Summary Points: The incidence of congenital syphilis has risen dramatically over the past decade in Virginia, from 3 cases in 2013 to 20 in 2022. Congenital syphilis is preventable if syphilis infections are detected and treated in time during pregnancy. Ensuring that pregnant women receive early prenatal care and appropriate syphilis screening throughout pregnancy is crucial to prevention efforts.

Congenital Syphilis in Virginia, 2013-2022

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Background

Congenital syphilis occurs when a pregnant woman infected with Treponema pallidum bacteria passes the infection to their baby during gestation or delivery.i,1 Congenital syphilis is of public health importance because of the seriousness of its consequences if untreated, including severe perinatal morbidity and mortality. Forty percent of infants born to mothers with untreated syphilis are either stillborn or die from infection.² Congenital syphilis can also cause miscarriage, premature birth, or low birth weight. Infants born with congenital syphilis may have bone damage, severe anemia, enlarged liver and spleen, jaundice, nerve problems causing blindness or deafness, meningitis, or skin rashes. Children with late congenital syphilis, when infection is diagnosed after 2 years of age, may develop cardiovascular involvement, meningovascular and neurologic manifestations (including deafness), and experience developmental delays.

How syphilis affects a baby's health depends on when syphilis was acquired during pregnancy and if, or when, the mother received treatment for the infection.³ Congenital syphilis cases can be prevented if syphilis infections among pregnant women are detected early and treated promptly with a penicillin regimen that is both appropriate for the stage of syphilis and initiated 30 days or more before delivery.⁴

Risk factors for congenital syphilis include infants born to mothers with untreated syphilis, to mothers treated with a non-penicillin regimen while pregnant, and to mothers who received appropriate syphilis treatment that started less than 30-days prior to delivery. Syphilis is a sexually transmitted infection (STI). Maternal risk factors for syphilis infection during pregnancy include sex with multiple partners; sex in conjunction with drug use or

transactional sex; late entry to prenatal care (*i.e.*, first visit during the second trimester or later) or no prenatal care; methamphetamine, fentanyl, or heroin use; incarceration of the woman or her partner; housing instability or homelessness; and living in a community with high syphilis incidence rates.⁵

After reaching a historic low in the early 2000s, congenital syphilis case reports in the United States have increased each year since 2013.⁶ In 2021, 2,855 cases of congenital syphilis were reported nationally, including 220 congenital syphilis-related stillbirths and infant deaths. The national congenital syphilis rate of 77.9 cases per 100,000 live births in 2021 represents a 30.5% increase relative to 2020 and a 747% increase relative to 2013.⁷ In 2021, almost all jurisdictions (46 states and the District of Columbia) reported at least one case of congenital syphilis; 37 of these jurisdictions saw increases.

These increases in congenital syphilis mirror increases in syphilis infections diagnosed among reproductive aged women. From 2020 to 2021 the rate of early syphilis (the primary and secondary stages of infection) increased 52.3% among women aged 15–44 years, impacting just over 10,500 women in the United States annually. Congenital syphilis is preventable if the infection is detected and treated in time during pregnancy. Therefore, identifying and treating syphilis infections among pregnant women is a public health priority. The purpose of this report is to summarize the current epidemiology of congenital syphilis in Virginia and inform efforts to address this re-emerging public health issue.

ⁱ All references to pregnant women in this report are intended to be inclusive of all pregnant persons.



Methods

The Virginia Department of Health (VDH) collects data on both syphilis and congenital syphilis through routine surveillance for notifiable conditions. This includes passive laboratory and morbidity case reporting as well as field investigations and surveillance follow-up with medical providers and cases. Because timely treatment may prevent disease, congenital syphilis is a high priority condition for both reporting and field investigation. All reports of congenital syphilis, or syphilis infections among pregnant women, receive public health priority.

Notifiable conditions are those that health providers are required to report to state or local public health officials when diagnosed (usually by law). Such notifiable diseases may be of public interest because of their contagiousness, severity, or frequency.

Because of the complexities involved in staging syphilitic infections and providing partner services, public health investigations of syphilis are conducted by trained STI/HIV health counselors known as Disease Intervention Specialists (DIS).¹⁰ When a positive syphilis laboratory report is received by VDH for a woman of childbearing age (approximately 15-44 years), it is flagged for priority field investigation and partner services. DIS are responsible for ascertaining the pregnancy status of all such women within two business days of investigation initiation. For pregnant women, the DIS confirms the case diagnosis, collaborates with medical providers to ensure proper treatment, attempts to contact partners and link them to proper testing and treatment, and follows the pregnancy until delivery to ascertain infant outcomes.

In addition to the case investigation work conducted by DIS, VDH has a Perinatal Surveillance Coordinator who monitors active syphilis and HIV case investigations for pregnant patients. This coordinator works with the DIS, private providers, and other VDH staff to ensure proper maternal and infant case management, evaluation, and treatment.

All data presented in this analysis represent cases of congenital syphilis reported as of July 4, 2023. Note that there may be some discrepancy between clinical case definitions (as determined by a medical provider) and surveillance case definitions. For this report, only cases

that met the national notifiable disease surveillance definition were used. This means that some infants may have been classified as having congenital syphilis based on surveillance case definition criteria, even if they did not exhibit any symptoms. Per the current surveillance reporting guidelines, a case must meet at least one of three criteria to be considered a reportable congenital syphilis (CS) case. 12

- To meet maternal criteria for CS, a mother must meet the surveillance case definition for syphilis during pregnancy and either not have been appropriately treated or not have started appropriate treatment within 30 days of delivery.
- 2) To meet infant criteria for CS, Treponema pallidum must be directly detected in neonatal tissue, lesions, body fluids, or nasal discharge via dark field microscopy, PCR, DFA, or special stain examinations, any of which would result in a confirmed congenital syphilis diagnosis. Alternatively, a case can be considered probable by infant criteria if the infant has a reactive nontreponemal test in addition to physical sign(s) of CS, evidence of CS on long bone X-rays, reactive cerebrospinal fluid (CSF) VDRL, or elevated CSF protein or white blood cell count in a non-traumatic lumbar puncture.
- 3) Finally, a case can be considered positive by syphilitic stillbirth criteria provided the mother meets the maternal criteria and the pregnancy results in fetal death either after at least 20 weeks gestation or weighing at least 500 grams.

CS cases were reported by date of birth, while syphilis infections among women were reported by diagnosis date. Rates were calculated per 100,000 population using 2020 Census population estimates and Virginia live birth statistics. A rate is a common calculation used in public health that offers a standardized way to compare the burden of a health condition across demographic groups or geographic areas regardless of population size.

Data on race and ethnicity were combined into three main categories: non-Hispanic white, non-Hispanic black, and Hispanic or Latino (individuals of any race reported as Hispanic). Due to low case counts, persons reported as other or multiple races/ethnicities were collapsed into one "other or multi-race" category to preserve individual privacy.



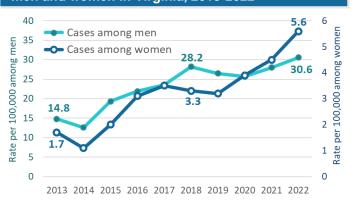
Results

Syphilis Infections among Women: While rates of syphilis have risen among all populations in Virginia, the rise among women has been particularly dramatic. Over the late decade (2013-2022), rates of early syphilis diagnoses among women in Virginia communities increased by 229% (from 1.7 to 5.6 per 100,000); rates among men increased by 107% (Figure 1). Early syphilis diagnoses include the primary and secondary stages of syphilis (as well as the early non-primary, non-secondary stage), which are the most contagious stages of infection. More recently, early syphilis rates among women increased 70% from 2018 to 2022. The equivalent case counts among women increased from 142 to 244 over this period. Fifty-nine percent of these cases occurred among women reported as non-Hispanic black, and 43% were between 20 and 29 years of age. Based on field investigations conducted by DIS, approximately 12% of reproductive age women (15-44 years) with reported early syphilis infections in 2022 were pregnant at the time of their diagnosis.

Congenital Syphilis Case Trends: As the number of syphilis infections reported among women in Virginia has increased, so too has the volume of reported CS cases (Figure 2). In 2022, 20 CS cases were reported in Virginia, the highest count in over three decades. Eight syphilitic stillbirths were reported between 2013 and 2022.

The rate of CS in Virginia remains lower than the national rate, but the progressive upward trend since historic lows in the early 2000s is concerning (**Figure 3**). In 2022, the national CS rate was 102.5 per 100,000; the rate in Virginia was 20.8 per 100,000. The national rate of CS was almost 5 times higher than in Virginia. The magnitude of observed increases has also been slower in

Figure 1. Early syphilis diagnosis rates among men and women in Virginia, 2013-2022



Virginia. From 2013 to 2022, CS rates increased 1,013% nationally and 608% locally. In just the last five years (2018 to 2022) rates in Virginia increased 87%, while national rates increased 194%.

Congenital Syphilis Case Geography: From 2013-2022, most CS cases were reported from the Eastern (29.4%) and Northern (29.4%) health regions in Virginia, based on the mother's residence at delivery (Figure 4). The Norfolk health district observed the greatest volume of cases (15 cases), followed by Prince William (9 cases), Fairfax and Arlington (8 cases each) (Figure 5). Twenty-six of the 35 health districts in Virginia have reported at least one CS case during this period.

Maternal Case Demographics: Of the 102 CS cases reported between 2013 and 2022, maternal race/ethnicity was reported as non-Hispanic black for over half (54%), which is considerably greater than 20% composition of this racial/ethnic group in Virginia's overall population based on 2020 US Census Bureau estimates (Figure 6).¹³ Hispanic or Latino mothers (any race) were also overrepresented in the CS case counts (18% of cases compared to 11% of the population). Twenty-four percent of mothers were non-Hispanic white. There has been a pronounced shift in the reported race/ethnicity of CS cases over the last five years. In 2018, 91% of all cases (10 out of 11) were diagnosed among non-Hispanic black mothers; by 2022, only 35% were.

From 2018 to 2022, the average maternal age at syphilis diagnosis was 27.3 years (range 17 to 45 years). The majority (65.3%) of mothers were between 20-29 years of age; 30.7% were 30-45 years; and 4.0% were 15-19 years.

Figure 2. Early syphilis in women and congenital syphilis diagnoses in Virginia, 2013-2022

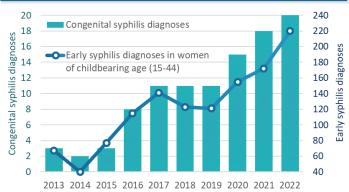




Figure 3. Congenital syphilis case rates in Virginia compared to the United States, 2013-2022

120 United States 102.5

OVIrginia

1000

OVIrginia

20

9.2

11.1

20.8

Figure 4. Congenital syphilis diagnoses by health region in Virginia, 2013-2022 (N = 102)

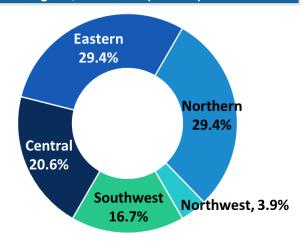


Figure 5. Congenital syphilis diagnoses by mother's health district at delivery, 2013-2022 (N = 102)

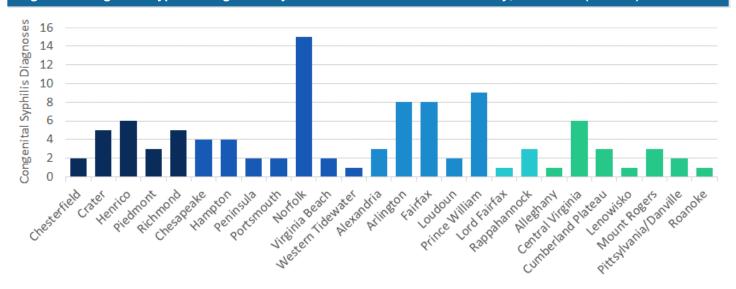


Figure 6. Maternal race/ethnicity compared to total percent share of Virginia population, 2013-2022

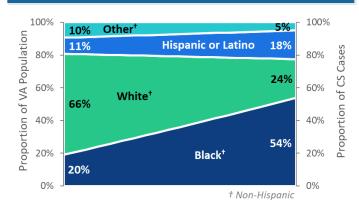


Figure 7. Temporal trends in congenital syphilis diagnoses by maternal race/ethnicity, 2018-2022

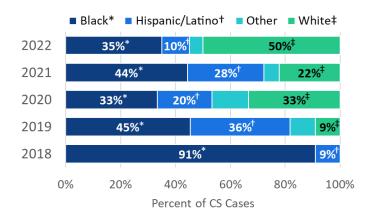




Table 1.	Congenital syphilis case characteristics a	at
delivery	2018-2022 (N = 75)	

delivery, 2018-2022 (N = 75)			
Extremely or very preterm (<32 weeks)	7 (9%)		
Moderate or late preterm (32-37 weeks)	25 (33%)		
Low birth weight (<2,500 grams)	21 (28%)		
Signs or symptoms at delivery	14 (19%)		
Abnormal long bone x-rays	13 (17%)		
Abnormal cerebrospinal fluid (CSF) result	32 (43%)		
Reactive RPR (rapid plasma reagin) test	54 (72%)		

Congenital Syphilis Case Characteristics: From 2018-2022, the average infant gestational age at delivery was 36.6 weeks (range 25 to 41 weeks). Forty-three percent were born preterm (<38 weeks gestation), and 28% weighed less than 2,500 grams at delivery (Table 1). Only 14 out of 75 cases were symptomatic at delivery (19%); however, 17% had abnormal long bone x-rays, 43% had abnormal cerebrospinal fluid (CSF) laboratory results (including reactive VDRL, elevated white blood cell count, or elevated protein), and 72% had a reactive RPR test.

Figure 8. Timing of first prenatal care visit among mothers of congenital syphilis cases in Virginia, 2018-2022 (N = 75)

Late prenatal care (3rd trimester)

No prenatal care 25%

9%

Timely prenatal care (1st/2nd trimester) 63%

Unknown timing of prenatal care; 3%

Maternal Screening, Treatment, and Missed

Opportunities: From 2018-2022, 25% of the 75 mothers of CS cases did not receive any prenatal care prior to delivery, and an additional 9% did not receive prenatal care until late in pregnancy (**Figure 8**). Sixty-three percent received timely prenatal care (prior to 28 weeks gestation), but still developed CS. Among the 56 mothers who received prenatal care, 79% were tested prior to 28 weeks gestation, 45% were tested early in the 3rd trimester (28-32 weeks), and 70% were tested at delivery (**Table 2**). Note that these percentages are not

cumulative, as women may be tested several times during pregnancy.

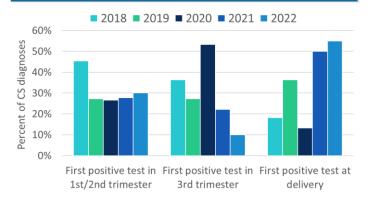
Some women who initially screened negative early in pregnancy were infected afterwards and tested positive for syphilis either later in pregnancy or at delivery (31 out of 56 cases diagnosed between 2018 and 2022). Based on these data, early 3rd trimester screening could have prevented 41% of the CS cases that occurred among pregnant women who received prenatal care.

The number of mothers diagnosed with syphilis at delivery has increased progressively over the last five years (**Figure 9**). In 2022, 11 (55%) mothers of CS cases were diagnosed at delivery, compared to only 2 (18%) in 2018. In contrast, fewer mothers tested positive for the first time at delivery in 2020, but instead the majority first tested positive for syphilis in the 3rd trimester. This is possibly due to delays in prenatal care associated with the COVID-19 pandemic disrupting the provision of routine clinical care in 2020.

Table 2. Timing of syphilis screening for mothers of congenital syphilis cases who received prenatal care in Virginia, 2018-2022 (N = 56)

44 (79%)
25 (45%)
39 (70%)
23 (41%)

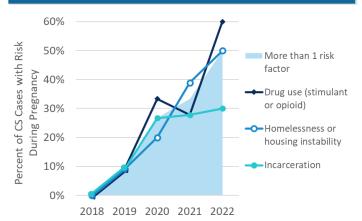
Figure 9. Timing of mother's first positive syphilis test among congenital syphilis cases in Virginia, 2018-2022 (N = 75)





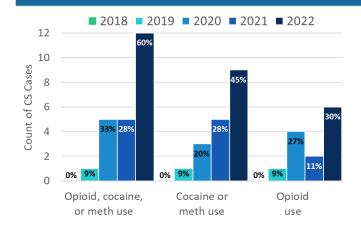
Maternal Risk Factors: Between 2018 and 2022, 24% of mothers had a history of previous syphilis infection prior to pregnancy. Housing instability or homelessness and incarceration were common, impacting 28% and 21% of mothers respectively (Figure 10). Substance misuse during, or in the year prior to, pregnancy was reported in 31% of cases. Half of women reported more than one risk factor during their pregnancies in 2022 (substance misuse, housing instability, and/or incarceration), roughly double the proportion with similar risk in 2020.

Figure 10. Maternal risk factors for syphilis during pregnancy, 2018-2022



In particular, there has been a drastic increase in the proportion of mothers reporting opioid or stimulant use in recent years, jumping from 0% in 2018 to 33% in 2020 and 60% in 2022 (**Figure 11**). Opioid use (including heroin and synthetic opioids) was reported for 30% of cases diagnosed in 2022, while 45% reported use of stimulants such as cocaine and methamphetamine. Neonatal abstinence syndrome (NAS) was previously uncommon among CS cases; however, three infants in 2020 and 4 infants in 2022 were diagnosed with NAS.

Figure 11. Maternal drug use during pregnancy, 2018-2022



Discussion

Notable disparities exist in the incidence of both syphilis and CS by race and ethnicity in Virginia. In 2022, the rate of early syphilis among black Virginians was 6.6 times that of white Virginians (50.1 vs. 7.6 per 100,000); rates of CS were roughly 2 times higher for black infants relative to white infants based on maternal race/ethnicity. While the proportion of all CS cases born to white mothers has increased in recent years, this is likely driven by increases in the prevalence of other risks during pregnancy, such as drug use, rather than improvements in racial/ethnic equity.

Lack of adequate prenatal care during pregnancy remains the greatest barrier to prevention of CS in Virginia. Successful prevention requires addressing challenges related to implementation of screening recommendations, awareness of infection among pregnant women and their providers, and access to and availability of care and treatment. In 2021, Virginia established its Congenital Syphilis and Perinatal HIV Case

Review Board (CRB), a group of private and public health care providers, professionals, and surveillance staff that meets yearly to review CS and perinatal HIV exposure cases. Recommendations from the CRB have included updating the prenatal syphilis testing requirements in the Administrative Code of Virginia, improving provider education and knowledge of available resources, and expanding Bicillin delivery to private providers under the 340B federal drug pricing program.¹⁵

Concerning trends have also been observed in the risk factors for syphilis. Substance use, especially methamphetamine misuse, during pregnancy has increased substantially over the last 5 years. Other risk factors such as being unhoused, housing instability, and incarceration are also increasingly common. This confluence puts women in vulnerable situations that are more difficult for healthcare providers and public health workers to reach.¹⁶



Data Considerations / Limitations

Our analysis of CS epidemiology is reliant on surveillance data, the quality and comprehensiveness of which depend on both notifiable disease reporting and adequate screening of pregnant women and infants. Reported cases are likely an undercount of the true burden of CS. These surveillance data are likely to miss miscarriages, early fetal demises, and stillbirths for which syphilis was never considered as a possible cause and/or syphilis testing was not conducted.

Furthermore, the COVID-19 pandemic negatively impacted the provision of routine sexual and reproductive health care, as well as STI prevention programs and DIS case investigations. Many clinics suspended operations or limited clinic appointments to

symptomatic patients, and most health department sexual health clinics have not yet returned to prepandemic capacity.

Since many STIs are asymptomatic, and screening is necessary for timely diagnosis and treatment, changes in healthcare access can affect the number of infections diagnosed and reported to surveillance systems.¹⁷ A 2021 analysis conducted by the Centers for Disease Control and Prevention estimated that syphilis diagnoses declined during the early months of the pandemic before rebounding for the rest of the year.¹⁸ The long-term impact on CS rates remains unclear, but delays in syphilis screening and treatment during the pandemic may have led to increased syphilis transmission in communities.

Prevention Recommendations

Screening: All pregnant patients should receive comprehensive screening for STIs, including syphilis and HIV, at their first prenatal visit. ¹⁹ For women (or other persons) who are at higher risk for syphilis acquisition during pregnancy, or whose risk status is unclear, serologic testing should also be performed *twice* during the **third trimester**: at 28-32 weeks' gestation and at delivery.

Pregnant women at higher risk of syphilis infection during pregnancy include:⁵

- ✓ Pregnant women who live in <u>communities</u> with high rates of syphilis.²⁰
- ✓ Women who have new sex partners, multiple sex partners, sex in conjunction with drug use, or transactional sex during their pregnancy.
- ✓ Women who use drugs, particularly methamphetamine or heroin.
- Women who are incarcerated, or whose partners are incarcerated.
- Women experiencing unstable housing or who are unhoused.

Any woman who has a fetal death after 20 weeks' gestation should be tested for syphilis. Any neonate at risk for CS should also receive a full evaluation and testing

No mother or neonate should leave the hospital without maternal serologic status having been documented at least once during pregnancy.

for HIV. Clinicians who see pregnant women for any reason, including at emergency department visits, should offer comprehensive STD and HIV screening, as this may be the only point of care during pregnancy for some vulnerable populations. Healthcare systems should employ assessments and interventions to increase compliance with screening guidelines among their providers.

Treatment: Pregnant women diagnosed with syphilis should be treated immediately with an appropriate regimen (please refer to the CDC's <u>2021 STI Treatment Guidelines</u>).⁴ Pregnant women who receive treatment at least 30-days prior to birth lower the risk of infection in their baby by 98%.²¹ Their sex partner(s) should also receive treatment to prevent the mother from becoming re-infected and to improve the health of her partner. Neonates should be screened and treated as needed.

Penicillin G benzathine (Bicillin L-A) is the only recommended treatment for syphilis during pregnancy and for CS; no proven therapeutic alternatives exist. Desensitization is therefore required for pregnant women who have a documented penicillin allergy.²² Private clinicians without access to Bicillin L-A are encouraged to work with their <u>local health department</u> to identify timely and affordable treatment options for their patients. Recent national shortages of Bicillin L-A further complicate prevention efforts. In the event of penicillin shortages, VDH has compiled <u>resources</u> for patient prioritization and possible alternative therapies.²³



Partner Services: Medical providers are encouraged to work with <u>DIS</u> to properly stage, treat, and counsel infected pregnant women as well as their partners. DIS can assist with locating sex partners and other contacts, as well as linkage to appropriate care to prevent reinfection of pregnant women. From a surveillance perspective, it is important to document pregnancy status for all syphilis infections among women of reproductive age (15-44 years), and to monitor pregnancies among women at high-risk of syphilis infection or re-infection.

Monitoring: Infants exposed to syphilis during pregnancy should be thoroughly evaluated at birth to assess for evidence of CS and need for treatment. These infants should also be closely followed post-delivery, regardless of initial evaluation or treatment, because infants with CS may not have any initial symptoms at birth but can later develop symptoms of CS if not treated appropriately. Infants with CS who are not treated appropriately within

the first 3 months of life are more likely to have lifelong complications of CS such as deafness, blindness, and intellectual disability.^{3,4}

Address Syndemics and Foster Partnerships: Preventing CS requires consideration not only of disease transmission dynamics, but also of the underlying social inequities and syndemics that hinder prenatal care and overall maternal and child health. Poverty or economic instability, lack of health insurance or access to healthcare, housing instability, substance misuse, incarceration, discrimination, mental health, and other socio-economic factors all have substantial impacts on health and disease risk. These may place women at higher risk not just for syphilis, but also for other infections such as HIV and hepatitis. Therefore, it is important to foster relationships with other partners in public health to comprehensively address the myriad factors relevant to CS prevention and help ensure healthy outcomes for families in Virginia.

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