

Monthly Public Health Webinar

Syphilis *Congenital Syphilis*

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December 14, 2023
New Hampshire Division of Public Health Services

Clinical Didactic on Syphilis

Syphilis: Not a disease of the past

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THE
STATE OF STDs
IN THE
UNITED STATES,
2021

**STDs remain far too high,
even in the face of a
pandemic.**

Note: These data are considered preliminary prior to official 2021 close-out. Data also reflect the effect of COVID-19 on STD surveillance trends.



1.6 million
CASES OF CHLAMYDIA
4.7% decrease since 2017



696,764
CASES OF GONORRHEA
25% increase since 2017



171,074
CASES OF SYPHILIS
68% increase since 2017



2,677
CASES OF SYPHILIS
AMONG NEWBORNS
185% increase since 2017

LEARN MORE AT: www.cdc.gov/std/

Syphilis is increasing among newborn babies in the U.S.

in 2021:



2,855

CASES OF NEWBORN SYPHILIS
203% increase since 2017



220

DEATHS OF BABIES FROM SYPHILIS
175% increase since 2017

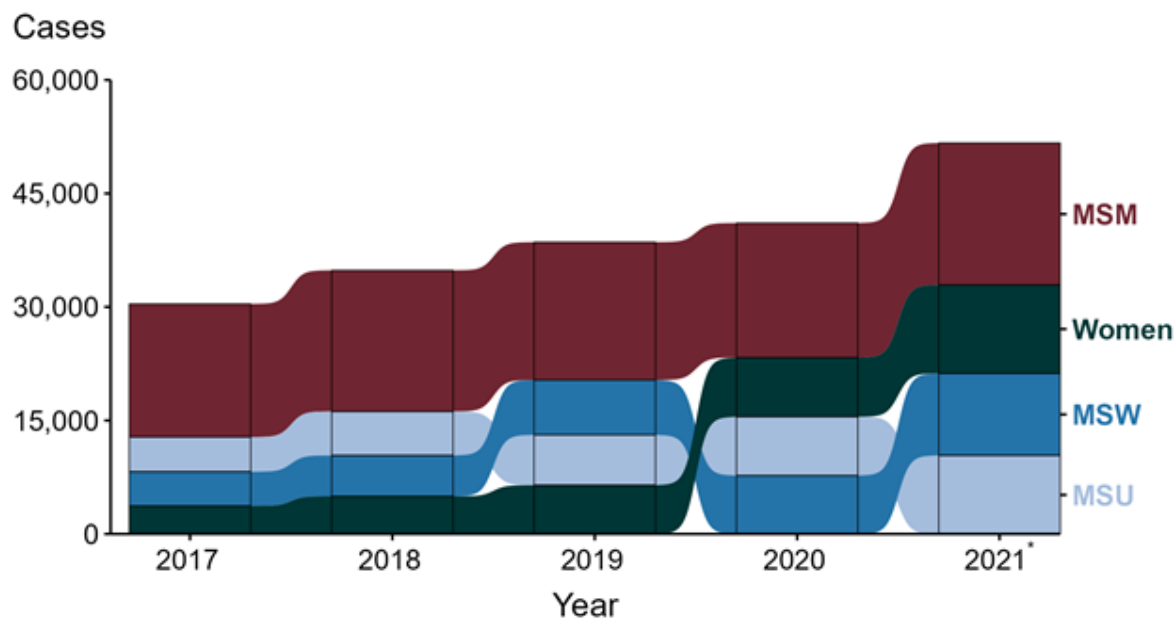


46

STATES WITH AT LEAST ONE CASE
up from 26 in 2011

Every case is one too many
when we have the tools to prevent it

Primary and Secondary Syphilis — Reported Cases by Sex and Sex of Sex Partners, United States, 2017–2021*



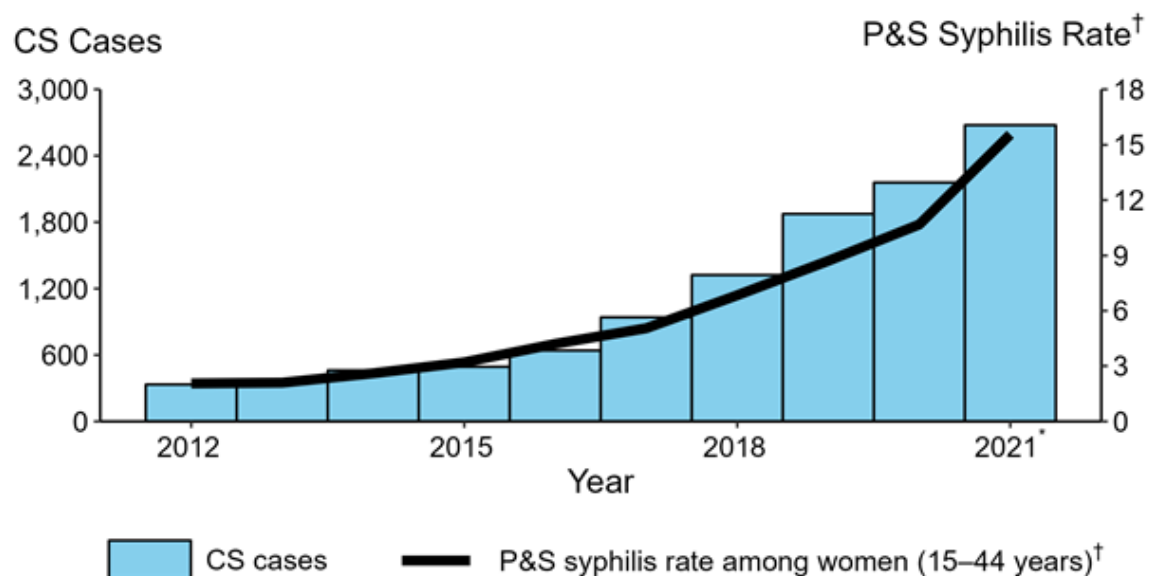
* Reported 2021 data are preliminary as of July 7, 2022

ACRONYMS: MSM = Gay, bisexual, and other men who have sex with men; MSU = Men with unknown sex of sex partners; MSW = Men who have sex with women only

NOTE: Over the five-year period, 0.4% of cases were missing sex and were not included.



Congenital Syphilis — Reported Cases by Year of Birth and Rates of Reported Cases of Primary and Secondary Syphilis Among Women Aged 15–44 Years, United States, 2012–2021*



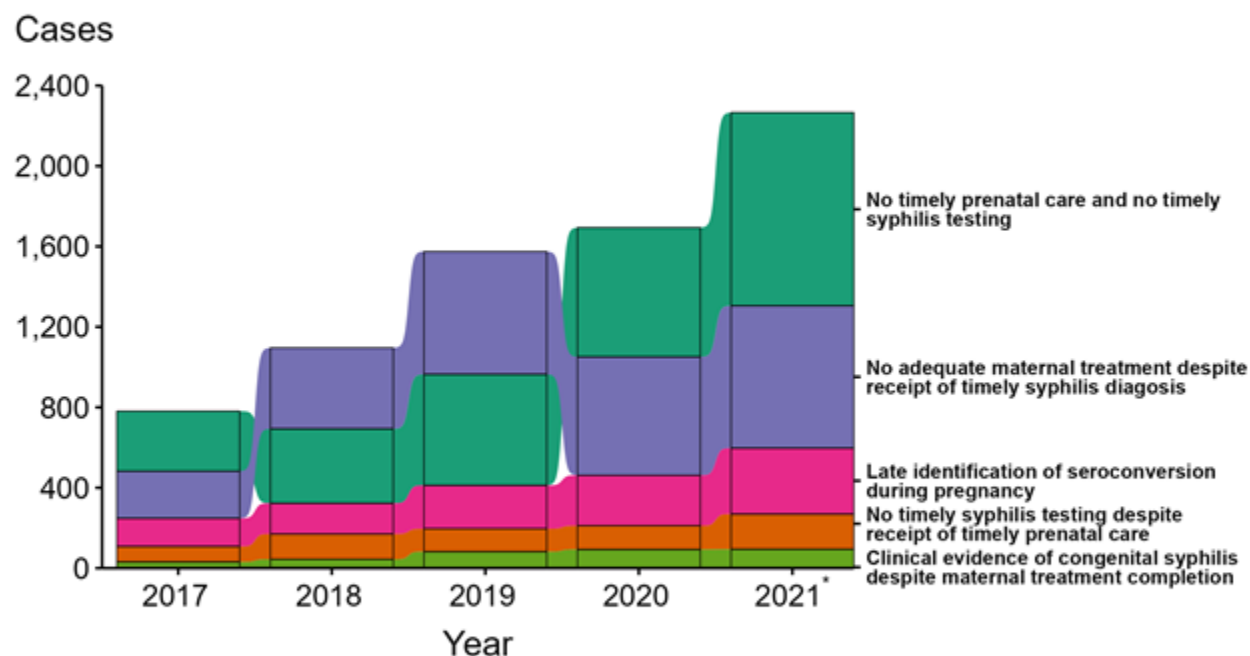
* Reported 2021 data are preliminary as of July 7, 2022

† Per 100,000

ACRONYMS: CS = Congenital syphilis; P&S = Primary and secondary syphilis



Congenital Syphilis — Missed Prevention Opportunities among Mothers Delivering Infants with Congenital Syphilis, United States, 2017–2021*



* Reported 2021 data are preliminary as of July 7, 2022

NOTE: Of the 8,974 congenital syphilis cases reported during 2017 to 2021, 1,562 (17.4%) were not able to have the primary missed prevention opportunity identified due to insufficient information provided to CDC related to maternal prenatal care, testing, or treatment.



Syphilis (*Treponema pallidum*)



- Can be acquired sexually, hematogenously, or via vertical transmission from mother to infant.
- If left untreated, is associated with significant complications.
- Can facilitate the transmission and acquisition of HIV infection.

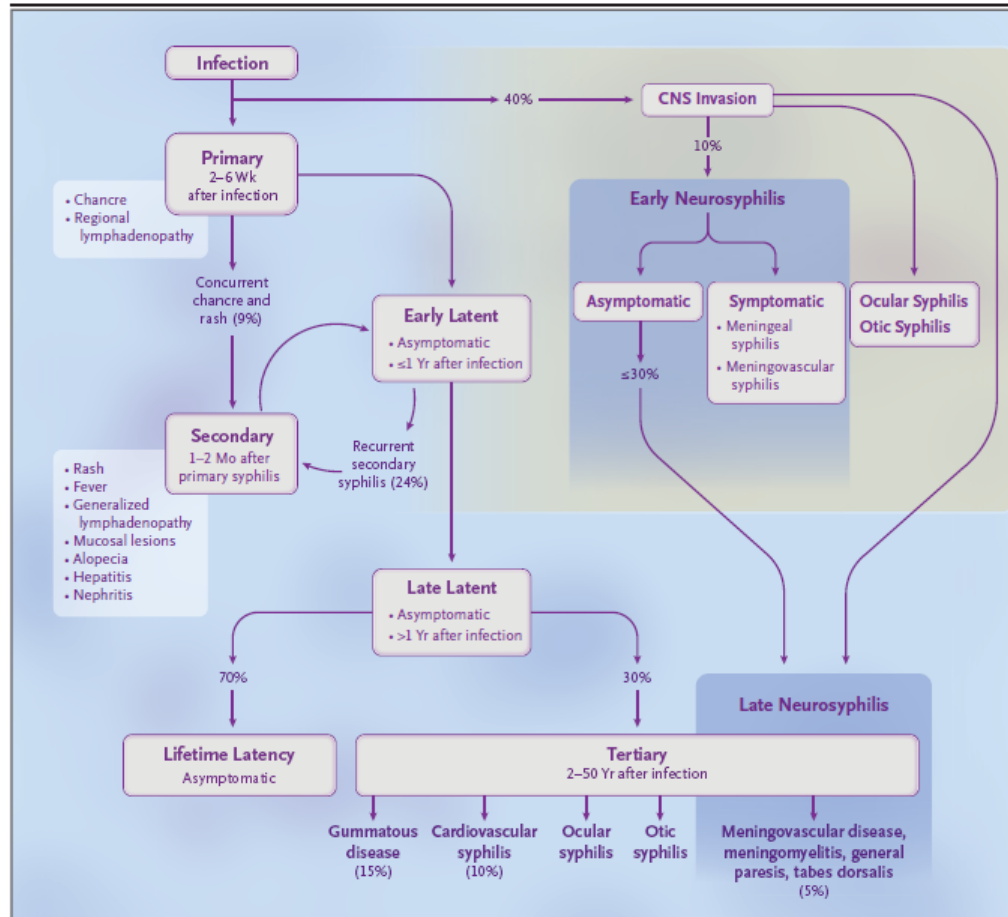
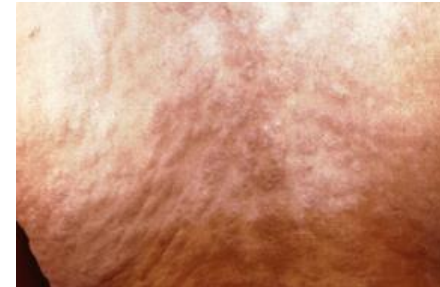


Figure 2. Natural History of Untreated Syphilis.

The time intervals between stages of syphilis are shown, along with the approximate percentages of persons progressing to the indicated stages. Invasion of the central nervous system (CNS) by treponemes may not be a necessary prerequisite for the development of certain forms of ocular syphilis. Adapted from Ho and Lukehart.¹⁰



Images: CDC

N Engl J Med 2020;382:845-54.
DOI: 10.1056/NEJMra1901593

USPSTF Screening Recommendations

Population	Recommendation	Grade
Asymptomatic, nonpregnant adolescents and adults who are at increased risk for syphilis infection	The USPSTF recommends screening for syphilis infection in persons who are at increased risk for infection.	A

* Risk of syphilis is higher in men who have sex with men; persons with HIV infection or other sexually transmitted infections; persons who use illicit drugs; and persons with a history of incarceration, sex work, or military service.

Population	Recommendation	Grade
Pregnant women	The USPSTF recommends early screening for syphilis infection in all pregnant women.	A



Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

Sexually Transmitted Infections Treatment Guidelines, 2021

Screening Recommendations and Considerations Referenced in Treatment Guidelines and Original Sources

By Disease

By Population

[STI Screening Recommendations \(cdc.gov\)](https://www.cdc.gov/sti/screening-recommendations)

Syphilis

Women	<ul style="list-style-type: none">• Screen asymptomatic women at increased risk (history of incarceration or transactional sex work, geography, race/ethnicity) for syphilis infection^{2,7}
Pregnant Women	<ul style="list-style-type: none">• All pregnant women at the first prenatal visit⁸• Retest at 28 weeks gestation and at delivery if at high risk (lives in a community with high syphilis morbidity or is at risk for syphilis acquisition during pregnancy [drug misuse, STIs during pregnancy, multiple partners, a new partner, partner with STIs])²
Men Who Have Sex With Women	<ul style="list-style-type: none">• Screen asymptomatic adults at increased risk (history of incarceration or transactional sex work, geography, race/ethnicity, and being a male younger than 29 years) for syphilis infection^{2,7}
Men Who Have Sex With Men	<ul style="list-style-type: none">• At least annually for sexually active MSM²• Every 3 to 6 months if at increased risk²• Screen asymptomatic adults at increased risk (history of incarceration or transactional sex work, geography, race/ethnicity, and being a male younger than 29 years) for syphilis infection^{2,7}
Transgender and Gender Diverse People	<ul style="list-style-type: none">• Consider screening at least annually based on reported sexual behaviors and exposure²
Persons with HIV	<ul style="list-style-type: none">• For sexually active individuals, screen at first HIV evaluation, and at least annually thereafter^{2,6}• More frequent screening might be appropriate depending on individual risk behaviors and the local epidemiology²

Syphilis in Pregnancy

- Transplacental transmission of *T. pallidum* can occur at any time during gestation but occurs with increasing frequency as gestation advances.
- Women with untreated primary or secondary syphilis are more likely to transmit syphilis to their fetuses than women with latent disease.
- If acquired within 4 years of delivery, can lead to infection in fetus in 80% of cases and may result in stillbirth or infant death in up to 40%.
 - The risk of transmission is only 2% after four years.
- *T. pallidum* is not transferred in breast milk, but transmission may occur if the mother has a chancre on her breast.

Complications of syphilis in pregnancy

- Miscarriage
- Preterm birth
- Stillbirth
- Impaired fetal growth
- Congenital infection
- Neonatal mortality

TABLE 2

Summary estimates of adverse pregnancy outcomes in untreated maternal syphilis

Qin et al (2014) ³³	Summary estimate (95% CI)
All adverse pregnancy outcomes	76.8% (68.8–83.2)
Congenital syphilis	36.0% (28.0–44.9)
Preterm birth	23.2% (18.1–29.3)
Low birthweight	23.4% (12.8–38.6)
Miscarriage	14.9% (11.4–19.4)
Stillbirth or fetal loss	26.4% (21.9–31.4)
Neonatal death	16.2% (10.1–25.1)
Gomez et al (2013) ³¹	
All adverse pregnancy outcomes	66.5% (58.0–74.1)
Clinical evidence of syphilis	15.5% (7.5–29.0)
Prematurity or low birthweight	12.1% (3.9–31.8)
Stillbirth and fetal loss	25.6% (18.5–34.2)
Neonatal death	12.3% (9.3–16.2)

Adapted from Qin et al,³³ and Gomez et al.³¹

CI, confidence interval.

Eppes. Syphilis in pregnancy. Am J Obstet Gynecol 2022.

Syphilis Screening in Pregnancy

- All pregnant women should be tested for syphilis at their first prenatal visit.
- For women at high risk for infection*, serologic testing should be performed twice during the third trimester: once at 28–32 wk gestation and again at delivery.
- Any woman who has a fetal death after 20 wk gestation should be tested for syphilis.
- No mother or neonate should leave the hospital without maternal serologic status having been documented at least once during pregnancy, and if the mother is considered high risk, documented at delivery.
- Concurrent HIV screening recommended for all pregnant woman.

*Women at high risk

- Diagnosed with a STI during pregnancy
- Exchanging sex for drugs or money
- Multiple sex partners
- Late entry into care (second trimester or later)
- No prenatal care
- Residence in an area of high syphilis prevalence
- Methamphetamine or heroin use
- Incarceration of woman or her partner
- Unstable housing or homelessness

Legal requirements for syphilis screening among pregnant women by time of test and state, 2018

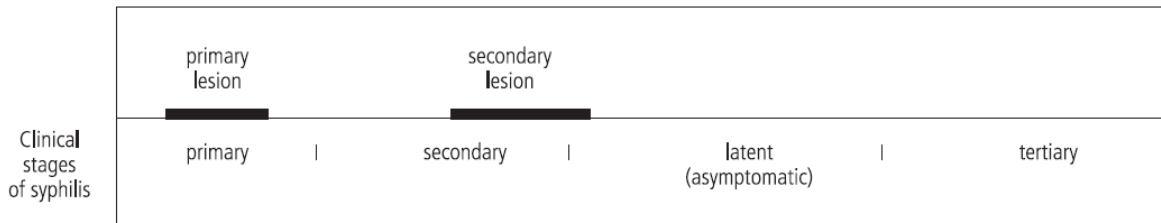
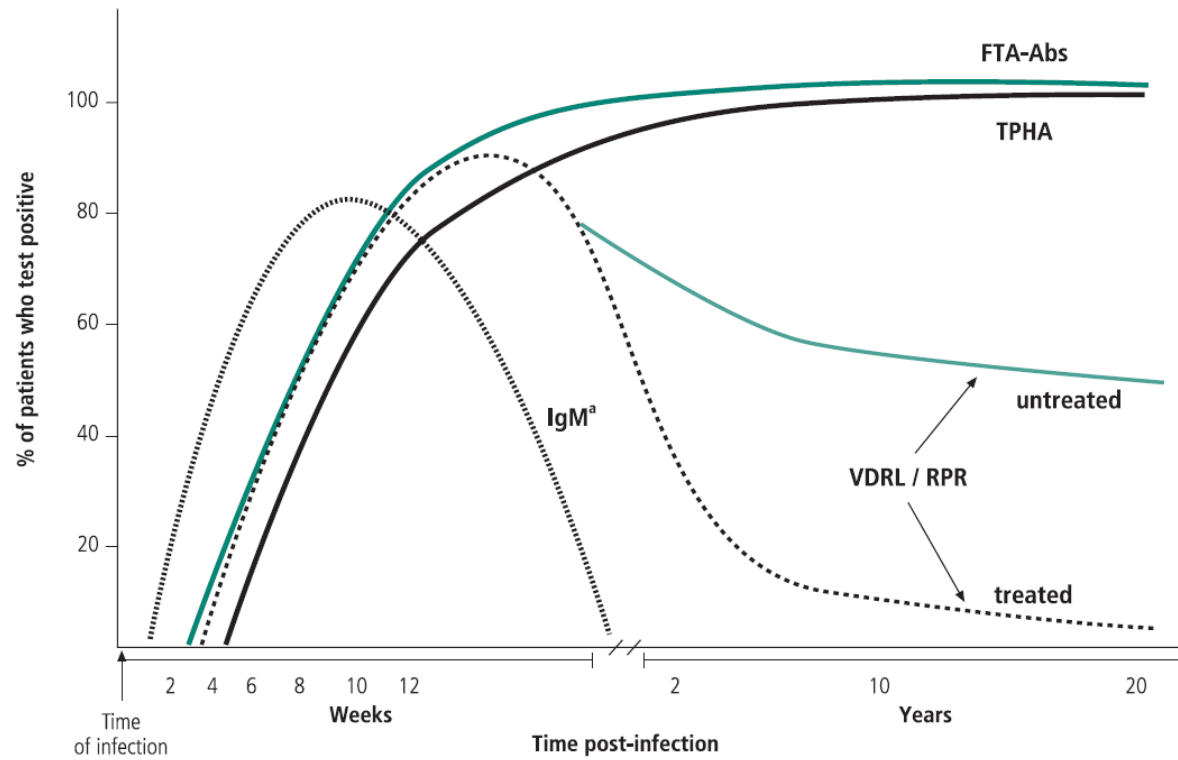
	First Visit	Third Trimester	Delivery
Alabama	X	O	X
Alaska	X		
Arizona	X	X	X
Arkansas	X	X	
California	X		
Colorado	X		
Connecticut	X	X	
Delaware	X	X	
DC	X	X	
Florida	X	X	O
Georgia	X	X	O
Hawaii			
Idaho	X		
Illinois	X	X	
Indiana	X	O	
Iowa			
Kansas	X		
Kentucky	X		
Louisiana	X	X	O
Maine			
Maryland	X	X	O
Massachusetts	X		
Michigan	X	X	O
Minnesota			
Mississippi			
Missouri	X	O	O
Montana	X		
Nebraska	X		
Nevada	X	X	
New Hampshire			

X	Screening required
O	Screening Required only if at increased risk

New Jersey	X		X
New Mexico	X		
New York	X		
North Carolina	X	X	X
North Dakota			
Ohio	X		
Oklahoma	X		
Oregon	X		
Pennsylvania	X	O	
Rhode Island	X		
South Carolina	X		
South Dakota	X		
Tennessee	X	O	
Texas	X	X	
Utah	X		
Vermont	X		
Virginia	X		
Washington	X		
West Virginia	X		
Wisconsin			
Wyoming	X		

Serologic Tests

- Nontreponemal – nonspecific, low cost, able to quantify response to treatment
 - Rapid plasma reagin (RPR)
 - Venereal Disease Research Laboratory (VDRL)
 - Tolidine Red Unheated Serum Test (TRUST)
- Treponemal – more complex, expensive, specific, qualitative
 - Fluorescent treponemal antibody absorption (FTA-ABS)
 - *T. pallidum* particle agglutination assay (TPPA)
 - *T. pallidum* enzyme immunoassay (TP-EIA)
 - Microhemagglutination test for antibodies to *Treponema pallidum* (MHA-TP)
 - Chemiluminescence immunoassay (CIA)

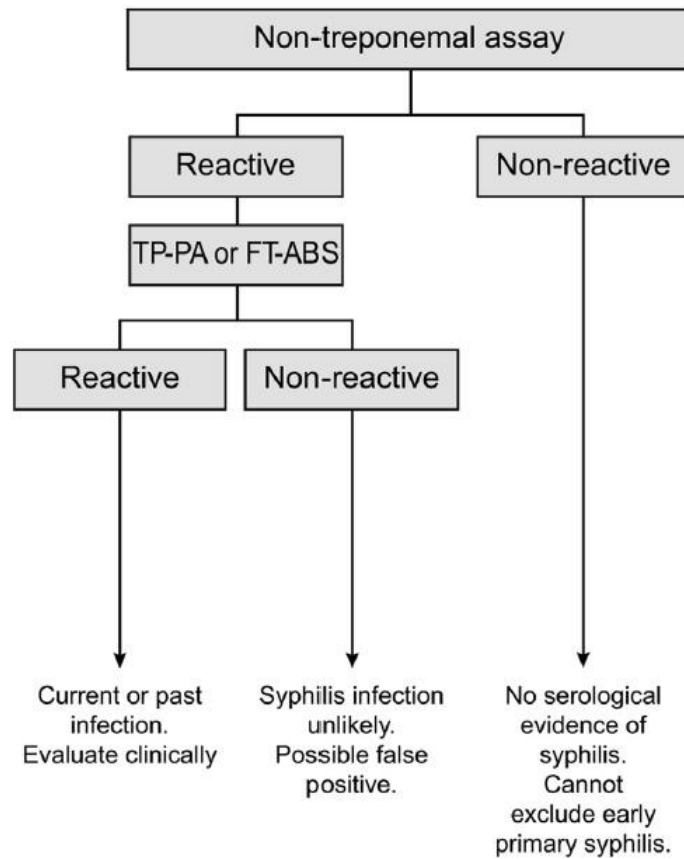


Rac et al. Syphilis during pregnancy: a preventable threat to maternal-fetal health. AJOG. 2017.

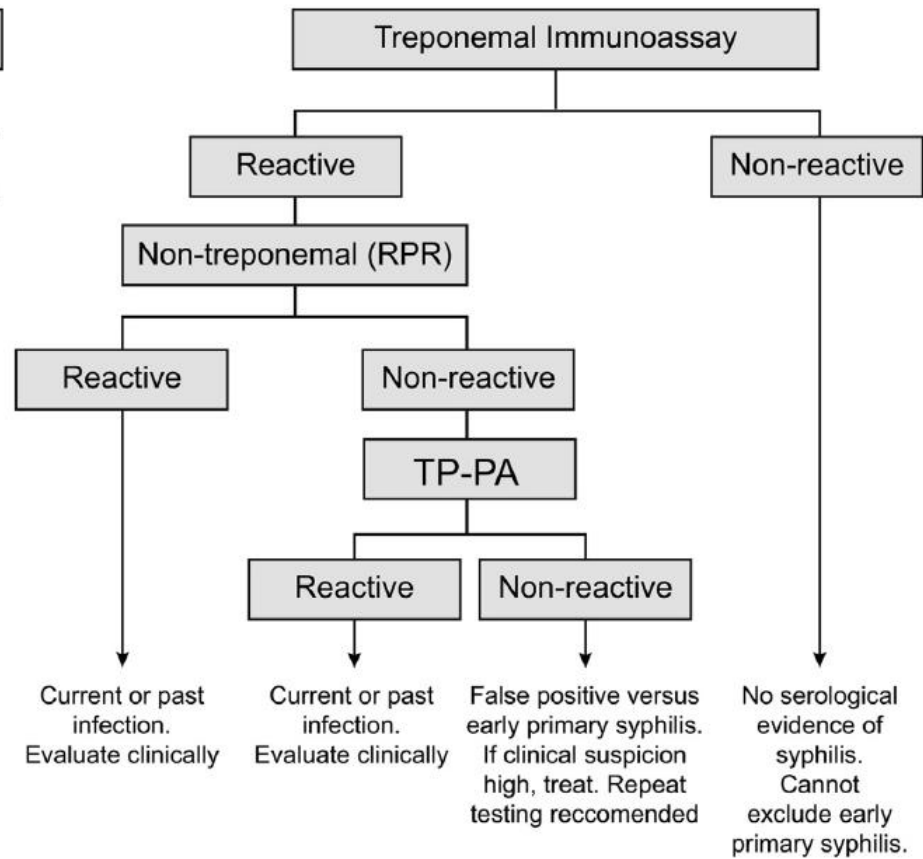
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Screening Algorithms

Traditional



Reverse



Syphilis or not?

RPR	<i>Negative</i> *
-----	-------------------

Syphilis IgG/IgM	<i>Negative</i>
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Syphilis IgG/IgM	<i>Positive</i> *	!
RPR	<i>Reactive</i> *	!
RPR Titer	<i>1:8</i> *	!

Syphilis IgG/IgM	<i>Positive</i> !
Syphilis Ab, TP-PA	
RPR	<i>Non-Reactive</i> *
RPR Response to Th...	
RPR, Response to T...	<i>Negative</i> *
T. pallidum Ab by ...	<i>Non-Reactive</i> *

Syphilis IgG	<i>Positive</i> *	!
Syphilis Ab, TP-PA	<i>Positive</i> *	!
RPR	<i>Negative</i> *	

False-positive nontreponemal tests

- 31% of pregnant women with positive VDRL was FP
 - Biologically due to pregnancy
 - Acute febrile illness
 - Recent immunization
 - Autoimmune disorders
 - IVDU
 - Chronic liver disease
 - HIV
- Hence all positive tests need confirmatory testing

Genitourin Med. 1990;66(2):76
Clin Microbiol Rev. 1995;8(1):1

False-positive treponemal tests

- 47-88% of pregnant women have with positive TP-EIA or CIA was FP
 - Biologically due to pregnancy
 - Advanced age
 - Tumor
 - Dialysis
 - Autoimmune disease
 - Other spirochetal infections, malaria, leprosy
- Hence all positive tests need confirmatory testing

J Med Assoc Thai. 2016;99(2):119
Clin Infect Dis. 2015;61(7):1049.
Sex Transm Dis. 2011;38(12):1126

False-negative nontreponemal test

- Very early infection (primary or secondary)
 - 20-30% of patients presenting with chancre will have negative nontreponemal test
- Prozone reaction
 - Antibody titers are high (as often seen in secondary syphilis), an overabundance of antibodies interferes with clumping of antigen-antibody complexes
 - Occurs in pregnancy, HIV and neurosyphilis
- Early treatment preventing antibody formation
- Late infection (nontreponemal tests become nonreactive over time)

Clin Infect Dis. 2010;51(6):700
Ann Intern Med. 1986;104(3):368

CNS involvement can occur during any stage of syphilis, and CSF laboratory abnormalities are common among persons with early syphilis, even in the absence of clinical neurologic findings. No evidence exists to support variation from recommended diagnosis and treatment for syphilis at any stage for persons without clinical neurologic findings, except tertiary syphilis. If clinical evidence of neurologic involvement is observed (e.g., cognitive dysfunction, motor or sensory deficits, cranial nerve palsies, or symptoms or signs of meningitis or stroke), a CSF examination should be performed before treatment.

Syphilitic uveitis or other ocular syphilis manifestations (e.g., neuroretinitis and optic neuritis) can occur at any stage of syphilis and can be isolated abnormalities or associated with neurosyphilis. All persons with ocular symptoms and reactive syphilis serology need a full ocular examination, including cranial nerve evaluation. If cranial nerve dysfunction is present, a CSF evaluation is needed. Among persons with isolated ocular symptoms (no cranial nerve dysfunction or other neurologic abnormalities), reactive syphilis serology, and confirmed ocular abnormalities on examination, CSF examination is unnecessary before treatment. CSF analysis might be helpful in evaluating persons with ocular symptoms and reactive syphilis serology who do not have ocular findings on examination. If ocular syphilis is suspected, immediate referral to and management in collaboration with an ophthalmologist is crucial. Ocular syphilis should be treated similarly to neurosyphilis, even if a CSF examination is normal.

Hearing loss and other otologic symptoms can occur at any stage of syphilis and can be isolated abnormalities or associated with neurosyphilis, especially of cranial nerve 8. However, among persons with isolated auditory symptoms, normal neurologic examination, and reactive syphilis serology, CSF examination is likely to be normal and is not recommended before treatment. Otosyphilis should be managed in collaboration with an otolaryngologist and treated by using the same regimen as for neurosyphilis.

Testing for Neurosyphilis

- CSF VDRL – highly specific but poor sensitivity (30%)
- CSF FTA-ABS – less specific but more sensitive
- Elevated WBC and protein – nonspecific
- Laboratory diagnosis of neurosyphilis usually depends on various combinations of reactive serologic test results, CSF cell count and protein, and a reactive CSF-VDRL with or without clinical manifestations.

Treatment of Syphilis

- Primary, secondary, or early latent (<1yr) syphilis
 - **Benzathine penicillin G 2.4 million units IM x 1**
 - Alternative: Doxycycline 100mg PO BID x 14 days
- Late latent (>1yr)
 - **Benzathine penicillin G 2.4 million units IM weekly x 3 weeks**
 - Alternative: Doxycycline 100mg PO BID x 28 days
- Neurosyphilis, ocular or otic syphilis
 - **IV Penicillin G x 14 days**
 - Alternative: Procaine penicillin G 2.4 million units IM once daily PLUS Probenecid 500 mg orally 4 times/day, both for 10–14 day

CDC 2021 STI Treatment Guidelines

[Syphilis - STI Treatment Guidelines \(cdc.gov\)](https://www.cdc.gov/std/treatment-guidelines/syphilis)


Treatment in Pregnancy

- **Penicillin is the gold standard for treatment.**
 - It is the only known effective antimicrobial for treating fetal infection and preventing congenital syphilis.
- Non-penicillin antibiotic regimens used for syphilis treatment in non-pregnant women are either contraindicated (eg, tetracycline, doxycycline), lack sufficient data regarding efficacy (eg, ceftriaxone), or do not cross the placental barrier completely so the fetus is not treated (eg, erythromycin, azithromycin).
- Missed doses >9 days between doses are not acceptable for pregnant women receiving therapy for late latent syphilis.

CDC 2021 STI Treatment Guidelines

[Syphilis During Pregnancy - STI Treatment Guidelines \(cdc.gov\)](https://www.cdc.gov/std/treatment-guidelines/syphilis-during-pregnancy)

Bicillin L-A® Shortage

The FDA has listed penicillin G benzathine injectable suspension products (Bicillin L-A®) on [their drug shortage webpage](#) , noting limited supply due to increased demand. The FDA website includes an expected duration for the shortage. CDC continues to monitor the situation and will post updates as needed.

Bicillin L-A® is the first-line recommended treatment for syphilis and the only recommended treatment option for some patients.

During this time, programs can see [Clinical Reminders during Bicillin L-A® Shortage](#) for priority actions they can take.

- Prioritize using Bicillin L-A® to treat **pregnant people** with syphilis and **babies with congenital syphilis** – penicillin is the only recommended treatment for these populations.
- Appropriately stage syphilis cases to ensure appropriate use of antimicrobials. Early syphilis (primary, secondary and early latent) only requires 2.4 million units of Bicillin L-A®.

Jarisch-Herxheimer reaction

- Acute systemic reaction that results from the rapid killing of spirochetes
 - Skin rash, fever/chills, tachycardia, arthralgias, pharyngitis, headache, leukocytosis
 - Onset 2-8 hours after treatment and resolves by 24 hours
 - Treatment is supportive
- More common in early stages of syphilis
 - 95% experience reaction with treatment of primary or secondary syphilis
- In pregnant women it can lead to preterm labor, fetal heart rate abnormalities and stillbirth (depending on severity of fetal infection)
 - Consider giving first dose of Penicillin under 24hr continuous fetal monitoring

Indian J Sex Transm Dis AIDS. 2022.

Eppes. Syphilis in pregnancy. AJOG. 2022.

Treatment Outcomes

- Maternal treatment is curative for fetal infection in most cases
 - Congenital infection occurs in 1-2% of treated women and 70-100% of untreated women
- Predictors of fetal treatment failure:
 - High nontreponemal titer at time of treatment or delivery
 - Ultrasound abnormalities suggestive of congenital syphilis
 - Early stage infection
 - Treatment <30 days before delivery
 - Delivery <36 wks

BMC Public Health. 2011;11 Suppl 3:S9.

Am J Obstet Gynecol. 2002;186(3):569

Rac. Syphilis during pregnancy. AJOG. 2017.

Syphilis can have very serious complications when left untreated.



[Addressing STIs: Ask. Test. Treat. Repeat. | TargetHIV](#)

Sexually Transmitted Infections Treatment Guidelines, 2021

[Syphilis - STI Treatment Guidelines \(cdc.gov\)](https://www.cdc.gov/std/treatment-guidelines)

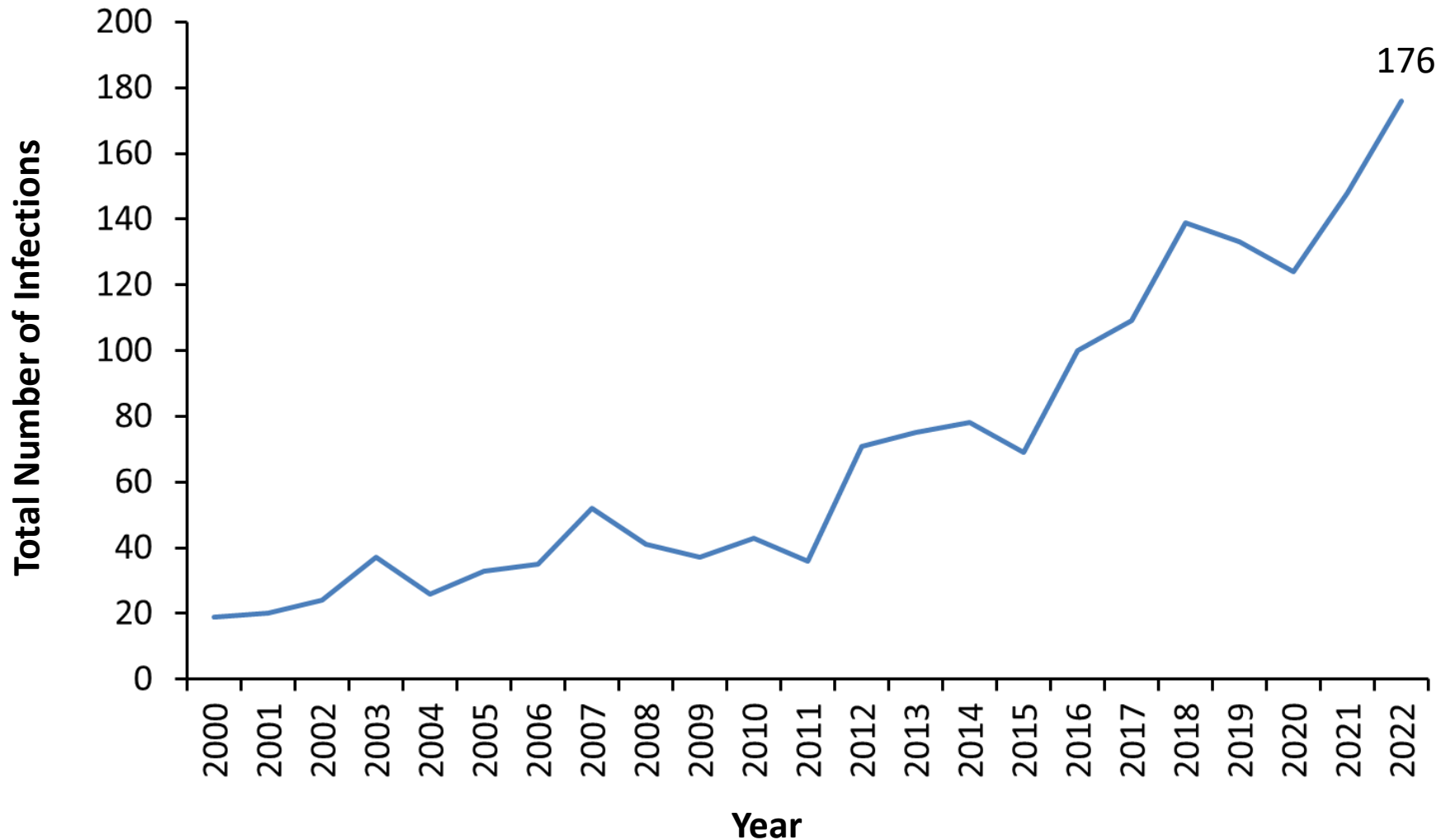


 National **STD** Curriculum

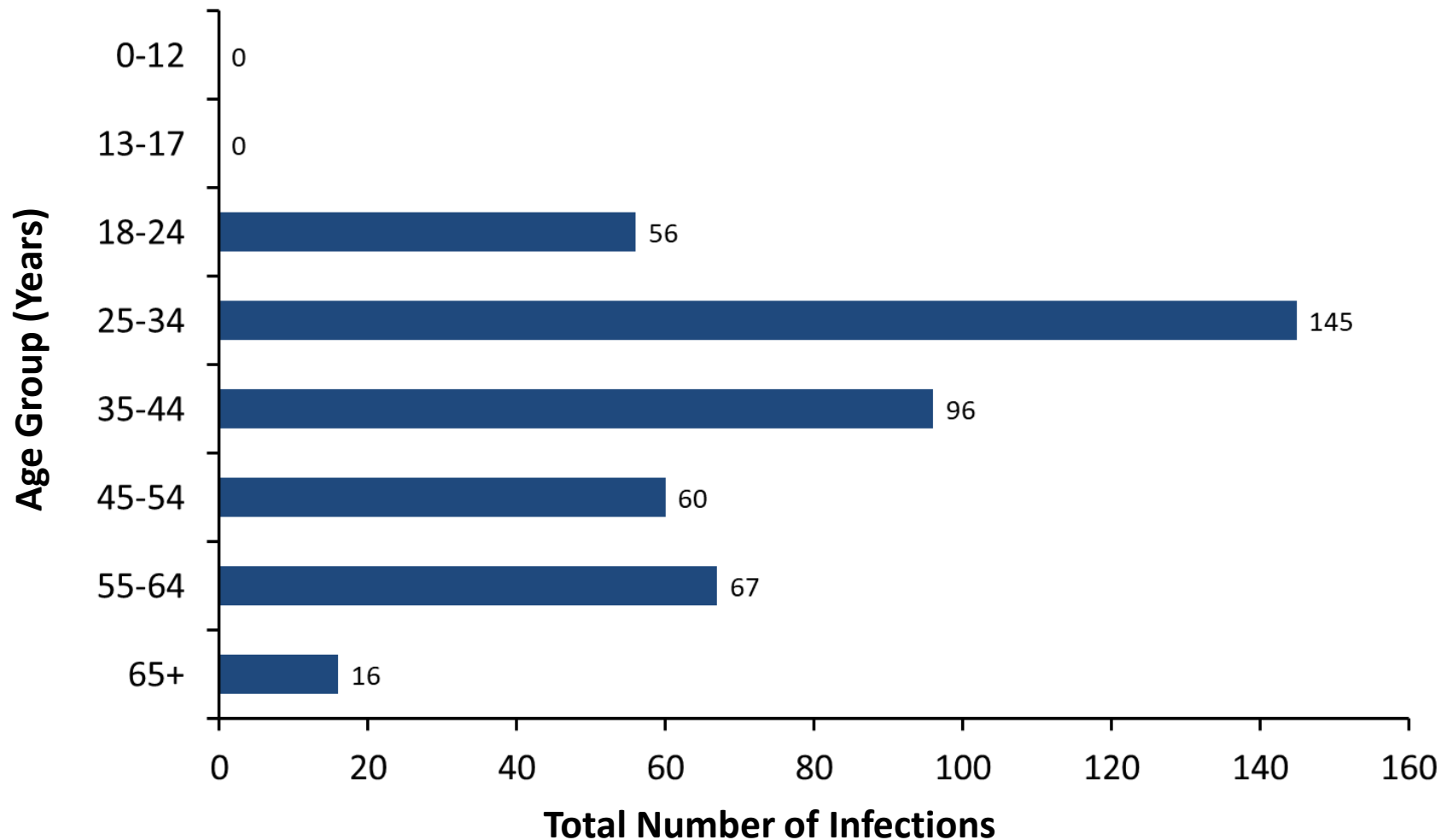
[Core Concepts - Syphilis - Self-Study Lessons 2nd Edition -
National STD Curriculum \(uw.edu\)](https://www.uw.edu/stdccn/core-concepts-syphilis-self-study-lessons-2nd-edition)

Syphilis in New Hampshire

Total Number of Syphilis Infections in NH Each Year (All Stages), 2000 – 2022

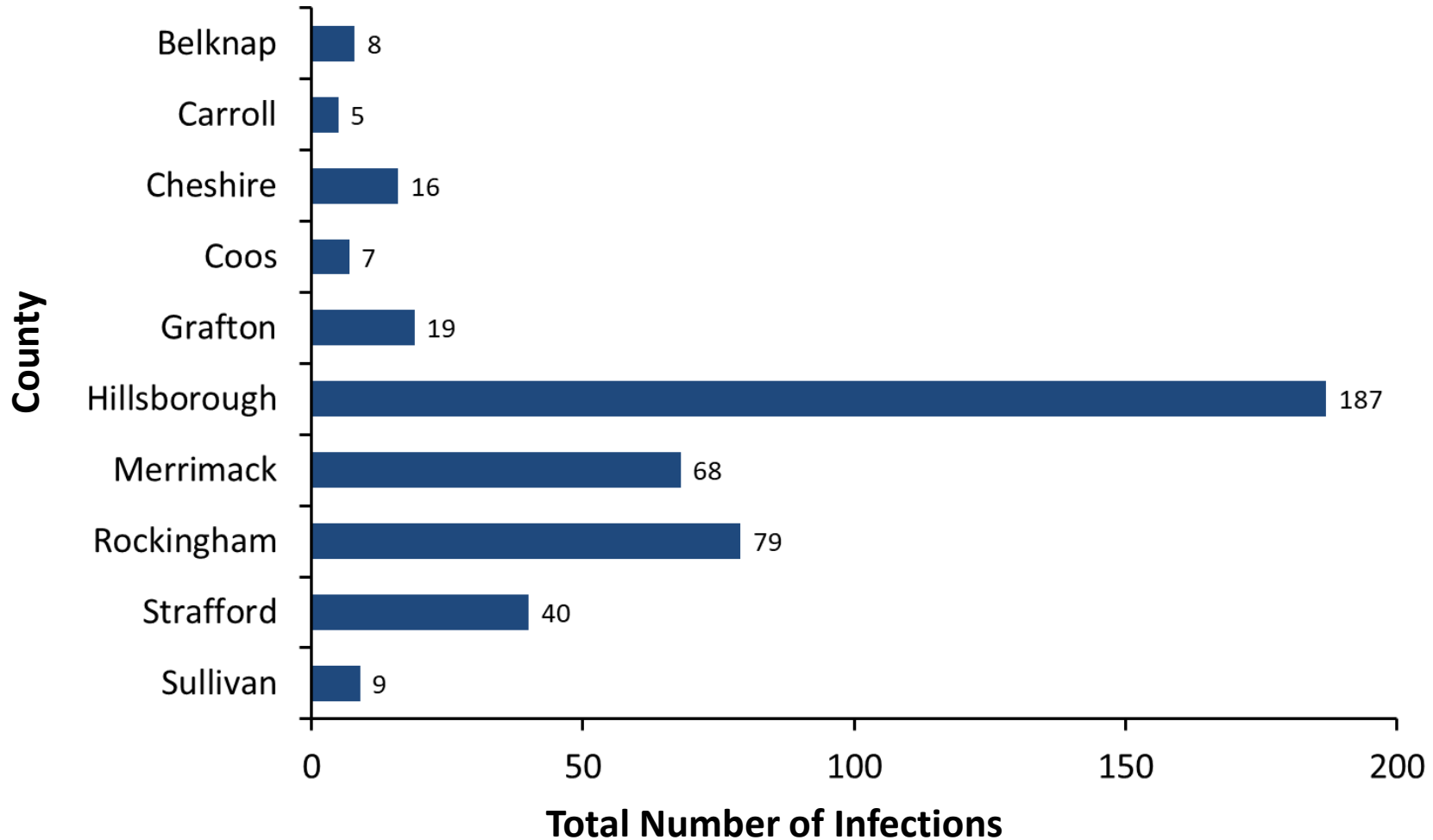


Total Number of Syphilis Infections in NH by Age (All Stages), 2021 – 2023* Combined



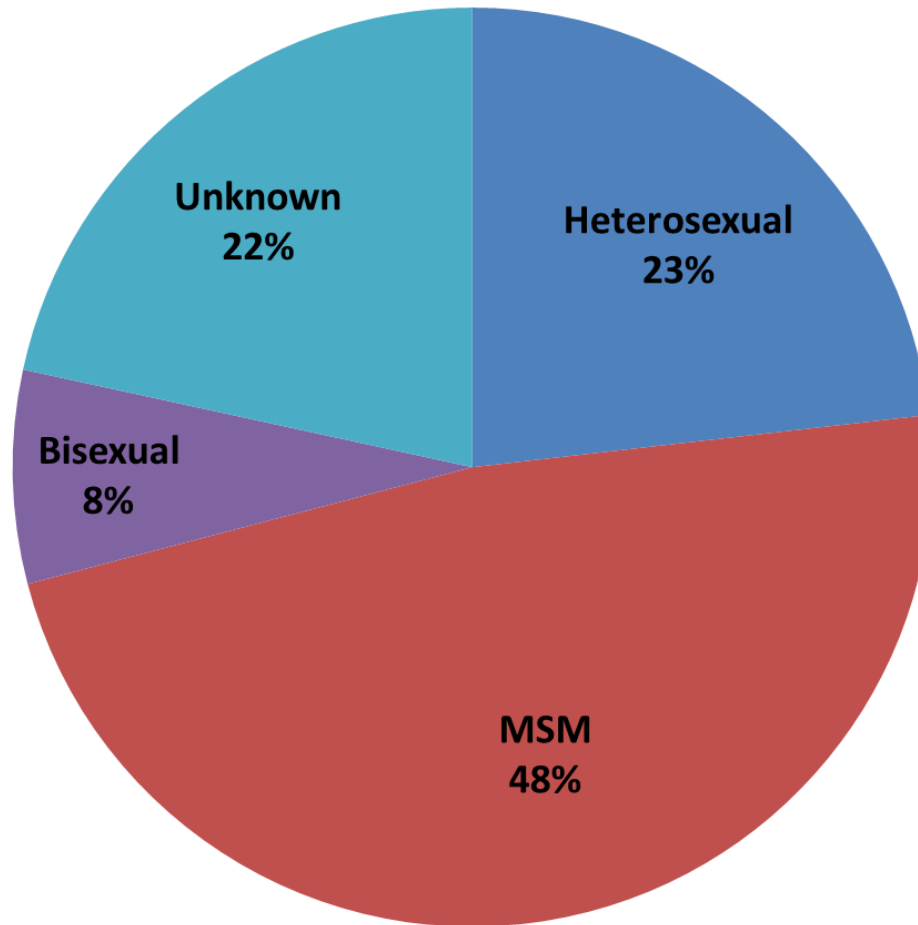
* 2023 data is incomplete and includes reported cases to date through the end of November 2023

Total Number of Syphilis Infections in NH by County (All Stages), 2021 – 2023* Combined



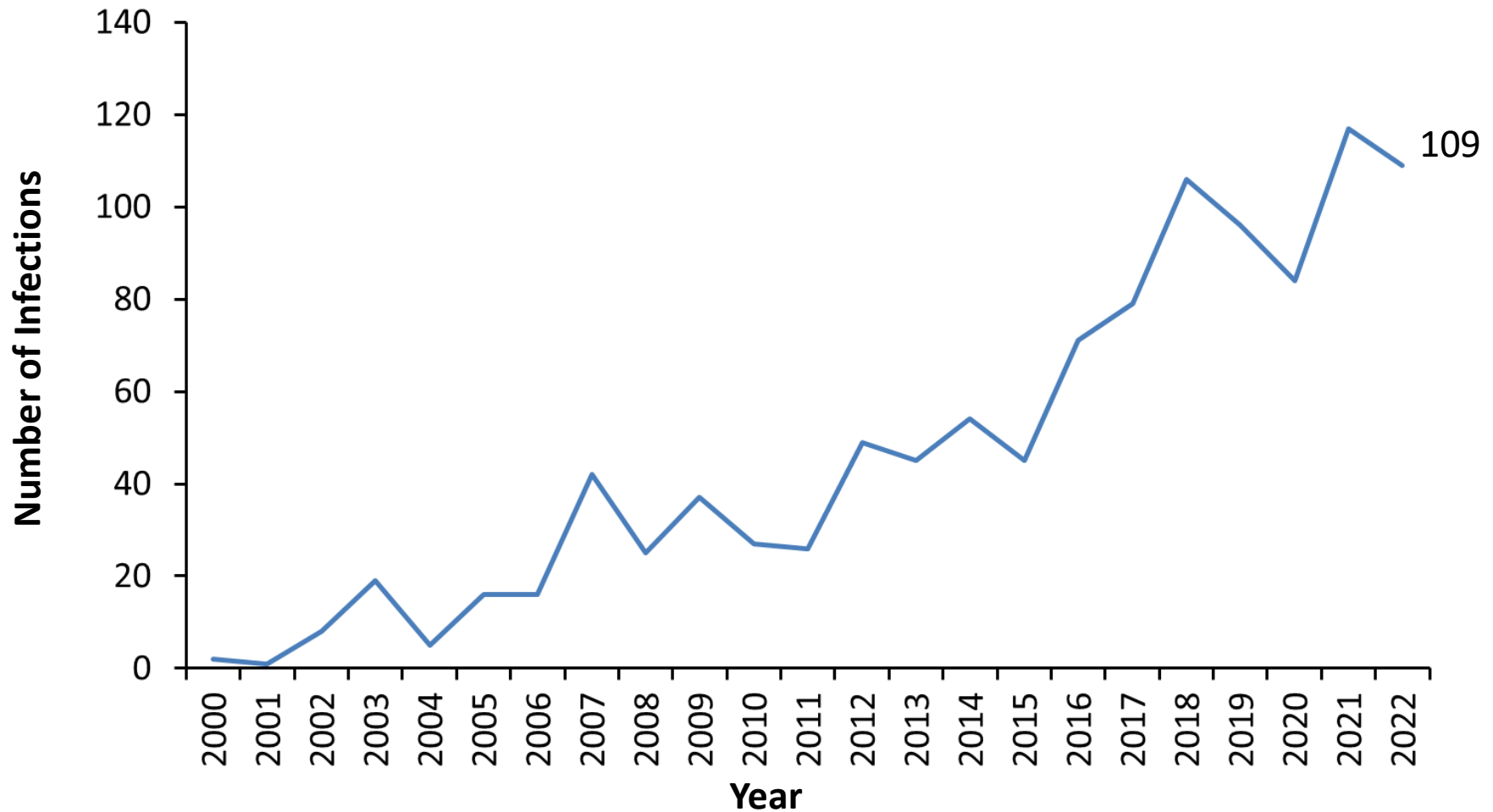
* 2023 data is incomplete and includes reported cases to date through the end of November 2023

Percent of Syphilis Cases with Reported Sexual Risk Factor in NH, 2021 – 2023* Combined



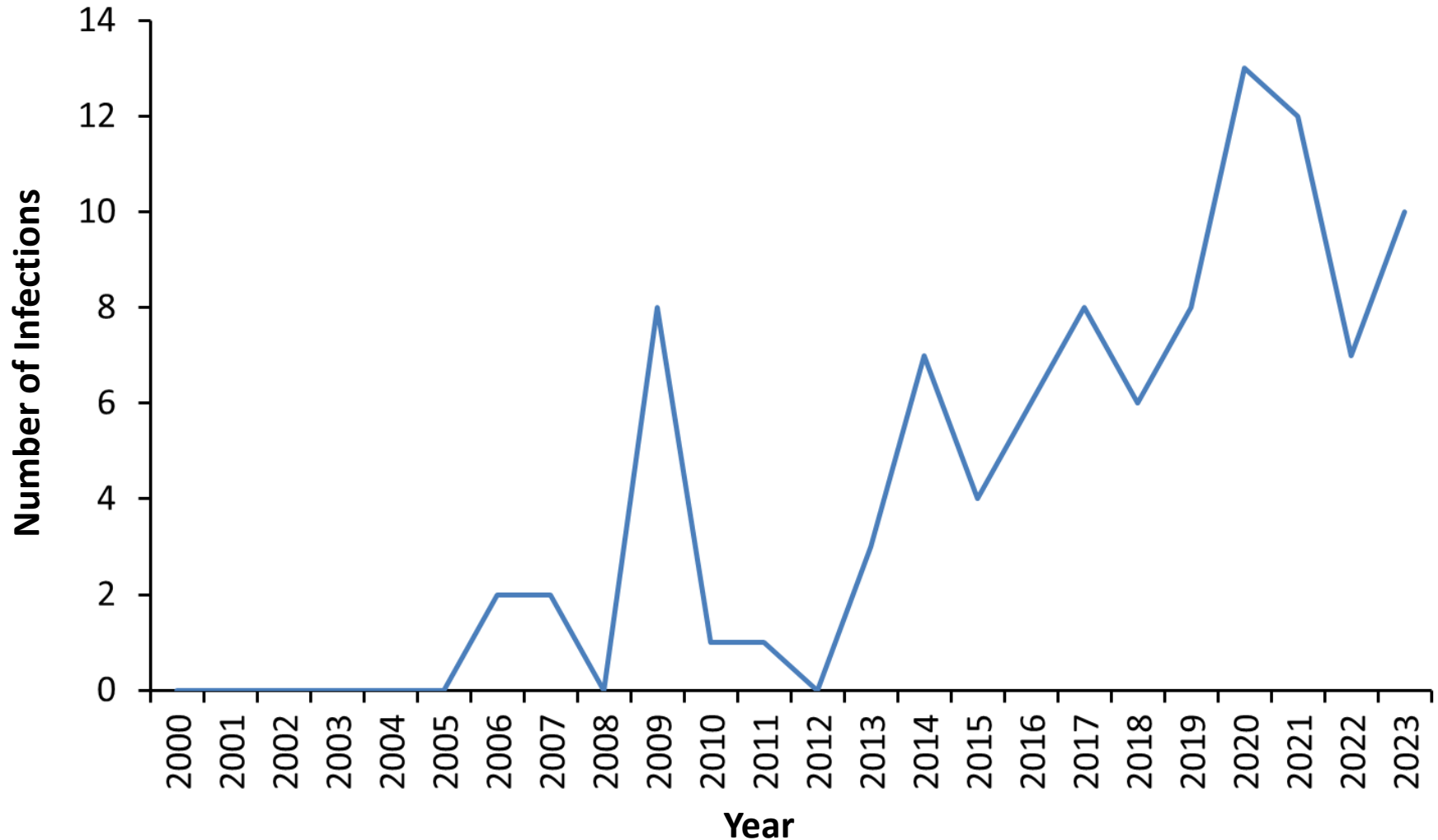
* 2023 data is incomplete and includes reported cases to date through the end of November 2023

Number of “Infectious Syphilis” Infections in NH Each Year, 2000 – 2022



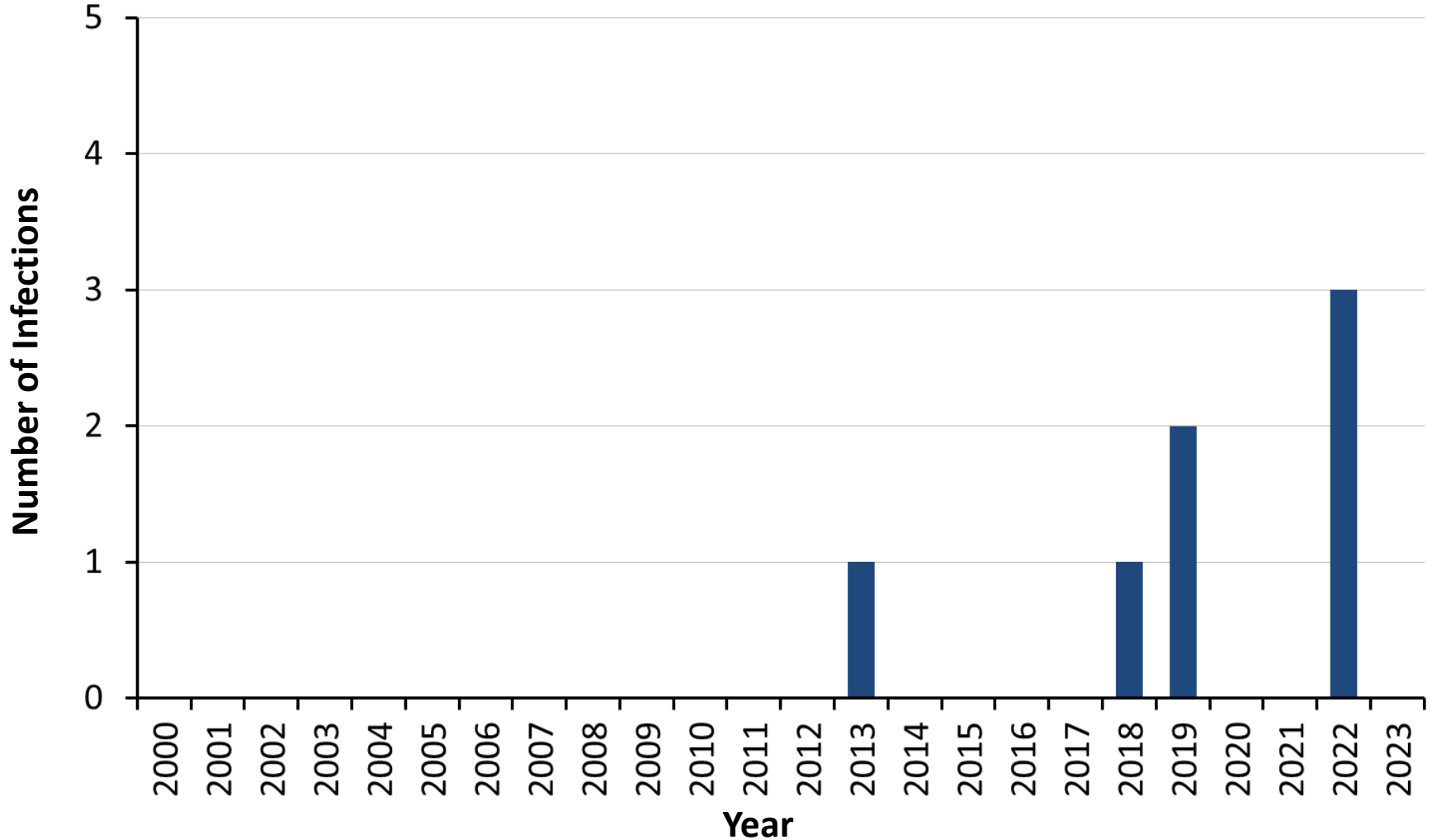
Note: “Infectious Syphilis” includes persons with primary, secondary, and other early syphilis infections determined to have occurred within the previous 12 months.

Number of “Infectious Syphilis” Cases in Females in NH Each Year, 2000 – 2023*



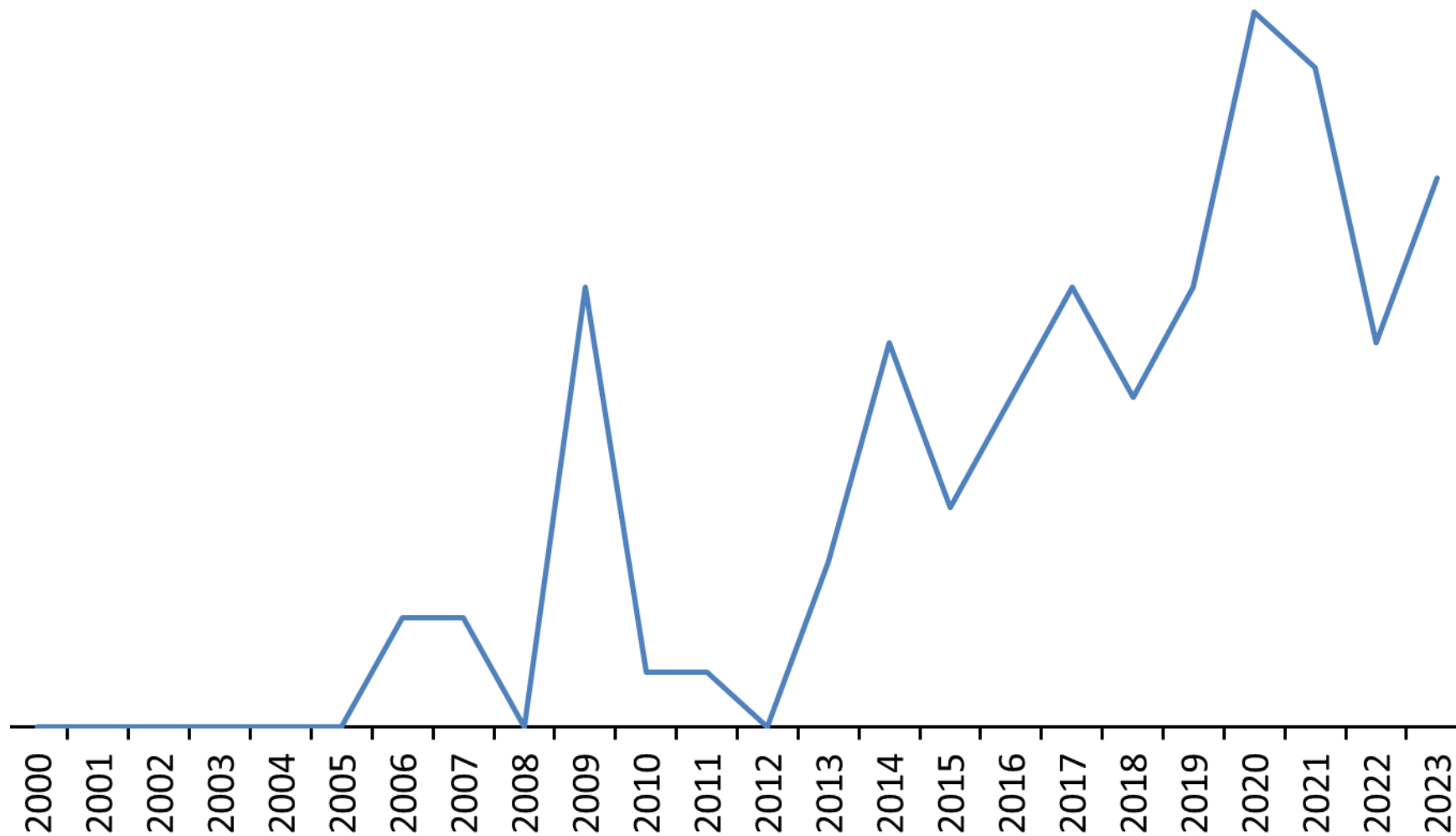
* 2023 data is incomplete and includes reported cases to date through the end of November 2023

Number of Congenital Syphilis Infections in NH Each Year, 2000 – 2023*

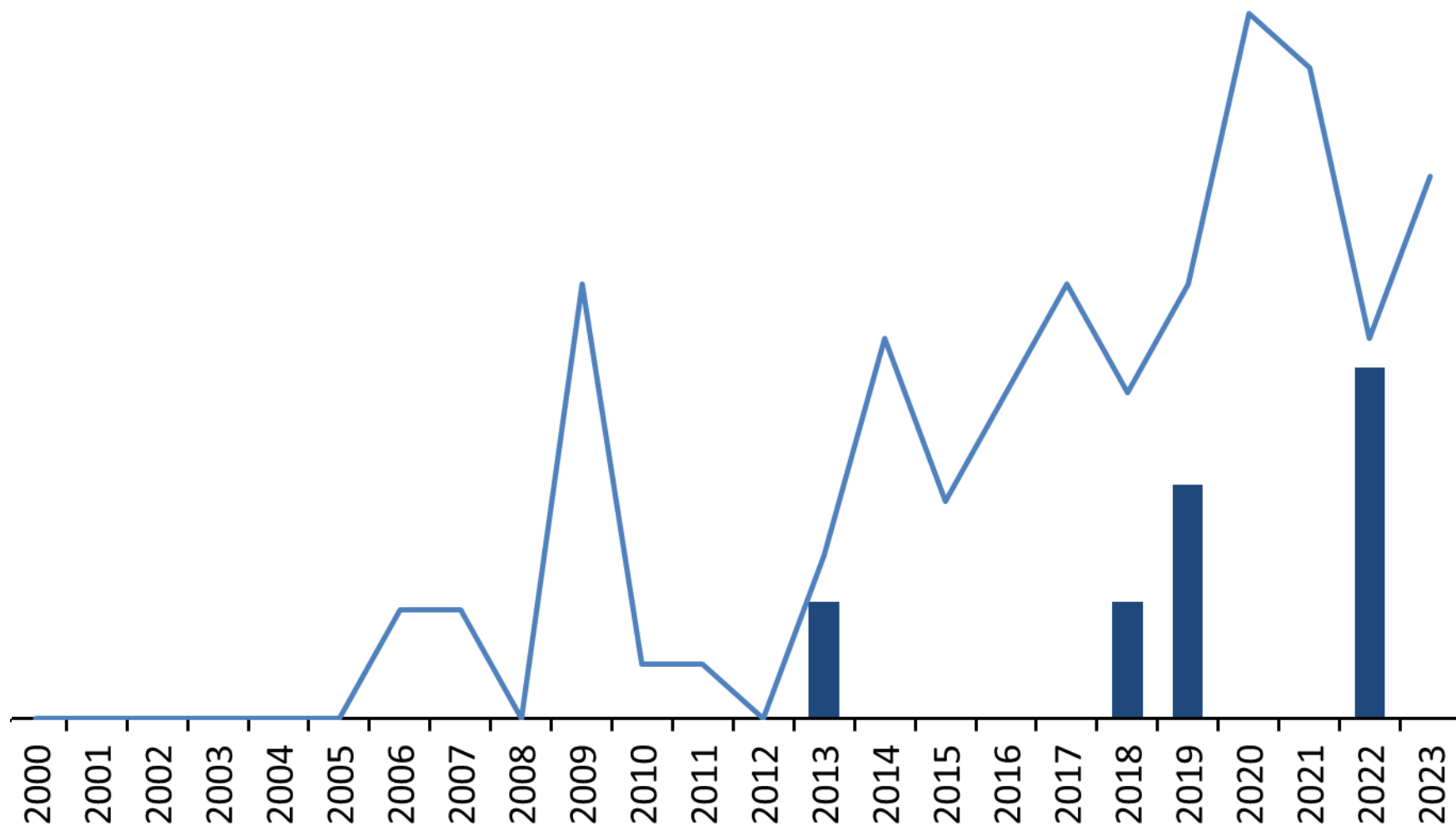


* 2023 data is incomplete and includes reported cases to date through the end of November 2023

As Syphilis Increases in Women of Child-Bearing Age...



As Syphilis Increases in Women of Child-Bearing Age... Congenital Syphilis Will Increase



Vital Signs: Missed Opportunities for Preventing Congenital Syphilis — United States, 2022

10x

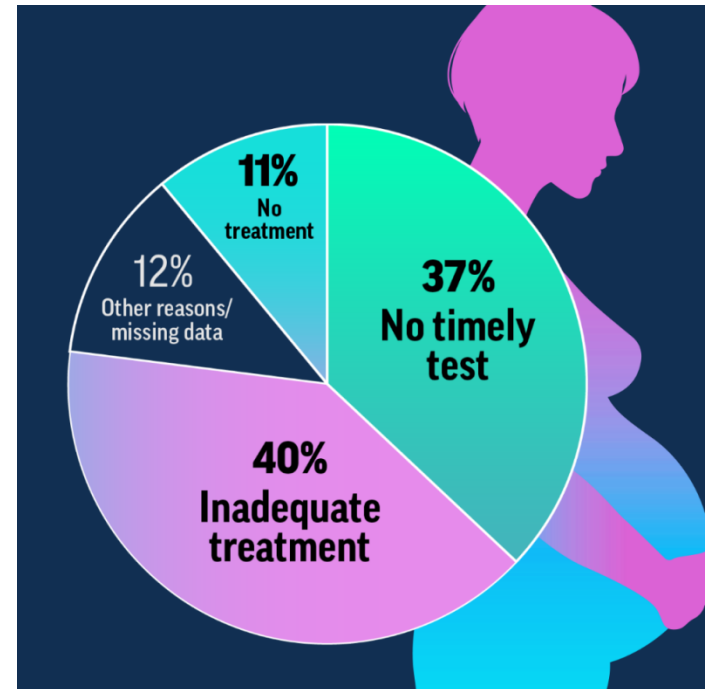
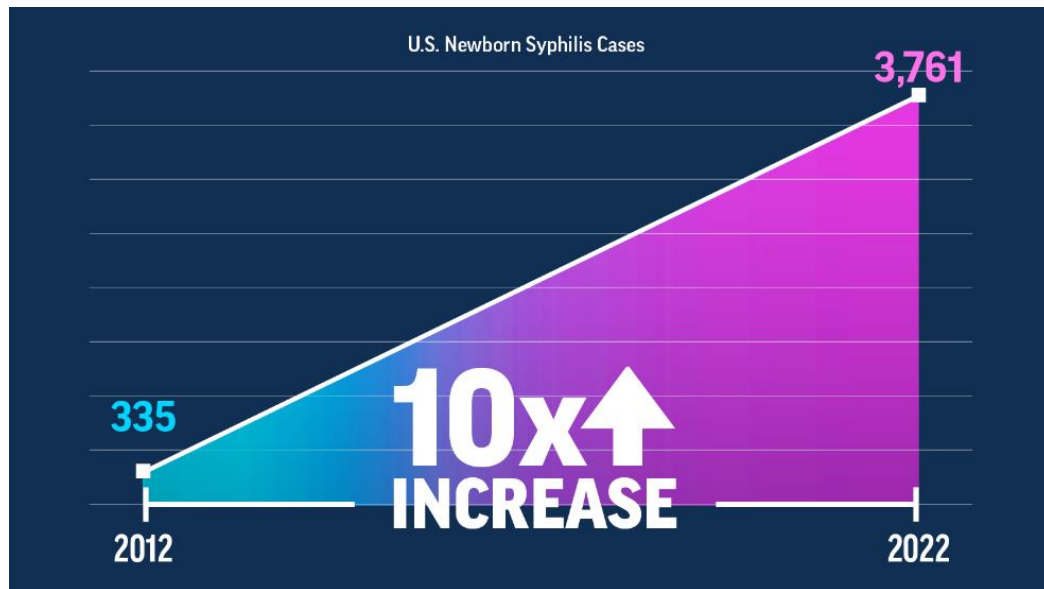
Over 10 times as many babies were born with syphilis in 2022 than in 2012.

9 in 10

Timely testing and treatment during pregnancy might have prevented almost 9 in 10 (88%) cases in 2022.

2 in 5

Two in 5 (40%) people who had a baby with syphilis did not get prenatal care.

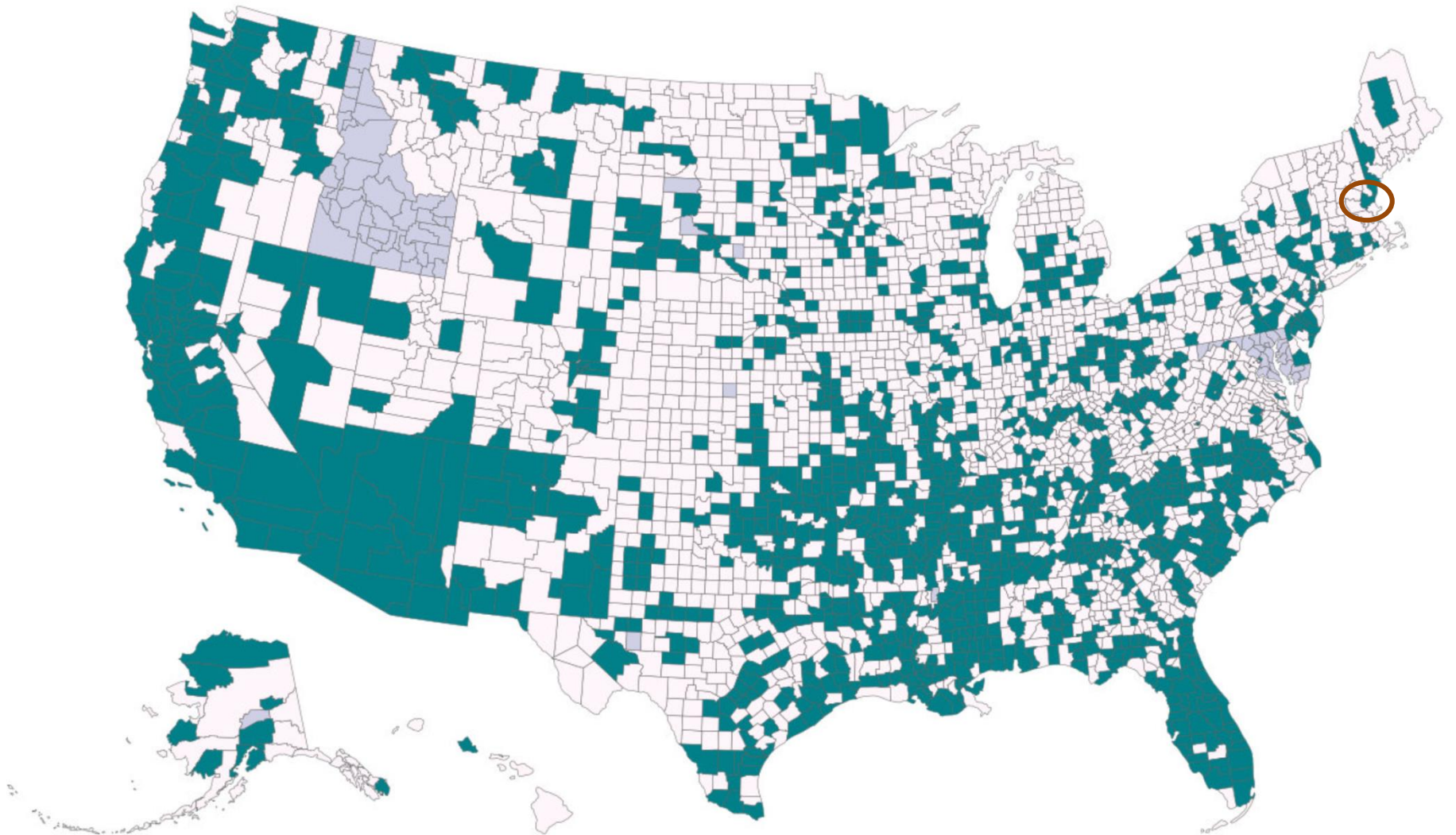


Vital Signs: Missed Opportunities for Preventing Congenital Syphilis — United States, 2022

- Consider geographic risk in addition to individual behaviors when determining the need for syphilis screening
- Make any healthcare encounter during pregnancy (e.g., ED visits) an opportunity to test and treat for syphilis
- Consider implementing rapid syphilis testing with immediate treatment of pregnant persons who are positive (while awaiting full confirmatory testing)
- Ensure appropriate treatment – Penicillin G is the only effective and recommended treatment for syphilis during pregnancy

County-Level Syphilis Rates Can Be Used to Inform Syphilis Screening

- A threshold for “high” levels of syphilis is not currently defined
- All areas should assess individual risk factors per existing [STI Screening Recommendations](#) to determine need for screening
- [Healthy People 2030 goal](#) is to reduce the rate of primary + secondary syphilis among women 15-44 years of age to **4.6 cases per 100,000** or less
- Therefore, CDC is suggesting that in counties with syphilis rates in women above this target rate, providers should offer syphilis screening to all sexually active persons aged 15-44 years to diagnose and treat syphilis BEFORE a pregnancy occurs



- Continue to assess individual risk factors to determine screening needs*
- Offer syphilis testing to all sexually active people aged 15-44**
- Suppressed†

<https://www.cdc.gov/nchhstp/atlas/syphilis/>

CDC Recommendations for Expanded Screening Based on Geographic Risk

DATA TABLE: Rates of primary & secondary syphilis among women aged 15-44 years by county, 2021

County	State	Rate per 100,000	Offer syphilis testing to all sexually active people aged 15-44 years*
Belknap	NH	0	No
Carroll	NH	0	No
Cheshire	NH	0	No
Coos	NH	0	No
Grafton	NH	0	No
Hillsborough	NH	1.2	No
Merrimack	NH	3.5	No
Rockingham	NH	7.3	Yes
Strafford	NH	0	No
Sullivan	NH	0	No

Alternative Analysis of Syphilis Rates in Females Aged 15-44 Years

- Rates of “Infectious Syphilis” (primary, secondary, and early latent) by NH county for 2021-2023 data combined:
 - Merrimack: 5.9 cases per 100,000 persons
 - Hillsborough: 3.7 cases per 100,000 persons
 - Rockingham: 3.7 cases per 100,000 persons
- Other NH counties had too few infections to calculate a rate for this population
- Numbers/rates fluctuate year-to-year, so making clinical decisions based on one year of data has limitations
- Compared to Rockingham County, the higher 3-year rate in Merrimack County, and similar 3-year rate for Hillsborough County suggests providers consider expanding syphilis screening in these counties as well

Summary

- Syphilis has steadily increased in NH
- An increasing number of infections in females has translated to an increase in congenital syphilis
- As STI rates increase, there will be a need for expanded testing/screening to control transmission
 - Rates of syphilis in NH are highest in Hillsborough, Merrimack, and Rockingham counties
- Appropriate timely treatment is necessary to prevent transmission and avoid adverse health outcomes – Penicillin G is the only effective and recommended treatment for syphilis during pregnancy!


Q&A

Webinar Slides Will Be Posted to our Healthcare Provider Resources Website

- <https://www.dhhs.nh.gov/programs-services/disease-prevention/infectious-disease-control/bidc-resources-healthcare-providers>

Monthly Webinar for Healthcare and Public Health Partners

The Division of Public Health Services (DPHS) continues to host monthly clinician webinars on the **2nd Thursday of each month from 12:00 – 1:00 PM EST** to provide updates on important and timely public health issues. To access the webinar, please use the link below:





- Webinar link: <https://nh-dhhs.zoom.us/j/94059287404>
- Call-in phone number: (646) 558-8656
- Webinar ID: 940 5928 7404
- Password: 353809

Join us for the next webinar on **Thursday, December 14th, 12:00 – 1:00 PM EST**, when the topics covered will be **syphilis and congenital syphilis**.

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