Syphilis and Congenital Syphilis

Ruth Lynfield, MD | State Epidemiologist & Medical Director

February 2, 2024

Disclosures

Drs. Lynfield, Contag, and Lehman have nothing to disclose

Agenda

- Clinical presentation, stages, and treatment of syphilis – Dr. Ruth Lynfield
- Rise in syphilis and congenital syphilis – Dr. Ruth Lynfield
- Updated MDH pregnancy syphilis screening recommendations – Dr. Ruth Lynfield
- Syphilis screening in the emergency department – Dr. Stephen Contag
- Clinical challenges – Dr. Alice Lehman

Clinical Presentation and Stages of Syphilis

Primary Syphilis

PRIMARY

Painless chancre, appears 1-12 weeks after exposure (average 21 days) on site of exposure to infectious lesion, highly infectious, resolves after 3-6 weeks

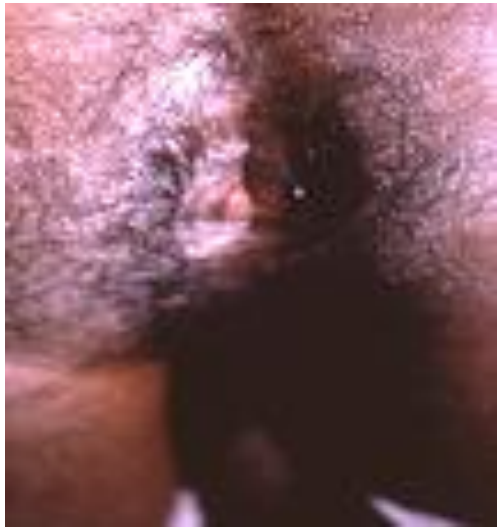
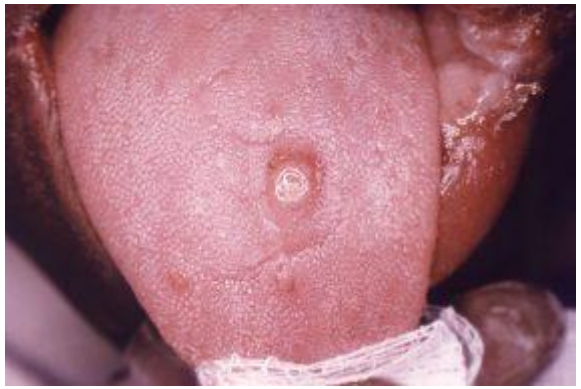


Photo credit: CDC



Chancre on tongue
Photo credit: CDC

Secondary Syphilis

SECONDARY

Symptoms appear 6 weeks to 6 months after chancre appears, including a rash anywhere on body, flu like symptoms, whitish-grey patches on mouth/lips, wart like lesions around genitals (condyloma lata), hair loss (less common)

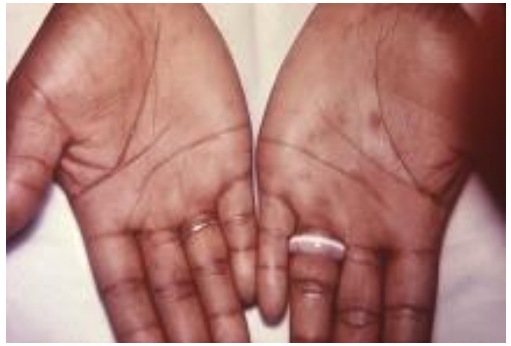


Photo credit: CDC

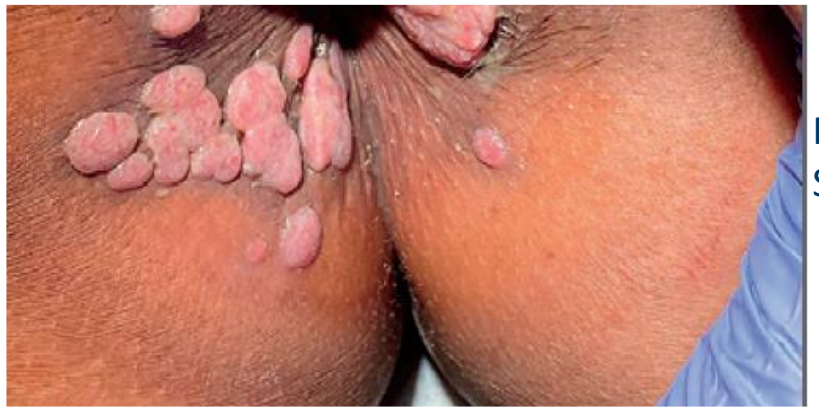


Photo credit:
Stafford, et al. NEJM 2024

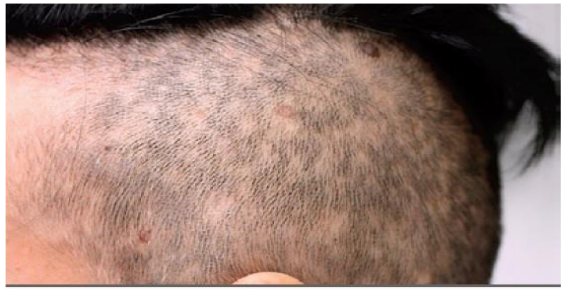


Photo credit:
Stafford, et al. NEJM 2024

Early Non-Primary Non-Secondary and Late Syphilis

- **EARLY NON-PRIMARY NON-SECONDARY (ENPNS)**
  - Asymptomatic, duration <1 year (negative syphilis screening within 12 months, confirmed exposure to early staged syphilis)
- **LATE**
  - Duration >1 year

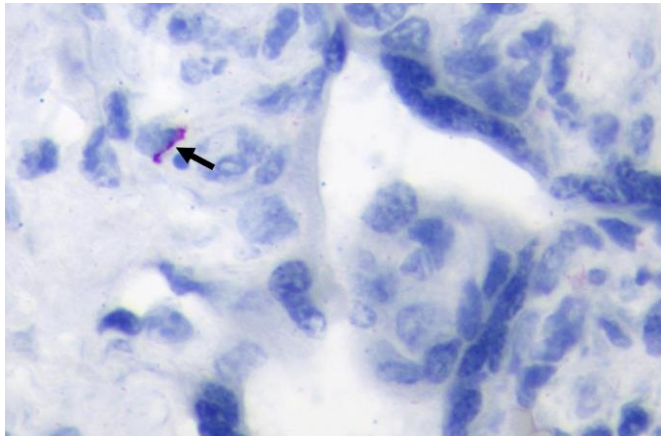
Tertiary and Neuro/Ocular/Otosyphilis

- **TERTIARY SYPHILIS**
  - Can appear 10-30 years after infection in about 30% of untreated patients
  - Multiple organ systems; can include brain, nerves, eyes, heart, blood vessels, liver, bones, joints
- **NEUROSYPHILIS, OCULAR SYPHILIS, OTOSYPHILIS**
  - Can occur at any stage

Congenital Syphilis

CONGENITAL SYPHILIS

- Fetal infection occurs from infection of placenta to fetus; less commonly, exposure to primary syphilis lesions during birth
- Risk to infection in fetus: 50-70% if pregnancy complicated by early syphilis to 15% if maternal infection >1 year prior to pregnancy
- Transmission can occur at any time during pregnancy



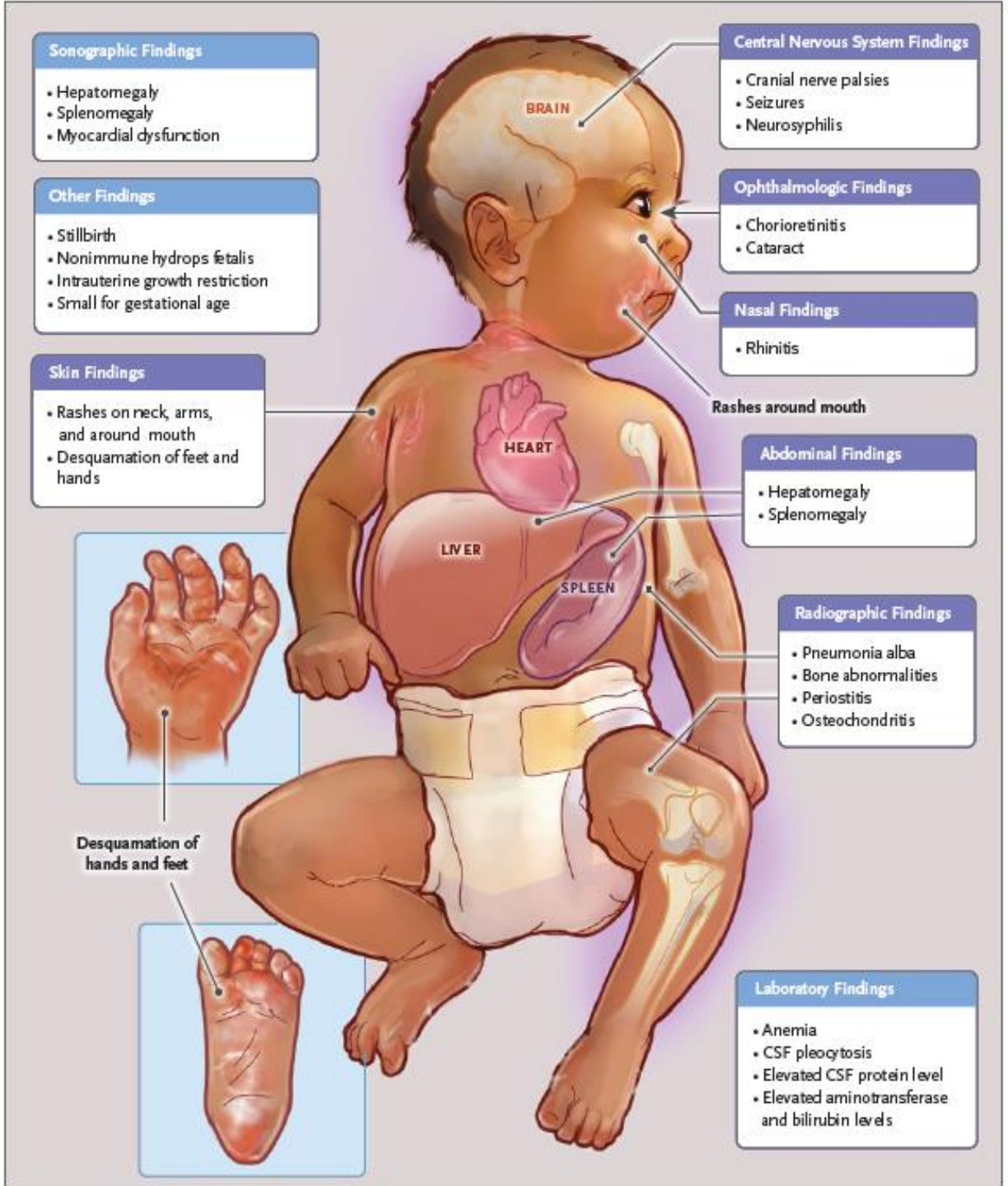
Treponema spirochete seen in placenta with immunohistochemistry

https://champshealth.org/resources

Congenital Syphilis (cont.)

- Fetal infection can result in miscarriage, stillbirth, small for gestational age, prematurity, infant death
- Symptoms at birth: hydrops, anemia, thrombocytopenia, rash, hepatic abnormalities, jaundice, bone abnormalities, syphilitic rhinitis, fever
    - Up to 60% symptomatic newborns have neurological involvement: seizures, cranial nerve palsies, cerebral infarcts, ophthalmologic abnormalities
- May be asymptomatic at birth
- Late manifestations (can occur after age 2 years): bony abnormalities in face, extremities, Hutchinson's teeth, ocular abnormalities, hearing loss

Stafford, Workowski, Bachmann. Syphilis Complicating Pregnancy and Congenital Syphilis
N Engl J Med 2024;390:242-53. DOI: 10.1056/NEJMra2202762



Stafford, Workowski, Bachmann. Syphilis Complicating Pregnancy and Congenital Syphilis
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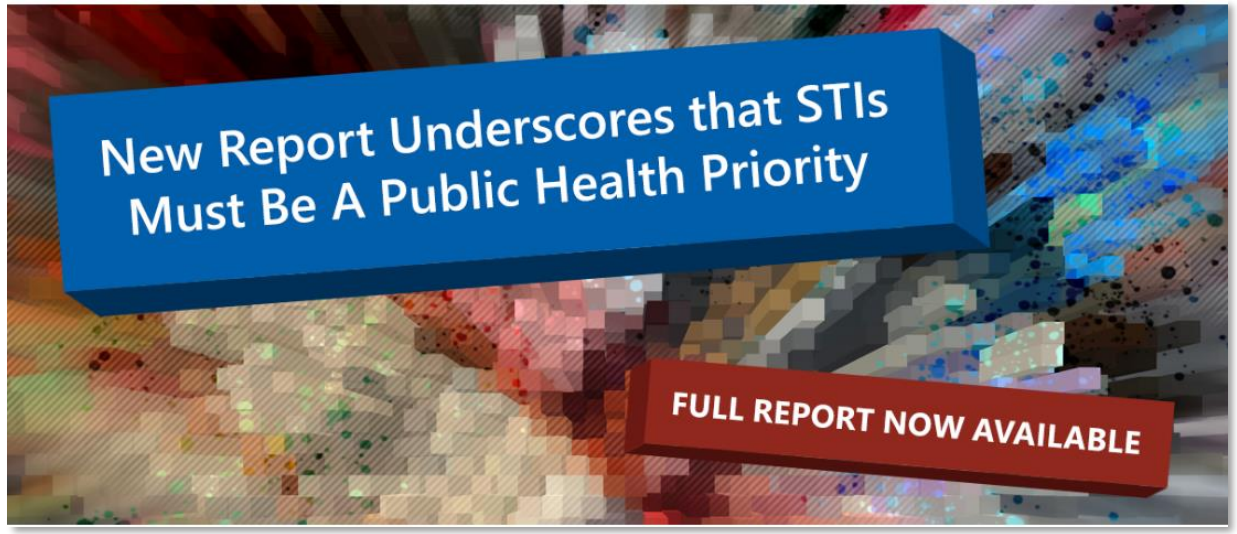
Syphilis Epidemiology

CDC Syphilis 2022 Data Report (Jan 30, 2024)



The New York Times

Jan. 30, 2024

Syphilis Is Soaring in the U.S.

Cases have risen by 80 percent since 2018, the C.D.C. reported.

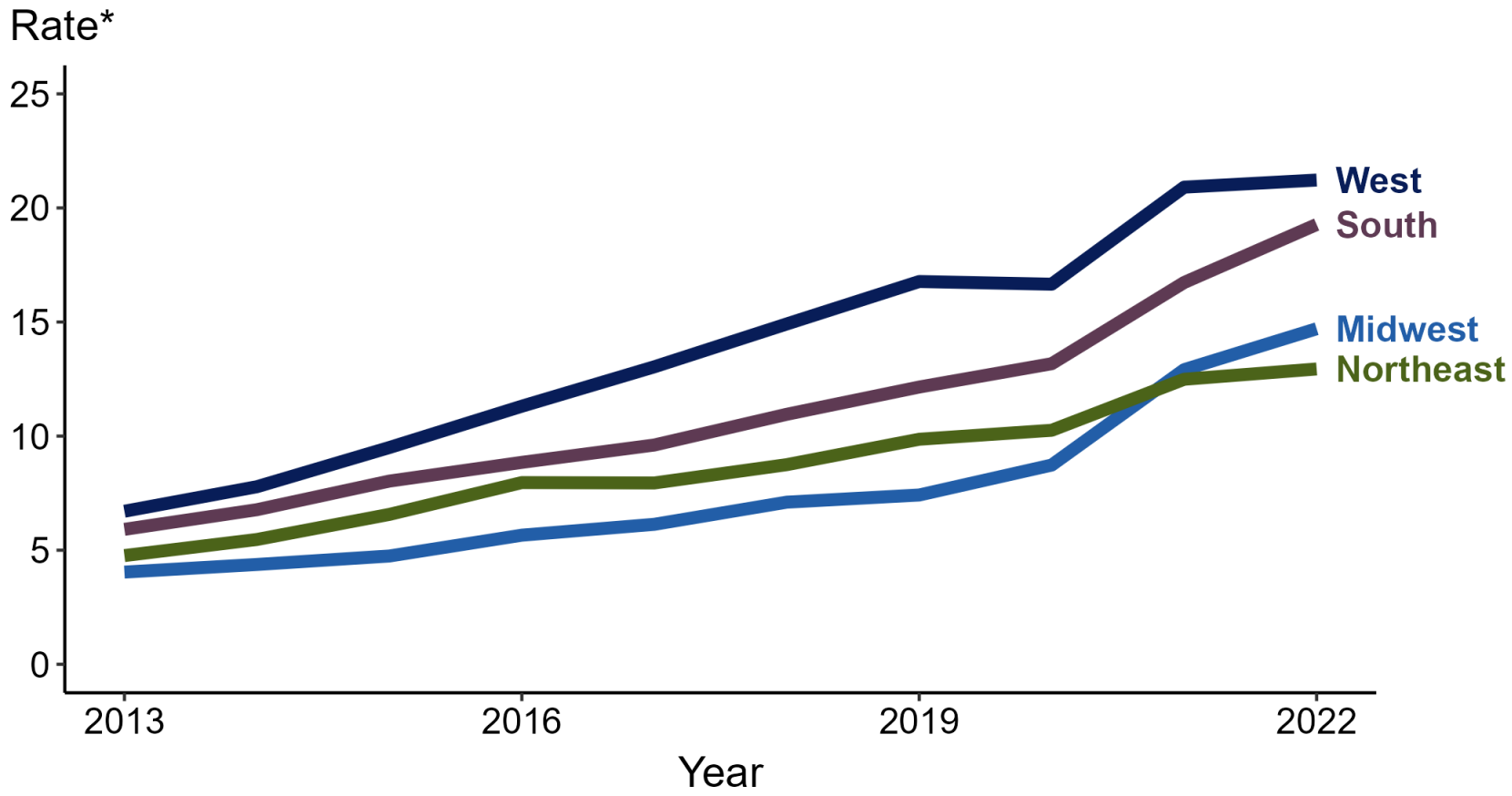
NBC NEWS NOW

Syphilis rates in the U.S. up 80% since 2018

Syphilis rates in the U.S. as high as they were in the 1940's.

Jan. 31, 2024

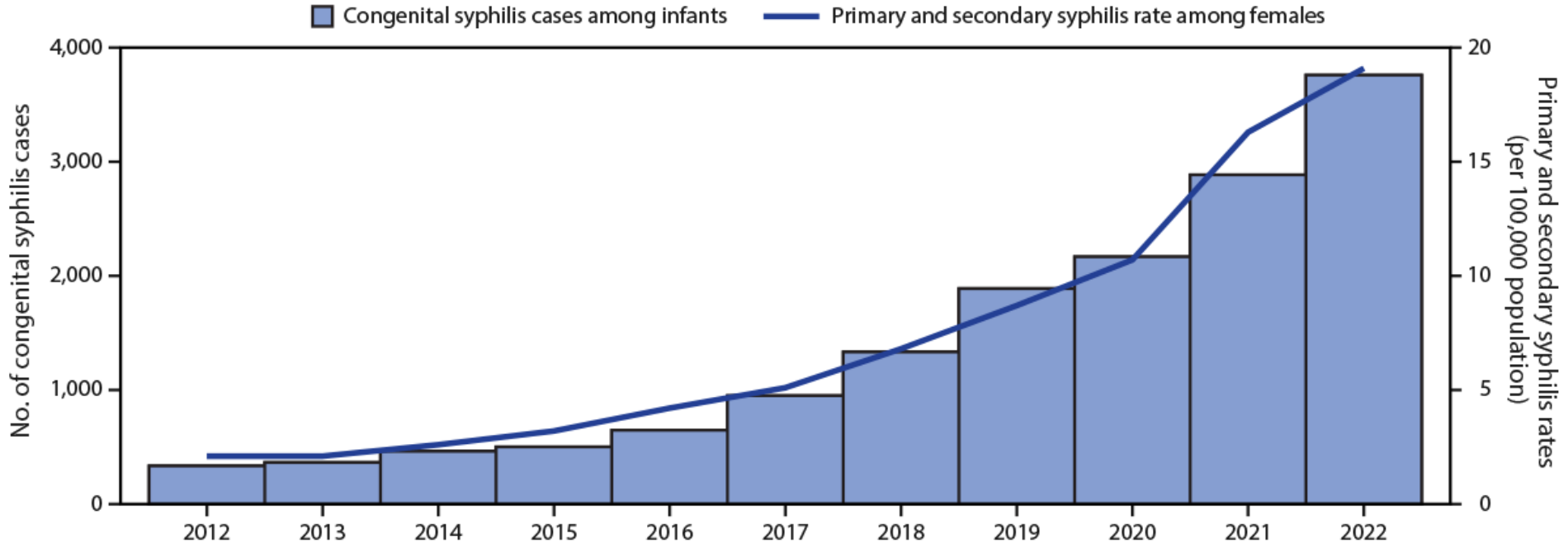
Primary and Secondary Syphilis — Rates of Reported Cases by Region, United States, 2013–2022



* Per 100,000

National Syphilis and Congenital Syphilis Trends 2012-2022

FIGURE 1. Reported number of cases of congenital syphilis among infants, by year of birth, and rates* of reported cases of primary and secondary syphilis† among females aged 15–44 years, by year — United States, 2012–2022



* Cases per 100,000 population.

† Primary and secondary syphilis case data for all U.S. territories and freely associated states and outlying areas were not available for all years; therefore, rates presented include only the 50 states and the District of Columbia.

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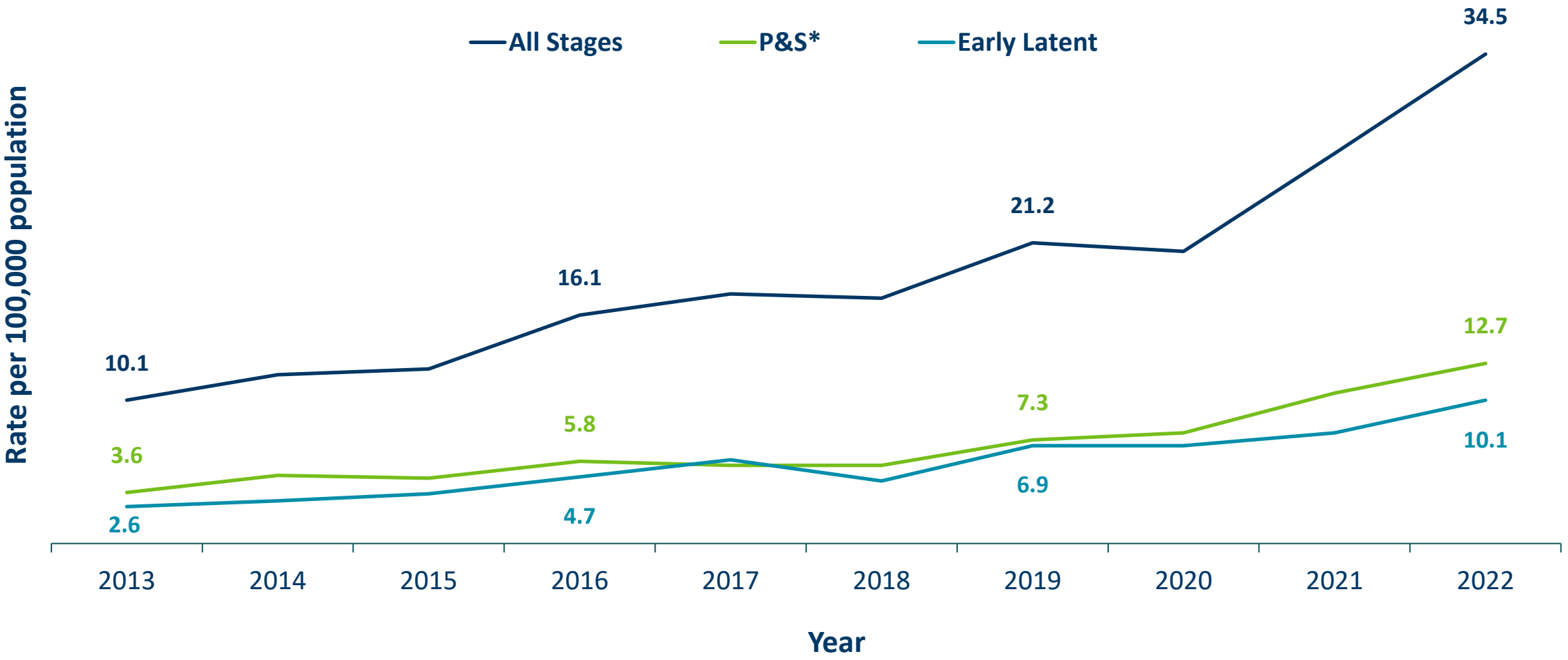
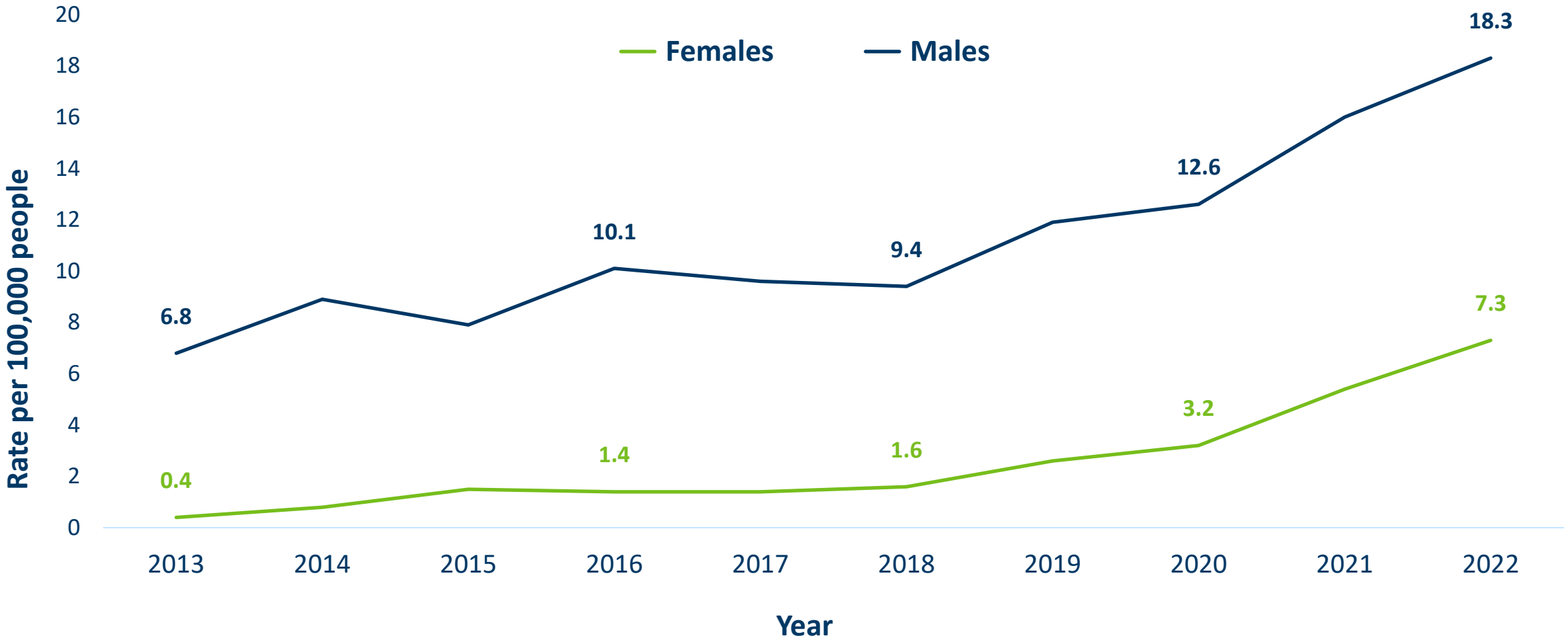
Syphilis Rates Increasing Across All Stages – Minnesota, 2013-2022



* P&S = Primary and Secondary

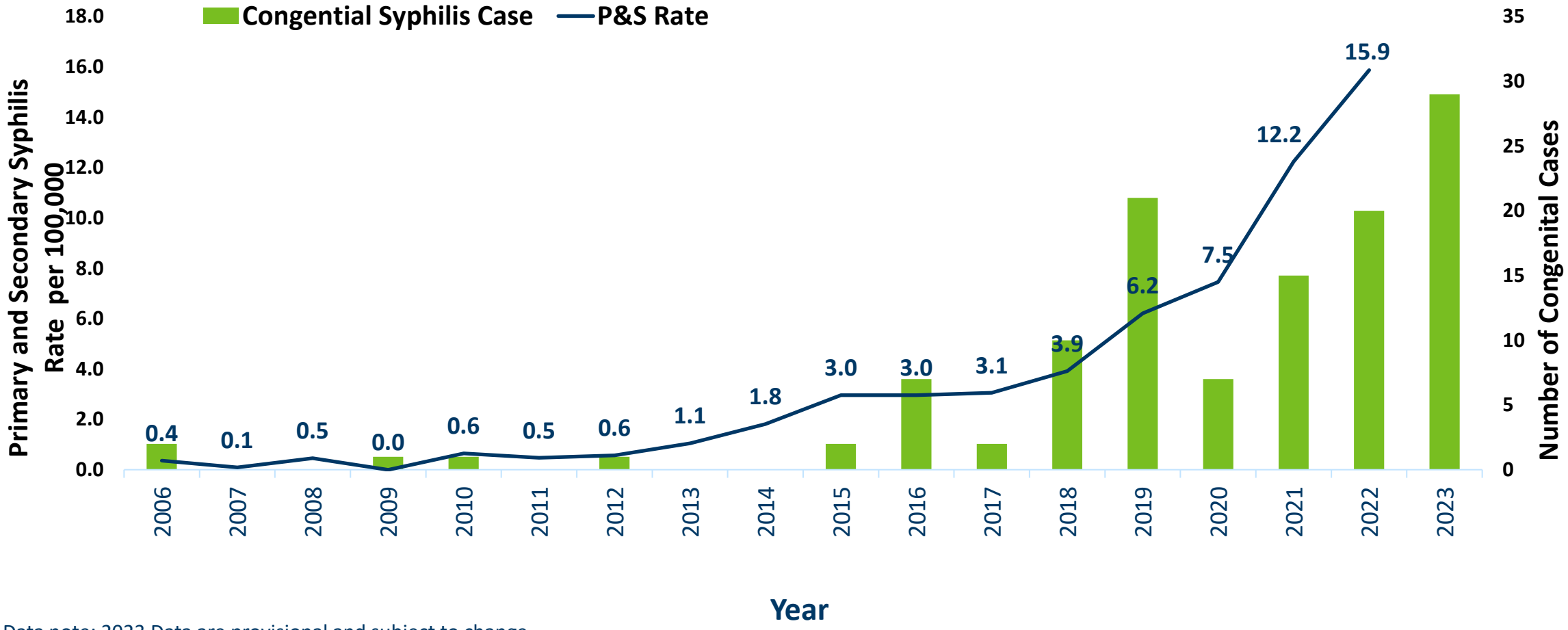
Data note: 2023 Data are provisional and subject to change

Primary & Secondary Syphilis Rates by Sex – Minnesota, 2013-2022



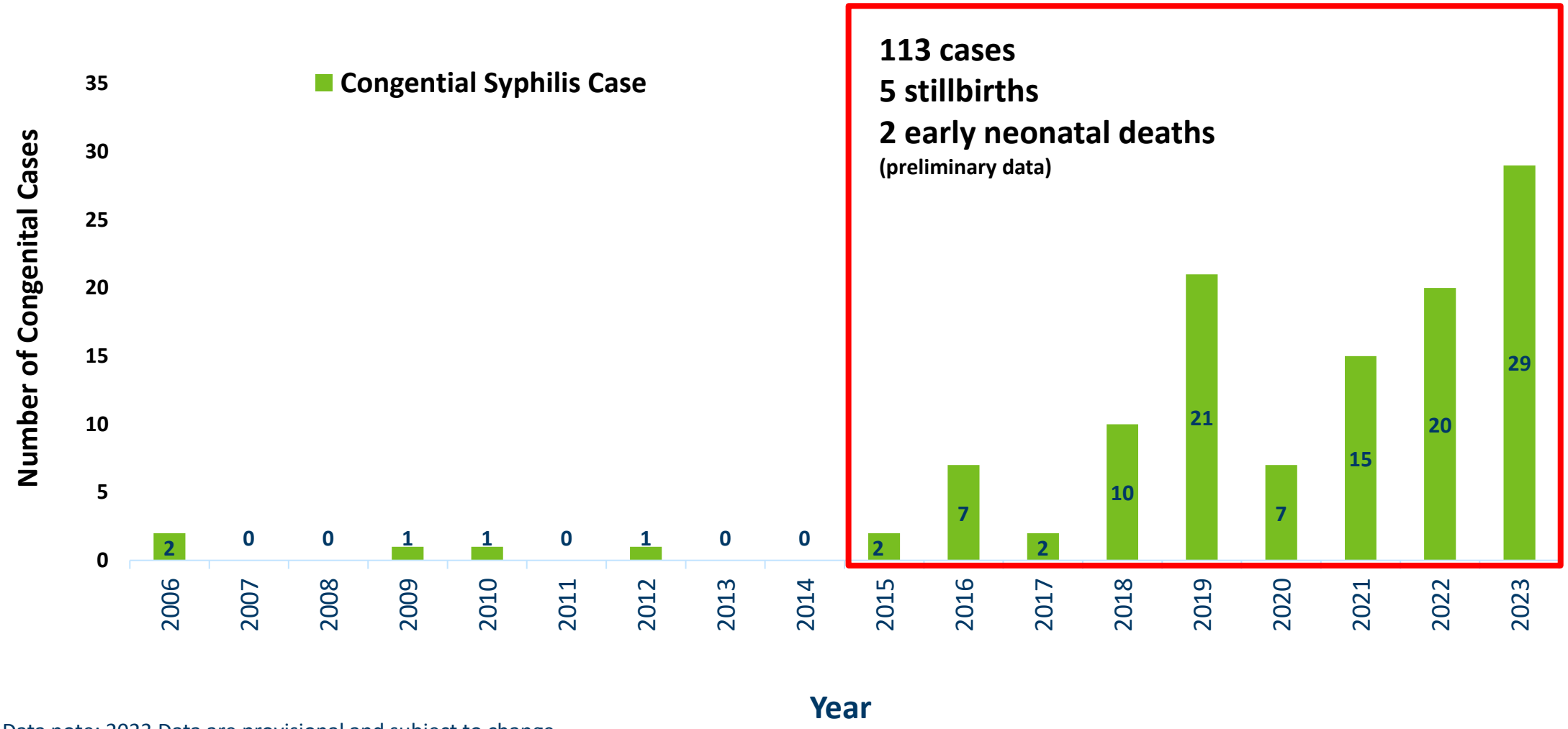
Data note: 2023 Data are provisional and subject to change

Primary and Secondary Syphilis Rates among Females aged 15-44 years and Number of Congenital Syphilis Cases – Minnesota, 2006-2023



Data note: 2023 Data are provisional and subject to change

Number of Congenital Syphilis Cases – Minnesota, 2006-2023



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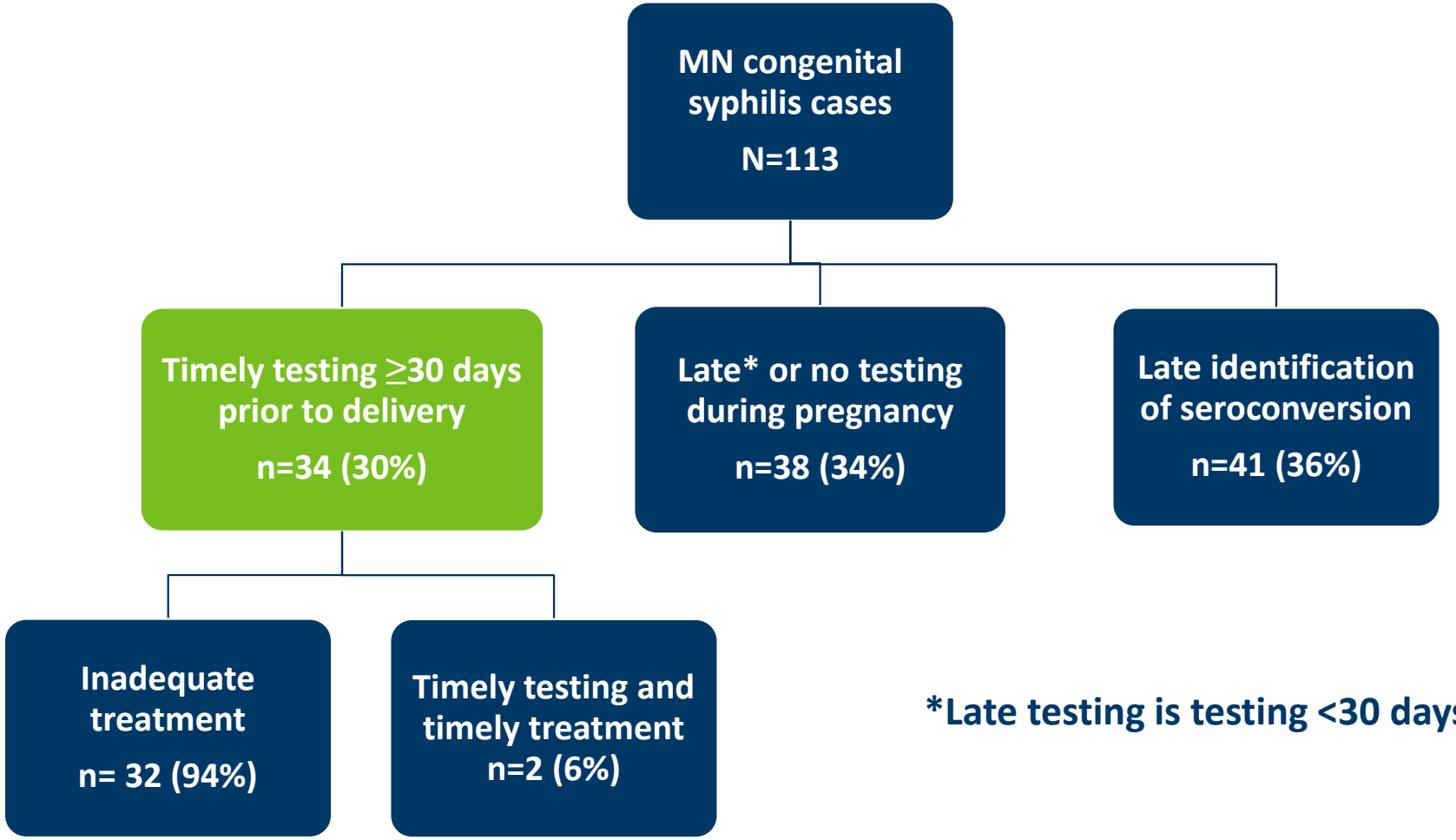
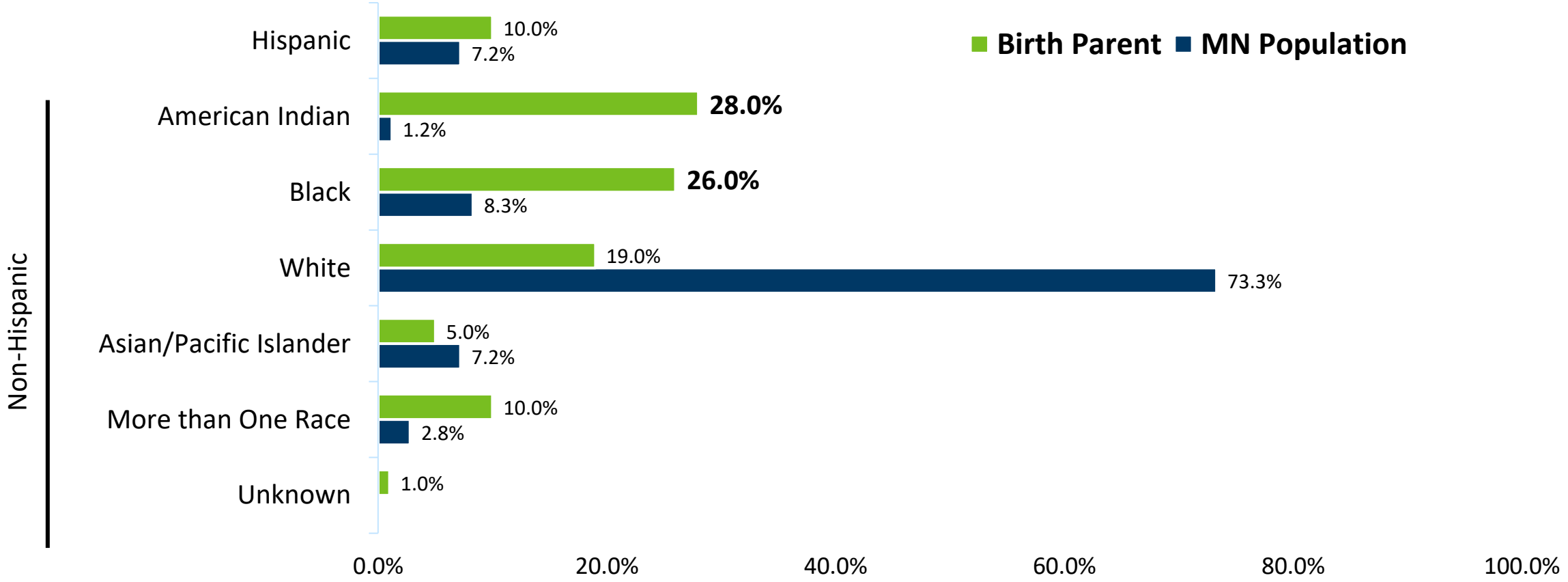
Minnesota Congenital Syphilis Cases, 2015-2023: Missed Opportunities



*Late testing is testing <30 days prior to delivery

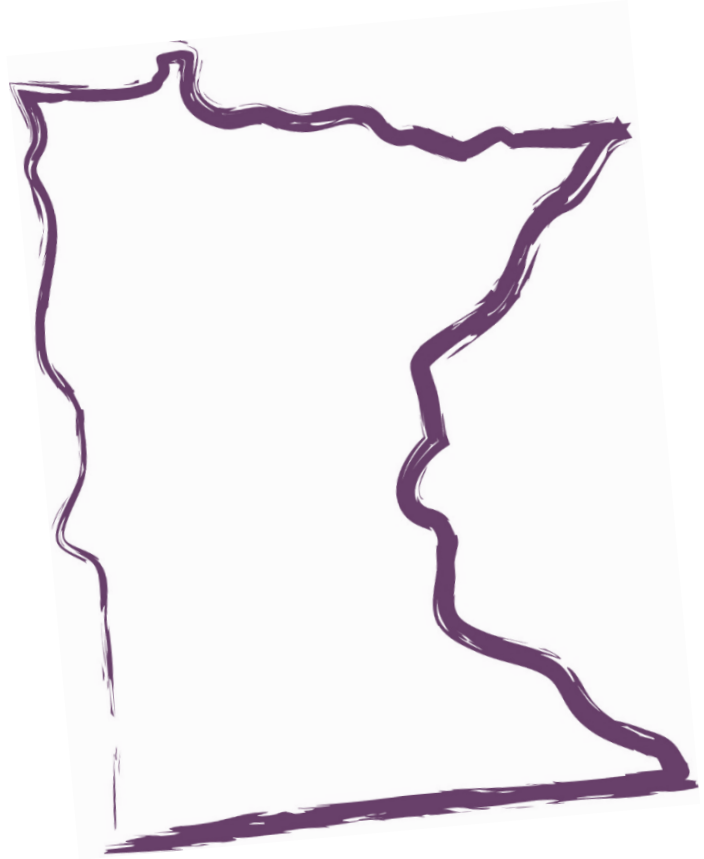
Minnesota Congenital Syphilis Cases, 2015-2023: Ethnicity and Race of Birth Parent (n=106)



Source: 2020 MN Population Estimate, CDC Wonder
Data note: All race categories exclude persons who self-identify as Hispanic

Syphilis in Minnesota

- Syphilis can affect anyone
- Minnesotans of all races, ethnicity, gender, and sexual orientation are increasingly impacted
- People who identify as American Indian, Black, and Hispanic are disproportionally impacted due to factors that may influence social determinants of health
  - Historical, current, and intergenerational trauma
  - Structural and individual racism
  - Discrimination
  - Differences in health insurance coverage, housing, and employment status
  - Access to preventive, screening, and curative services



MDH Screening Recommendations

MDH 2024 Pregnancy Syphilis Screening Recommendations

Providers should screen all pregnant people three times during pregnancy

1. **At first prenatal encounter – ideally during the 1st trimester**
   - Pregnant people not accessing prenatal care and not previously screened for syphilis should be tested in any health care setting
2. **Early in the 3rd trimester (28-32 weeks' gestation)**
   - Important to allow enough time for treatment to occur prior to delivery to prevent congenital syphilis
3. **At delivery**
   - Including pregnant people who experience a stillbirth (fetal death after 20 weeks' gestation or fetus weighs greater than 500 g)

Pregnancy Syphilis Screening Recommendations and FAQs (state.mn.us)

MDH 2024 Pregnancy Syphilis Screening Recommendations: Important Considerations

- Screen in any health care setting (not limited to prenatal care), including emergency departments, urgent care centers, correctional facilities, substance use treatment facilities, and primary care clinics
  - Link to prenatal care
- The reverse algorithm is generally preferred for screening in pregnant people to detect early infection and late, untreated infection
  - However, either algorithm is acceptable, and local factors should be considered in determining clinical and laboratory approach to syphilis screening in pregnancy
  - If traditional algorithm is used, consider also sending a treponemal test for pregnant people

Pregnancy Syphilis Screening Recommendations and FAQs (state.mn.us)

California Prevention Treatment Center's Clinical Interpretation of Syphilis Screening Algorithms

MDH 2024 Pregnancy Syphilis Screening Recommendations: Important Considerations

- Test at other times if exposed, other STI, patient concerns, or request
- Providers should review all syphilis results, including from-delivery, of the birthing parent before birthing parent and infant leave the facility
    - If not feasible, confirm syphilis test is performed and follow-up is assured

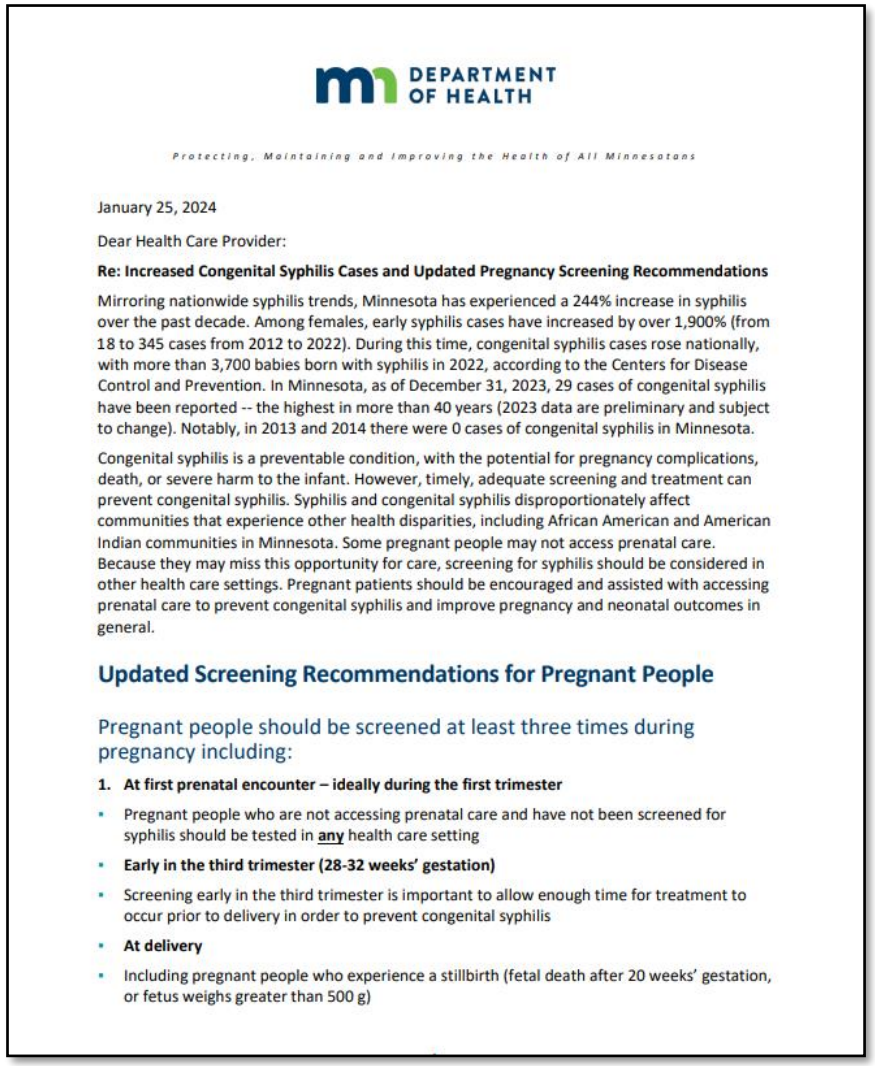
Pregnancy Syphilis Screening Recommendations and FAQs (state.mn.us)

MDH 2024 Pregnancy Syphilis Screening Recommendations: Important Considerations

- Test and treat sex partners of patients with syphilis
- Due to increased burden of syphilis statewide think about syphilis and consider syphilis screening for sexually active adolescents and adults
- Updated screening guidelines for non-pregnant people will be forthcoming from MDH in 2024

Pregnancy Syphilis Screening Recommendations

MDH 2024 Pregnancy Syphilis Screening: Health Care Provider Letter



DEPARTMENT OF HEALTH

Protecting, Maintaining and Improving the Health of All Minnesotans

January 25, 2024

Dear Health Care Provider:

Re: Increased Congenital Syphilis Cases and Updated Pregnancy Screening Recommendations

Mirroring nationwide syphilis trends, Minnesota has experienced a 244% increase in syphilis over the past decade. Among females, early syphilis cases have increased by over 1,900% (from 18 to 345 cases from 2012 to 2022). During this time, congenital syphilis cases rose nationally, with more than 3,700 babies born with syphilis in 2022, according to the Centers for Disease Control and Prevention. In Minnesota, as of December 31, 2023, 29 cases of congenital syphilis have been reported -- the highest in more than 40 years (2023 data are preliminary and subject to change). Notably, in 2013 and 2014 there were 0 cases of congenital syphilis in Minnesota.

Congenital syphilis is a preventable condition, with the potential for pregnancy complications, death, or severe harm to the infant. However, timely, adequate screening and treatment can prevent congenital syphilis. Syphilis and congenital syphilis disproportionately affect communities that experience other health disparities, including African American and American Indian communities in Minnesota. Some pregnant people may not access prenatal care. Because they may miss this opportunity for care, screening for syphilis should be considered in other health care settings. Pregnant patients should be encouraged and assisted with accessing prenatal care to prevent congenital syphilis and improve pregnancy and neonatal outcomes in general.

Updated Screening Recommendations for Pregnant People

Pregnant people should be screened at least three times during pregnancy including:

1. **At first prenatal encounter – ideally during the first trimester**
   - Pregnant people who are not accessing prenatal care and have not been screened for syphilis should be tested in **any** health care setting
   - **Early in the third trimester (28-32 weeks' gestation)**
   - Screening early in the third trimester is important to allow enough time for treatment to occur prior to delivery in order to prevent congenital syphilis
   - **At delivery**
   - Including pregnant people who experience a stillbirth (fetal death after 20 weeks' gestation, or fetus weighs greater than 500 g)

Endorsed by:

Minnesota Affiliate of American College of Nurse-Midwives (MN ACNM)
Melissa Kitzman, APRN, CNM, WHNP-BC, Co-President
Lizi Seefeldt, DNP, APRN, CNM, Co-President
Dominique Jones, DNP, APRN, CNM, PHN, Vice President
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Eileen Crespo, MD, Chapter President

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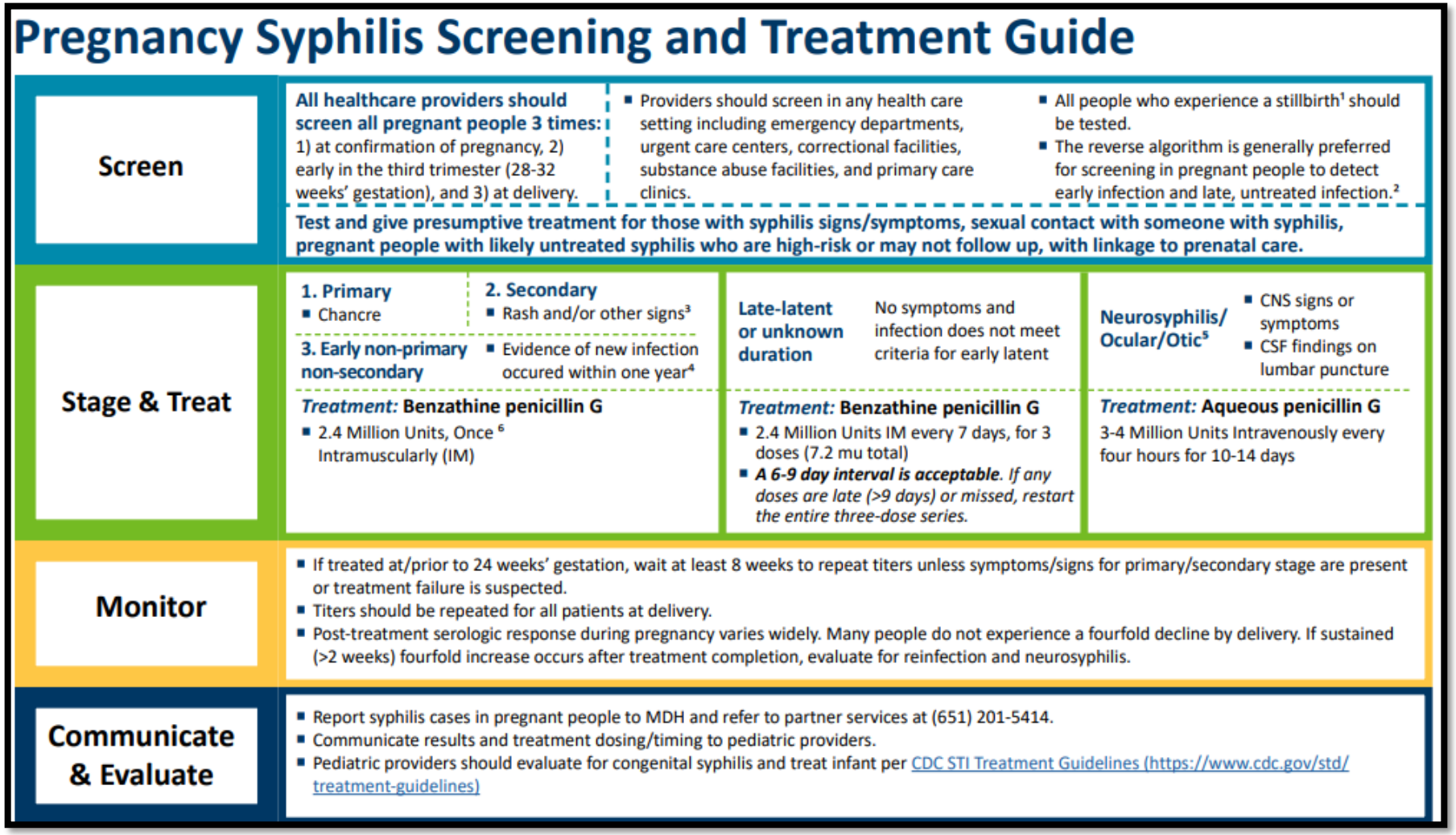
Elizabeth Slagle, MD, Chair

[Congenital Syphilis Provider Recommendations Letter (state.mn.us)]

MDH Pregnancy Syphilis Screening and Treatment Guide



Pregnancy Syphilis Screening and Treatment Guide

Screen

All healthcare providers should screen all pregnant people 3 times: 1) at confirmation of pregnancy, 2) early in the third trimester (28-32 weeks' gestation), and 3) at delivery.

- Providers should screen in any health care setting including emergency departments, urgent care centers, correctional facilities, substance abuse facilities, and primary care clinics.
- All people who experience a stillbirth[1] should be tested.
- The reverse algorithm is generally preferred for screening in pregnant people to detect early infection and late, untreated infection.[2]

Test and give presumptive treatment for those with syphilis signs/symptoms, sexual contact with someone with syphilis, pregnant people with likely untreated syphilis who are high-risk or may not follow up, with linkage to prenatal care.

Stage & Treat

1. Primary
- Chancre

2. Secondary
- Rash and/or other signs[3]

3. Early non-primary non-secondary
- Evidence of new infection occured within one year[4]

Treatment: **Benzathine penicillin G**
- 2.4 Million Units, Once [6] Intramuscularly (IM)

Late-latent or unknown duration

No symptoms and infection does not meet criteria for early latent

Treatment: **Benzathine penicillin G**
- 2.4 Million Units IM every 7 days, for 3 doses (7.2 mu total)
- ***A 6-9 day interval is acceptable****. If any doses are late (>9 days) or missed, restart the entire three-dose series.*

Neurosyphilis/ Ocular/Otic[5]
- CNS signs or symptoms
- CSF findings on lumbar puncture

Treatment: **Aqueous penicillin G**

3-4 Million Units Intravenously every four hours for 10-14 days

Monitor

- If treated at/prior to 24 weeks' gestation, wait at least 8 weeks to repeat titers unless symptoms/signs for primary/secondary stage are present or treatment failure is suspected.
- Titers should be repeated for all patients at delivery.
- Post-treatment serologic response during pregnancy varies widely. Many people do not experience a fourfold decline by delivery. If sustained (>2 weeks) fourfold increase occurs after treatment completion, evaluate for reinfection and neurosyphilis.

Communicate & Evaluate

- Report syphilis cases in pregnant people to MDH and refer to partner services at (651) 201-5414.
- Communicate results and treatment dosing/timing to pediatric providers.
- Pediatric providers should evaluate for congenital syphilis and treat infant per CDC STI Treatment Guidelines (https://www.cdc.gov/std/treatment-guidelines)

[Pregnancy Syphilis Screening and Treatment Guide (state.mn.us)]

MDH Pregnancy Syphilis Treatment Guide

1. Primary ▪ Chancre **2. Secondary** ▪ Rash and/or other signs[3]	**Late-latent or unknown duration**	No symptoms and infection does not meet criteria for early latent	**Neurosyphilis/ Ocular/Otic[5]**	▪ CNS signs or symptoms ▪ CSF findings on lumbar puncture
3. Early non-primary non-secondary	▪ Evidence of new infection occured within one year[4]			
Treatment: **Benzathine penicillin G** ▪ 2.4 Million Units, Once [6] Intramuscularly (IM)		***Treatment:*** **Benzathine penicillin G** ▪ 2.4 Million Units IM every 7 days, for 3 doses (7.2 mu total) ▪ ***A 6-9 day interval is acceptable****. If any doses are late (>9 days) or missed, restart the entire three-dose series.*		***Treatment:*** **Aqueous penicillin G** 3-4 Million Units Intravenously every four hours for 10-14 days

[Pregnancy Syphilis Screening and Treatment Guide (state.mn.us)]

Syphilis Reporting

- Health care practitioners and laboratories are required to report all laboratory-confirmed cases of syphilis to MDH within one working day
  - Include pregnancy status in laboratory reports
- **Syphilis in a pregnant person, possible congenital syphilis case, or syphilitic stillbirth should be reported promptly to MDH**
  - Please call MDH by phone at (651) 201-5414 or (877) 676-5414
- Notify MDH if a pregnant person with syphilis is refusing treatment or is lost to follow-up and remains untreated
- Whenever available, report names and addresses of exposed partners to MDH

MDH Partner Services

- Free and confidential statewide services for people with syphilis
  - Provided by Disease Intervention Specialists (651) 201-5414 or (877) 676-5414
  - Partner notification
  - Referrals for testing, treatment and prevention, and other supportive services
  - Prevention counseling
- Participation is voluntary
- Partner Services questions: Brian Kendrick (651-201-4021) or Brian.Kendrick@state.mn.us or Marcie Babcock (651-201-4003) or Marcie.Babcock@state.mn.us

MDH STD/HIV Partner Services Program

MDH Syphilis Consultation

- MDH maintains record of **positive** syphilis test results and treatments
- Health care providers can access current and historical syphilis testing and treatment information to inform diagnosis and case management
- Consultations regarding the medical management of syphilis available
- To request a syphilis check or for a consultation call (651) 201-5414 or (877) 676-5414 during regular business hours and ask to speak with syphilis surveillance
- For after-hours emergencies or urgent matters request to speak with the person on call: MDH Infectious Disease Epidemiology, Prevention and Control staff available for disease consultation and reporting 24 hours a day, 7 days a week

Bicillin Shortage

Penicillin G Benzathine (Bicillin L-A) Shortage

- FDA has listed penicillin G benzathine (Bicillin L-A) on their drug shortage webpage
- Bicillin L-A is the only recommended treatment option for pregnant people and infants with possible congenital syphilis
- Prioritize the use of Bicillin L-A to treat pregnant people and infants
- Use doxycycline to treat non-pregnant people with syphilis
- Inventory your current stock of Bicillin L-A
- Contact MDH at (651) 201-5414 or (877) 676-5414 if your site is experiencing a shortage of Bicillin® L-A

Health Advisory: Bicillin Shortage for Syphilis Treatment (state.mn.us)
Syphilis Information for Health Professionals - MN Dept. of Health (state.mn.us)
FDA Drug Shortages

Availability of Extencilline

- CDC has informed partners that to address the current Bicillin L-A shortage, the FDA is temporarily allowing the importation of Extencilline (benzathine benzylpenicillin)
- Extencilline is not FDA-approved, but has been determined to be equivalent to Bicillin L-A and is authorized for use in other countries (including in France)
- MDH supports use of this alternative when Bicillin L-A is unavailable
- Key similarities and differences between Extencilline and Bicillin L-A
- MDH Syphilis for Providers webpage for precautions and how to place an order

Photo credit:
Laboratoires Delbert, France

Syphilis Information for Health Professionals - MN Dept. of Health (state.mn.us)

FDA Drug Shortages

FDA Announcement on Availability of Extencilline (cdc.gov)

Dr. Stephen Contag, MD

UNIVERSITY OF MINNESOTA
Driven to Discover®

Partnering with Emergency Department

Population identified

- Population:
  - Limited access to health care
  - Substance use disorder (no required reporting for pregnancy MN statute 260E.31)
  - Mood or behavioral disorders
- A population that is difficult to follow up

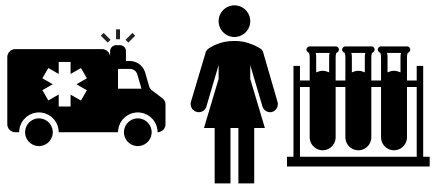
1: Stafford IA, Workowski KA, Bachmann LH. Syphilis Complicating Pregnancy and Congenital Syphilis. N Engl J Med. 2024 Jan 18;390(3):242-253.
2: Vital Signs: Missed Opportunities for Preventing Congenital Syphilis-United States, 2022. Pediatr Infect Dis J. 2024 Jan 1;43(1):39. Nov 30. PMID: 38048643.
3: Kachikis A, Schiff MA, Moore K, Chapple-McGruder T, Arluck J, Hitti J. Risk Factors Associated with Congenital Syphilis, Georgia, 2008-2015. Infect Dis Obstet Gynecol. 2023 Nov 8;2023

Team

- Emergency department
- Laboratory
- Infectious disease
- Infectious disease laboratory
- IT-EMR screening questions to guide management
- MDH-DIS for history of treatment and contact tracking

Congenital Syphilis (ca.gov)
Syphilis — OPQC
Syphilis | Florida Department of Health (floridahealth.gov)
Scott K, Faryar KA, Patil N, Gripshover B, Hammond C, Purohit M, Schmotzer C, Suleman-Civis L, Niforatos J, Avery A, Yax J. Evaluation of an emergency department opt-out provider-driven HIV and syphilis screening and linkage-to-care program. Am J Emerg Med. 2023 Dec 20;77:187-193.

Dr. Alice Lehman, MD, CTropMed



ER visit for abdominal pain.

Pregnancy and prenatal tests sent including treponemal antibody with reflex to RPR.

Results return and informed have + RPR 1:16.

Sees local clinic and received 1 dose penicillin given concern for early latent syphilis.

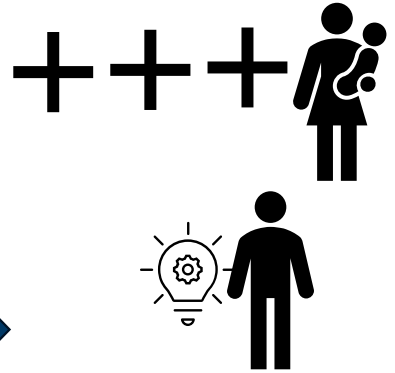
No expedited partner treatment offered.

Represents for delivery.
No other prenatal care.
Delivers at outside facility, no ER labs at time.

Testing for Treponemal antibody and pending at time of discharge.

Spontaneous Vaginal delivery, no neonatal complications.

Discharge home

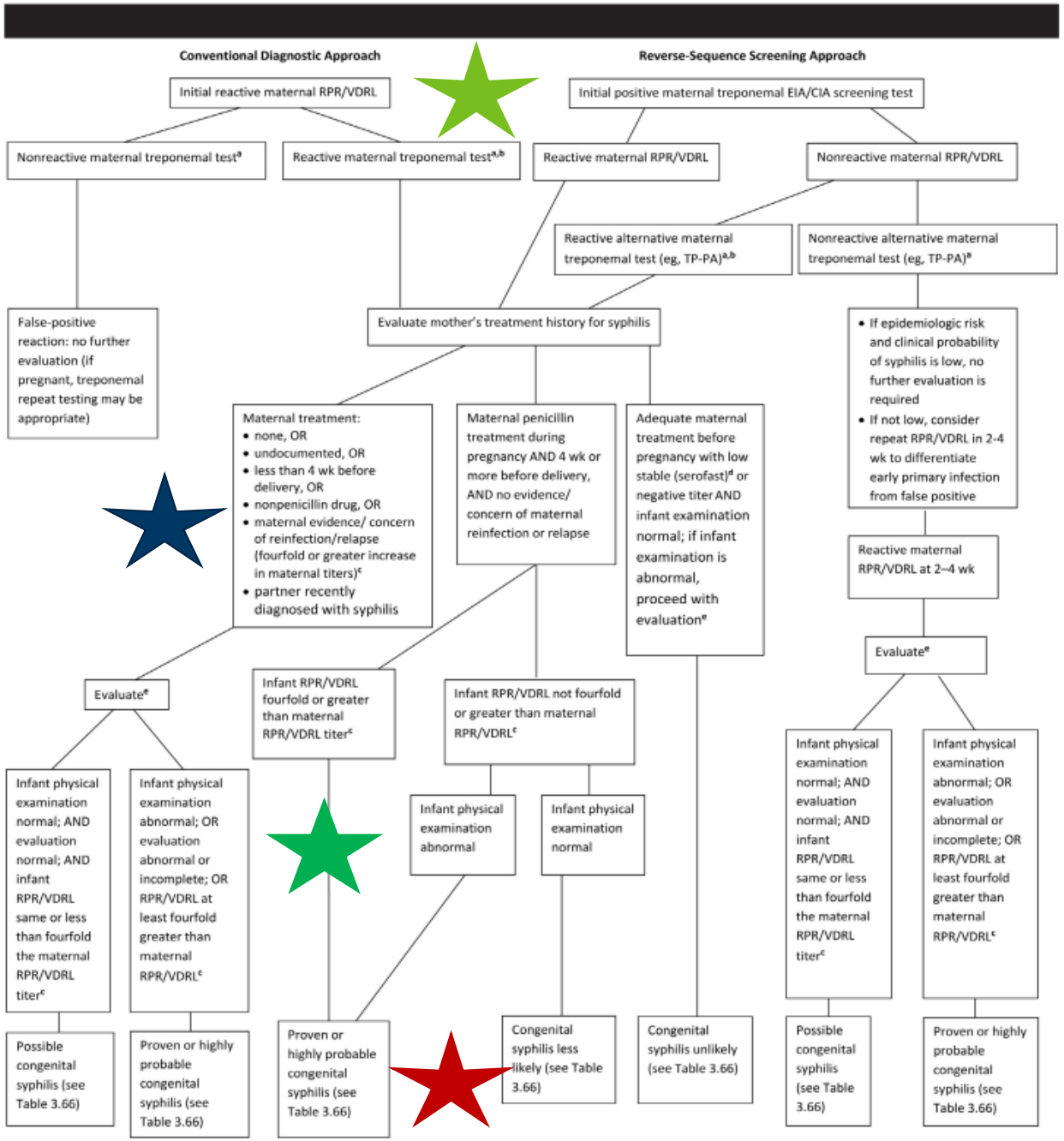


Infant and mother see Pediatrician at DOL4 day.

Pediatrician gets call that RPR in mother, rose 1:64.

Discover positive partner never treated.

What should the pediatrician do now?



Evaluation of the neonate is complex.

Knowledge of maternal testing

Knowledge of maternal treatment and risk for new infection

Neonatal evaluation that may include blood draw and lumbar puncture

Consolidation of clinical history, neonatal examination and labs to determine risk for congenital syphilis

RedBook AAP

Full evaluation requires admission for evaluation and initiation of empiric treatment

- Thorough examination
- Labs – **infant quantitative RPR**, complete blood count with platelets, liver function tests
- **Lumbar puncture** – evaluate for cell count with differential, protein and quantitative VDRL
- Long bone radiographs, eye examination, chest radiograph, neuroimaging, auditory brain stem response (if clinically indicated)

Consolidate information to determine treatment of neonate

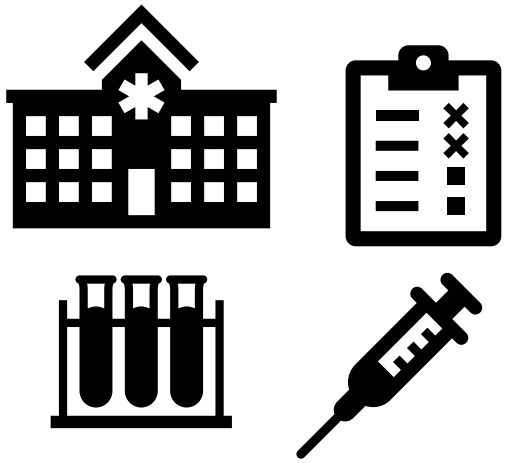
- Proven or highly probable congenital syphilis → 10 days of penicillin IV/IM
- Possible congenital syphilis → 10 days of penicillin IV/IM > Single dose of penicillin IM*
- Congenital syphilis less likely → Single dose of penicillin IM
- Congenital syphilis unlikely → No treatment

Resources are available

Call Minnesota Department of Health to get information on maternal testing and treatment.

Call Pediatric Infectious Diseases Consultation to talk through a case.

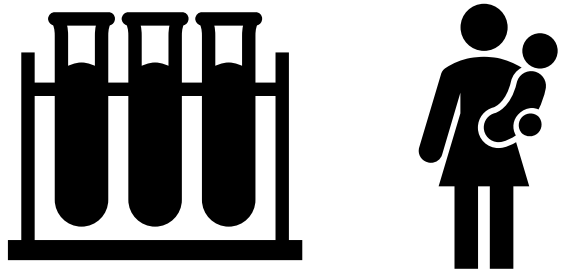
University of Minnesota
Childrens Minnesota
Mayo Clinic
Hennepin Healthcare



Admission for neonatal evaluation as concern repeat exposure from partner in late pregnancy therefore leading to re-infection.

Full evaluation demonstrating concern for possible congenital syphilis. Infant RPR 1:32 and negative exam and CSF analysis

Receives 10 days of IV penicillin G.



Follows up with Pediatrician for RPR recheck at 6 months of age and nonreactive.

Pearls from neonatal evaluation

1. Pregnant person’s syphilis testing and treatment is essential to evaluate neonate

2. Know pregnant persons syphilis history prior to discharge after delivery

3. Infant quantitative RPR is essential to determine risk for congenital syphilis

4. Full infant evaluation is best done in a hospital admission

5. Use resources and call Pediatric Infectious Diseases and Minnesota Department of Health

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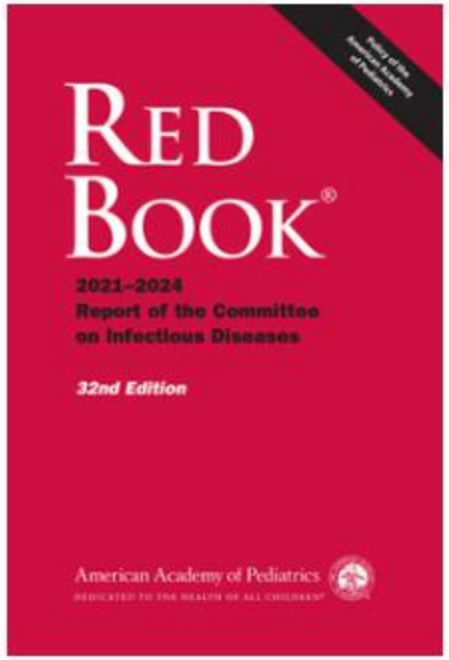
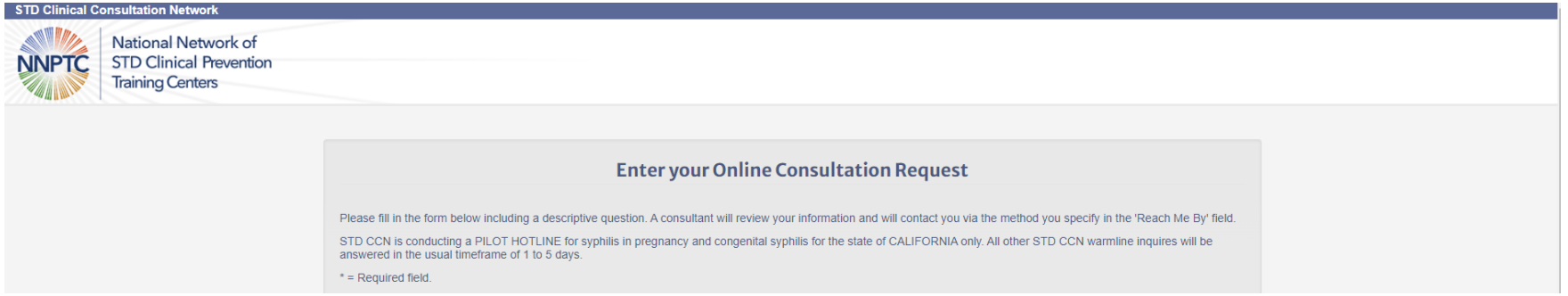


National Network of STD Clinical Prevention Testing Centers

https://stdccn.org/controller/Public/AddPublicConsultRequestStep1



Resources

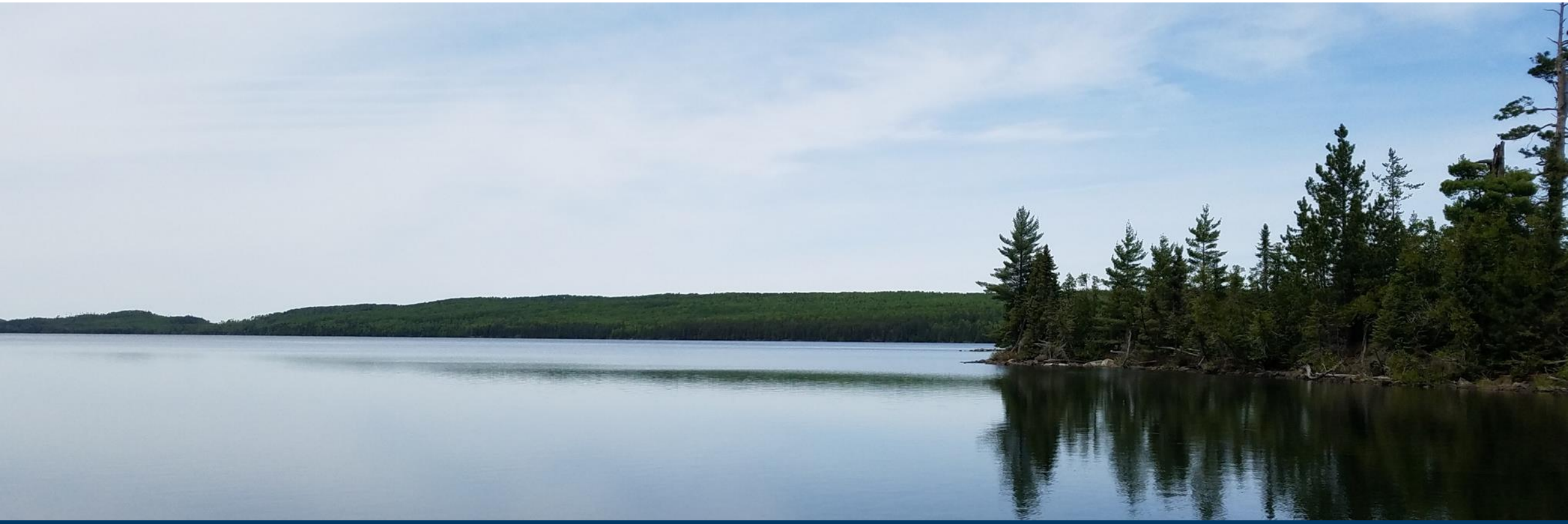
Minnesota Department of Health Resources

- **Call MDH at (651) 201-5414 for questions on past and current syphilis screening, diagnosis, or treatment in pregnancy, or to report cases (including syphilitic stillbirths) among pregnant persons**
- **Refer partners to the MDH STD/HIV Partner Services Program at (651) 201-5414**
- MDH pregnancy screening recommendations, FAQs, one-page resource on syphilis in pregnancy, and additional information on the MDH Syphilis Information for Health Professionals web page
- To request syphilis training by MDH, complete the MDH request a syphilis training/presentation form
- The 2022 MN Syphilis Virtual Learning Series

Additional Resources

- CDC STI Treatment Guidelines for evaluation and treatment guidelines for pregnant people, including penicillin allergy recommendations, and infants
- California Prevention Treatment Center's Clinical Interpretation of Syphilis Screening Algorithms
- Free STD consultation service for providers through the STD Clinical Consultation Network
- CDC Syphilis Pocket Guide for Providers
- National STD Curriculum (Self Study Clinician Lessons)
- California Department of Public Health Clinician's Resource for STDs in Gay Men and other MSM

DEPARTMENT OF HEALTH



Thank You!

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