



How Can We Reach Pregnant Persons at Risk for Congenital Syphilis?

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**CONGENITAL SYPHILIS
IS PREVENTABLE**
IF SYPHILITIC MOTHERS WILL TAKE
ADEQUATE TREATMENT DURING THE
LAST FIVE MONTHS OF PREGNANCY
NEW YORK STATE DEPARTMENT OF HEALTH

Disclosures

The findings and conclusions in this presentation are those of the presenter and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Outline

- 1 Overview
- 2 Epidemiology
- 3 Missed Opportunities
- 4 Challenges and Approaches in Clinical Settings
- 5 Innovation Around Service Delivery



Congenital Syphilis

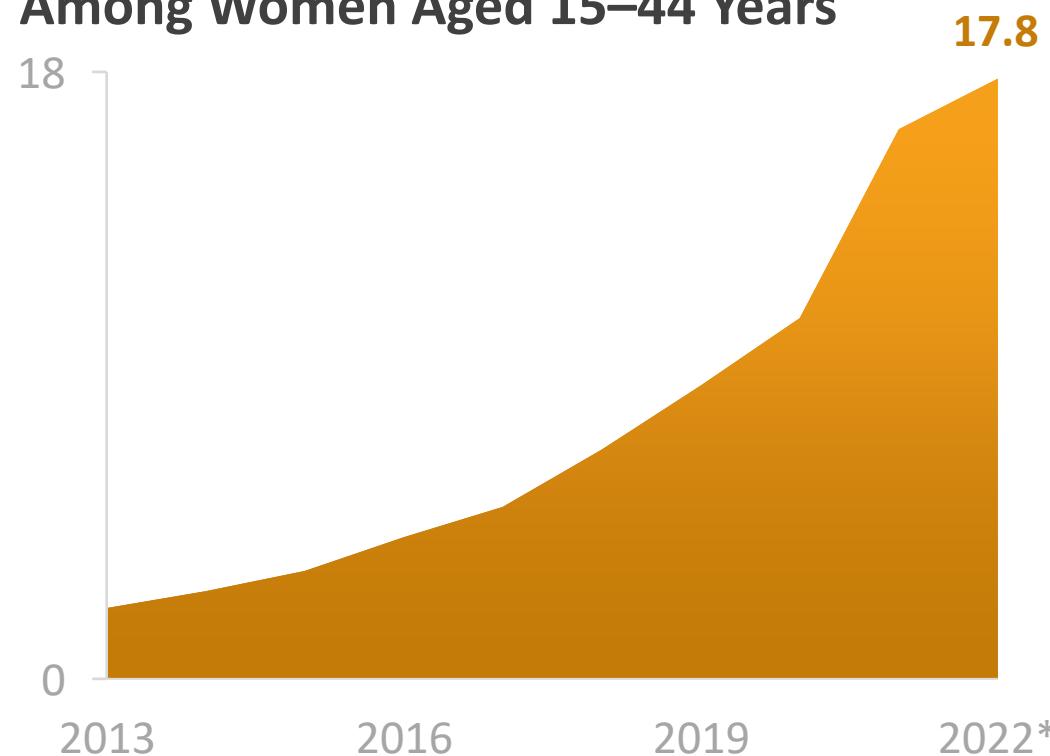


*An infection with *Treponema pallidum* acquired in an infant or fetus when a pregnant person has untreated or inadequately treated syphilis*

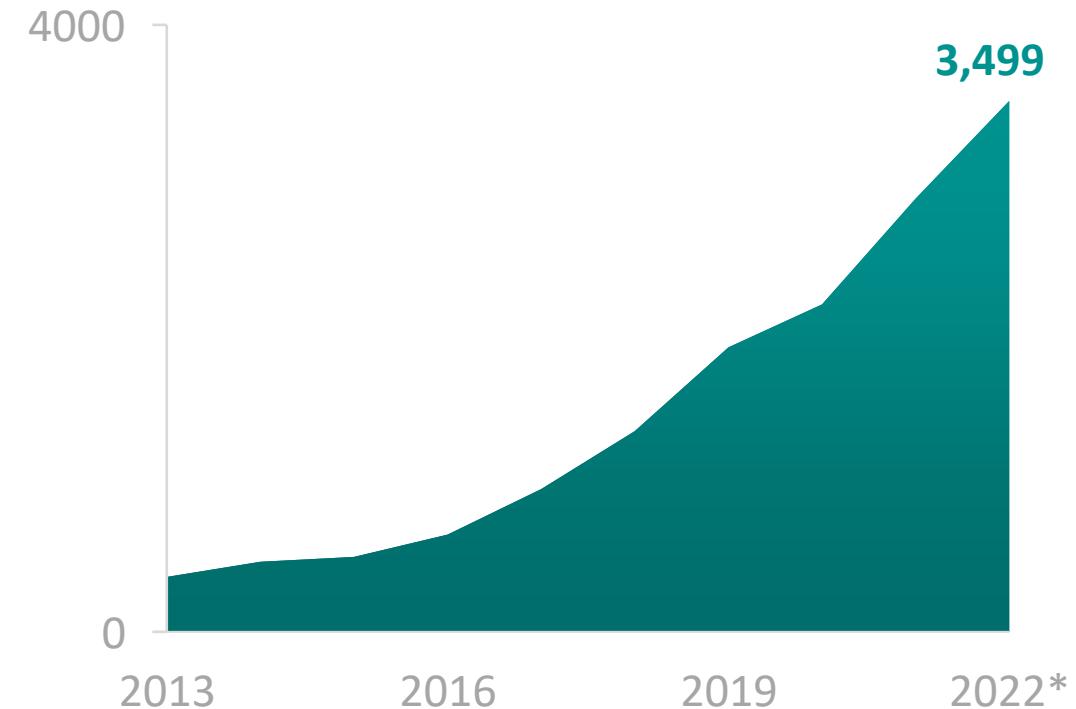
Epidemiology

Congenital Syphilis Mirrors Syphilis Trends Among Women Aged 15-44 Years in the United States

Primary and Secondary Syphilis Rate[†] Among Women Aged 15–44 Years

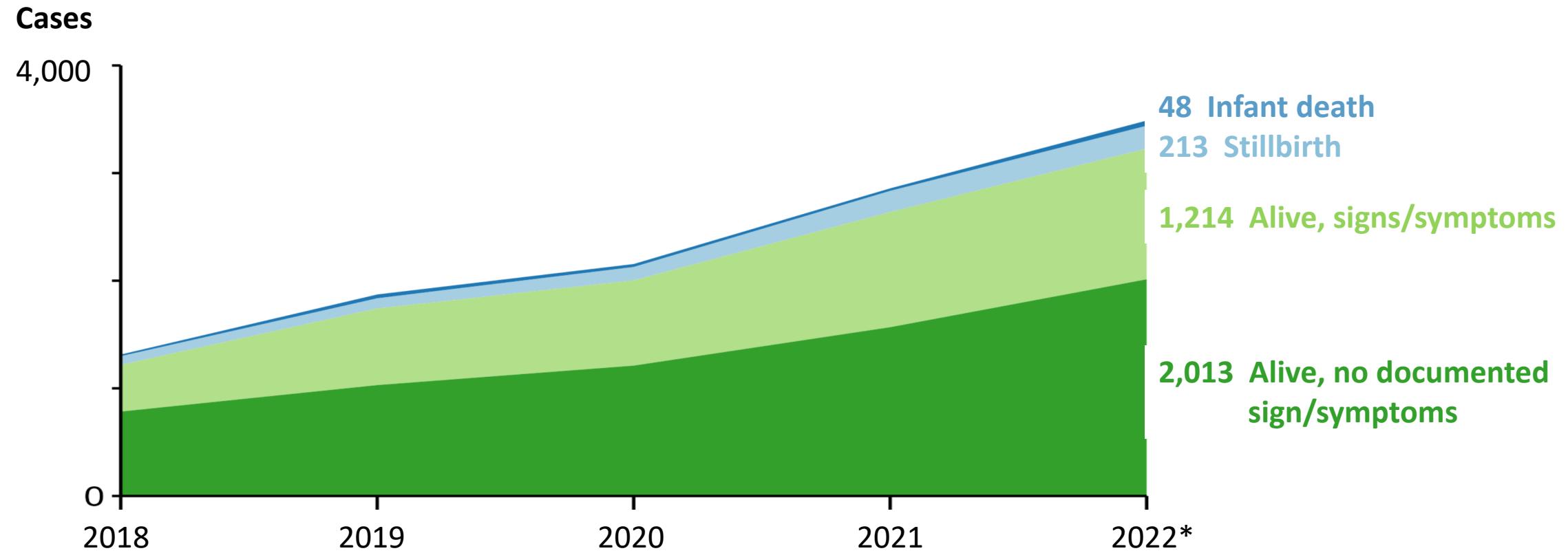


Reported Congenital Syphilis Cases by Year of Birth



*Reported 2022 data are preliminary as of June 21, 2023; † Per 100,000

Congenital Syphilis — Reported Cases by Vital Status and Clinical Signs and Symptoms* of Infection, United States, 2018–2022*

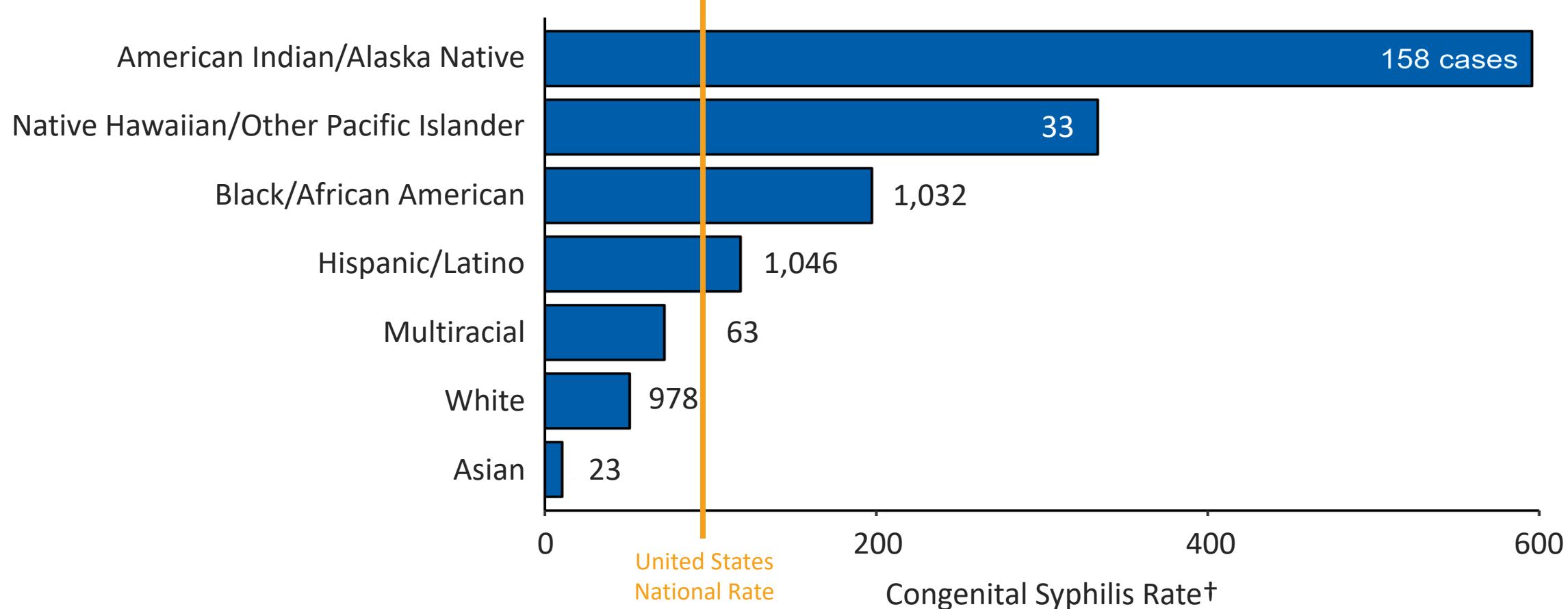


* Reported 2022 data are preliminary as of June 21, 2023; Infants with signs/symptoms of congenital syphilis have documentation of at least one of the following: long bone changes consistent with congenital syphilis, snuffles, condylomata lata, syphilitic skin rash, pseudoparalysis, hepatosplenomegaly, edema, jaundice due to syphilitic hepatitis, reactive CSF-VDRL, elevated CSF WBC or protein values, or evidence of direct detection of *T. pallidum*.
NOTE: Of the 11,719 congenital syphilis cases reported during 2018 to 2022, 32 (0.3%) did not have sufficient information to be categorized.

In 2022, 3 in 10 Congenital Syphilis Cases Were Among Hispanic/ Latino Mothers

Congenital Syphilis: Case Counts and Rates of Reported Cases by Race/Hispanic Ethnicity of Mother,

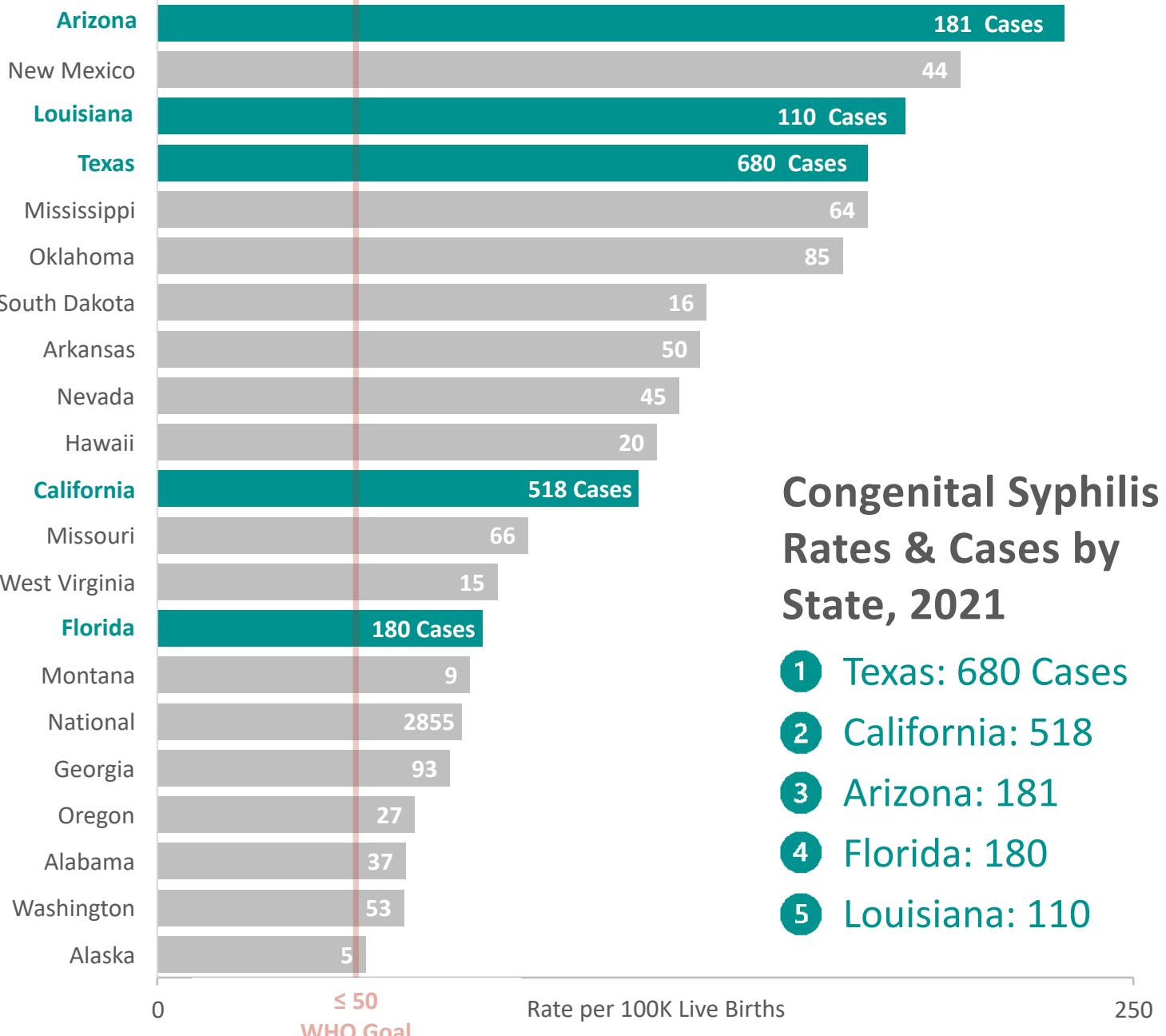
*United States, 2022**



* Reported 2022 data are preliminary as of June 21, 2023; †Per 100,000 live births

NOTE: In 2022, a total of 166 congenital syphilis cases (4.7%) had missing, unknown, or other race and were not reported to be of Hispanic ethnicity.

5 States Accounted for 58% of the 2,855 Congenital Syphilis Cases Reported in 2021



Characteristics Compared Between Patients With and Without Syphilis Infection in Pregnancy (N=15,341,868)

Maternal factors associated with syphilis infection (N=17,408) during pregnancy in multivariable analysis*:



Concurrent infection with gonorrhea or chlamydia

Gonorrhea (aOR 7.24; 95% CI, 6.79-7.72); chlamydia (aOR 3.74; 95% CI 3.55-3.93)



Low educational attainment – less than high school

(aOR 4.40;
95% CI 3.93-4.92)



Non-Hispanic Black race/ethnicity

(aOR 3.81;
95% CI 3.65-3.98)



Medicaid insurance

(aOR 2.13;
95% CI 2.03-2.23)



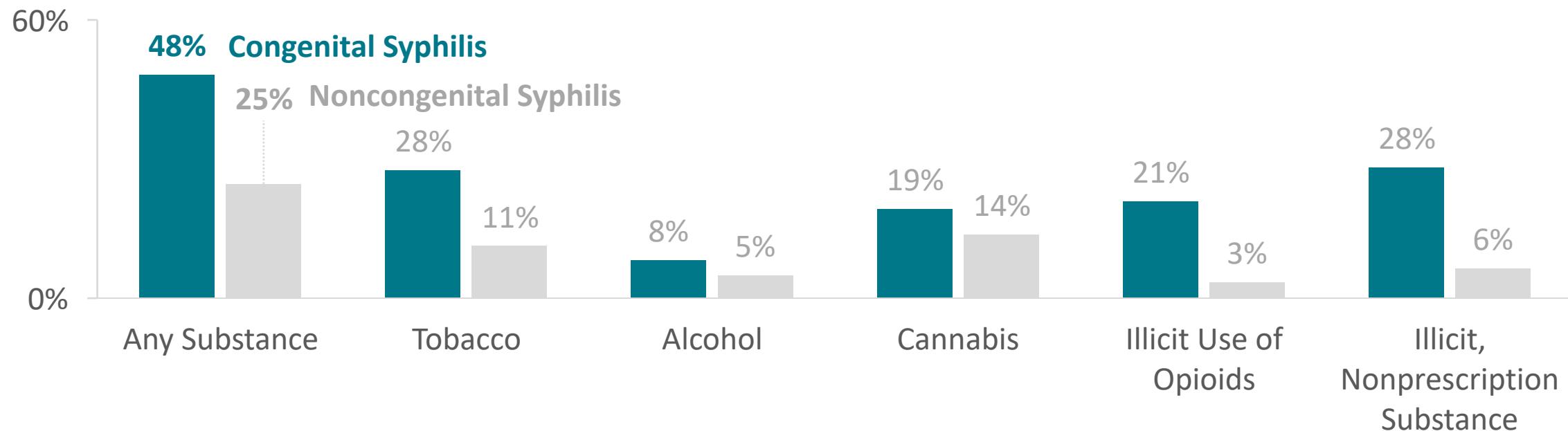
Initiation of prenatal care

2nd (RR 2.07; 95% CI 2.00-2.15)
3rd (RR 2.58; 95% CI 2.44-2.72)
No prenatal care (RR 3.98; 95% CI 3.67-4.21)

The Prevalence of Substance Use Among Persons with Syphilis During Pregnancy Is Higher for Those with a Congenital Syphilis Pregnancy Outcome than Those Without

Percent of Reported Substance Use Among Pregnant Persons with Syphilis, by Congenital Syphilis Pregnancy Outcome, Arizona and Georgia, 2018-2021

Surveillance for Emerging Threats to Pregnant People and Infants Network



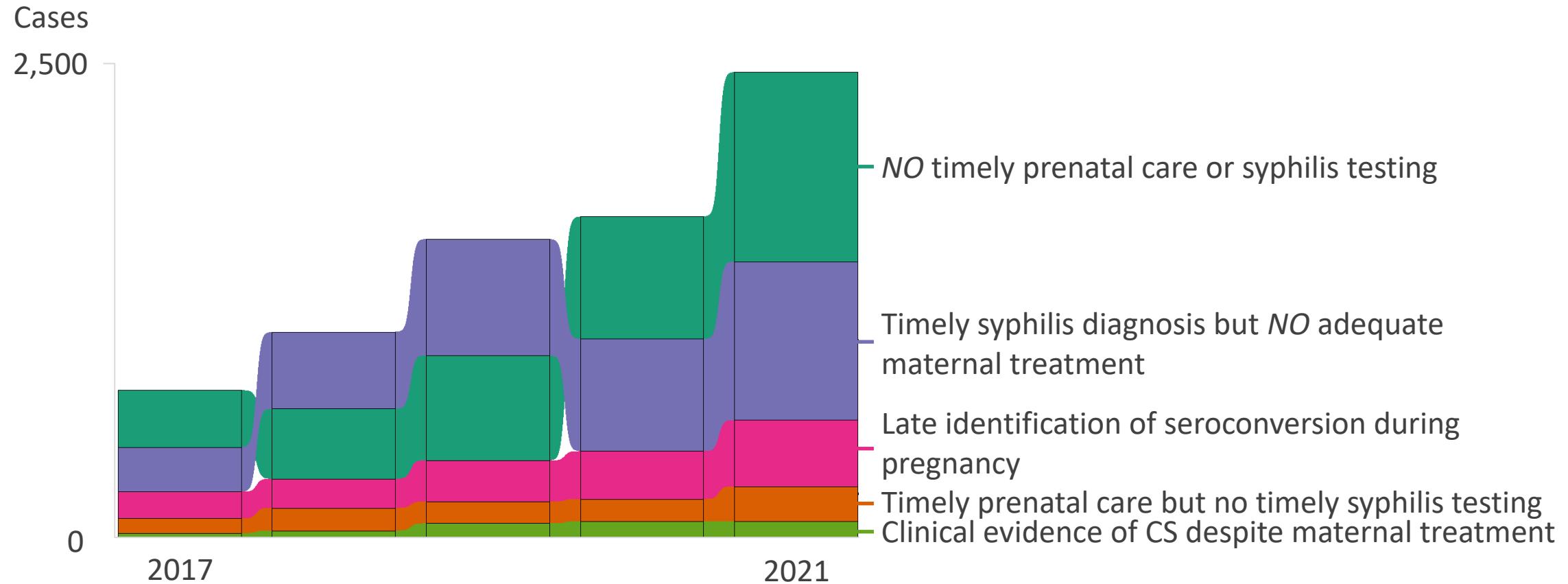
Risk of Adverse Pregnancy and Neonatal Outcomes Associated With Syphilis

Significantly increased risk for:

- ✓ Preterm birth (<37 weeks - 15.4% vs 10.0%; <32 weeks – 3.8% vs 2.1%)
- ✓ Low birth weight (14.3% versus 8.3%)
- ✓ Congenital structural abnormalities (0.5% vs 0.3%)
- ✓ Low 5-minute Apgar scores (3.3% vs 2.0%)
- ✓ NICU admission (20.9% vs 9.0%)
- ✓ Antibiotic treatment for suspected neonatal sepsis (7.5% vs 2.2%)
- ✓ Immediate ventilation (7.2% vs 4.3%)
- ✓ Prolonged ventilation (2.9% vs 1.5%)

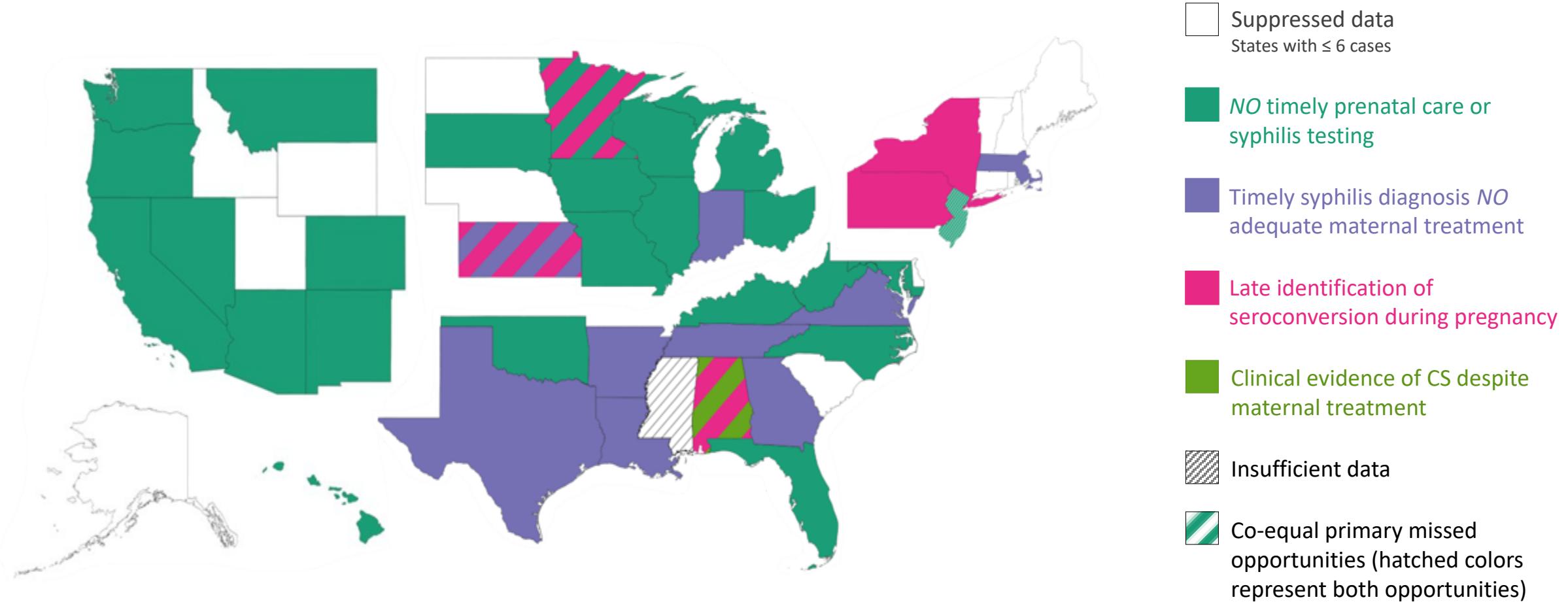
Reaching Pregnant Persons: Missed Opportunities

Missed Prevention Opportunities Among Mothers Delivering Infants With Congenital Syphilis, United States, 2017–2021



NOTE: Of the 9,141 congenital syphilis cases reported during 2017 to 2021, 1,553 (17.0%) 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.

Most Common Missed Prevention Opportunities Among Mothers Delivering Infants With Congenital Syphilis by State, United States, 2021



Most Common Missed Prevention Opportunities Among Mothers Delivering Infants With Congenital Syphilis, by Census Region, United States, 2021

Key

 Suppressed data
States with ≤ 6 cases

 *NO* timely prenatal care or
syphilis testing

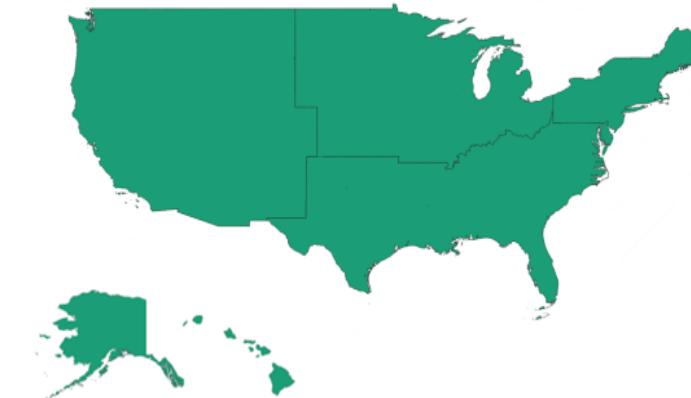
 Timely syphilis diagnosis *NO*
adequate maternal treatment

 Late identification of sero-
conversion during pregnancy

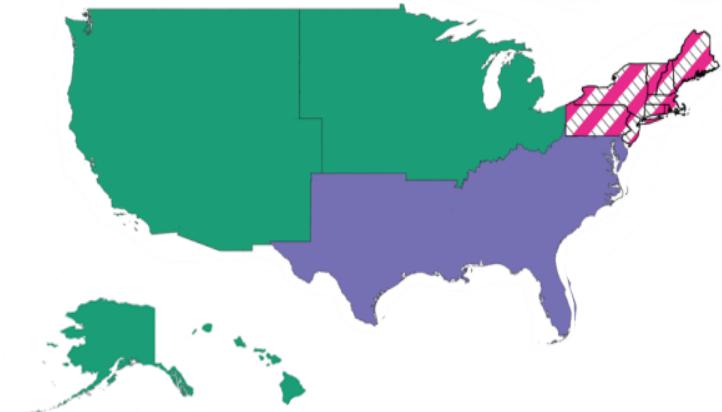
 Insufficient data

 Co-equal primary missed
opportunities (hatched colors
represent both opportunities)

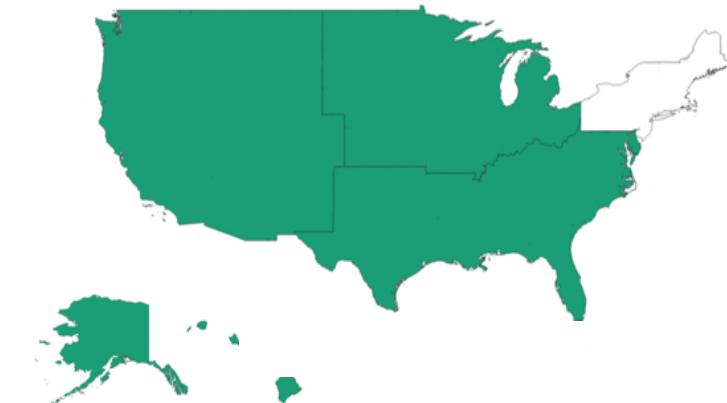
White non-Hispanic



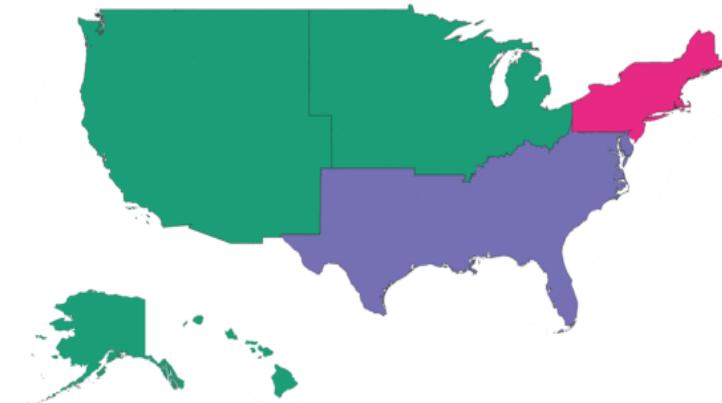
Black non-Hispanic



American Indian/Alaskan Native non-Hispanic



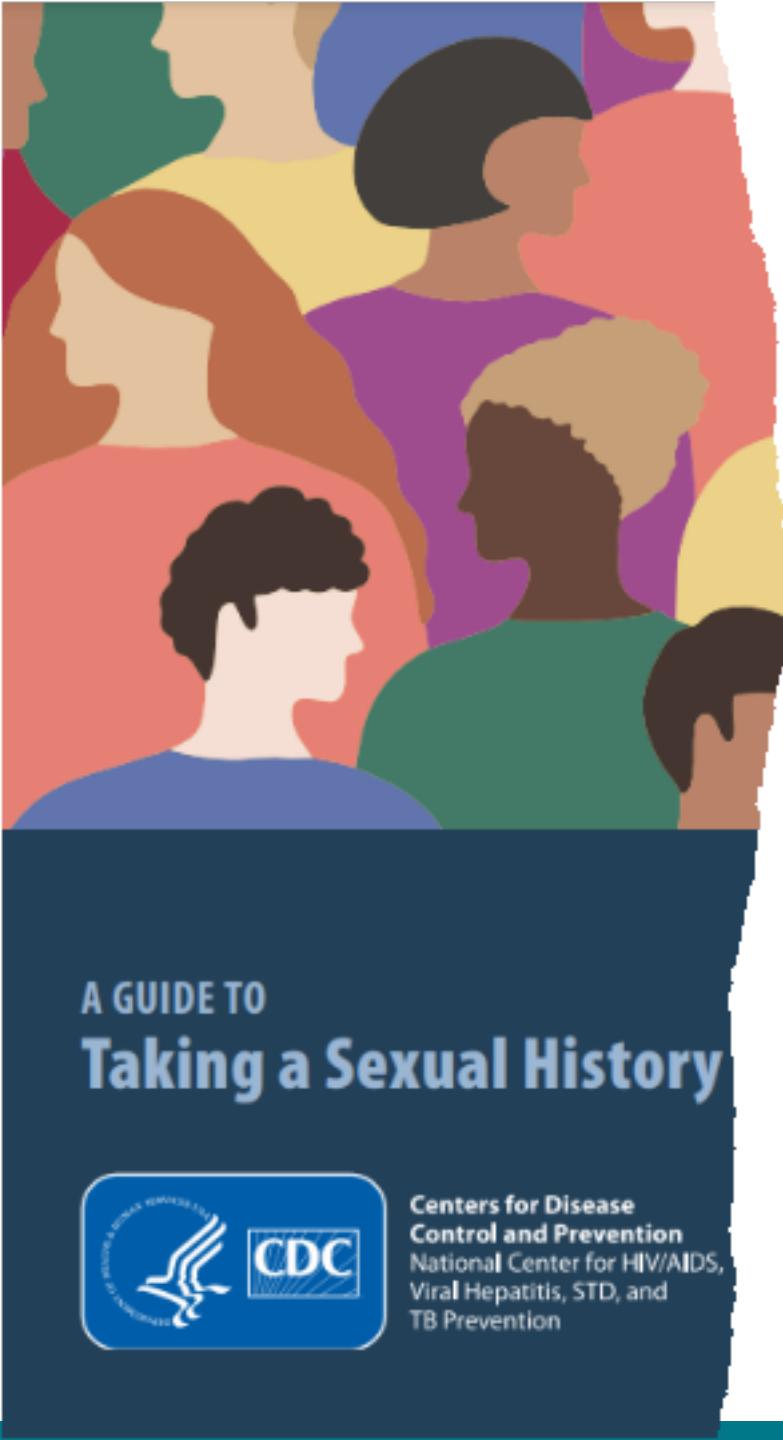
Hispanic



Challenges and Approaches in Clinical Settings

Recognize the Signs!





Key Aspects of Sexual Health

⚠️ Not exhaustive!

- Incorporate sexual history into routine care
- Ask about pregnancy intention and offer/refer for contraception if appropriate
 - ⚠️ If syphilis diagnosed, important to know status of patient/partner**
- Implement screening per guidelines
- Recognize signs and symptoms of syphilis
- Provide timely treatment with recommended regimens
- Link patients to Disease Intervention Specialist (DIS) for partner services as appropriate
- Discuss prevention approaches
- Provide wrap around services

A GUIDE TO **Taking a Sexual History**



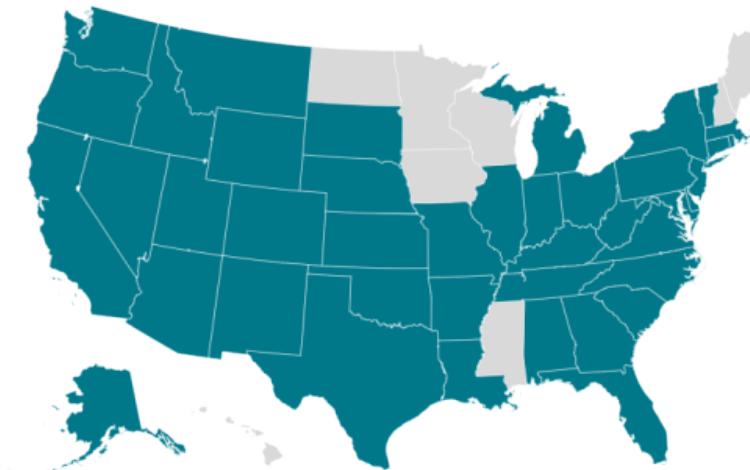
Centers for Disease
Control and Prevention
National Center for HIV/AIDS,
Viral Hepatitis, STD, and
TB Prevention

Prenatal Screening Laws for Syphilis

As of July 2021

Screening at 1st Visit

42 states require



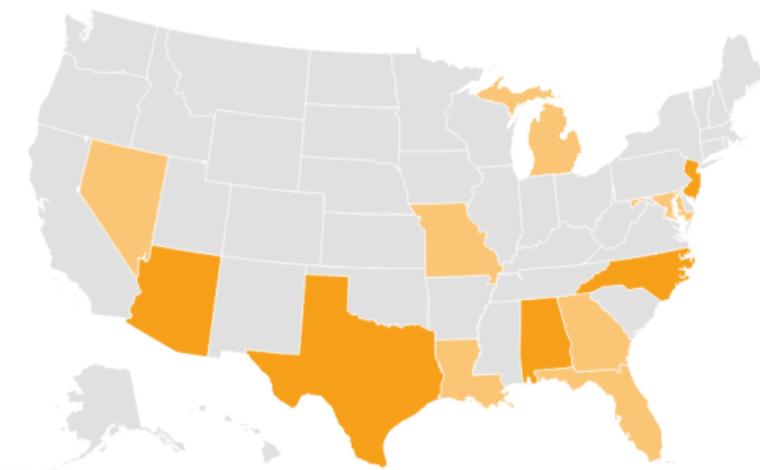
Screening at 3rd Trimester

13 states require
6 states require if patient is
at increased risk



Screening at Delivery

5 states require
7 states require if patient
is at increased risk

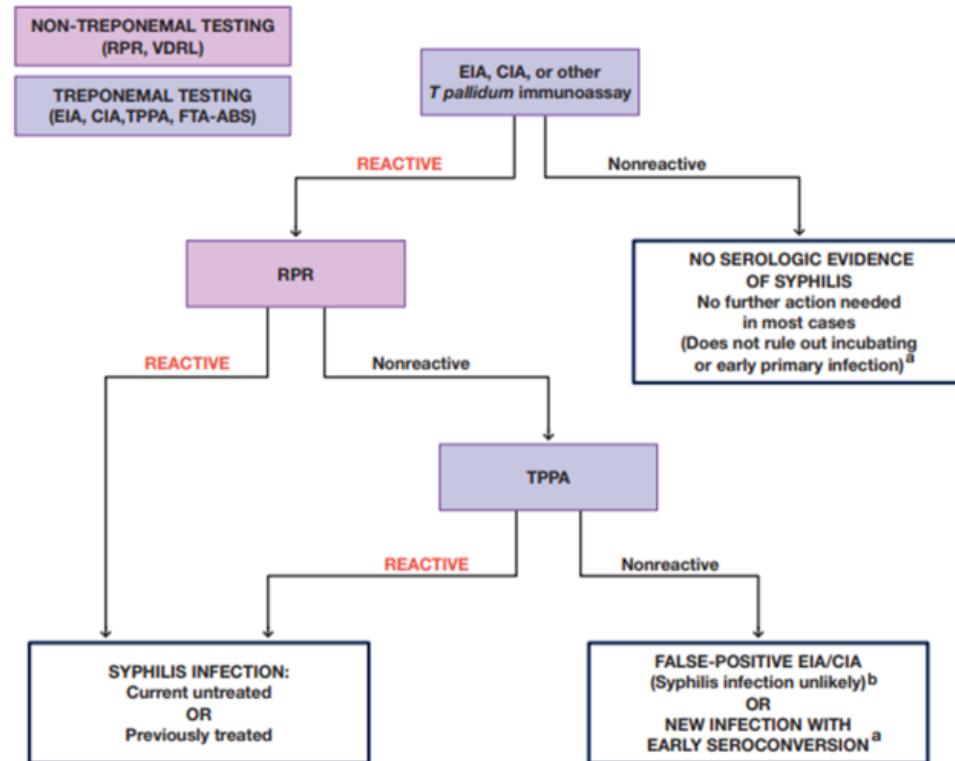


8 States Have No Screening Laws

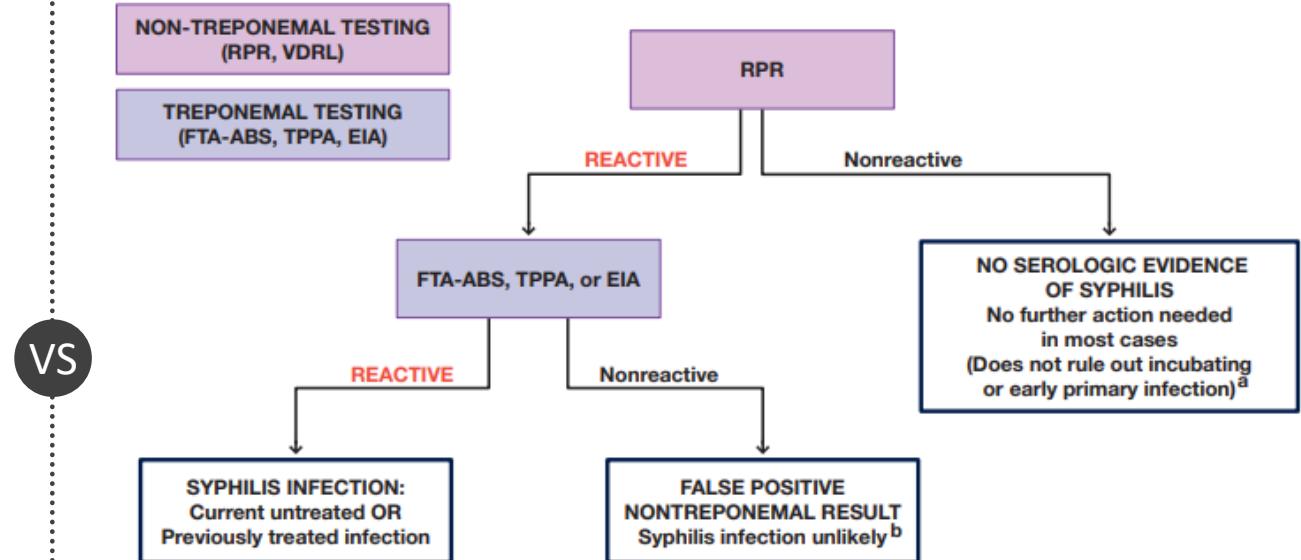
Hawaii, Iowa, Maine, Minnesota, Mississippi, New Hampshire, North Dakota, and Wisconsin

Syphilis Diagnostics: A Picture Is Worth 1000 Words!

Reverse-Sequence Algorithm



Traditional Algorithm



VS

Syphilis Diagnostics: A Picture Is Worth 1000 Words!

Reverse-Sequence Algorithm



Traditional Algorithm



Better (Less Complicated) Tests Are Needed!

Syphilis Treatment - 2021 CDC STI Treatment Guidelines

Primary, Secondary & Early Latent:

Benzathine penicillin G 2.4 million units IM x 1 dose

Late Latent and Unknown Duration:

Benzathine penicillin G 7.2 million units total, given as 3 IM doses of 2.4 million units each at 1-week intervals

Neurosypilis:

Aqueous crystalline penicillin G 18-24 million units IV daily administered as 3-4 million IV q4hr for 10 -14 days

Syphilis Treatment - 2021 CDC STI Treatment Guidelines

Primary, Secondary & Early Latent:

Benzathine penicillin G 2.4 million units IM x 1 dose



Pregnant people must receive benzathine penicillin

Neurosyphilis:

Aqueous crystalline penicillin G 18-24 million units IV daily administered as 3-4 million IV q4hr for 10 -14 days

HEALTH

Pfizer warns of a looming penicillin supply shortage

June 16, 2023 • 3:20 AM ET

By Ayana Archie



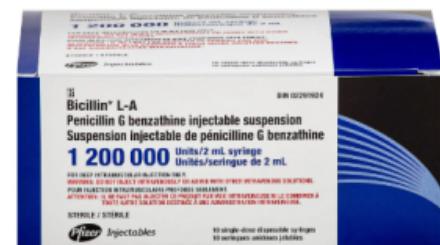
The Pfizer logo is displayed on the exterior of a former Pfizer building in New York.

The New York Times

July 7, 2023

Antibiotic Shortage Could Worsen Syphilis Epidemic

The primary drug used to treat the sexually transmitted infection could be scarce into next year, Pfizer warns.



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

s should:

[CDC's treatment recommendations](#). Penicillin G benzathine (Bicillin L-A®) is the only treatment for pregnant people infected with or exposed to syphilis. 2 mg PO BID for two weeks (for early syphilis) or for four weeks (for late latent or syphilis or congenital syphilis) is an alternative for the treatment of non-pregnant people with a penicillin allergy.

Use Bicillin L-A® to treat pregnant people and babies with congenital syphilis.

To monitor the situation, notify DSTDP (stdshortages@cdc.gov) of stock-outs of Bicillin L-A® in the jurisdiction.

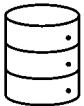
which patients diagnosed with syphilis are not being treated due to the inability to procure the jurisdiction.

to the Pfizer Supply Continuity Team at 844-646-4398 (select 1 and then select 3).

Alternative Treatments for Syphilis During Pregnancy



Comprehensive search



3 databases



Approx. 50 years
(1/1/1970 – 12/31/2018)



Non-penicillin treatments of syphilis in pregnant patients



6 publications with alternative treatments in 21 patients

- 13 with beta-lactam antibiotics
- 7 with macrolides
- 1 with tetracycline



0 publications reporting >15 cases/any RCT/comparative controlled trials

Conclusions:

- Amoxicillin holds promise (*not an option for PCN allergy though*)
- 3rd generation cephalosporins should be explored
- Macrolide and azalide antibiotics did not perform well (limited transplacental transfer)

Effectiveness of Oral Amoxicillin in Pregnant Women With Active Syphilis

– Japan, 2010-2018

- Nationwide retrospective study in Japan
- 80 pregnant women with active syphilis treated with amoxicillin or ampicillin 2010-2018
- 21% (15/71) had pregnancies that resulted in CS

0

CS cases among
26 patients with
early syphilis

33%

15(33%) cases of
late syphilis among
45 individuals with
late syphilis

14%

8 (14%) had CS
among 57 patients
who started
treatment \geq 60 days
before delivery

Conclusions:

- Oral amoxicillin potentially ineffective at preventing CS in late syphilis but potentially effective in early syphilis
- Prospective studies needed

Phase II Trial Evaluating the Clinical Efficacy of Cefixime for Treatment of Active Syphilis in Non-pregnant Women in Brazil - CeBra Study



Objectives

1

To demonstrate the efficacy of Cefixime, as measured by a **4-fold decrease in Rapid Plasma Reagin (RPR)** titer from baseline up to 6 months after treatment

2

To **determine the drug safety**, during or after treatment with Cefixime and the tolerability of the regimen.

- **Study design:** Randomized, non-comparative phase 2 efficacy trial

- **Population:**



Non-pregnant women

18+

Ages 18 and over

RPR $\geq 1:16$

Diagnosed with active syphilis

- **Randomization:**



140 cefixime
400mg PO bid x 10 days

70 penicillin

- **Follow up:** 15 days, 3-, 6- and 9-months following treatment with cefixime

Prevention



Doxycycline use as post-exposure prophylaxis (Doxy as PEP)

- So far efficacy in cis-women disappointing
- Will use of doxycycline as PEP have impact of decreasing STIs at the population level → indirectly reducing syphilis in individuals of reproductive potential and CS?



Is there a syphilis vaccine in the future?

The time for disruptive innovation
is now!

Innovation in Testing and Treatment Strategies

Non-traditional settings

Mobile vans and other field-based outreach

Partner facilities
(i.e., substance use treatment facilities, syringe exchange programs, homeless service providers, community-based organizations, emergency departments)

Increased implementation of point-of-care syphilis tests needed



Field treatment

Expanded role for Disease Intervention Specialists (DIS)

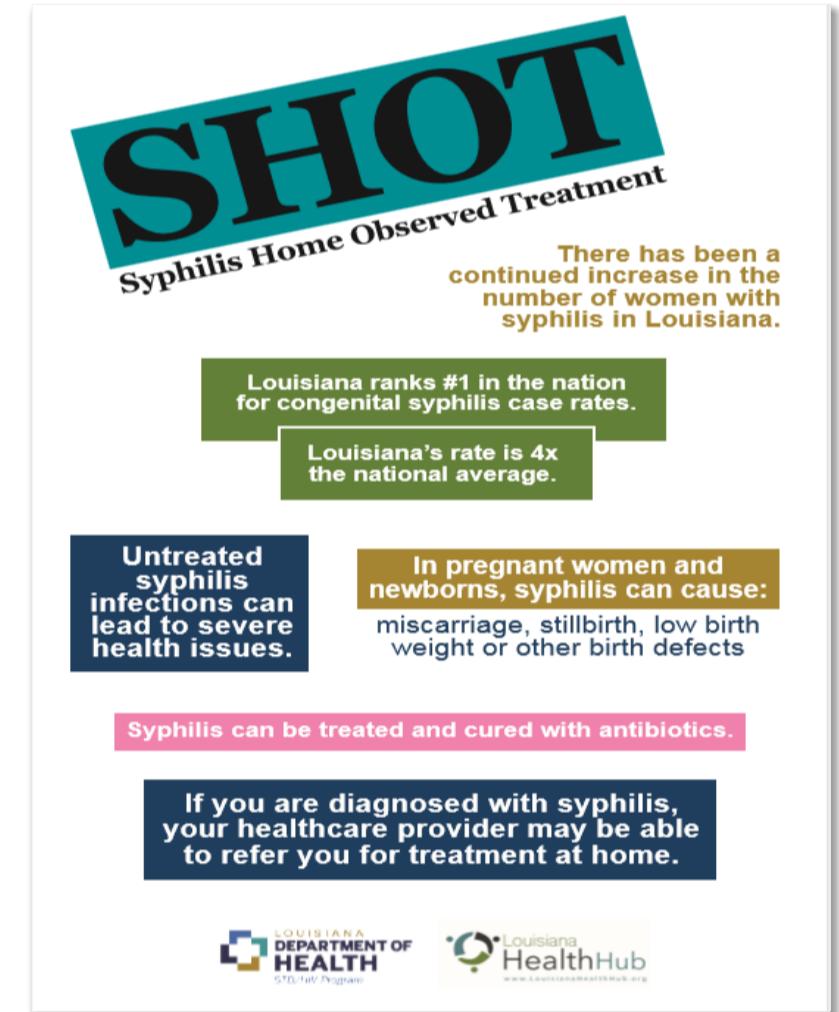
SHOT



Syphilis Home Observed Treatment

Louisiana DOH – Syphilis Home Observed Treatment (SHOT) Protocol

- Developed to facilitate treatment of pregnant people to intervene on increasing congenital syphilis rates.
- Focus on pregnant people unable to access treatment for syphilis at a clinic
- Decision to treat in home made by STD nurse clinician and DIS in consultation with regional Medical Director
- DIS and public health nurse visit pregnant person and partner in the field
- Protocol outlines parameters
- Expanded to non-pregnant individuals



Delivery of Medications to Medical Practices

- Louisiana DOH developed a program that allows DIS to deliver BIC (non-340b stock) to community physician offices.
- Advantages:
 - ① Strengthens partnership between the medical practice and public health
 - ② Allows DIS opportunity to interview patient on-site



From Oct. 2019-Jun. 2022,
575 practices
took advantage of this service

Congenital Syphilis Activities: Florida

- 1 Hospital partnership with Jackson Memorial Hospital to deliver **syphilis screening to women of reproductive age in the emergency department**

From December 2022 – July 2023:

 **11,000+**
syphilis tests
performed

 **292**
People requiring syphilis
treatment

 **42**
Pregnant people tested
for syphilis

 **10**
Pregnant people requiring
syphilis treatment

- 2 University collaboration with the University of Miami's IDEA program, a syringe-service provider, **to test and treat women of reproductive age** who use that facility

From July 2022:

Roughly 1 in 3
women tested positive for syphilis

2 of 3 pregnant women identified
were diagnosed with syphilis

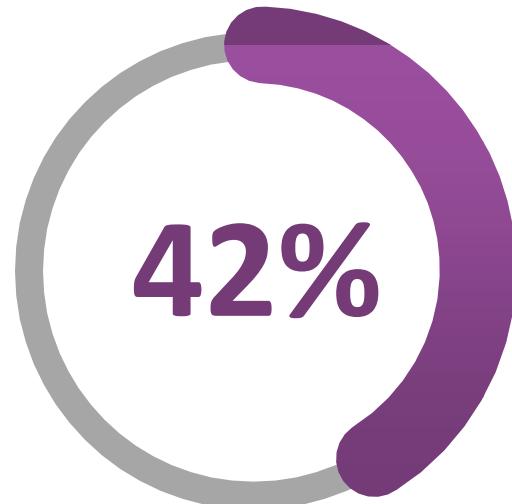
Congenital Syphilis Activities: California

Pregnancy Connections, or PCONN, Clinic

An open access prenatal care clinic for women experiencing homelessness and/or substance use

- ✓ Established with the local health department in San Joaquin County and a local FQHC look-a-like
- ✓ Opened the clinic in mid-January 2022

Of patients seen by a PCONN provider (n=31)



were diagnosed with syphilis during their current pregnancy.

Conclusions

- ✓ The congenital syphilis epidemic is **multi-faceted** and **complicated**
- ✓ **No one entity** can address the epidemic in isolation
- ✓ **Partnerships**, old and new, will be required
- ✓ Data should be used to **tailor interventions**
- ✓ **Training providers** to deliver good clinical care remains a goal
- ✓ **Innovation** around diagnosis, treatment and care delivery desperately needed
- ✓ We have many tools already, but **how to implement them?**
- ✓ **Optimizing biomedical** approaches important but likely not sufficient if social determinants of health not addressed
- ✓ Important to **take a broader approach** to the congenital syphilis epidemic

Acknowledgements

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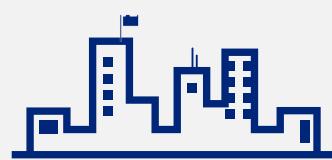
Challenges and Opportunities: Structural Contributors to Health Inequity

Address Structural Contributors to Health Inequity

STI control has historically focused on individual risk factors and individual behavior change or a specific organism



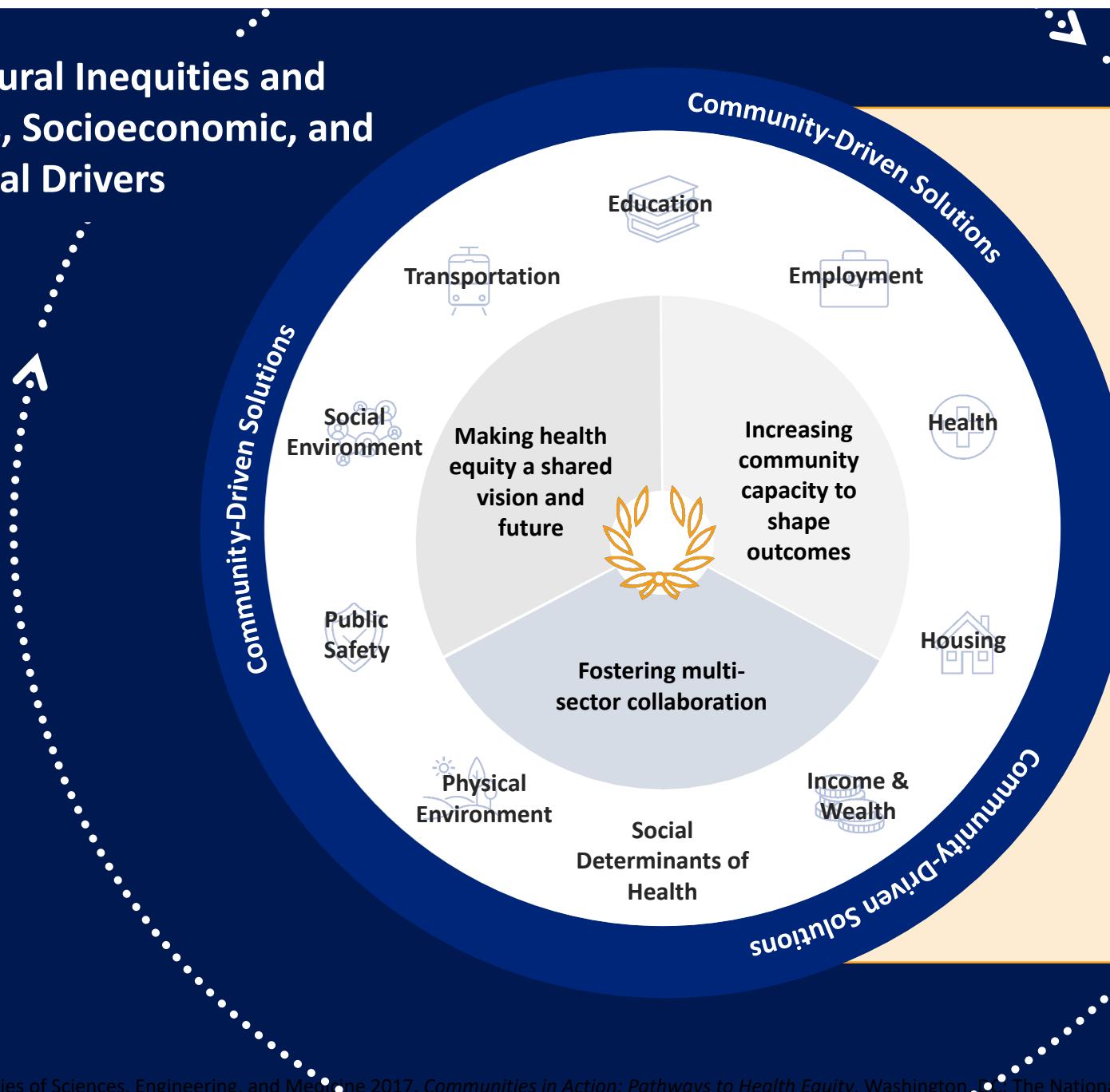
Multi-level factors have not been addressed to the same extent: institutional, community, and structural factors



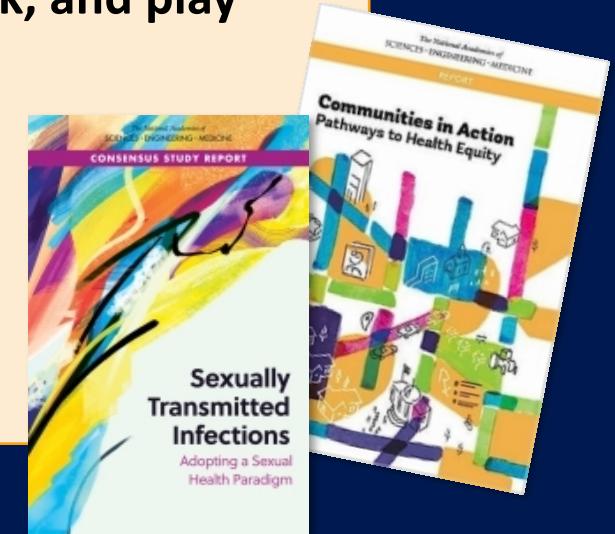
The majority of affected individuals are marginalized; while optimizing biomedical approaches important, this is probably not sufficient



Structural Inequities and Biases, Socioeconomic, and Political Drivers



Healthier, more equitable communities in which individuals and families live, learn, work, and play



A Heuristic Framework to Inform Future Directions for Mitigation

Eight Key Principles of SDOH Mechanisms Shaping Inequities

1

SDOH are underlying causes of health inequities

2

SDOH shape health inequities through contextual influences

3

SDOH contextual disadvantage is not deterministic

4

SDOH shape health over the life course

5

SDOH operate through biological embedding

6

SDOH operate intergenerationally

7

SDOH shape clustering and synergies of health inequities

8

Unjust social processes shape SDOH mechanisms to produce health inequalities

- **Upstream efforts needed to prevent syphilis in the general population including men.**
- **Pregnant persons**
 - In clinical settings – comprehensive sexual health approach that includes:
 - Screen for syphilis at time pregnancy identified
 - Repeat screening based on prevalence and individual risk
 - Treat persons with syphilis as soon as possible
 - Identify signs/symptoms of syphilis in timely manner and treat (even before confirmation)
 - Institute approaches to facilitate screening and treatment for people who cannot access prenatal care
 - Where to find pregnant people who have not accessed prenatal care?
 - Emergency departments
 - Correctional facilities
 - Substance use treatment facilities – heterosexual syphilis and drug use are intersecting epidemics
 - Needle exchange programs
 - Facilities serving individuals experiencing housing instability/homelessness
 - Treat partners of pregnant persons

is: síntomas y riesgos de una de las infecciones de transmisión sexual que más creció en la Argentina



ta de una enfermedad que, si no se atiende, tiene consecuencias graves para la salud - LA
2, 2023

JN The Japan News

Syphilis Cases Exceed 5000 in Japan, Fastest Pace on Record

More than 5,000 people have been diagnosed with syphilis this year, according to the National Institute of Infectious Diseases.

May 24, 2023

CNN

Rates of congenital syphilis are skyrocketing in the US. Here's why

Venus Johnson entered the world clinging to life. She stopped breathing shortly after delivery, and doctors massaged her tiny chest and held...

Mar 1, 2023

own sexually transmitted infections at an alarming rate.

The Guardian

Syphilis cases at highest level for 75 years in England this year

Figures also show gonorrhoea diagnoses rose by 50% to 82600 – the highest figure since records began in 1918.

1 month ago



Reuters

Insight: Syphilis cases in babies skyrocket in Canada amid healthcare failures

TORONTO, March 31 (Reuters) - The numbers of babies born with syphilis in Canada are rising at a far faster rate than recorded in the United States...

Mar 31, 2023

The Yucatan Times

Syphilis on the verge of tripling in Yucatan this year

In Yucatan, syphilis is on the verge of tripling, since only last week a case was reported as the highest figure in two months...

WS

Genital syphilis cases recorded in 2022 'too many' - experts

Health services are calling for extra funding to address a dramatic spike in syphilis cases since 2019.

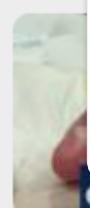
Mar 24, 2023



The Guardian

Mississippi sees 900% rise in number of infants born with congenital syphilis

Medical professionals attribute the increasing cases of disease to inadequate prenatal health care and staff shortages.



Guardian

PAHO

With rising trends of syphilis and congenital syphilis in some countries in the Americas, PAHO calls for reinforcement of ...

In 2020, countries in the region reported 29147 cases of congenital syphilis, and preliminary figures for 2021 indicate more than 30000.

Jul 5, 2022