoms and go to a doctor, while others are detected through screening or partner notification. Patients of either sex are not likely to be infectious to their sexual partners beyond the early latent stage, but finding these cases is still important, as long-term outcomes of untreated syphilis can be severe.¹²

Pregnant women can pass syphilis to their infants at any stage. Exposure to syphilis while in utero can result in stillbirth or infant death, especially when the pregnant woman is not treated during pregnancy. Up to 40% of babies born to women with untreated syphilis may be stillborn or die from the infection as a newborn. Infants

¹⁰Centers for Disease Control and Prevention (2018). Gonococcal Isolate Surveillance Project (GISP) Profiles, 2017. Updated March 27, 2018. Accessed July 2, 2019. Retrieved from <u>https://www.cdc.gov/std/statistics/gisp-profiles/default.htm</u>.

¹¹Centers for Disease Control and Prevention (2019). Conjunctivitis (pink eye) in newborns. Updated January 4, 2019. Retrieved April 9, 2019. https://www.cdc.gov/conjunctivitis/newborns.html.

¹²Centers for Disease Control and Prevention (2017). Syphilis-CDC detailed fact sheet. Updated January 30,2017. Accessed April 9, 2019. Retrieved from https://www.cdc.gov/std/syphilis/stdfact-syphilis-CDC detailed fact sheet. Updated January 30,2017. Accessed April 9, 2019. Retrieved from https://www.cdc.gov/std/syphilis/stdfact-syphilis-CDC detailed fact sheet. Updated January 30,2017. Accessed April 9, 2019. Retrieved from https://www.cdc.gov/std/syphilis/stdfact-syphilis-CDC detailed fact sheet. Updated January 30,2017. Accessed April 9, 2019. Retrieved from https://www.cdc.gov/std/syphilis/stdfact-syphilis-detailed.htm.

¹³Centers for Disease Control and Prevention (2018). Syphilis 2018 case definition-CSTE position paper. Updated January 1, 2018. Accessed April 9, 2019. Retrieved from https://ndc.services.cdc.gov/case-definitions/syphilis-2018/.

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that are born with congenital syphilis can have a skin rash, low birth weight, jaundice, bone and joint deformities, and eye and ear nerve damage.¹³ Congenital syphilis is preventable provided that pregnant women receive consistent and timely prenatal care. North Carolina Administrative Code states pregnant women shall be tested for syphilis at first prenatal visit, at 28-32 weeks, and at delivery. If the syphilis infection is not detected during pregnancy or at the time of delivery, and the infant does not have initial physical symptoms, congenital syphilis diagnosis may not occur until years later.¹⁴ If a confirmed or probable case of congenital syphilis is detected at delivery the infant can be treated at the hospital before discharge.

Nongonococcal urethritis (NGU) and Pelvic Inflammatory Disease (PID)

Nongonococcal urethritis (NGU) and pelvic inflammatory disease (PID), are syndromic in nature. NGU and PID are diagnosed by symptom presentation and exclusion of other causative organisms. NGU is a diagnosis of exclusion that requires specific physical manifestations which include the inflammation of the urethra, painful urination and penile and/or rectal discharge.¹⁴ Diagnosis is determined by the documented absence of *N. gonorrhoeae*, the causative agent in gonorrheal urethritis. Although NGU is caused by several different organisms, *C. trachomatis* may be responsible for many infections; however, these NGU cases are not tested for chlamydia.¹⁵ Most NGU cases in North Carolina are diagnosed at local health department clinics.

Similarly, PID occurs when an untreated sexually transmitted infection spreads to the uterus and the reproductive organs. PID symptoms can include cervical motion tenderness, discharge, fever, lower back pain, and painful urination.¹⁵ Many different types of microorganisms can cause PID; therefore, this STD is considered a polymicrobial infection. Sexually transmitted disease pathogens *N. gonorrhoeae* and *C. trachomatis* have frequently been identified among women with PID infection (one third to half of cases); most cases of PID are caused by these organisms.¹⁶ Quick detection and antibiotic treatment is critical to prevent long term sexual reproductive organ damage.

Rare Bacterial Sexually Transmitted Infections

Chancroid is caused by *Haemophilus ducreyi* organism. Symptoms include painful genital ulcer and tender suppurative inguinal adenopathy.¹⁷ Cases are rarely reported in North Carolina. Laboratory diagnosis is complex since no PCR tests for detection are cleared by the FDA and the culture media for *H. ducrey* is not widely available. Two other rare bacterial STDs are reportable in North Carolina. Lymphogranuloma venereum (LGV) is caused by a variant of *C. trachomatis*. The physical symptoms can include tender inguinal and or femoral lymphadenopathy, a lesion, proctocolitis, and other symptoms. The diagnostic criteria for LGV include *C. trachomatis* culture and serology.¹⁸ Granuloma inguinale is caused by *Klebsiella granulomatis*, and the symptom is a genital ulcer.¹⁹ North Carolina DHHS investigates less than 10 possible cases of these conditions each year. Because these STDs are so

¹⁴Centers for Disease Control and Prevention (2017). Congenital syphilis-CDC fact sheet. Updated January 31,2017. Accessed April 9, 2019. Retrieved from https://www.cdc.gov/std/syphilis/stdfact-congenital-syphilis.htm.

¹⁵Centers for Disease Control and Prevention (2015). Diseases characterized by urethritis and cervicitis. Updated June 4, 2015. Accessed April 9, 2019. Retrieved from https://www.cdc.gov/std/treatment-guidelines/urethritis-and-cervicitis.htm.

¹⁶Centers for Disease Control and Prevention (2015). Pelvic Inflammatory Disease (PID)-CDC basic fact sheet. Updated December 11, 2015. Accessed April 9, 2019. Retrieved from https://www.cdc.gov/std/pid/stdfact-pid.htm.

¹⁷Centers for Disease Control and Prevention (2015). Chancroid-2015 STD Treatment Guidelines. Updated June 4, 2015. Accessed April 9, 2019. Retrieved from https://www.cdc.gov/std/tg2015/2015-poster-press.pdf.

¹⁸Centers for Disease Control and Prevention (2015). Lymphogranuloma venereum (LGV)-2015 STD Treatment Guidelines. Updated June 4, 2015. Accessed April 9, 2019. Retrieved from https://www.cdc.gov/std/treatment-guidelines/lgv.htm.

¹⁹Centers for Disease Control and Prevention (2015). Granuloma Inguinale (Donovanosis)-2015 STD Treatment Guidelines. Updated June 4, 2015. Accessed April 9, 2019. Retrieved from https://www.cdc.gov/std/treatment-guidelines/donovanosis.htm.

rare, most clinicians have little experience in diagnosis and reporting, and it is possible that these diseases are underreported.

Non-Reportable Sexually Transmitted Diseases (STDs) in North Carolina

In order to get a clear picture of STDs in North Carolina, it is worth mentioning four non-reportable diseases that impact North Carolinians. The following section will explain the significance of human papillomavirus, genital herpes, *Mycoplasma genitalium*, and trichomoniasis.

Human Papillomavirus (HPV)

Genital human papillomavirus (HPV) is the most common sexually transmitted infection.²⁰ The CDC estimates that about 13 million Americans become infected each year with HPV.²¹ More than 40 strains of HPV can be sexually transmitted. Most strains produce no symptoms in infected individuals, but there are a few strains associated with genital warts and others associated with the development of cancer in both women and men.²² Since most infected people are asymptomatic, extensive screening would be required to diagnose the majority of infections. Current screening efforts focus on the detection of cancer, in particular cervical cancer in females, rather than on HPV infection.²¹ The most recent data available estimated that 333 cases of cervical cancer were reported in North Carolina in 2017.²³

There are three vaccines licensed by the US Food and Drug Administration (FDA) to protect against HPV infection, and all three have high efficacy (close to 100%).²⁴ The HPV vaccination is recommended or preteen girls and boys at age 11 or 12. For more information, visit the CDC website: https://www.cdc.gov/vaccines/vpd/hpv/public/index.html.

Genital Herpes

The CDC estimates that 572,000 people are newly infected with genital herpes each year. Around 12% of people aged 14 to 49 have a genital herpes simplex virus type 2 (HSV-2) infection.²⁵ In 2015-2016, prevalence of HSV-1 was 48% and prevalence of HSV-2 was 12% in the U.S. population.²⁶ Asymptomatic shedding of the virus is not uncommon. Many infected patients are unaware of being infected and represent a source of transmission in the community.²⁴

HSV-2 infection is more common in women than in men, but transmission from an infected male to a female partner is more likely than from an infected female to a male partner.²⁴ Symptoms are most severe immediately following the initial infection and subsequent outbreaks decrease in severity. A rare but extreme consequence of

²¹Centers for Disease Control and Prevention (2019). About HPV. Updated July 23, 2021. Accessed August 16, 2022. Retrieved from https://www.cdc.gov/hpv/parents/about-hpv.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fhpv%2Fparents%2Fwhatishpv.html.
²²Centers for Disease Control and Prevention (2016). What is HPV? Updated December 13, 2016. Accessed April 9, 2019. Retrieved from https://www.cdc.gov/std/hpv/default.htm.

²⁰Centers for Disease Control and Prevention (2017). Genital HPV Infection-CDC fact sheet. Updated November 16, 2017. Accessed April 9, 2019. Retrieved from https://www.cdc.gov/std/hpv/stdfact-hpv.htm.

²³North Carolina State Center for Health Statistics (2019). Cancer incidence rates by race, North Carolina, 2017. Updated March 18, 2019. Accessed November 12, 2014. Retrieved from https://schs.dph.ncdhhs.gov/schs/CCR/incidence/2017/race v2.pdf

²⁴Centers for Disease Control and Prevention (2016). About HPV vaccines. Updated December 15, 2016. Accessed April 9, 2019. Retrieved from https://www.cdc.gov/vaccines/vpd/hpv/hcp/vaccines.html.

²⁵Centers for Disease Control and Prevention (2021). Genital herpes-CDC detailed fact sheet. Updated July 22, 2021. Accessed September 2,2022. Retrieved from <u>https://www.cdc.gov/std/herpes/stdfact-herpes-detailed.htm</u>.

²⁶Centers for Disease Control and Prevention (2018). Prevalence of herpes simplex virus type 1 and 2 in persons aged 14-49: United States, 2015-2016. Updated February 7, 2018. Accessed April 9, 2019. Retrieved from https://www.cdc.gov/nchs/products/databriefs/db304.htm.

genital herpes is transmission to newborns during birth.²⁴ Since active disease causes ulcerative lesions, herpes infection is believed to increase the risk of HIV transmission and acquisition.¹⁹ The CDC does not recommend routine serological screening for herpes in asymptomatic people.²⁷

Mycoplasma genitalium

Mycoplasma genitalium infections cause urethritis in men and cervicitis in women. Many cases are asymptomatic. *M. genitalium* is associated as a causative organism in NGU and PID diagnoses.²⁸ *M. genitalium* is responsible for approximately 15%-20% of NGU cases, and 4%-22% of PID cases.²⁷

Trichomoniasis

Trichomoniasis is caused by the protozoan *Trichomonas vaginalis* that affects more than 2 million patients annually in the US.²⁹ Symptoms can include urethritis in males and diffuse malodorous vaginal discharge with vulvar irritation in females; asymptomatic infection also occurs.

Some studies have suggested that vaginal trichomoniasis is a risk factor for HIV acquisition, and up to 53% of women with HIV are also infected with *T. vaginalis*. In pregnant women, adverse pregnancy outcomes are associated with infection including premature rupture of membranes and low birth weight infants. Trichomoniasis usually responds to a single dose of metronidazole or tinidazole, although resistance to treatment can occur. Partner treatment is necessary to prevent re-infection.²⁸

²⁷Centers for Disease Control and Prevention (2022). Genital herpes screening FAQ. Updated July 11, 2022. Accessed September 2, 2022. Retrieved from https://www.cdc.gov/std/herpes/screening.htm.

²⁸Centers for Disease Control and Prevention (2021). 2015 STD Treatment Guidelines-Emerging Issues-*Mycoplasma genitalium*. Updated July 22, 2021. Accessed September 2, 2022. Retrieved from <u>https://www.cdc.gov/std/treatment-guidelines/mycoplasmagenitalium.htm</u>.

²⁹Centers for Disease Control and Prevention (2022). Trichomoniasis-CDC detailed fact sheet. Updated January April 25, 2022. Retrieved September 2, 2022. <u>https://www.cdc.gov/std/trichomonas/stdfact-trichomoniasis.htm</u>.

Appendix A: STD Surveillance Notes and Case Definitions

About the Authors

North Carolina law requires that diagnoses of certain communicable diseases, including STDs, be reported to local health departments that in turn report the information to the state. The HIV/STD/Hepatitis Surveillance Unit is the designated recipient for STD, viral hepatitis B (HBV) and hepatitis C (HCV), and HIV morbidity reports at the state level. From these reports, the HIV/STD/Hepatitis Surveillance Unit is responsible for aggregating these reports and providing county, regional, and statewide data to the public and the CDC. The HIV/STD/Hepatitis Surveillance Unit is part of the Communicable Disease Branch within the North Carolina Department of Health and Human Services, Division of Public Health.

Chlamydia Surveillance Data

Chlamydia case reports represent people who have a laboratory-confirmed chlamydial infection (isolation of *Chlamydia trachomatis* by culture or detection of antigen or nucleic acid)³⁰. Chlamydial infection is often asymptomatic in both males and females and most cases are detected through screening. Therefore, changes in the number of reported cases may be due to changes in screening practices rather than changes in true disease incidence. The disease can cause serious complications in females, such as pelvic inflammatory disease and infertility, so a number of screening programs are in place to detect chlamydia infection in young women. No comparable screening programs exist for young men. For this reason, chlamydia case reports are always highly biased with respect to gender.

Reports are summarized by the date of diagnosis.

Determining whether the prevalence of chlamydia infections is changing is difficult because chlamydia reporting is dependent on screening practices.

Gonorrhea Surveillance Data

Gonorrhea case reports represent people who have a laboratory-confirmed gonorrhea infection. Gonorrhea is often symptomatic in males and slightly less so in females. Many cases are detected when patients seek medical care. Other cases are detected through routine testing even if no symptoms are present. Classification of gonorrhea is based on the presence of a gram-negative intracellular diplococci in a urethral smear (male) or endocervical smear (female) (probable case) OR the isolation of a gramnegative, oxidase-positive diplococci by culture (presumptive *Neisseria gonorrhoeae*) from clinical specimen OR *N. gonorrhoeae* by detection of antigen or nucleic acid amplification (confirmed case).³¹

³⁰Centers for Disease Control and Prevention (2010). National Notifiable Disease Surveillance System (NNDSS): *Chlamydia trachomatis* infection 2010 case definition. Retrieved from https://ndc.services.cdc.gov/case-definitions/chlamydia-trachomatis-infection-2010/. ³¹Centers for Disease Control and Prevention (2014). National Notifiable Disease Surveillance System (NNDSS): Gonorrhea (*Neisseria gonorrhoeae*) 2014 case definition. Retrieved from https://ndc.services.cdc.gov/case-definitions/chlamydia-trachomatis-infection-2010/. ³¹Centers for Disease Control and Prevention (2014). National Notifiable Disease Surveillance System (NNDSS): Gonorrhea (*Neisseria gonorrhoeae*) 2014 case definition. Retrieved from https://ndc.services.cdc.gov/case-definitions/gonorrhea-2014/.

Gonorrhea can cause serious complications for females, and a number of screening programs exist targeting this population. Screening programs focused on female patients are predominately conducted at public clinics and health departments, which can cause the reported cases to be biased toward those attending public clinics. Males are less likely to be diagnosed by routine screening; however, they are more likely to have symptoms that would bring them to an STD clinic. Therefore, gender bias in gonorrhea reporting is not considered to be large.

Reports are summarized by the date of diagnosis.

Determining whether the prevalence of gonorrhea infections is changing is difficult because gonorrhea reporting is dependent on screening practices; in 2018, these changes included an increase in screening for infection in pharyngeal and rectal sites, which may lead to the detection of more cases in the absence of a true increase in disease.

Syphilis Surveillance Data

Syphilis cases are reported by stage of infection, which is determined through a combination of laboratory testing and patient interviews. Primary and secondary syphilis have characteristic symptoms, so misclassification of these stages is highly unlikely. Primary, secondary, and early non-primary non-secondary (formerly early latent syphilis) are considered "early syphilis," and all stages of early syphilis are considered a priority for public health action.

North Carolina performs patient interviews, partner notification, and contact tracing on all early syphilis cases; therefore, the quality of early syphilis case data is good. Screening programs are more likely to detect asymptomatic cases, which may result in more complete reporting of cases in the screened populations (pregnant women, jail inmates, and others). However, thorough contact tracing further aids in case detection and reduces these biases.

For more complete case definition of the stages of syphilis, please refer to the CDC's websites (<u>https://ndc.services.cdc.gov/case-definitions/syphilis-2018/</u>). CDC and the Council for Territorial and State Epidemiologists (CSTE) periodically update case definitions. Included below are the syphilis case definitions that were in using during the collection of the data in this report.

The 2018 case definitions for all stages of syphilis are summarized below.

2018 Case Definition of Primary Syphilis

- *Confirmed: T. pallidum* in clinical specimen by dark field microscopy that was not obtained from the oropharynx AND one or more ulcerative lesions (such as chancre), which may differ in appearance.
- *Probable:* One or more ulcerative lesions AND a reactive serologic test (nontreponemal: Venereal Disease Research Laboratory [VDRL], rapid plasma reagin [RPR], or equivalent serologic methods; treponemal: fluorescent treponemal antibody absorbed [FTA-ABS], *T. pallidum*

particle agglutination [TP-PA], enzyme immunoassay [EIA], chemiluminescence immunoassay [CIA] or equivalent serologic methods).³²

2018 Case Definition of Secondary Syphilis

- *Confirmed: T. pallidum* in clinical specimens by darkfield microscopy that was not obtained from the oropharynx AND at least one sign or symptom common with secondary syphilis (lesions, rash, or localized lymphadenopathy).
- *Probable:* At least one sign or symptom common with secondary syphilis as stated above AND a nontreponemal serologic test (VDRL, RPR, or equivalent serologic methods) AND a reactive treponemal serologic test (FTA-ABS, TP-PA, EIA, CIA, or equivalent serologic methods).³³

2018 Case Definition of Early Non-Primary Non-Secondary Syphilis (Formerly Early Latent Syphilis)

- *Probable:* No clinical symptoms evidence of having acquired the infection within the past 12 months (but no signs or symptoms of primary or secondary syphilis) AND has one of the following:
 - No past diagnosis of syphilis AND a current reactive nontreponemal test (VDRL, RPR, or equivalent serologic methods) AND a reactive treponemal test (FTA-ABS, TP-PA, EIA, CIA, or equivalent serologic methods); OR
 - A prior history of syphilis AND a current nontreponemal test titer demonstrating fourfold or greater increase from the last nontreponemal test titer, unless there is evidence that this increase was not sustained for ≥ 2 weeks; AND
 - Evidence having acquired the infection within the past 12 months based on 1.) documented seroconversion or fourfold or greater increase in titer of nontreponemal test during previous 12 months, unless there is evidence this increase was not sustained for ≥ 2 weeks, 2.) documented seroconversion of a treponemal test during previous 12 months, 3.) a history of symptoms consistent with primary or secondary syphilis during the previous 12 months, and 4.) has a history of sexual exposure to a partner within the previous 12 months who had primary, secondary, or early non-primary non-secondary syphilis (documented ≤ 12 months) or only sexual contact was within the previous 12 months.³³

2018 Case Definition of Unknown Duration or Late Syphilis

- *Probable:* A person with no clinical signs or symptoms of primary or secondary syphilis AND who has no evidence of acquiring the infection within 12 months AND who meets one of the following:
 - No prior history of syphilis and a current reactive nontreponemal test (VDRL, RPR, or equivalent serologic methods), and a current reactive treponemal test (FTA-ABS, TP-PA, EIA, CIA, or equivalent serologic methods); OR
 - A prior history of syphilis with a current nontreponemal test titer demonstrating a fourfold or greater increase from the last nontreponemal test titer, unless there is evidence that this increase was not sustained for more than two weeks; OR
 - Clinical signs or symptoms and laboratory results that meet the likely or verified criteria for neurological, ocular, otic, or late clinical manifestations (15-30 years of untreated syphilis).³³ More information about neurological, ocular, otic, or late clinical

³²Centers for Disease Control and Prevention (2018). National Notifiable Disease Surveillance System (NNDSS): Syphilis (*Treponema pallidum*) 2018 case definition. Retrieved from https://ndc.services.cdc.gov/case-definitions/syphilis-2018/.

³³ Centers for Disease Control and Prevention (2018). National Notifiable Disease Surveillance System (NNDSS): Syphilis (*Treponema pallidum*) 2018 case definition. Retrieved from <u>https://ndc.services.cdc.gov/case-definitions/syphilis-2018/</u>.

manifestations can be found on the CDC's website, under "Comments": <u>https://ndc.services.cdc.gov/case-definitions/syphilis-2018/</u>.

2018 Case Definition of Congenital Syphilis

A condition caused by in utero infection with *T. pallidum*. A wide spectrum of severity exists, which includes stillbirth.³³

- *Confirmed:* Demonstration of *T. pallidum* by:
 - Darkfield microscopy of lesions, body fluids, or neonatal nasal discharge; OR
 - PCR or equivalent direct molecular methods of lesions, neonatal nasal discharge, placenta, umbilical cord, or autopsy material; OR
 - Immunohistochemistry or specific stains of specimens from lesions, neonatal nasal discharge, placenta, umbilical cord, or autopsy material.
- *Probable:* A condition affecting an infant whose mother had untreated or inadequately treated syphilis at delivery, regardless of signs in the infant OR an infant or child who has a reactive treponemal test for syphilis AND one of the following:
 - Any evidence of congenital syphilis on physical examination or radiographs of long bones;
 - A reactive cerebrospinal fluid VDRL;
 - \circ $\;$ An elevated cerebrospinal fluid cell count or protein; or
 - In a non-traumatic lumbar puncture, an elevated cerebrospinal fluid leukocyte (white blood cell) count or protein.³³

³³ Centers for Disease Control and Prevention (2018). National Notifiable Disease Surveillance System (NNDSS): Syphilis (*Treponema pallidum*) 2018 case definition. Retrieved from https://ndc.services.cdc.gov/case-definitions/syphilis-2018/.