



The Quiet Crisis of Congenital Syphilis in Illinois: Why we need to care right now

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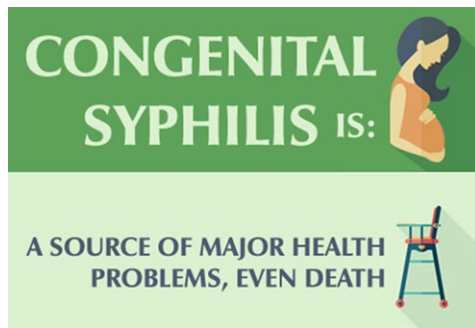
June 16, 2023

Objectives

- Brief review of congenital syphilis/staging
- Review clinical implications of congenital syphilis
- Understand testing and treatment of syphilis in pregnancy
- Improve knowledge of the missed opportunities in diagnosis and treatment
- Obtain updates on state programs for family planning services

What is Congenital Syphilis (CS)?

- A preventable and treatable spirochete infection acquired by the fetus during pregnancy, transmitted through sexual contact to the pregnant person and across the placenta to the fetus
 - *Adequate treatment for syphilis during pregnancy is 98% effective in reducing congenital syphilis*
- A disease that causes significant morbidity and mortality
 - 25% untreated pregnancies result in **pregnancy loss** or other adverse outcomes
 - Neonatal death, prematurity, low birth weight, **lifetime morbidity including developmental delay and hearing loss**
 - 21% increased risk for stillbirth



Neonatal CS clinical findings

- Rhinitis “snuffles” : which is contagious
- Hepatosplenomegaly
- Desquamating skin rash
- Hutchinson’s Triad
 - Notched teeth
 - Deafness
 - Interstitial keratitis
- Anemia
- Meningitis

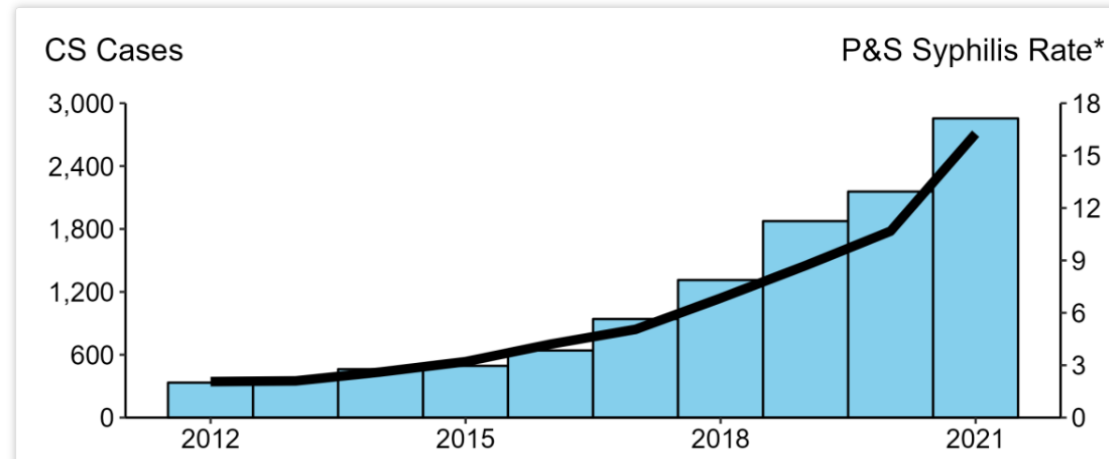


But...syphilis is gone from the US right?

- CS decreased during 1991–2005
 - Started increasing slightly by 2008
- By 2014, it had sharply risen to 11.6 per 100K live births;
- By 2018 it had reached 33 per 100K live births
- By 2021 it was 77.6 per 100k live births
 - >200% increase since 2017

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

[Print](#)



CDC 2021 report on
Congenital Syphilis

And who is this happening to?

TABLE 1. Number and rate* of congenital syphilis (CS) cases by race/ethnicity of mother and region of birth of infant — United States, 2008–2014†

Characteristic	2008		2009		2010		2011		2012		2013		2014	
	No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate
Race/ethnicity of mother														
White, non-Hispanic	67	2.9	65	2.9	63	2.9	50	2.3	50	2.3	61	2.8	80	3.2
Black, non-Hispanic	226	35.9	216	35.1	216	36.3	211	35.9	189	32.1	185	31.4	201	38.2
Hispanic	135	13.0	128	12.8	91	9.6	73	8.0	80	8.8	92	10.2	111	12.2
Asian/Pacific Islander	7	2.9	11	4.6	9	3.8	14	5.7	6	2.3	9	3.5	19	7.7
American Indian/Alaska Native	6	13.8	5	11.8	1	2.5	2	5.0	2	5.1	5	12.8	5	12.8
Other	1	N/A	2	N/A	3	N/A	3	N/A	4	N/A	3	N/A	7	N/A
Unknown	4	N/A	4	N/A	4	N/A	5	N/A	3	N/A	4	N/A	13	N/A
Region of birth of infant[§]														
Northeast	37	5.5	30	4.5	26	4.0	23	3.6	17	2.7	17	2.7	30	4.8
Midwest	37	4.2	41	4.7	45	5.3	41	4.9	57	6.8	53	6.4	71	8.5
South	265	16.4	263	16.7	253	16.6	234	15.5	206	13.7	213	14.1	234	15.5
West	107	10.1	97	9.5	63	6.4	60	6.2	54	5.5	76	7.9	123	12.8
Total	446	10.5	431	10.4	387	9.7	358	9.1	334	8.4	359	9.1	458	11.6

* CS rates during 2008–2013 were calculated as cases per 100,000 live births by using annual live birth data as denominators. Available at <http://wonder.cdc.gov/natality-current.html>.

Not the 1950s again

- Black women had a 4.5 times higher odds of birthing a child with congenital syphilis
- Hispanic women : 1.8 times higher odds
- Low income : 2.8 times higher odds
- Rural: 2.0 times higher odds
- Immigrant: 4.6 times higher odds
- Use of cocaine: 9.3 times higher odds

Characteristics of Pregnant Women With Syphilis and Factors Associated With Congenital Syphilis at a Chicago Hospital

[Corinne Thornton](#),¹ [Lelia H Chaisson](#),² and [Susan C Bleasdale](#)²

Women with psychiatric illness and noninjection substance use each had a >5-fold increased odds of having an infant with congenital syphilis.

Cases with congenital syphilis were more likely to have **late or scant prenatal care** and **initiated treatment nearly 3 months later in pregnancy.**

There's
more....

Other Congenital syphilis risk factors

High community syphilis rates

Multiple partners

Presence of other STI including HIV

Recent immigration to the US

Incarceration

Transactional sex

Unstable housing

Limited access to prenatal care

- Although national data from 2012-2016 showed almost half of CS cases lacked traditional risk factors
 - Trividi et al, Obstet Gynecolo 2019;133:27-32

The Urgent Need for Provider Based Reporting

- Public health systems experience challenges linking pregnancy data with syphilis results
- In the United States and in IL, congenital syphilis is a national notifiable disease
- For reporting purposes, congenital syphilis includes:
 - Stillbirths due to syphilis
 - Cases of congenital syphilis detected in newborns
 - Cases of congenitally acquired syphilis in infants and children.
- But we need to find the moms first before the children develop congenital syphilis!

Who can and should report

Persons Required to Report Disease in IL

- Physicians
- Physician assistants
- Nurses
- Nursing assistants
- Dentists
- Health care practitioners
- Emergency medical services personnel
- Any institution, school, college/university, child care facility or camp personnel
- Pharmacists
- Poison control center personnel
- Blood bank and organ transplant personnel
- Coroners, funeral directors, morticians and embalmers
- Medical examiners
- Veterinarians
- Correctional facility personnel
- Food service management personnel
- Any other person having knowledge or a known or suspected case or carrier or a reportable communicable disease or communicable disease death
- The master, pilot or any other person in charge of any bus, train, ship or boat, and the commander, pilot or any other person in charge of any aircraft within the jurisdiction of the state
- Researchers

IL STI reporting code

**TITLE 77: PUBLIC HEALTH
CHAPTER I: DEPARTMENT OF PUBLIC HEALTH
SUBCHAPTER k: COMMUNICABLE DISEASE CONTROL AND IMMUNIZATIONS
PART 693 CONTROL OF SEXUALLY TRANSMISSIBLE INFECTIONS CODE
SECTION 693.30 REPORTING**

Section 693.30 Reporting

- a) Every health care professional shall report each case in which the health care professional has diagnosed or treated a case of AIDS, HIV infection, syphilis, gonorrhea, chlamydia, or chancroid.
 - 1) The reportable STI case report shall state the name, address and telephone number of the health care professional who diagnosed or treated the case. The STI case report shall be submitted **within seven days after the diagnosis or treatment.**
 - 2) If the health care professional diagnoses or treats a reportable STI in a county or city governed by a local health department, the STI report shall be sent to that local health department. In all other cases, the STI report shall be sent directly to the Department.

First, the mom: Primary syphilis



Fig. 1. Vulvar chancre of primary syphilis. Image courtesy of Dr. Alejandra Perez-Moore. Used with permission. Adhikari. *Syphilis in Pregnancy. Obstet Gynecol* 2020.

- ~ 3 weeks after exposure
- Painless chancre
 - Highly infectious
- Localized lymphadenopathy

Secondary syphilis

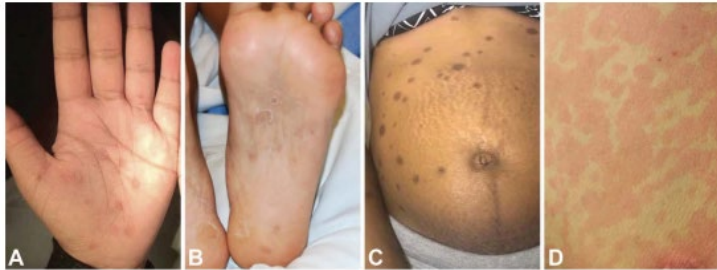


Fig. 2. Vulvar condyloma lata of secondary syphilis. Image courtesy of Dr. Edward Wells. Used with permission. Adhikari. *Syphilis in Pregnancy. Obstet Gynecol* 2020.

- Occurs in 25% if untreated
- ~ 4 – 10 weeks after chancre
- 90% with rash on palms soles
- 10-20% with oral lesions or condyloma lata
- Lymphadenopathy, malaise, fever
- Resolves in 1-6 months

Latent infection

Early latent

- < 1 year from initial infection
- Intermittent seeding of spirochetes in bloodstream
- 25% with recurrence of secondary lesions/rash

Late latent

- > 1 year from initial infection
- Often incomplete clearance of organisms
- 15-40% eventually develop tertiary syphilis

Tertiary Syphilis

- Occurs in 40% of untreated patients
- Benign gummas
 - Slowly progressive, painless nodules/plaques
- CV symptoms, vascular aneurysms

Neurosyphilis

Early

- Can occur with any stage
 - In 1% of secondary syphilis
- Aseptic meningitis
- Cranial nerve palsies – vision/hearing loss, vertigo
- Gradual progression

Late

- Decades after initial infection
- General paresis, dementia, psychiatric symptoms
- Tabes dorsalis, ataxia
- Argyll Robinson pupils (do not react to light)

Now the baby: Congenital Syphilis

Early

- Diagnosed younger than 2 y/o
- Growth restriction, hydrops/IUFD
- Rash, hepatomegaly, snuffles
- Progressive

Late

- Asymptomatic at birth
- Diagnosed after age 2
- Huthcheson's triad
 - Notched teeth, deafness, keratitis
- Bone deformations/saber shin
- CNS involvement
- Chronic and progressive

Perinatal transmission risk by syphilis stages

- Primary, Secondary, early latent syphilis: Highest risk (50 – 80%) of transplacental transmission from pregnant person to fetus
- Late latent with 10% risk of fetal infection
- Greater transmission as pregnancy progresses
 - Likely related to increased placental size

Clinical obstetric implications of CS

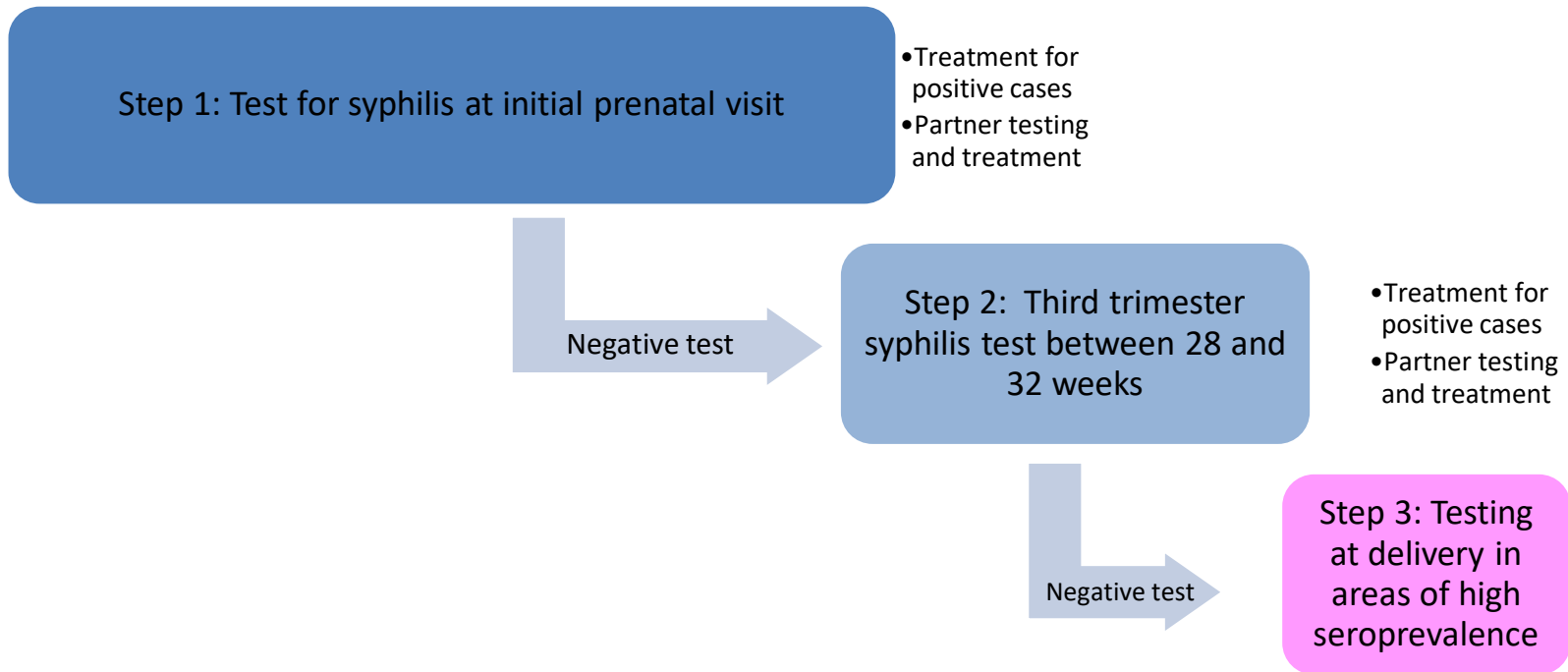
- 21% increased risk of stillbirth if untreated
- 9% increased risk of neonatal death
- Miscarriage
- Prematurity
- IUGR

Syphilis Testing during Pregnancy: What is the Law in Illinois?

- For all pregnancies in IL, both first visit and third-trimester syphilis testing are required.
 - Ideally early third trimester : 28 weeks is preferred
- There are documented disparities and poor adherence with IL mandate.¹

1. Clement AC, Fay KE, Yee LM. Disparities in state-mandated third-trimester testing for syphilis. Am J Obstet Gynecol MFM. 2022 May;4(3):100595. doi: 10.1016/j.ajogmf.2022.100595. Epub 2022 Feb 15. PMID: 35176505; PMCID: PMC9081215.

IL Congenital Syphilis Prevention Cascade



Third trimester treatment is not too late!

- Early treatment is optimal
- But, if detected in early 3rd trimester can still be effective!
- Treatment is most effective when initiated >30 days prior to delivery
 - Note that this means testing at 28-32 weeks, earlier than third trimester testing for GBS

Prenatal testing

Non treponemal

- RPR/VDRL
 - Measures ab to cardiolipin, contained within T pallidum and damaged host cells
- False positive (1% RPR false pos in pregnant people)
- Can become negative with time
- Titers can be used for monitoring tx response
 - Fourfold change in titer (2 dilutions) is clinically meaningful
 - (1:16 -> 1:4 or 1:8 -> 1:32)

Treponemal

- FTA/EIA/TPPA/MHA/TP-PA
 - Automatic immunoassay
- Majority of patients will remain positive
- 15-25% treated in *primary* stage will become negative

Testing algorithms

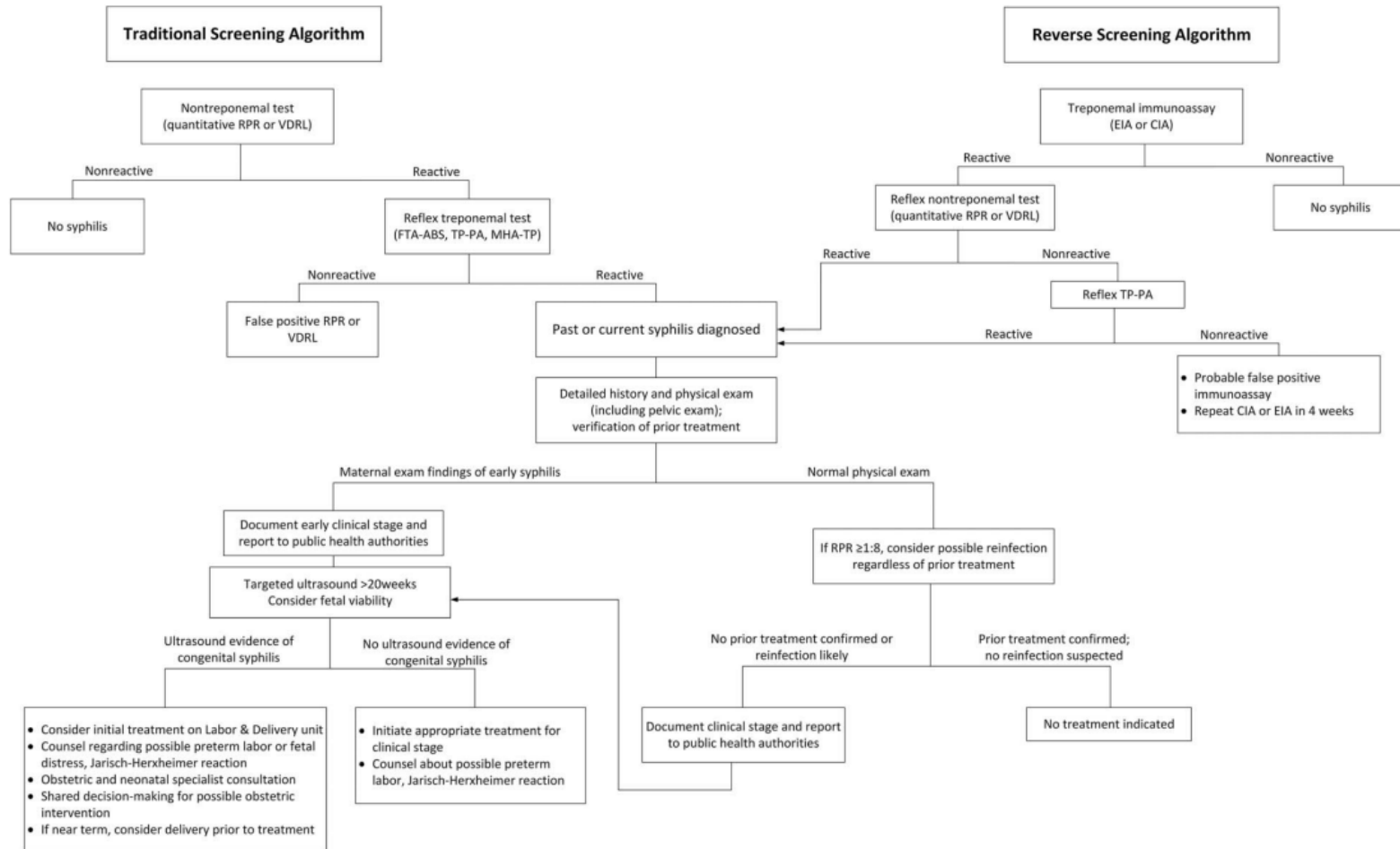


Fig. 6. Clinical evaluation for syphilis in pregnancy using the traditional or reverse sequence algorithms. RPR, rapid plasma reagin; VDRL, venereal disease research laboratory test; EIA, enzyme immunoassay; CIA, chemiluminescence immunoassay; FTA-ABS, indirect fluorescent-antibody; TP-PA, *Treponema pallidum* particle agglutination assay; MHA-TP, microhemagglutination assay.

Adhikari. *Syphilis in Pregnancy. Obstet Gynecol* 2020.

Why the change to reverse screening?

- This algorithm is cheaper and automated for high volume labs
- For non pregnant patients, treponemal tests are very specific
- In pregnant women, treponemal tests are:
 - 97-100% sensitive BUT
 - 40-80% false positives in pregnancy which is why confirmatory test is warranted with a second treponemal test targeting a different antigen (TPPA, FTA-ABS, CIA, TP-EIA)

Lin et al. Screening for syphilis infection in pregnant women: updated evidence report and systematic review for the US Preventive Services Task Force. JAMA 2018;320:918-25.

“Reverse” Syphilis Testing Interpretation During Pregnancy

1. Treponemal Ab (EIA or CIA)	2. Reflex RPR or VDRL	3. Reflex to 2nd treponemal test	Interpretation and Actions
Negative	Not performed	Not performed	No evidence of syphilis. No treatment.
Positive	Positive	Not performed	Syphilis is confirmed. <u>Treat with parenteral PCN according to stage of maternal syphilis.</u> Test and treat partner. Treat for syphilis with one possible exception: there is documented prior treatment of syphilis with reduction in RPR titers and the RPR has remained low and stable (termed serofast). In these patients, if no ongoing risk of syphilis, might withhold treatment.
Positive	Negative	Positive	Syphilis is confirmed– either current or in the past. <ul style="list-style-type: none"> • <u>If no history of treatment of syphilis in the past, treat for appropriate stage of syphilis.</u> If unknown stage, treat with 3 weekly Benzathine PCN shots. Test and treat partner(s). • If well-documented history of syphilis and adequate treatment and no ongoing risk, no further treatment is necessary.
Positive	Negative	Negative	If low seroprevalence region, low behavior risk and no history of treated syphilis, the treponemal ab is likely false positive, but <u>examine patient for primary or secondary syphilis AND test & examine partner(s) for syphilis AND repeat mother’s tests in 4 weeks.</u> If test 2 and 3 remain negative, no treatment is indicated. If, +/-/- but additional follow-up is uncertain, <u>treat</u> with 1 dose of Benzathine PCN G IM.

A fingerprick away! Point of care syphilis testing

- FDA has approved point of care testing!

Test	Specimen for Testing/ Sample Type	Test Type/ Target Antibody	Sensitivity	Specificity	Regulatory Approval
Syphilis Health Check (Diagnostic Direct, Youngstown, OH, USA)	Whole blood, serum, plasma	Treponemal	50-100	50-100	CE marked § FDA cleared †
Chembio DPP HIV/ Syphilis (Chembio Diagnostic Systems, Hauppauge, NY, USA)	Whole blood, serum, plasma	HIV	90.6-100	97.2-99.6	CE marked § FDA cleared †
		Treponemal	47.4-98.8	97-100	WHO pre-qualified ‡

§ CE marked: European Conformity marking for in-vitro medical diagnostics; † FDA: US Food and Drug Administration; ‡ WHO pre-qualification: World Health Organization marketing authorisation.

Pham et al, 2022



Diagnosis is challenging

Obstet Gyn 2020;135:1121-35

FUTURE DIRECTIONS IN SYPHILIS DIAGNOSIS

As described, the diagnosis of syphilis is still currently made based clinical history, physical examination, and indirect (serologic) testing. The recent evolution in syphilis serologic tests (with accompanying reverse sequence algorithm) resulted from major advances in the field over the past 20 years. The complete genome of *T pallidum* was sequenced in 1998.⁴⁹ This achievement spurred the development of new diagnostic techniques using recombinant treponemal antigens, such as the previously described treponemal-specific immunoassays. Admittedly, diagnostic quandaries are common, and lead to patient (and physician) distress.

As our ability to study syphilis is made easier using new technologies, DNA and polymerase chain reaction-based molecular tests will likely play a role in the evolution of syphilis diagnosis over the next 20 years.⁵⁰⁻⁵²

- Refer to CDPH or IDPH STI clinics if cost/desensitization challenges
- Hotline in process to help with clinical guidance and connect to data on previous serology/treatment

Syphilis treatment, there is an app for that!

STI Treatment Guide Mobile App

STI Treatment Guide Mobile App

- More Comprehensive
- More Integrated
- More Features

Download CDC's free app for iPhone and Android devices.

Available on the App Store

GET IT ON Google Play

CDC

The new app is free and available for iPhone and Android devices.

Treatment of syphilis in pregnancy

STAGE OF SYPHILIS		REGIMEN	DOSE
Early Syphilis	Primary and Secondary Early non-primary/non-Secondary (less than 12 months)	Benzathine Penicillin G* (Bicillin-LA)	2.4 million units IM single dose
Late Syphilis	Unknown Duration or Late (greater than 12 months)	Benzathine Penicillin G* (Bicillin-LA)	7.2 million units IM given as 3 doses at 1- week intervals

Benzathine Penicillin G is the *only* CDC-approved treatment for pregnant women

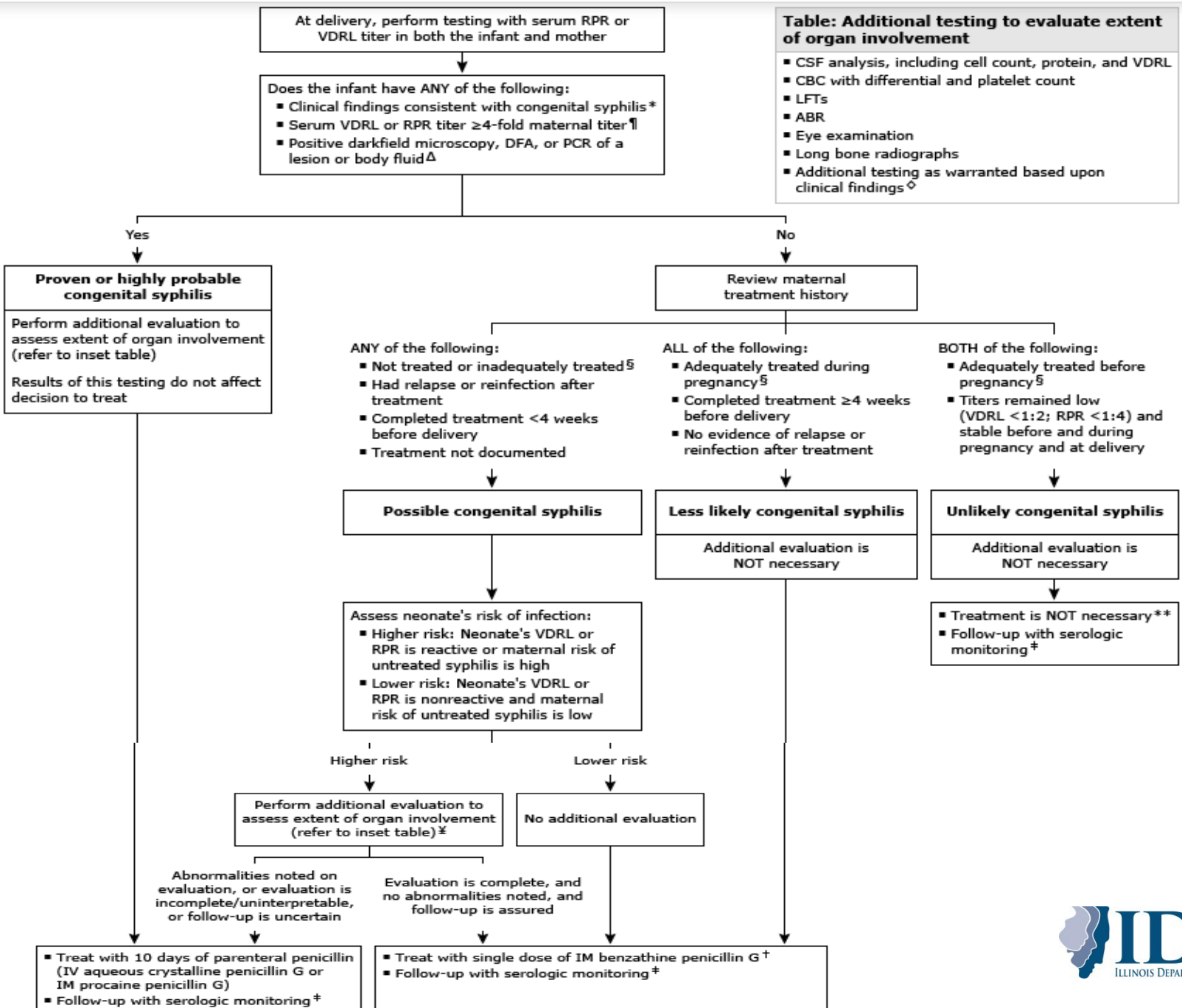
Interval can be NO LONGER than 9 days

Patients with PCN allergy need desensitization

PCN only option in pregnancy

- Penicillin is recommended for all clinical stages of syphilis, and **no proven alternatives exist** for treating neurosyphilis, congenital syphilis, or syphilis during pregnancy.
- For persons among whom the only therapy option is a penicillin antibiotic (e.g., a patient with neurosyphilis or a **pregnant woman with syphilis**) and among whom a penicillin skin test is positive, induction of penicillin tolerance (also referred to as desensitization) is required (675).


Approach to evaluation and management of newborns born to mothers who tested positive for syphilis during pregnancy





Sexually Transmitted Infections Treatment Guidelines, 2021

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 should:

- Continue to follow [CDC's treatment recommendations](#). Penicillin G benzathine (Bicillin L-A®) is the only recommended treatment for pregnant people infected with or exposed to syphilis.
 - Doxycycline 100mg PO BID for two weeks (for early syphilis) or for four weeks (for late latent or syphilis of unknown duration) is an alternative for the treatment of non-pregnant people with a penicillin allergy.
- Prioritize the use of Bicillin L-A® to treat pregnant people and babies with congenital syphilis.
- To help CDC continue to monitor the situation, notify DSTDP (stdshortages@cdc.gov) of:
 - Shortages or stock-outs of Bicillin L-A® in the jurisdiction.
 - Situations in which patients diagnosed with syphilis are not being treated due to the inability to procure Bicillin L-A® in the jurisdiction.
- Report any shortages to the Pfizer Supply Continuity Team at 844-646-4398 (select 1 and then select 3).

Follow-up after treatment

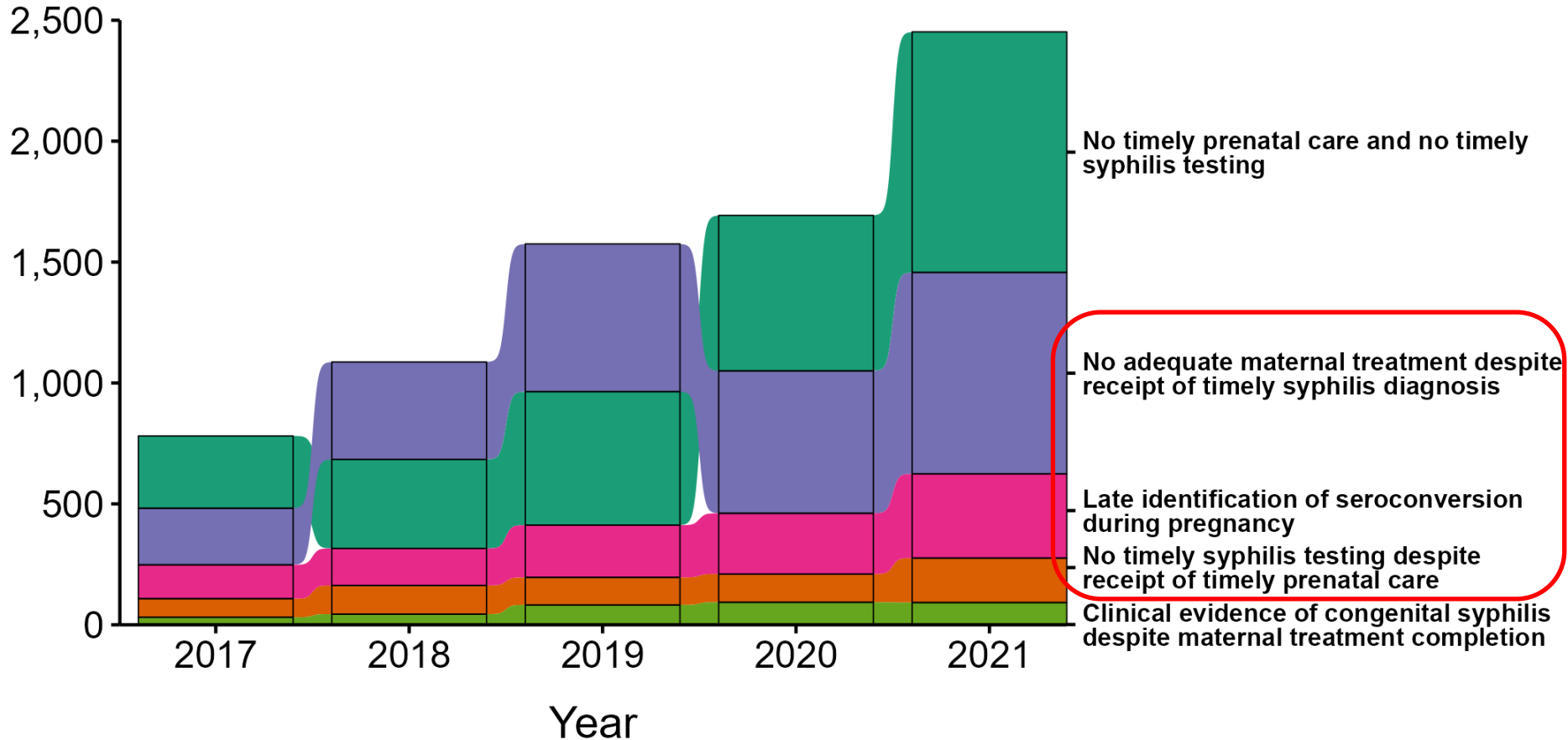
- FU essential to ensure tx response
- If tx at or before 24 weeks
 - Repeat titers in 8 weeks and at delivery
 - Sooner if concern for reinfection or tx failure
- If treated after 24 weeks
 - Repeat titers at delivery
- RPR 6-12 months after tx

Following titers

- Majority of patients will NOT have fourfold titer decrease before delivery
- But, if fourfold INCREASE and sustained for > 2 weeks
 - Concerning for reinfection or tx failure

Why is this happening: Missed opportunities US 2018

Cases

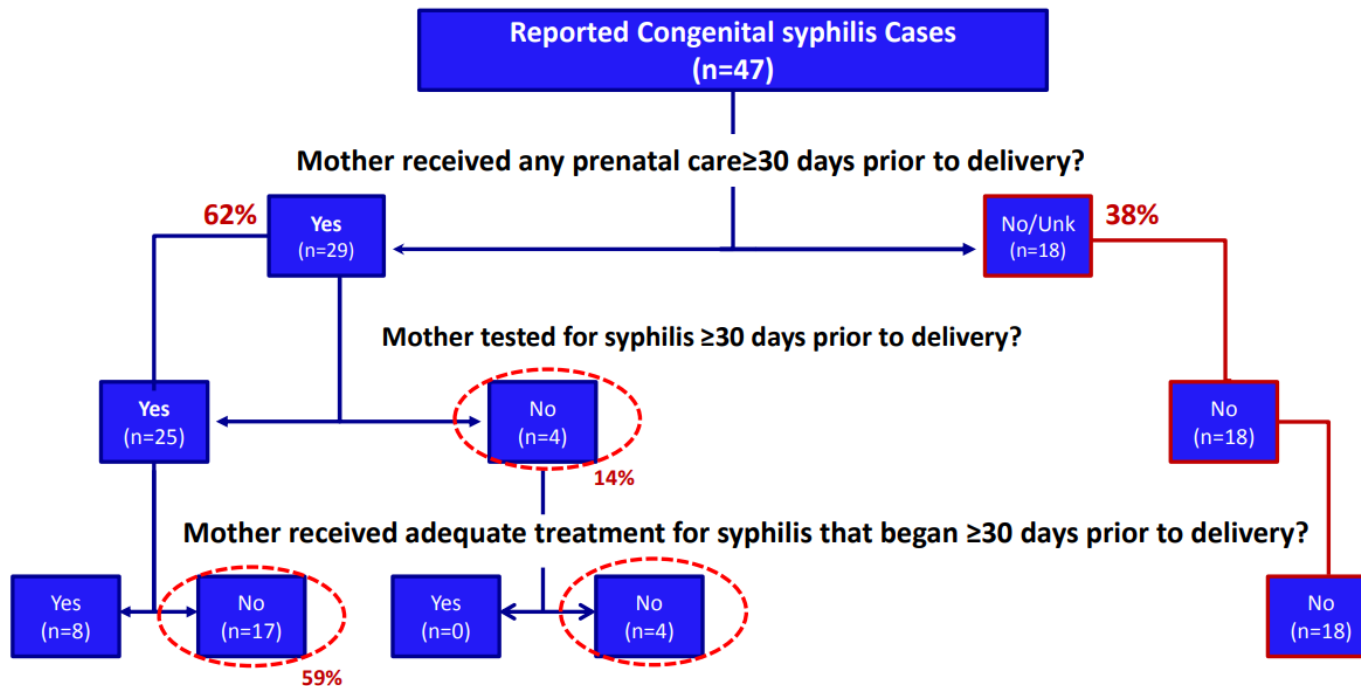


Slide Courtesy: Dr. Tabidze- Chicago Dept. Of Public Health

Missed opportunities 2015 – 2017 Chicago

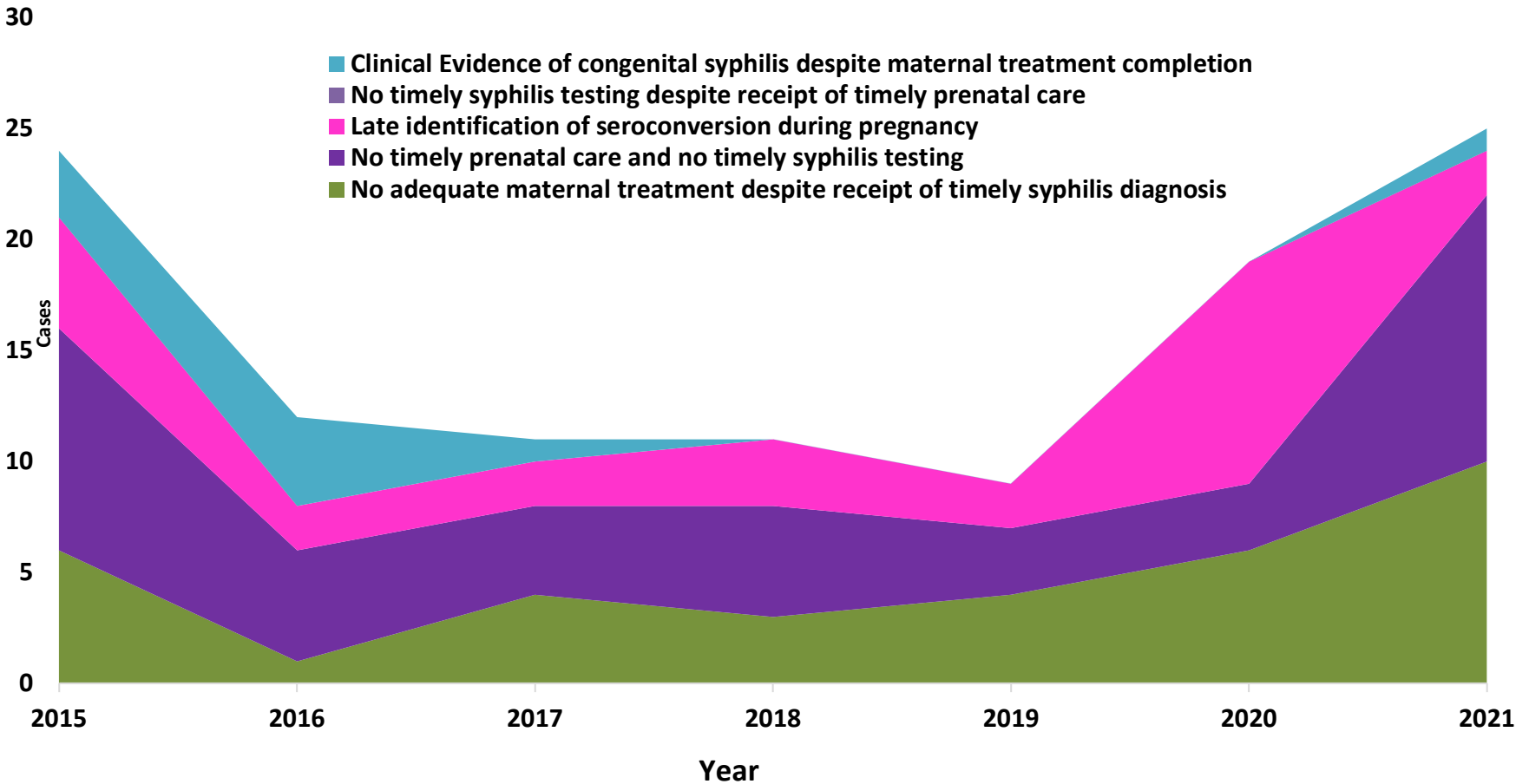
(21 of 47 cases had inadequate testing or treatment)

Prenatal care, testing, and treatment status of mothers of reported Congenital Syphilis Cases (n=47), Chicago, 2015-2017



Slide Courtesy: Dr. Tabidze- Chicago Dept. Of Public Health

Missed opportunities 2015 – 2021 Chicago



Slide Courtesy: Dr. Tabidze- Chicago Dept. Of Public Health

Update on state family planning services (less complications in planned pregnancies, including CS!)

IDPH-Illinois Family Planning Program



Illinois Family Planning Program – Title X is dedicated to providing comprehensive family planning and related health services. Below is a list of service provisions we offer:

ELIGIBILITY

- Patients receive immediate eligibility, with no predetermined termination date.
- Income is assessed against sliding fee scale annually. No one can be denied services due to inability to pay.
- IFPP is not a pre-requisite of any other program. Voluntary participation is essential.
- No residency requirement. Individuals are eligible regardless of home address.
- No restriction for adolescents
- No restrictions based on citizenship
- No restrictions for incarcerated individuals

RANGE OF METHODS

- Available on site or by prescription
- 340b Discount Pricing available for contraceptives, medicine, and supplies
- Male and female sterilizations
- Hormonal/Cooper IUD
- Up to 12-month Oral Contraceptives
- Progestin – only contraceptive pills
- Hormonal patch
- Vaginal Ring
- Hormonal Injection
- Male and female condoms

- Lubricants
- Emergency Contraceptive
- Fertility Based Awareness Methods
- Same day services available

ESSENTIAL SCREENING

- Pregnancy testing
- STI Screening/treatment
- HIV testing, education, and counseling
- Cervical and Breast cancer screening
- Genitourinary infections screening/treatment
- Blood pressure/BMI/Glucose monitoring

FUNDING

- Reimbursement based on expenses claimed through *reimbursement certification form* and a bill procedure documentation report.
- Administrative reimbursement for clients navigated through third party insurance, Medicaid, or other public programs.

SLIDING FEE SCALE (sample)

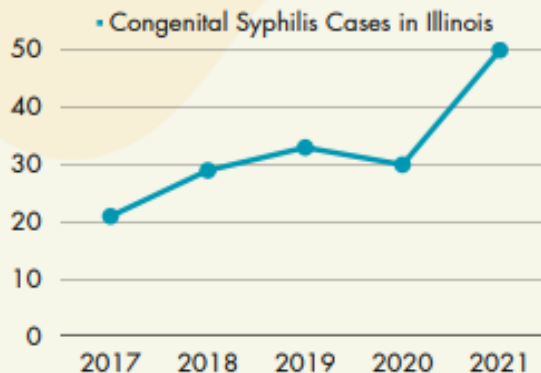
Family Size	Annual Income										
	<100% Poverty Level	101 - 138% Poverty Level	139 - 175% Poverty Level	176 - 213% Poverty Level	214-250% Poverty Level	>250% Poverty Level					
1	\$0	\$13,590	\$13,591	\$18,754	\$18,755	\$23,783	\$23,784	\$28,947	\$28,948	\$33,975	\$33,976
	← IDPH IFPP ←		← HFS SPA ELIGIBLE ←					IDPH IFPP →			

SLIDING FEE SCALE (sample)

Family Size	Annual Income										
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	← IDPH IFPP ←		← HFS SPA ELIGIBLE ←					IDPH IFPP →			

- Title X Family Planning clinics expanding telehealth services and adding sterilization services
- New HFS Family Planning Program (State Plan Amendment)
 - Enacted November 2022
 - Expanded Medicaid access, at any site (not only Title X)
 - Individual income, not family

Syphilis During Pregnancy



Congenital syphilis is on the rise. Nationwide, congenital syphilis has risen **203%** since 2017!

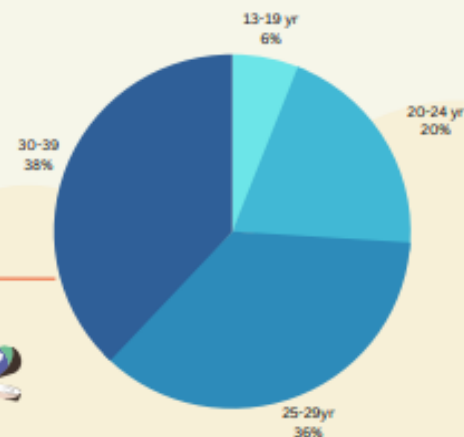


In Summary

In 2021, **60%** of congenital syphilis cases in Illinois were among **African American** pregnant persons.



In 2021, **56%** of congenital syphilis cases in Illinois were among pregnant persons 20-29 years of age.



Congenital syphilis is **PREVENTABLE.**

For the 2021 Centers for Disease Control and Prevention Treatment Guidelines



Resources

In Chicago/CDPH

- In Chicago

CS Reporting

For Clinical Questions Or To Report Suspect Cases, Contact:

The CDPH Disease Reporting Hotline at [312-743-9000](tel:312-743-9000)

**After hours, weekends, and holidays, call [311](tel:311) and ask for the communicable disease physician on-call (or [312-744-5000](tel:312-744-5000) if outside the City of Chicago)*

In Illinois/IDPH

REPORT ALL SYPHILIS CASES

Local Health Departments employ confidential means to locate and notify the partners of all early syphilis cases to prevent continued transmission.

- Reporting of all new syphilis cases within seven days of diagnosis to public health is required by law in Illinois; timely reporting of new cases is critical to the success of prevention and partner notification efforts
- STD Morbidity Report Forms should be completed and faxed to your local health department within seven days of disease diagnosis or treatment for presumed syphilis
- Additional information about disease reporting in Illinois can be found at: <http://dph.illinois.gov/topics-services/diseases-and-conditions/infectious-diseases/stds>

Please help us increase awareness among your patients of this serious statewide rise in early syphilis infections and what they can do to prevent infection. If your patients would like to learn more about syphilis or other STDs and how to prevent them, please refer them to CDC's STD website, <http://www.cdc.gov/std/>.

We appreciate your commitment to maintaining and promoting the health of all Illinoisans. For any questions or assistance please contact the Illinois STD Section at 217-782-2747.



THANK YOU! Questions?

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