Challenges and opportunities in the treatment of syphilis

Guest speakers: Laura Hinkle Bachmann & Pâmela Cristina Gaspar
Moderator: Esther Bettiol
Host: Victor Kouassi

19 August 2025

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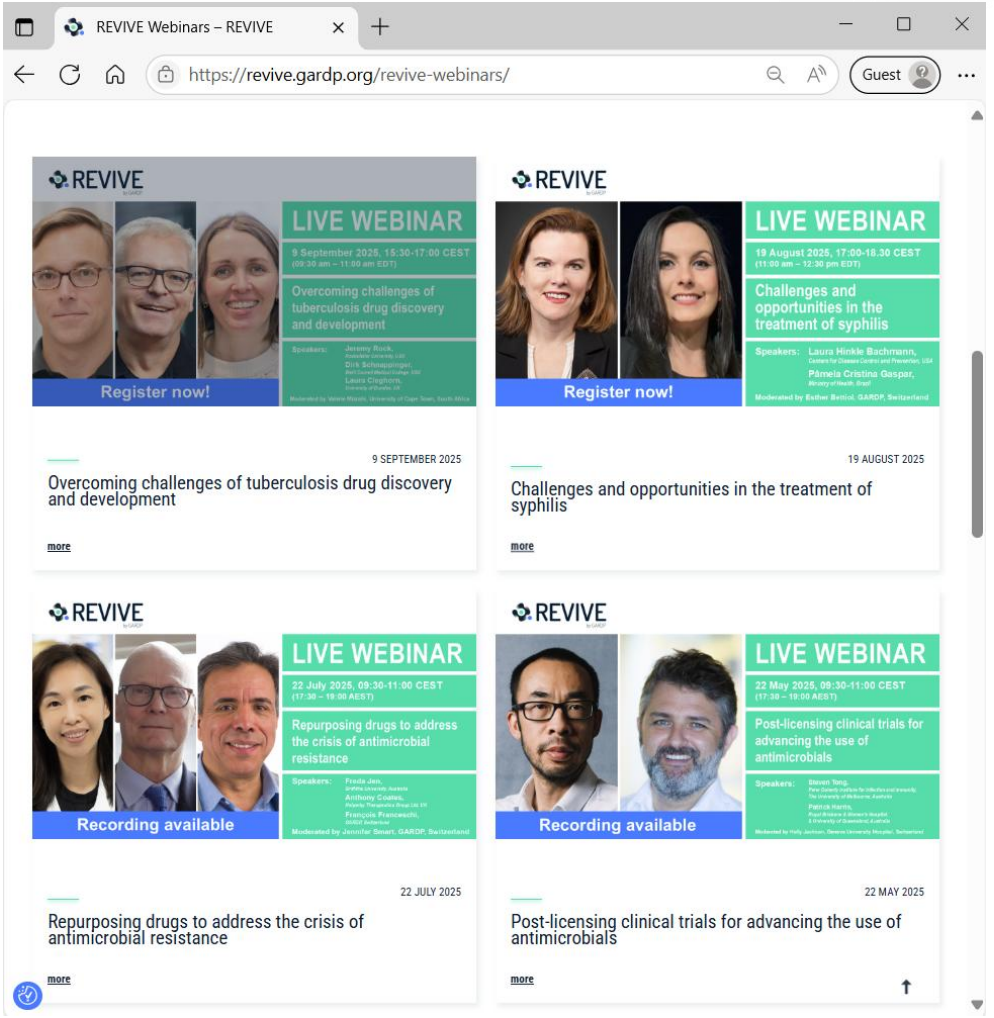

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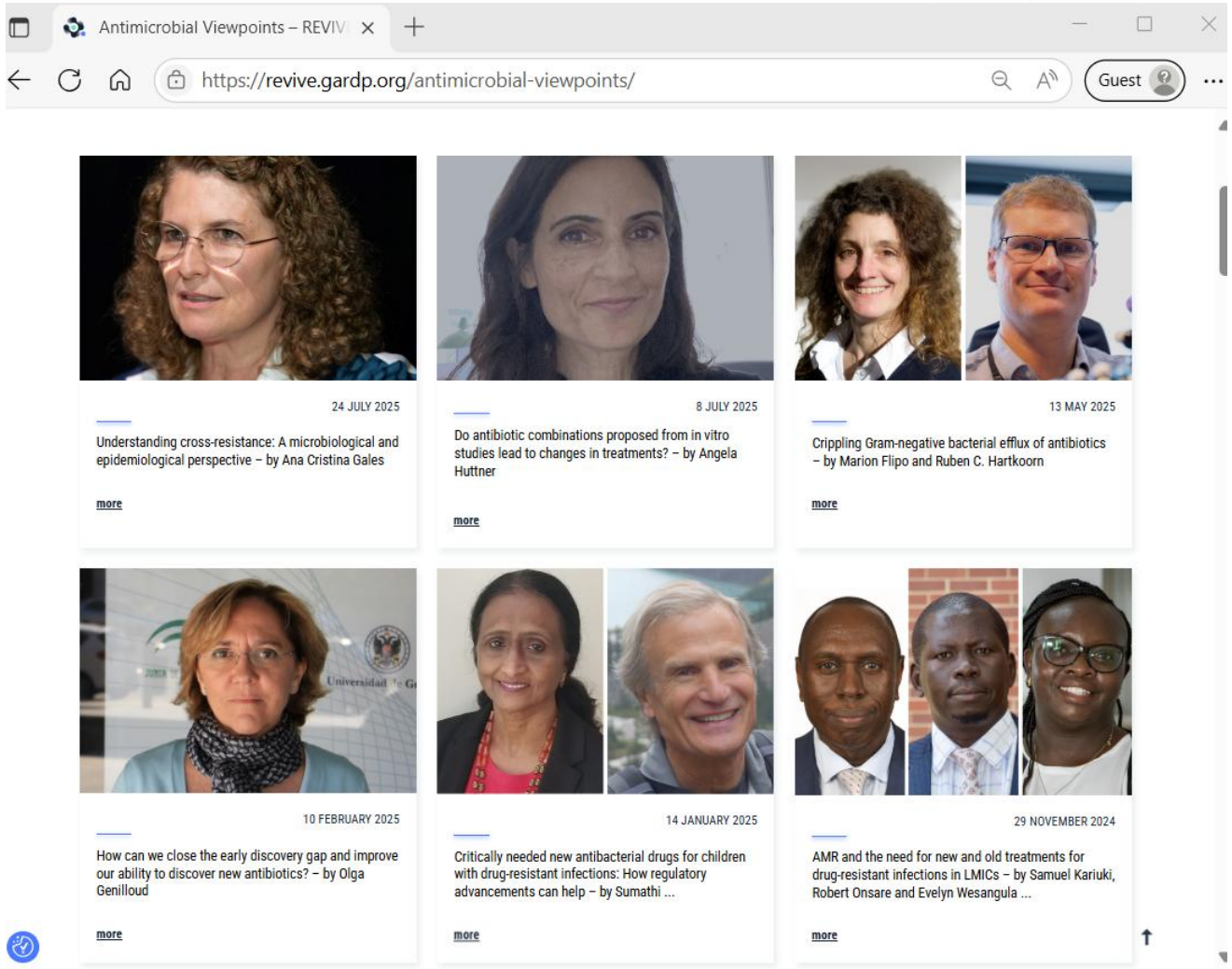

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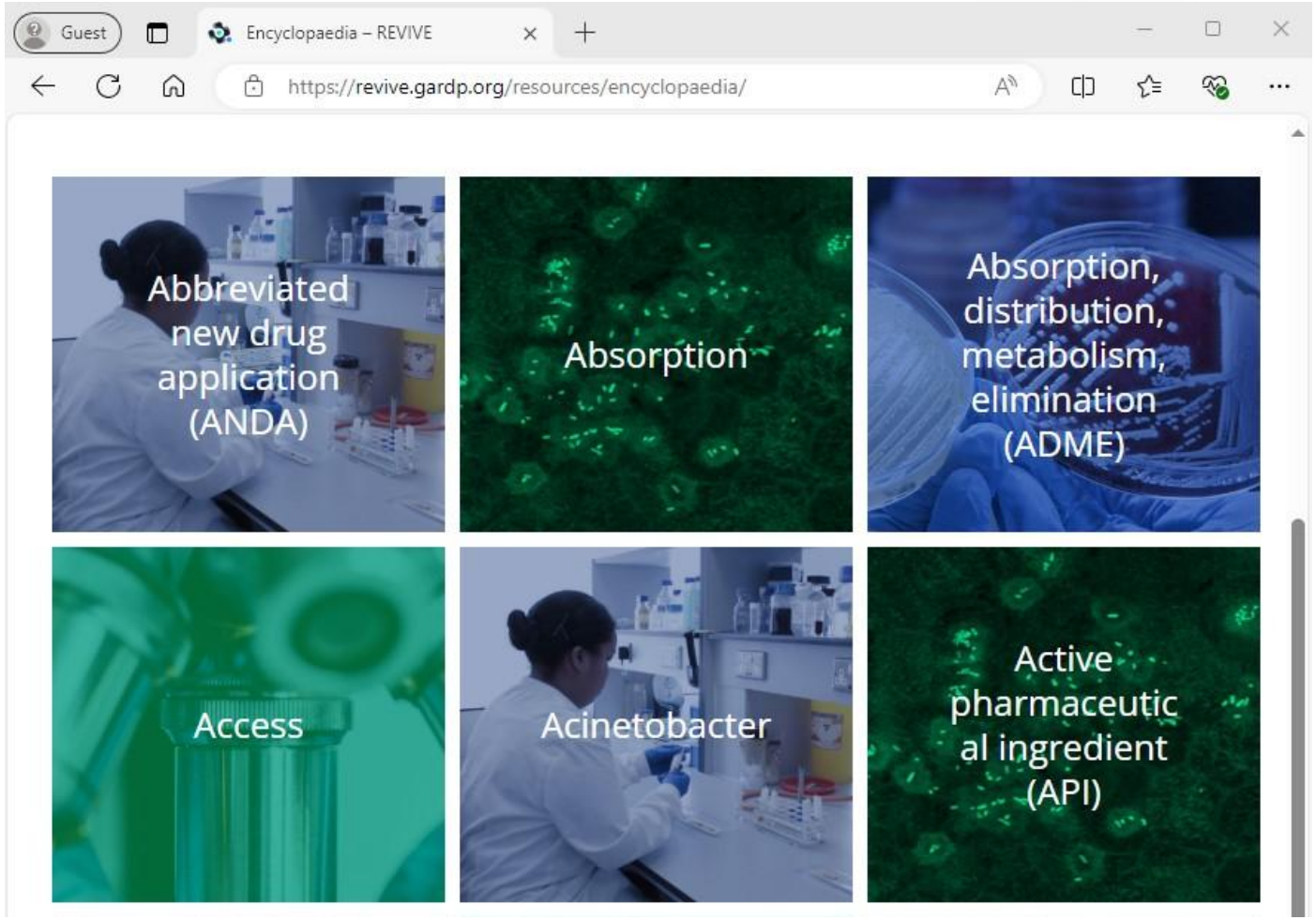

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How to submit your questions

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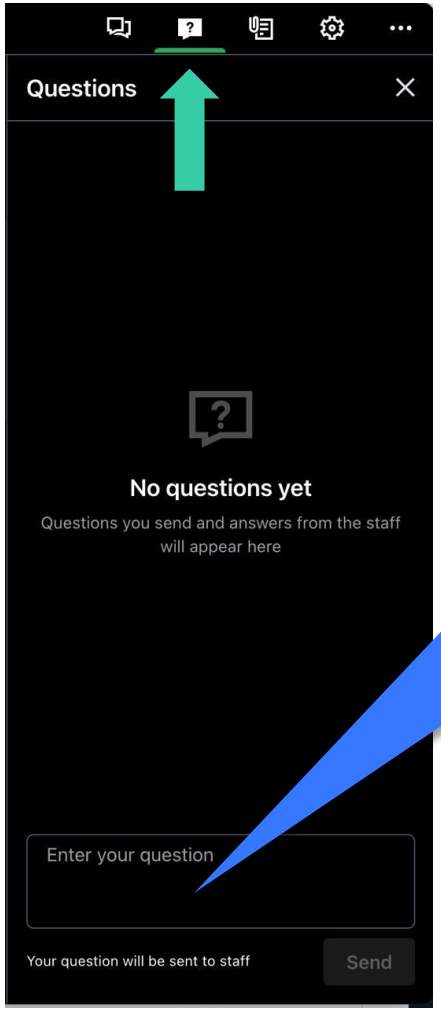
If your question is addressed to a specific speaker, please include their name when submitting the question.



Please submit your questions through the box provided after clicking the ‘questions’ button. We will review all questions and respond to as many as possible after the presentation.

Today's speakers

REVIVE by GARDP

Challenges and opportunities in the treatment of syphilis

Moderator:
Esther Bettiol
GARDP,
Switzerland

Laura Hinkle Bachmann
Centers for Disease Control and Prevention, USA

Pâmela Cristina Gaspar
Ministry of Health, Brazil

Laura Hinkle Bachmann

Laura Hinkle Bachmann is the Chief Medical Officer in the Division of STD Prevention, National Center for HIV, Viral Hepatitis, STD and TB Prevention at the U.S. Centers for Disease Control and Prevention. Prior to joining CDC in 2018, Laura was Professor of Medicine at Wake Forest University Health Sciences and Medical Director in the Guilford County Department of Health and Human Services, Public Health Division (NC).

Within Internal Medicine and Infectious Diseases, Laura specializes in STI and HIV care. She has over 30 years of experience practising in academic and public health settings. Her research has addressed a variety of STI/HIV control issues in both clinical and non-clinical settings. Laura has authored over 90 peer-reviewed manuscripts and book chapters.

Challenges and Opportunities in the Treatment of Syphilis

Laura Hinkle Bachmann, MD, MPH, FIDSA, FACP
Chief Medical Officer, Division of STD Prevention
National Center for HIV, Viral Hepatitis, STD and TB Prevention
Centers for Disease Control and Prevention

REVIVE
August 19, 2025

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.

Mapping the Spread: Understanding Syphilis Epidemiology

THE HEALTH GAP | SEX

Why syphilis is rising around the world

By Krupa Padhy 8th July 2023

(Image credit: Getty Images)

Syphilis Cases in Tokyo Keep Climbing, Rise Seven-Fold in 10 Years

In recent years, Japan's seen a huge spike in syphilis cases. The latest numbers aren't any better, with Tokyo reporting its fourth consecutive...

Jan 8, 2025

The Japan N

Syphilis Cases Exceed 5000 in Japan, Fas Record

More than 5,000 people have been diagnosed with syphilis t National Institute of Infectious Diseases.

May 24, 2023

DW

STIs in Europe: Gonorrhea and syphilis hit record high

Sexually transmitted infections are rising in Europe, especially gonorrhea and syphilis, among younger adults. But one STI has seen a huge drop in cases.

BBC

Syphilis and drug resistant gonorrhoea cases on the increase

New cases of the sexually transmitted infection syphilis have risen again in England, continuing a trend dating back to the early 2000s.

Jun 3, 2025

Casos de sífilis se duplican en Uruguay desigualdades sociales

Montevideo, 12 ago (Sputnik).- Uruguay, un país referente de acceso a la salud, enfrenta una «epidemia...

1 day ago

The Guardian

Frontiers

Rising congenital syphilis rates in Canada, 1993–2022

Results: The national rate of confirmed early congenital syphilis was 127-fold higher in 2022 than in 1993, increasing from 0.3 to 32.7 cases...

Jan 16, 2025

congenital syphilis

Medical professionals attribute the increasing cases of disease to inade

Australian Government Department of Health, Disability and Ageing

Syphilis declared a Communicable Disease Incident of National Significance

Infectious syphilis cases have been on the rise across Australia, resulting in tragic

WHO Estimates

New infections of syphilis

8 million

in adults 15 to 49 in 2022

Cases of congenital syphilis

700,000

in 2022

Adverse birth outcomes from syphilis

390,000

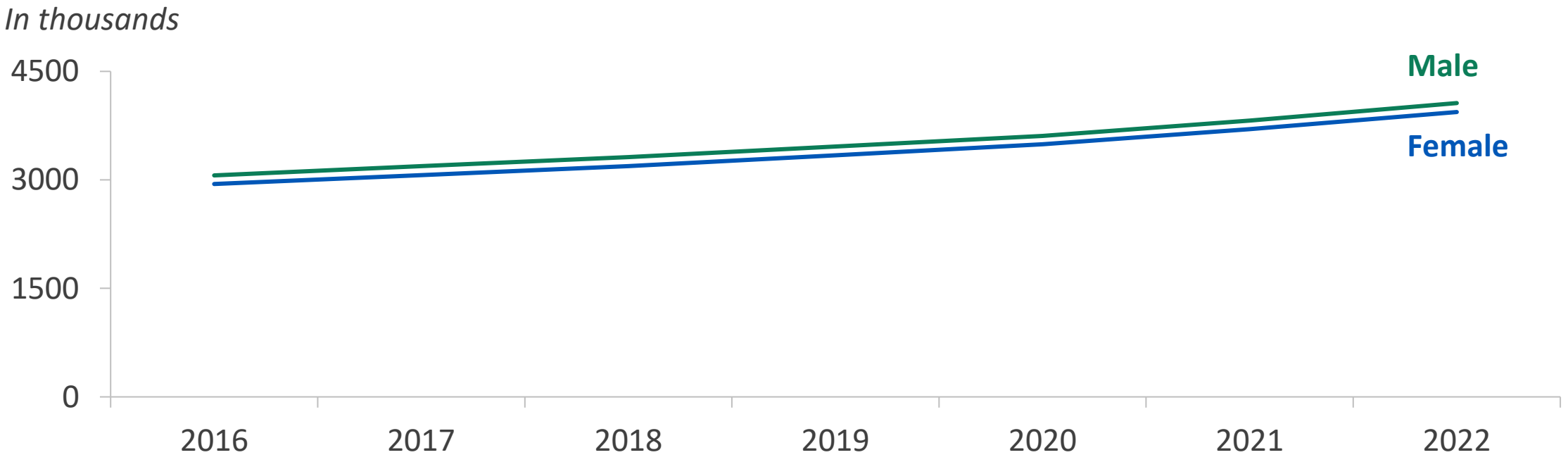
in 2022

These included:

- 150 000 early fetal deaths and stillbirths
- 70 000 neonatal deaths
- 115 000 infants with a clinical diagnosis of congenital syphilis.

Globally, New Cases of Active Syphilis in 15-49 Year Olds Are Rising

Incident Cases of Active Syphilis in 15-49 Year Olds



Source: WHO

Congenital Syphilis Global Trends

Rates per 100K Live Births, 2013-2024

DRC

Brazil

EU (without UK)

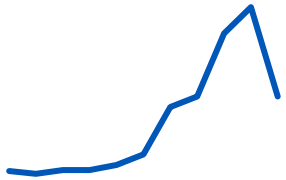
UAE

Sri Lanka

Malaysia

Zimbabwe

Canada



Germany

Tajikistan

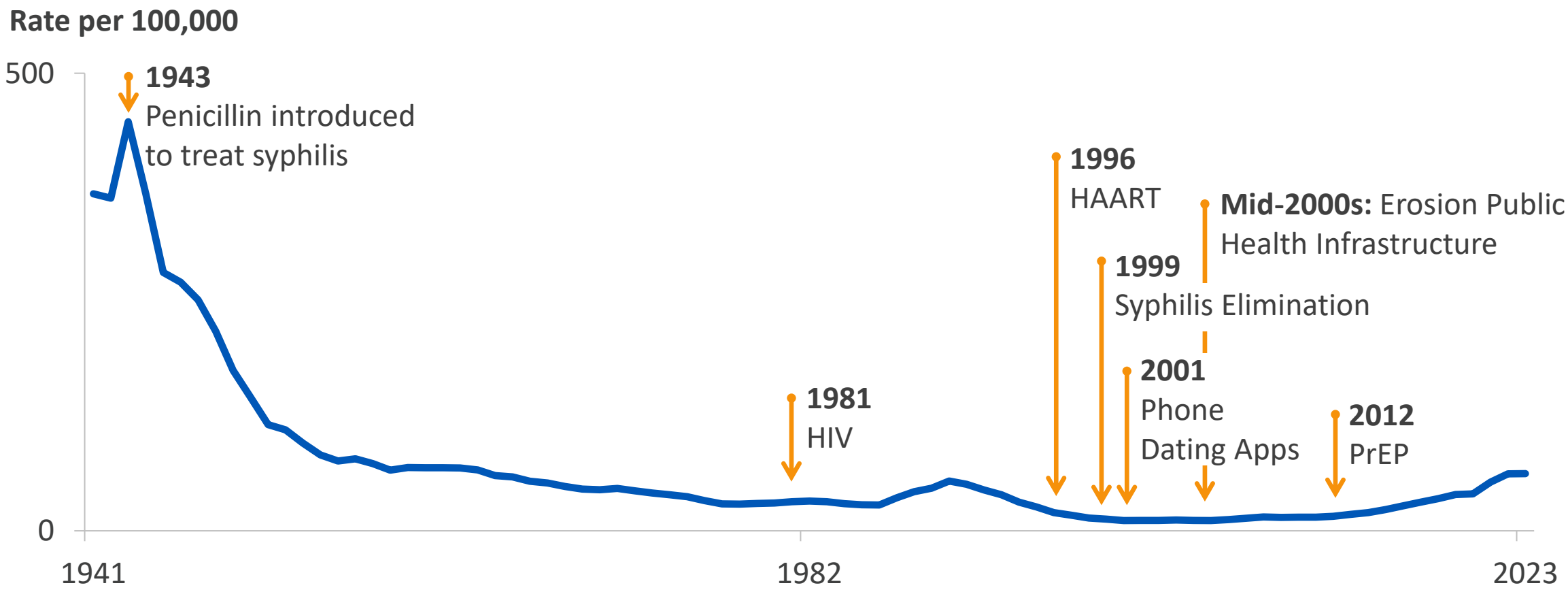
Thailand

Mongolia

Source: WHO

In the United States, Syphilis Has Decreased Significantly from the 1940s . . .

Syphilis — Rates of Reported Cases by Year, United States, 1941–2023

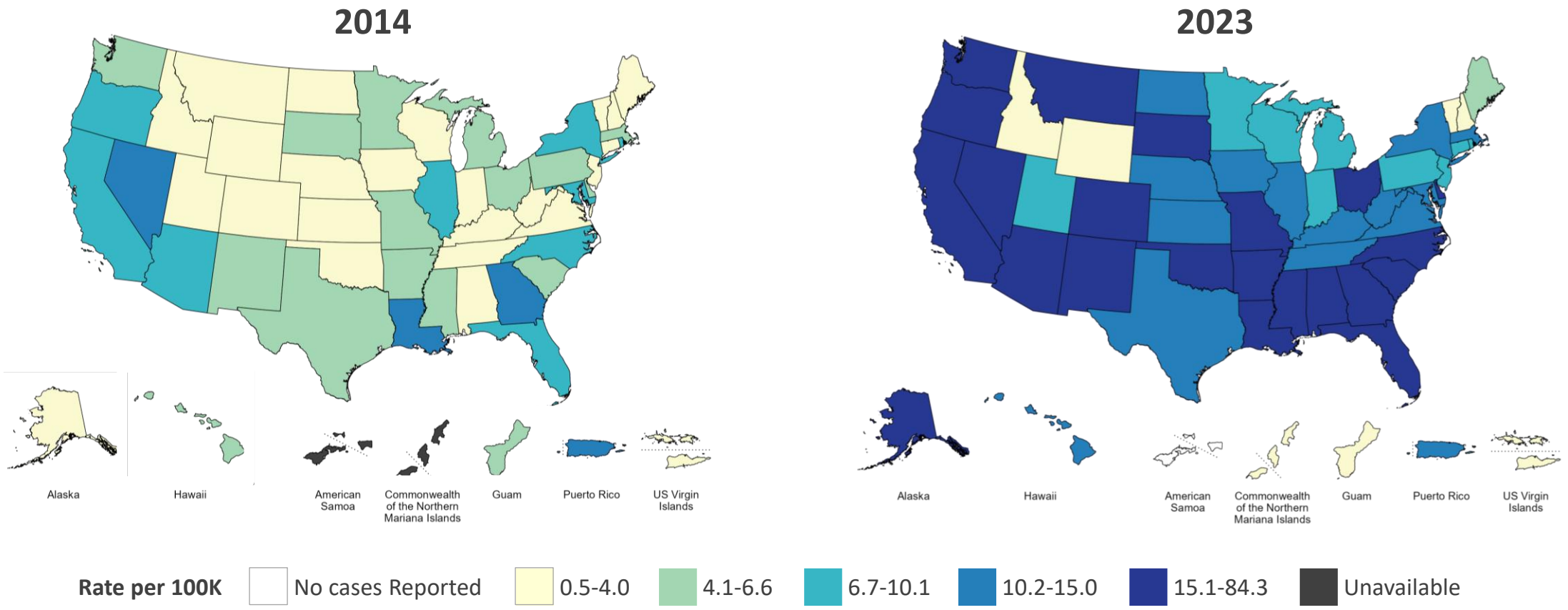


NOTE: Includes all stages of syphilis and congenital syphilis.

Centers for Disease Control and Prevention. Sexually Transmitted Disease Surveillance 2023. Atlanta: US Department of Health and Human Services; 2024.

However in the Past Decade, Syphilis Rates Have Skyrocketed

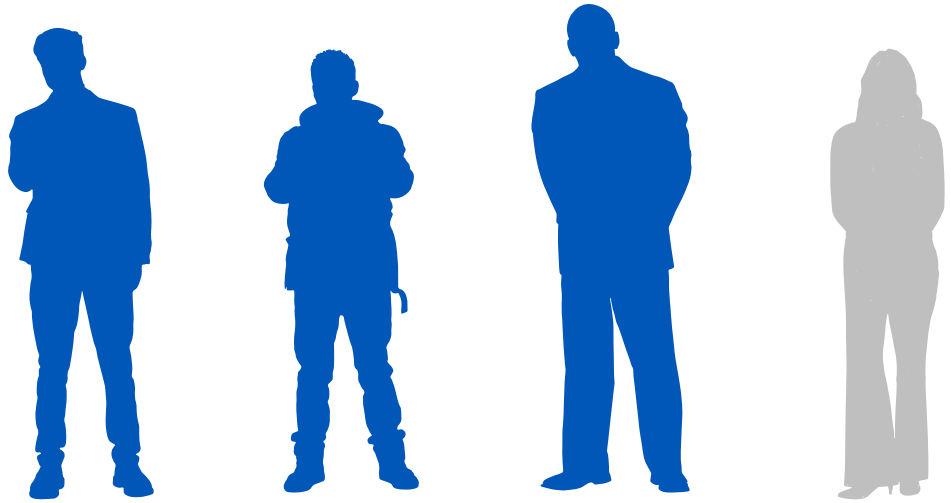
Primary and Secondary Syphilis — Rates of Reported Cases by Jurisdiction, United States and Territories, 2014 and 2023



Centers for Disease Control and Prevention. Sexually Transmitted Disease Surveillance 2023. Atlanta: US Department of Health and Human Services; 2024.

3 in 4 Cases of Reported Primary and Secondary Syphilis cases in 2023 in the U.S. **Were Among Men**

74%
P&S Syphilis Cases Among Men
39,188 cases in 2023

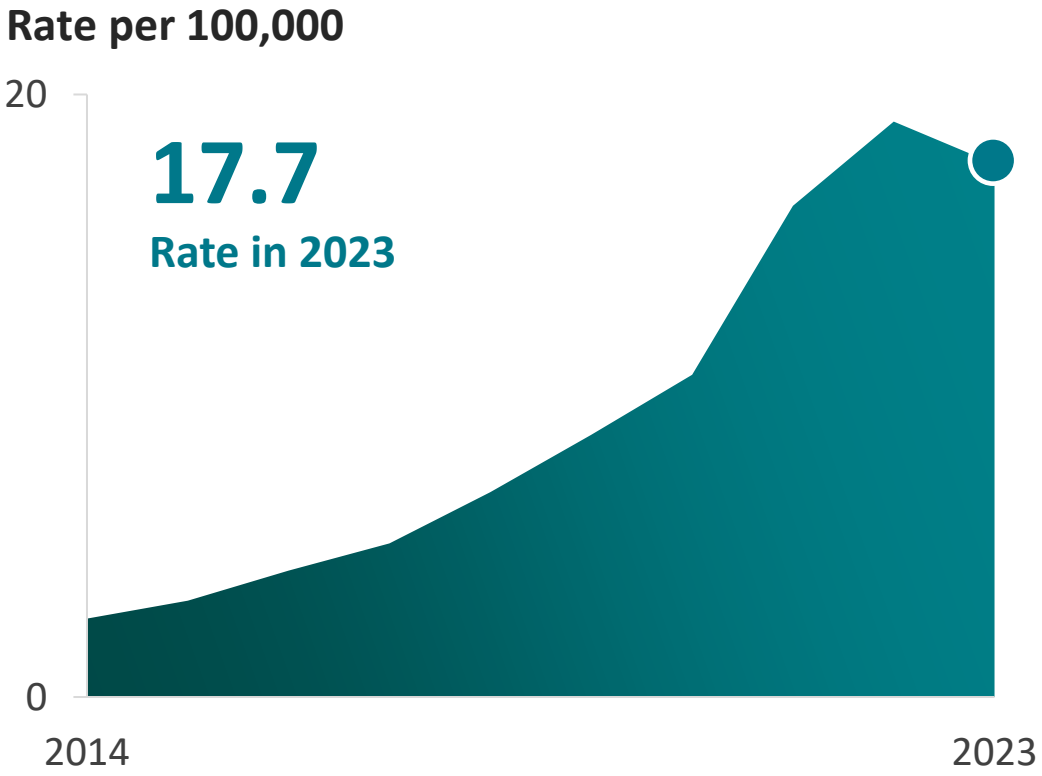


26%
P&S Syphilis Cases Among Women
13,763 cases in 2023

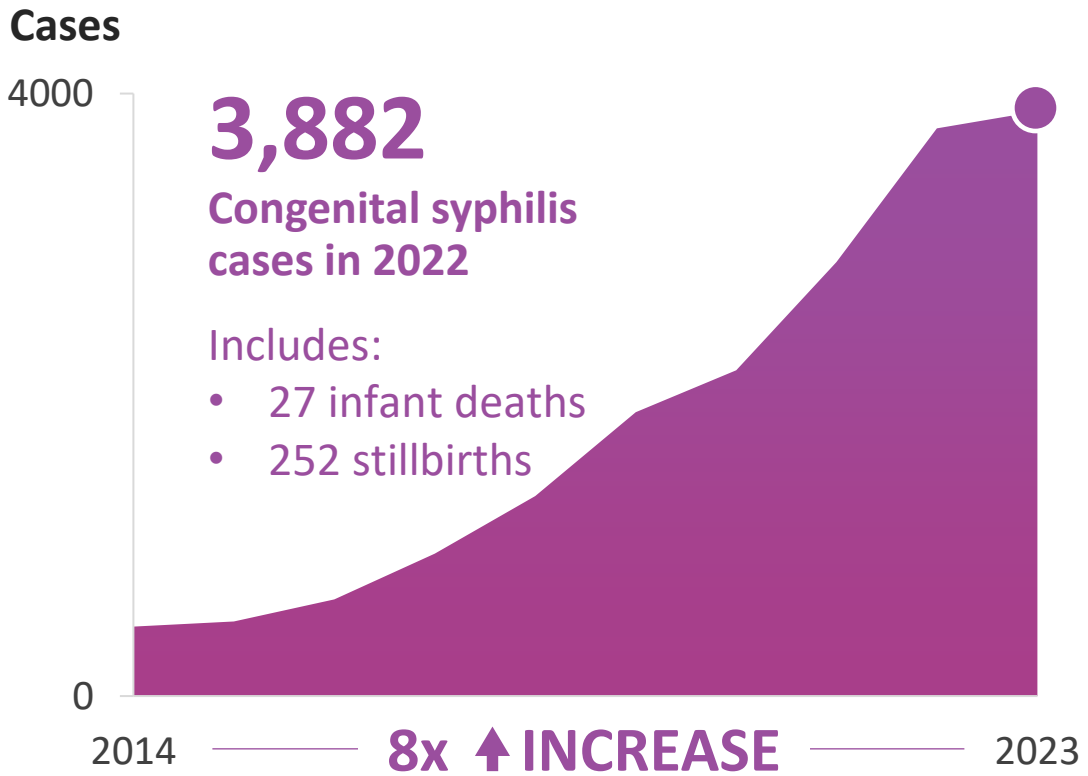
P&S = Primary and Secondary; Note: 0.1% (56 cases) of P&S syphilis cases had an unknown sex

Congenital Syphilis Cases in 2023 Continue to Mirror Increases of Primary and Secondary Syphilis Among Females Aged 15-44 Years

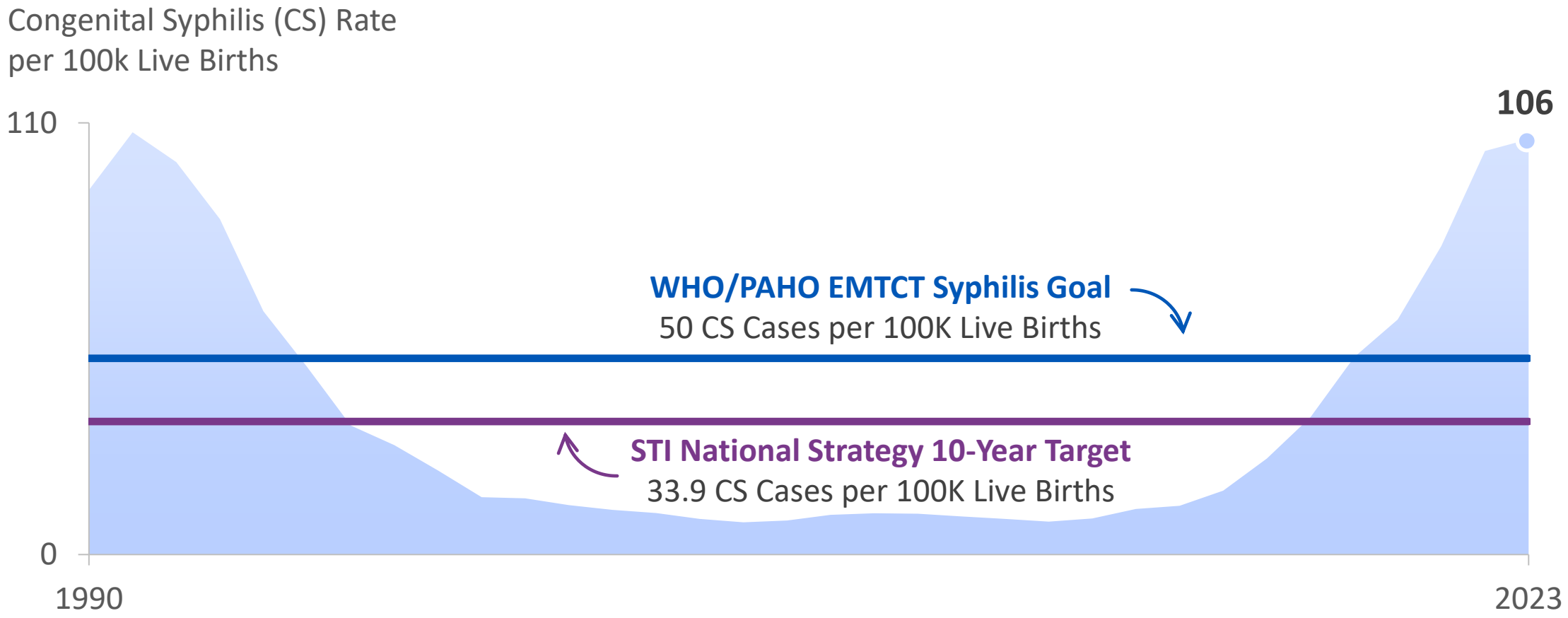
Primary and Secondary Syphilis Rate Among Females Aged 15–44 Years



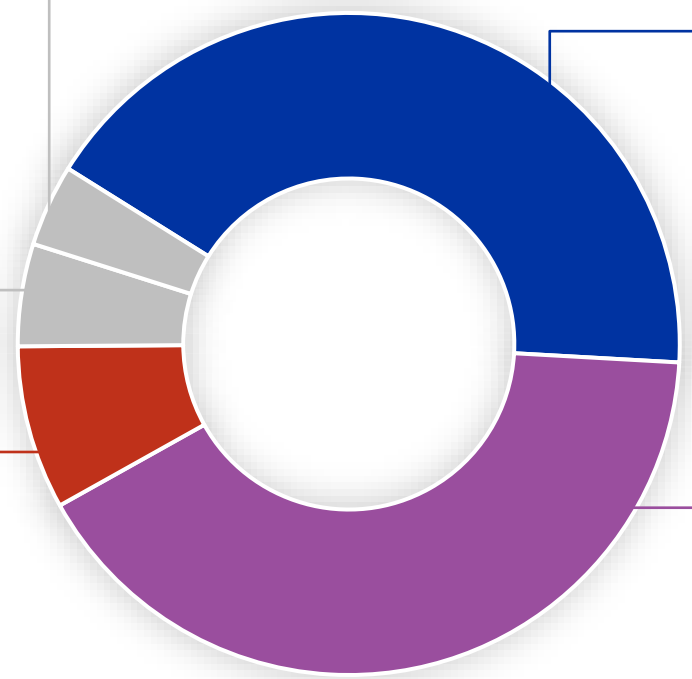
Reported Congenital Syphilis (CS) Cases by Year of Birth



In 2023, There Were 3,882 Congenital Syphilis Cases With a Rate of 106 per 100,000 Live Births



9 in 10 Cases of Congenital Syphilis Might Have Been Prevented With Timely Testing or Adequate Treatment During Pregnancy in 2023



4%
Evidence of congenital syphilis despite maternal treatment completion

5%
Other

8%
Late seroconversion

42%
No documented timely test

41%
Timely test, but no or in adequate maternal treatment

Missed Opportunities for Preventing Congenital Syphilis, 2023. Figure numbers may not add to 100 due to rounding.

Syphilis during pregnancy can lead to:

- Stillbirth
- Miscarriage
- Infant death
- Maternal and infant morbidity
- Severe lifelong health problems

Natural History: From Infection to Symptoms

Syphilis Overview

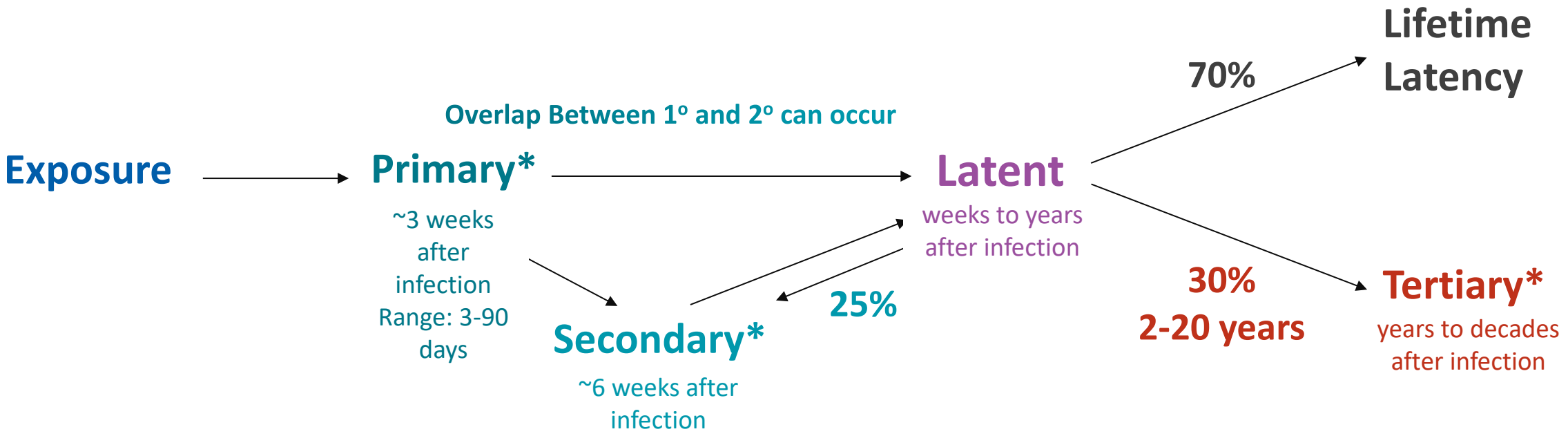
- Systemic, sexually transmitted infection
- Causative organism: *Treponema pallidum*, a spirochete bacterium, that replicates in approximately 30 hours
- Incubation period: 10-90 days
- Characterized by episodes of active disease interrupted by periods of latent infection
- Remains chronic without treatment or resolves

Syphilis: Pathogenesis

- Only infects humans
- Penetrates through macro and microscopic abrasions
- Local replication leads to chancre (1o)
- Spread to local lymphatics followed by widespread dissemination within hours via bloodstream (2o)
  - The smaller the inoculum the longer the incubation period
- Systemic disease, with involvement of many organs (2o and latent)
- Late lesions characterized by endarteritis (CNS and CV) or poorly formed granulomas (gumma)

Syphilis Natural History

*Symptomatic stages



Early Syphilis: ≤ 1 year duration

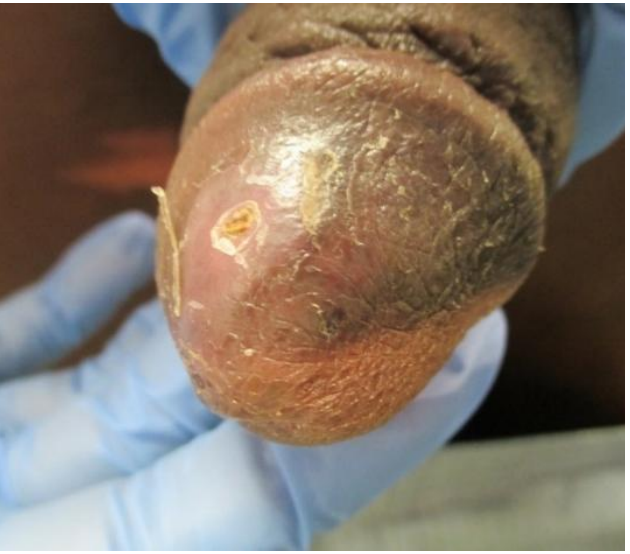
Late Syphilis: > 1 year duration

Neurosyphilis can occur at any stage

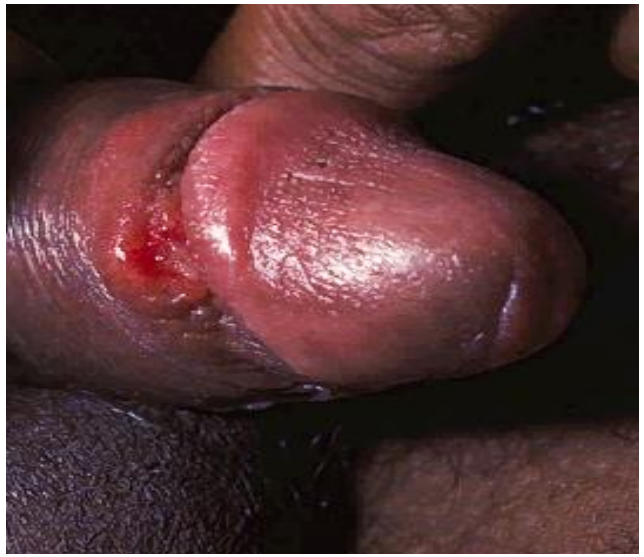
Slide courtesy: Susan Philip, SF DPH and M. Urban, U Rochester

Primary Syphilis | Chancre

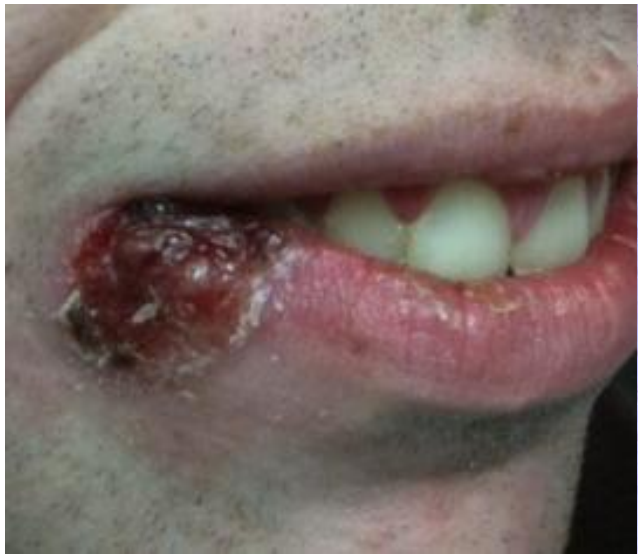
- Appears about 3 weeks (range: 10-90 days) after infection at the site of inoculation
- Typically single, painless, indurated, clean-based lesion with rolled edges
- Sore goes away even if person is not treated



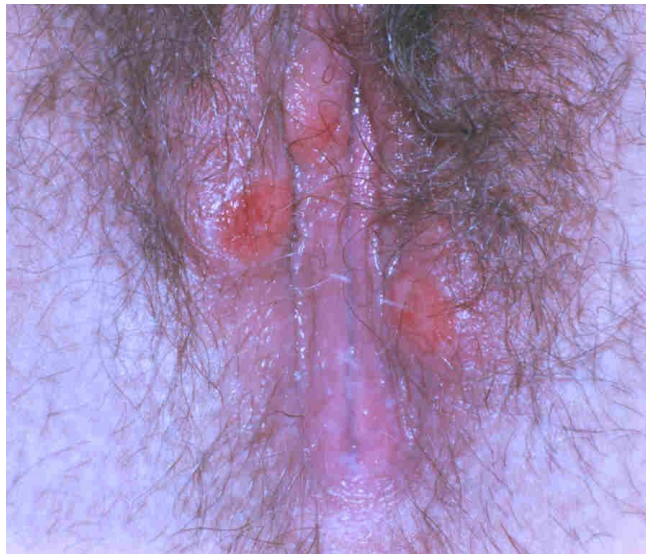
Penile Chancre



Penile Chancre, STD Atlas, 1997 Mosby



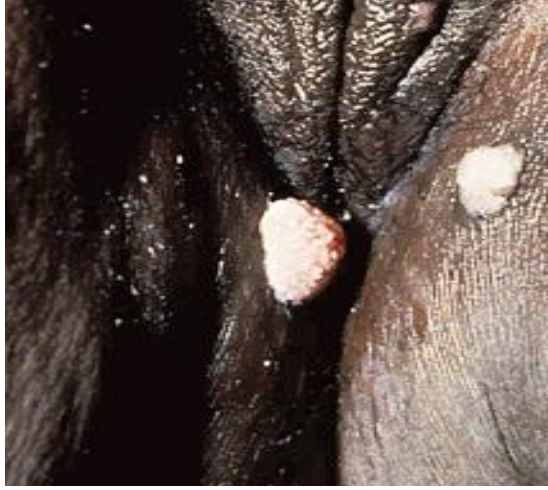
Chancre, Mouth

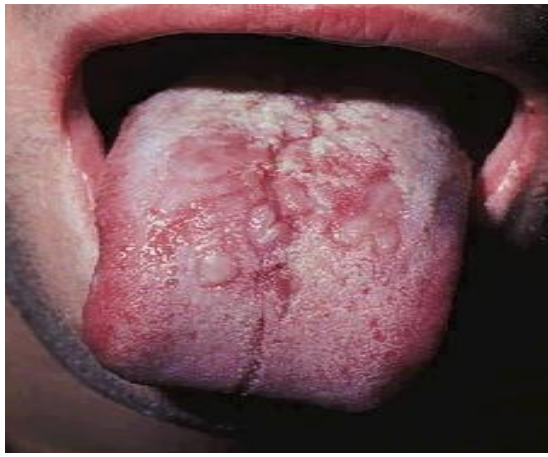


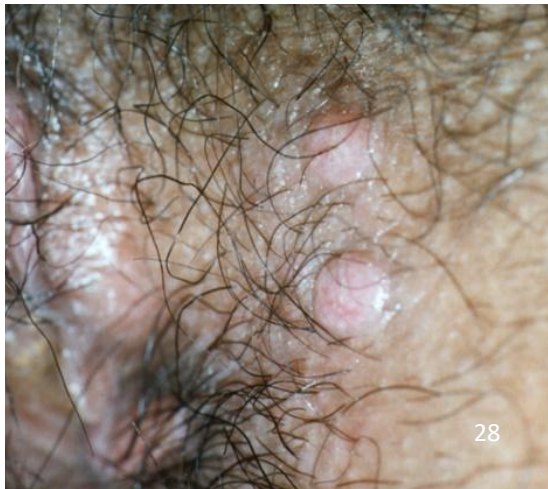
Dr. Joseph Engelman, San Francisco City Clinic

Secondary Syphilis | Signs & Symptoms

- Usually occurs 3-6 weeks after primary chancre
- Symptoms
  - Rash (75-90%)
  - Generalized lymphadenopathy (70-90%)
  - Constitutional symptoms (50-80%)
  - Mucous patches (5-30%)
  - Condyloma lata (5-25%)
  - Patchy alopecia (10-15%)
  - Symptoms of neurosyphilis (1-2%)
  - Less common: meningitis, hepatitis, arthritis, nephritis

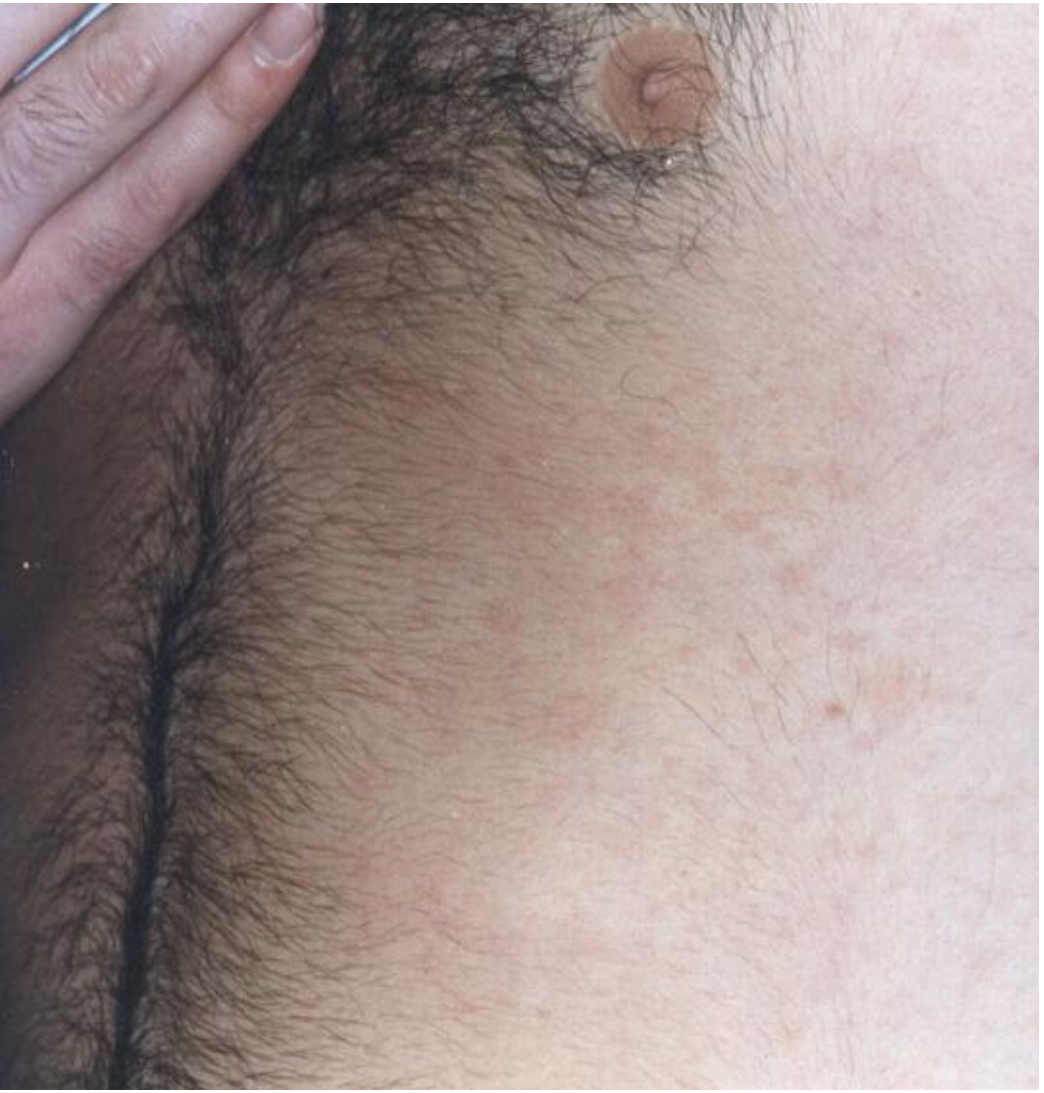


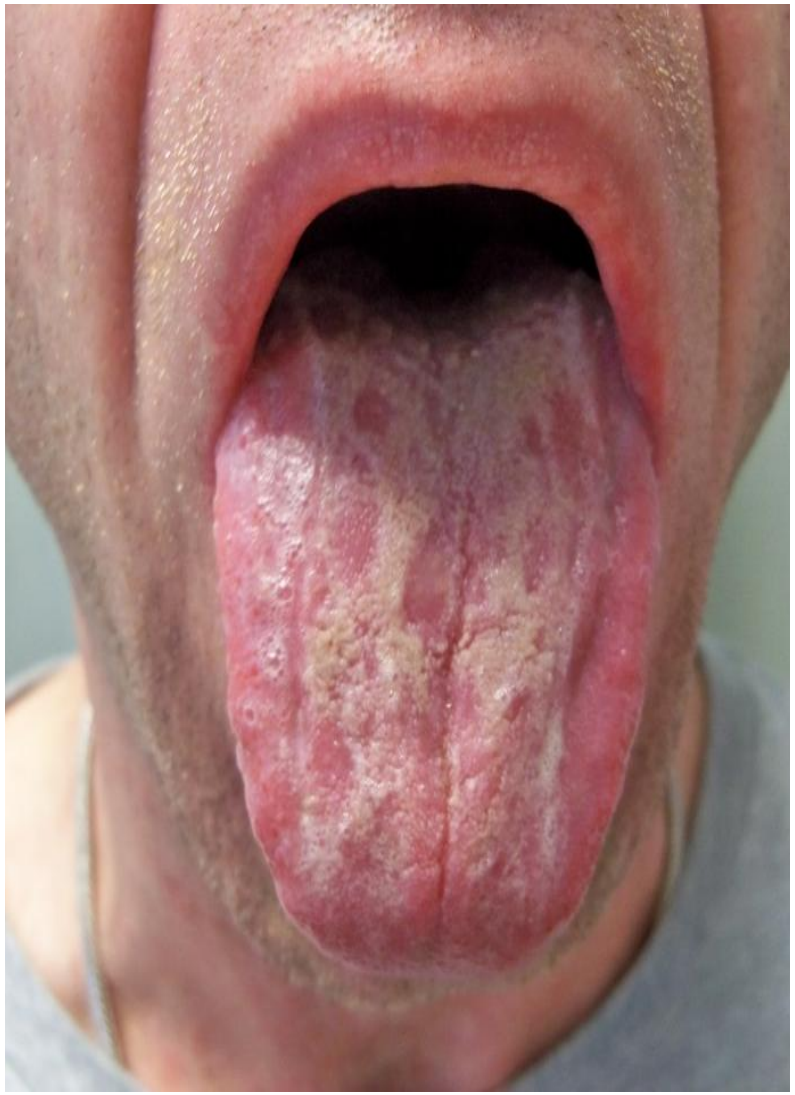


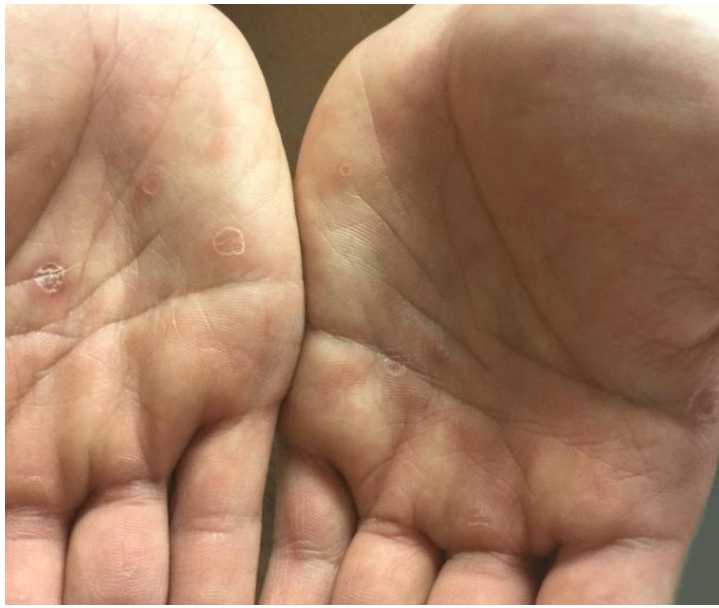


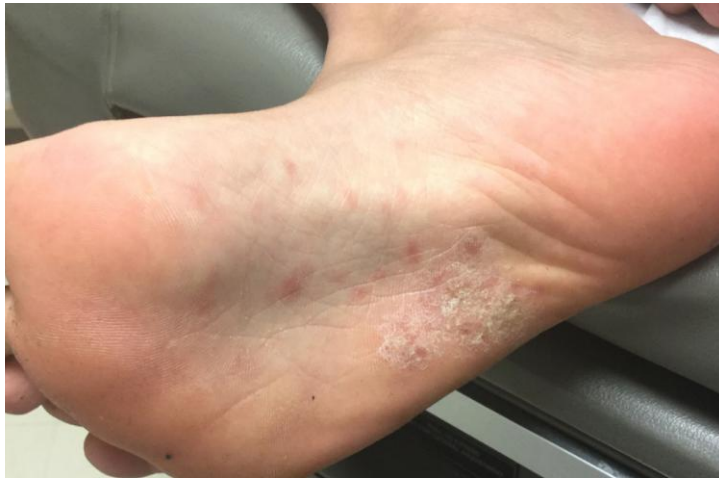
Images Top: Condyloma lata; Middle: Mucous patches, *STD Atlas, 1997* Mosby; Bottom: Condyloma lata, Dr. Joseph Engelman, San Francisco City Clinic

Secondary Syphilis





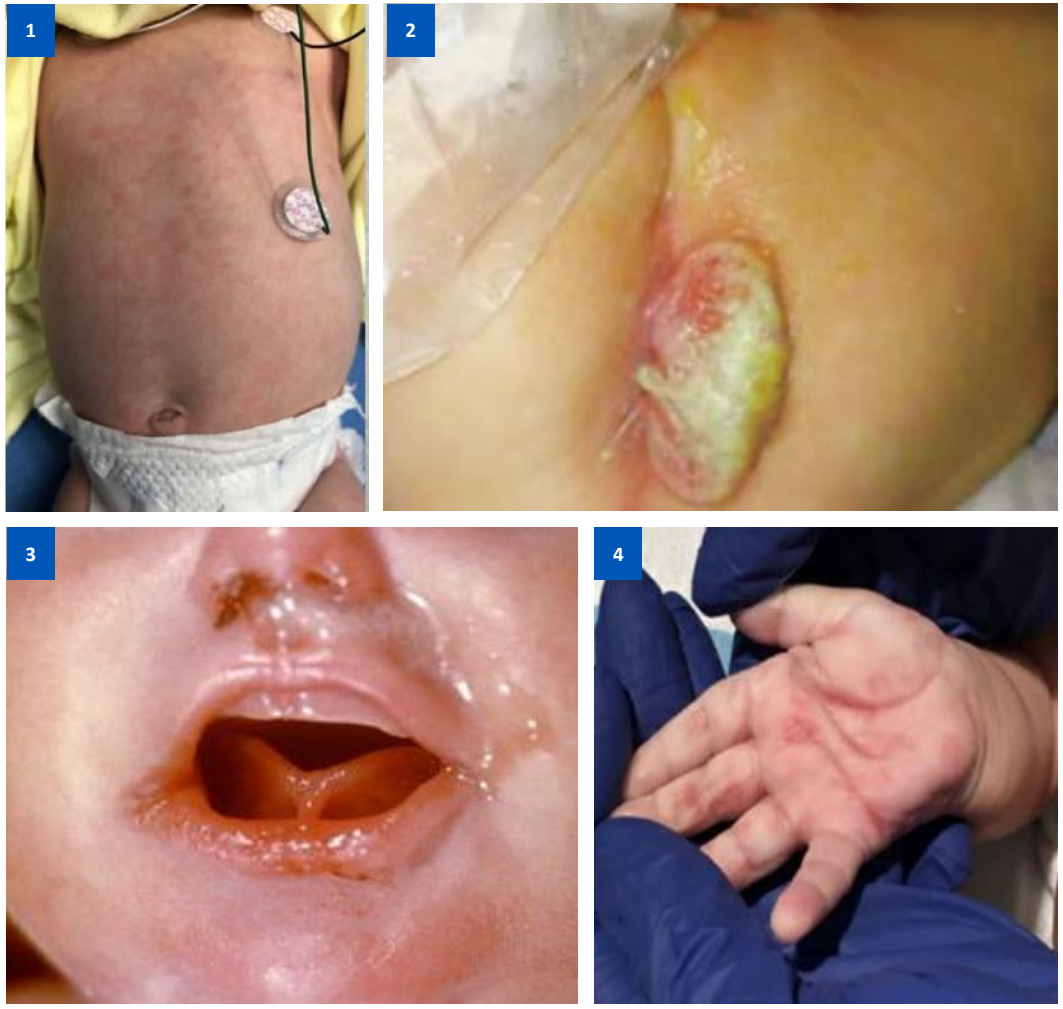




Images Left: Subtle Macular Form, Chest, Dr. Joseph Engelman, San Francisco City Clinic; Middle: Mucous patches; Right: Maculopapular rash on palms of hands and feet, Negusse Ocbamichael, PA, Public Health—Seattle & King County STD Clinic

Syphilis in a Newborn

- Clinical, laboratory or radiographic evidence of syphilis in a baby exposed to syphilis
  - Hepatosplenomegaly
  - Jaundice
  - Rash
  - Snuffles
  - Bone abnormalities
- A mother that was not adequately treated for her state of syphilis at least 30 days before delivery



[1] Catueno, S., Tsou, P.-Y., Wang, Y.-H., Becker, E., & Fergie, J. (2022). Congenital Syphilis and the Prozone Phenomenon: Case Report. The Pediatric Infectious Disease Journal, 41(6), e268-e270. https://doi.org/10.1097/inf.0000000000003522; [2] Arrieta, A. C., & Singh, J. (2019). Congenital Syphilis. *New England Journal of Medicine, 381(22), 2157-2157. https://doi.org/doi:10.1056/NEJMicm1904420 ;* [3] CDC Public Health Image Library - https://phil.cdc.gov/Default.aspx; [4] Jacobs, K., Vu, D. M., Mony, V., Sofos, E., & Buzi, N. (2019). Congenital Syphilis Misdiagnosed as Suspected Nonaccidental Trauma. Pediatrics, 144(4). https://doi.org/10.1542/peds.2019-1564

Diagnostics

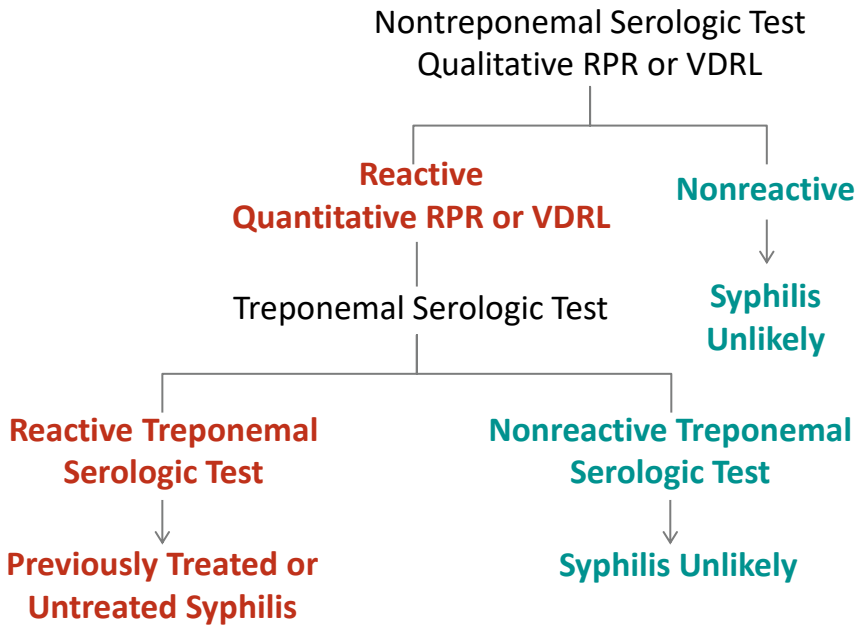
There Are 2 Types of Serologic Tests for Syphilis

Tests	Non-Treponemal	Treponemal
Examples	RPR, VDRL	FTA-ABS, TPPA, EIA, CIA
Method	Detects NON-specific antibodies caused by inflammation	Detects specific antibodies against *T. pallidum*
Results	Quantitative	Qualitative
Positivity	Positive in active disease	**Remains positive forever (85%)**

BOTH a nontreponemal test
and a treponemal test
are **needed to confirm** the
diagnosis of syphilis.

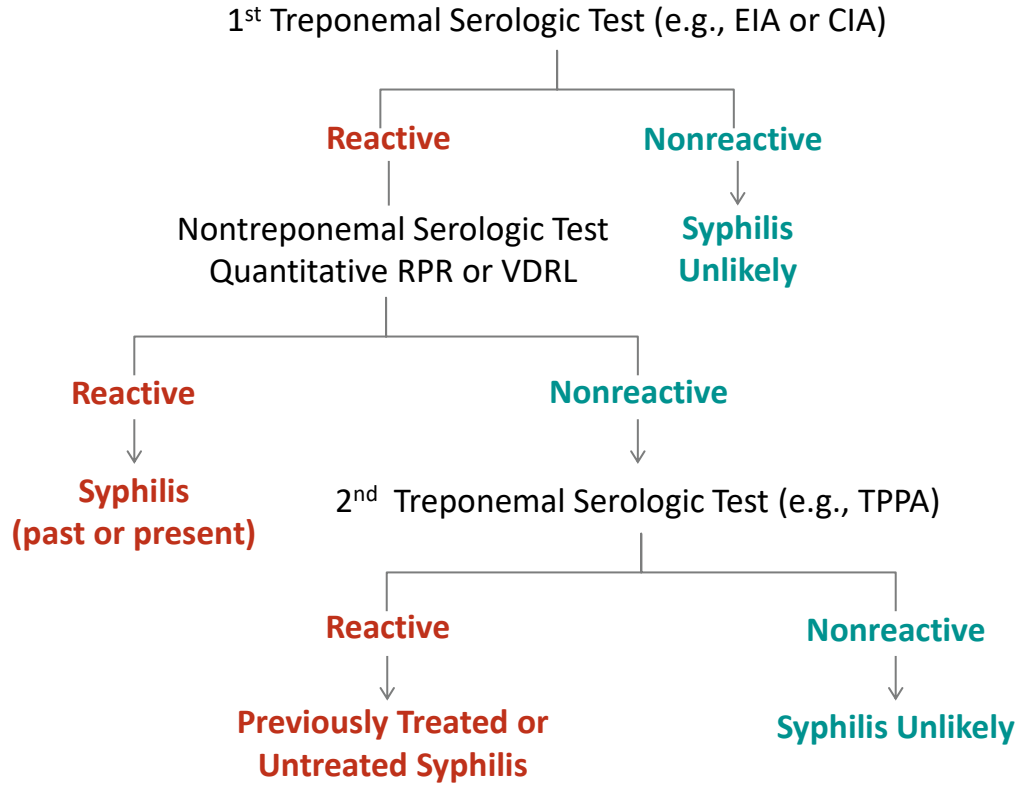
Either Lab-based Algorithm Is Acceptable for Syphilis Testing

Traditional Algorithm



VS

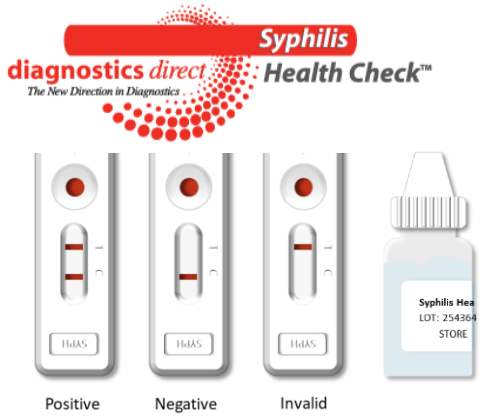
Reverse-Sequence Algorithm



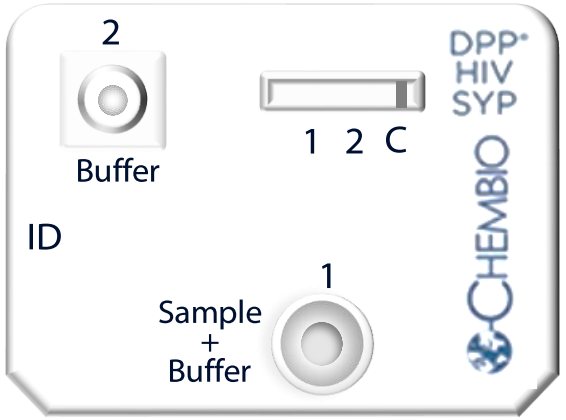
Point-of-Care (POC) Treponemal Tests Are Available, but Anyone With a Positive POC Should Have Lab-based Testing

Example POC Tests

Syphilis Health Check™



Chembio DPP® HIV/ Syphilis Test Kit



POC Tests Provide Fast and Accurate Results

	Time to Results	Shelf-life	Cost per Test	Sensitivity & Specificity
Diagnostics Direct, LLC (syphilis)	10 min.	30 months	Approx. $10	95-99% Sensitivity 94-97% Specificity
Chembio Diagnostics, Inc. (syphilis and HIV)	15 min.	24 months	Approx. $7-10	47-97% Sensitivity 99-100% Specificity

Bristow CC, Klausner JD, Tran A. Clinical Test Performance of a Rapid Point-of-Care Syphilis Treponemal Antibody Test: A Systematic Review and Meta-analysis. Clin Infect Dis. 2020 Jun 24;71(Suppl 1):S52-S57. |

FDA Approves the First Syphilis Self-Test

FDA NEWS RELEASE

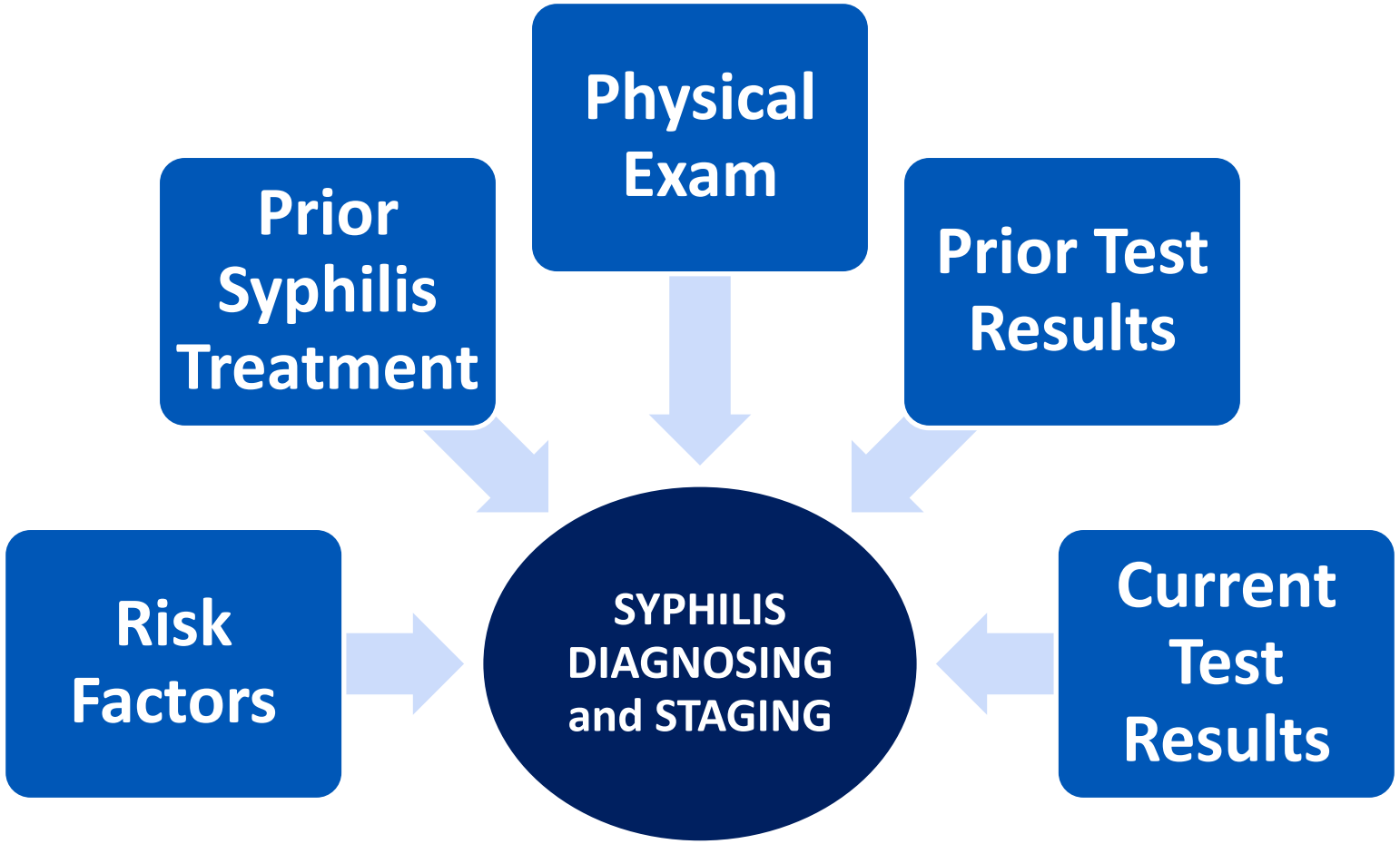
FDA Marketing Authorization Enables Increased Access to First Step of Syphilis Diagnosis

First Home Antibody Test Can Inform Patients of Current or Past Infection and Lead to Confirmatory Testing with Health Care Provider

For Immediate Release: August 16, 2024

fda.gov

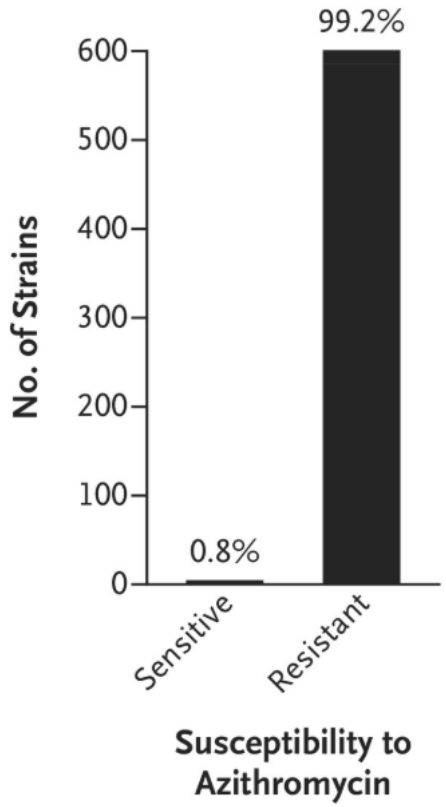
Diagnosis and Staging Are Based on More Than Just Current Test Results

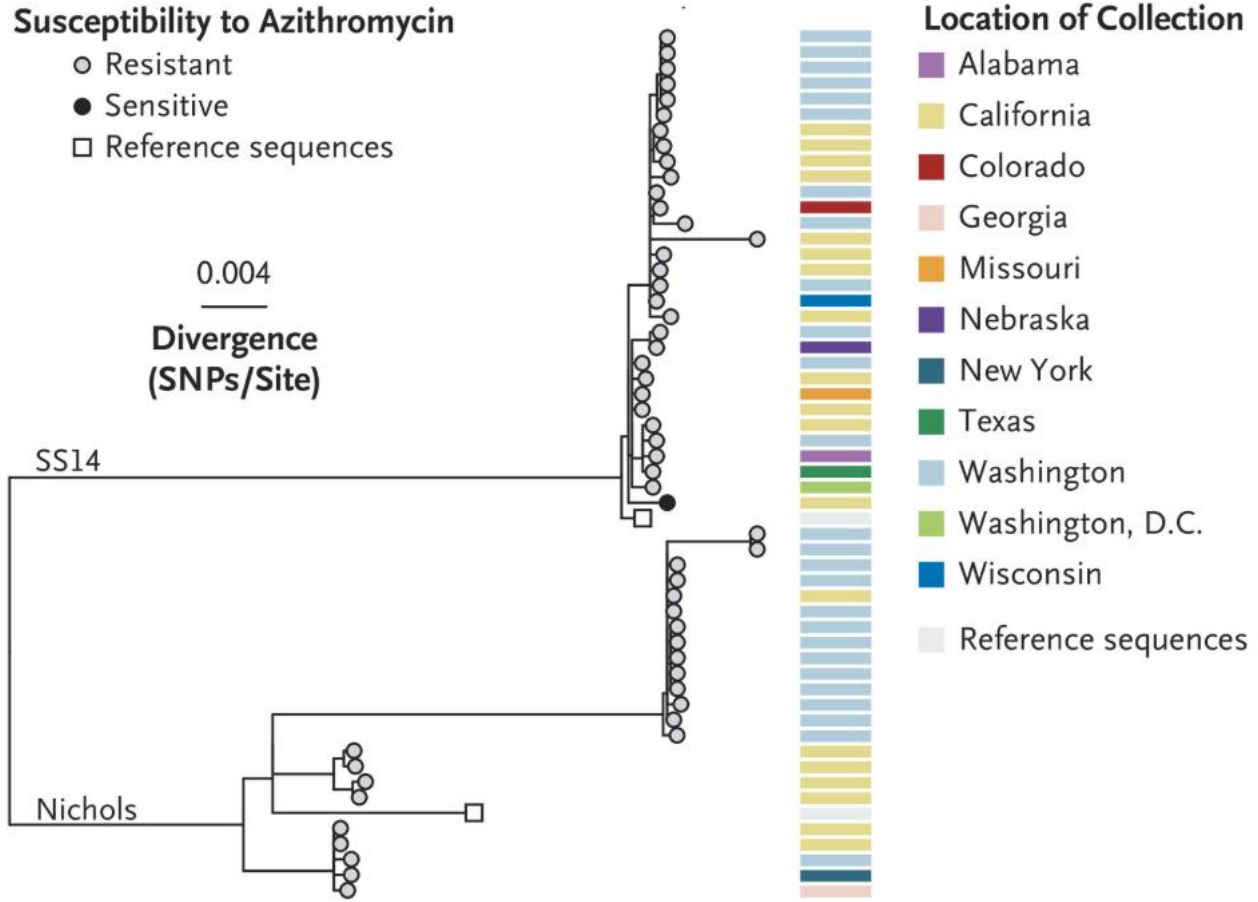


Treatment and Future Prevention Methods

Near-Universal Resistance to Macrolides of *Treponema pallidum* in North America

Azithromycin Resistance in Tested Treponema pallidum Strains.





N Engl J Med 2024;390:2127-2128

The NEW ENGLAND JOURNAL of MEDICINE

CORRESPONDENCE

Disseminated Syphilis Caused by Two Recombining *Treponema pallidum* Strains

Lieberman NAP et al. NEJM April 16, 2025

Penicillin Is the Only Recommended Regimen for Syphilis in the 2021 CDC STI Treatment Guidelines

Primary, Secondary & Early Latent	Late Latent & Latent Unknown Duration	Neurosyphilis, Ocular Syphilis or Otosyphilis
Benzathine penicillin G 2.4 million units IM in a single dose	**Benzathine penicillin G** 7.2 million units total, administered as 3 doses of 2.4 million units IM each at 1-week intervals	**Aqueous crystalline penicillin G** 18–24 million units per day, administered as 3–4 million units IV every 4 hours or continuous infusion for 10–14 days

Above recommendations are for adults. See Sexually Transmitted Infections Treatment Guidelines, 2021 for the complete list of recommendations on treating syphilis including treatment for children and congenital syphilis.

Penicillin Is the Only Recommended Regimen for Syphilis in the 2021 CDC STI Treatment Guidelines

Primary, Secondary & Early Latent	Late Latent & Latent Unknown Duration	Neurosyphilis, Ocular Syphilis or Otosyphilis
single dose	2.4 million units IM each at 1-week intervals	units IV every 4 hours or continuous infusion for 10–14 days

Pregnant women must receive benzathine penicillin

Above recommendations are for adults. See Sexually Transmitted Infections Treatment Guidelines, 2021 for the complete list of recommendations on treating syphilis including treatment for children and congenital syphilis.

Syphilis Treatment Newborn

Recommended Regimens, Confirmed or Highly Probable Congenital Syphilis

Aqueous crystalline penicillin G 100,000–150,000 units/kg body weight/day, administered as 50,000 units/kg body weight/dose by IV every 12 hours during the first 7 days of life and every 8 hours thereafter for a total of 10 days

OR

Procaine penicillin G 50,000 units/kg body weight/dose IM in a single daily dose for 10 days

Recommended Regimens, Possible Congenital Syphilis

Aqueous crystalline penicillin G 100,000–150,000 units/kg body weight/day, administered as 50,000 units/kg body weight/dose by IV every 12 hours during the first 7 days of life and every 8 hours thereafter for a total of 10 days

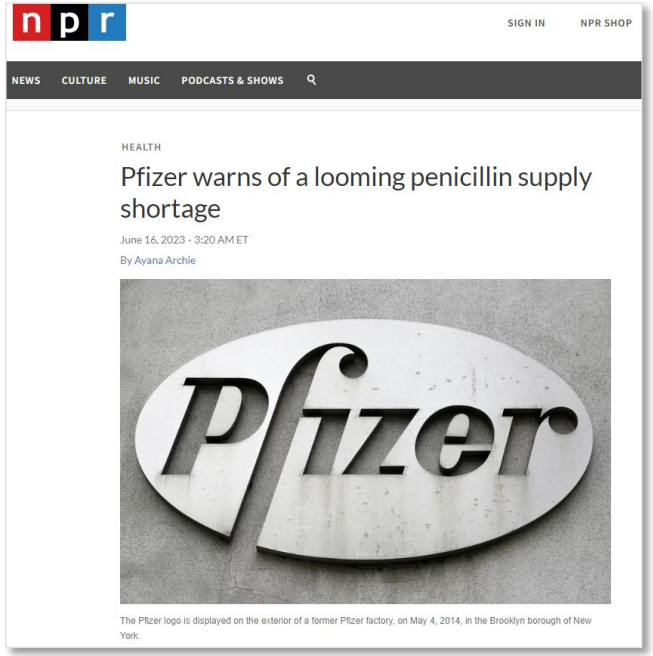
OR

Procaine penicillin G 50,000 units/kg body weight/dose IM in a single daily dose for 10 days

OR

Benzathine penicillin G 50,000 units/kg body weight/dose IM in a single dose

Treating Syphilis



Bicillin L-A® Shortage

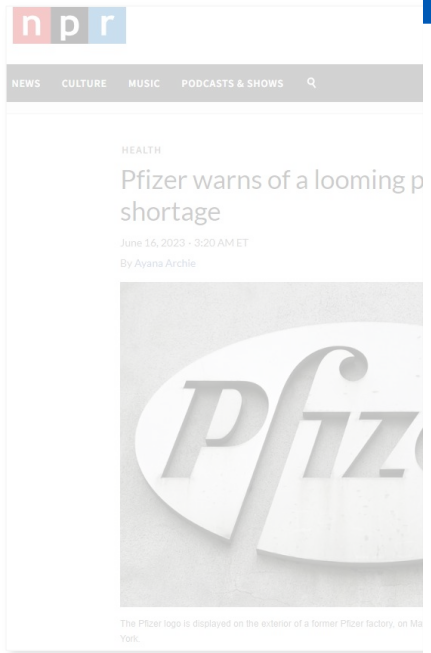
The FDA has listed penicillin G benzathine injectable suspension products (Bicillin L-A®) on their drug shortage webpage, noting limited supply due to increased demand. The FDA website includes an expected duration for the shortage. CDC continues to monitor the situation and will post updates as needed.

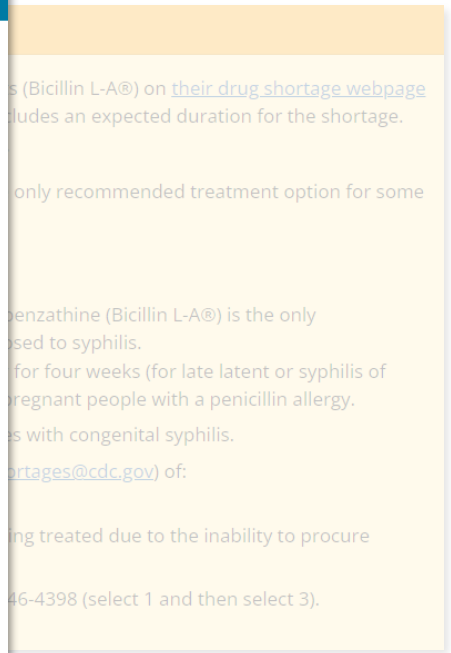
Bicillin L-A® is the first-line recommended treatment for syphilis and the only recommended treatment option for some patients.

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).

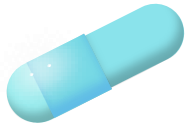
Treating Syphilis





Two Alternative Treatments Have Been Used for Years

Primary, Secondary, and Latent Syphilis

Antimicrobial	Dose	Duration*
 Doxycycline	100 mg orally 2 times/day	14 or 28 Days
 Tetracycline	500 mg orally 4 times/day	14 or 28 Days

*Duration is dependent on the stage of syphilis. Primary, secondary, and early latent syphilis duration is 14 days. Late latent or syphilis of unknown duration is 28 days.

3 Meta-Analyses

- Minor differences in inclusion criteria & outcome measured
- One only early syphilis, other all syphilis
- One study combined doxy & tetracycline
- Vary in included number of patients treated with doxy and penicillin
- All came to same conclusion

Open Forum Infectious Diseases

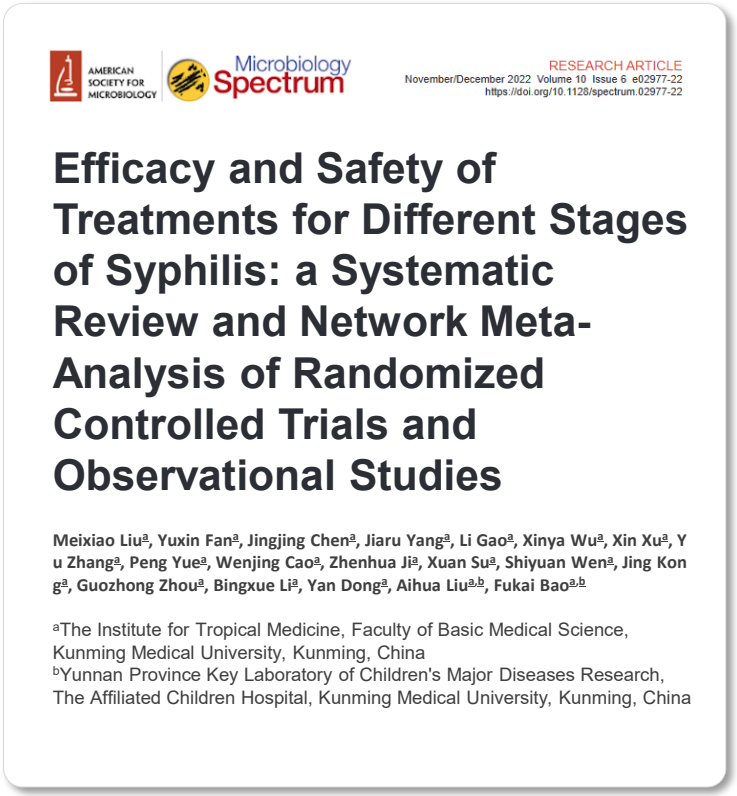
MAJOR ARTICLE

IDSA Infectious Diseases Society of America | hivma hiv medicine association | OXFORD

Syphilis Treatment: Systematic Review and Meta-Analysis Investigating Nonpenicillin Therapeutic Strategies

Gustavo Yano Callado,[1] Maria Celidonio Gutfreund,[1] Isabele Pardo,[1] Mariana Kim Hsieh,[1] Vivian Lin,[1] Mindy Marie Sampson,[2] Guillermo Rodriguez Nava,[2] Tássia Aporta Marins,[3] Rodrigo Octávio Deliberato, [4,5] Marinês Dalla Valle Martino,[1] Marisa Holubar, [2] Jorge L. Salinas,[2] and Alexandre R. Marra[1,6]

[1]Faculdade Israelita de Ciências da Saúde Albert Einstein, Hospital Israelita Albert Einstein, São Paulo, São Paulo, Brazil, [2]Division of Infectious Diseases & Geographic Medicine, Stanford University, Stanford, California, USA, [3]Faculdade de Medicina, Centro Universitário de Adamantina, Adamantina, São Paulo, Brazil, [4]Department of Biomedical Informatics, University of Cincinnati College of Medicine, Cincinnati, Ohio, USA, [5]Biomedical Informatics Division, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio, USA, and [6]Carver College of Medicine, Iowa City, Iowa, USA



AMERICAN SOCIETY FOR MICROBIOLOGY | Microbiology Spectrum

RESEARCH ARTICLE
November/December 2022 Volume 10 Issue 6 e02977-22
https://doi.org/10.1128/spectrum.02977-22

Efficacy and Safety of Treatments for Different Stages of Syphilis: a Systematic Review and Network Meta-Analysis of Randomized Controlled Trials and Observational Studies

Meixiao Liu[a], Yuxin Fan[a], Jingjing Chen[a], Jiaru Yang[a], Li Gao[a], Xinya Wu[a], Xin Xu[a], Yu Zhang[a], Peng Yue[a], Wenjing Cao[a], Zhenhua Ji[a], Xuan Su[a], Shiyuan Wen[a], Jing Kong[a], Guozhong Zhou[a], Bingxue Li[a], Yan Dong[a], Aihua Liu[a,b], Fukai Bao[a,b]

[a]The Institute for Tropical Medicine, Faculty of Basic Medical Science, Kunming Medical University, Kunming, China
[b]Yunnan Province Key Laboratory of Children's Major Diseases Research, The Affiliated Children Hospital, Kunming Medical University, Kunming, China

PLOS ONE

RESEARCH ARTICLE

Comparison of efficacy of treatments for early syphilis: A systematic review and network meta-analysis of randomized controlled trials and observational studies

Hong-yeLiu[1,2], Yan Han[1], Xiang-sheng Chen[1], Li Bai[2], Shu-ping Guo[2], Li Li[2], Peng Wu[3], Yue-ping Yin[1]

1 Reference STD Lab, National Center for STD Control, Chinese CDC, Institute of Dermatology, Chinese Academy of Medical Sciences, Peking Union Medical College, Jiangsu Key Laboratory of Molecular Biology for Skin Diseases and STIs, Nanjing, China, **2** Department of Dermatology and Venereology, First Affiliated Hospital of Shanxi Medical University, Taiyuan, China, **3** Health Statistics Teaching and Research Section, School of Public Health, Shanxi Medical University, Taiyuan, China

In Addition, for Early Syphilis...

Several RCTs have demonstrated:

- 1 dose (2.4 MU) benzathine penicillin G IM non-inferior to 3 doses (7.2 MU) as measured by serologic response at 6 months in people with and without HIV (Andrade 2017; Hook 2023)
- 2 doses of benzathine penicillin G inferior to 10 days of ceftriaxone 1gm IV daily for 10 days (Cao 2017)
- Linezolid 600mg orally daily for 5 days inferior to 2.4 MU benzathine penicillin G (Ubals 2024)
- Cefixime holds some promise though sample size small (Stayfylis 2021)

Alternatives With Limited Clinical Studies or Resistance Concerns

Primary, Secondary, and Early Latent Syphilis

Antimicrobial	Dose	Duration
 Azithromycin	Single 2 g oral dose ***Do not recommend*** *as documented treatment failures and potential macrolide resistance*	--
 Ceftriaxone	1 g daily either IM or IV *Optimal dose and duration have not been defined*	10 Days

WHO Treatment: Syphilis in Adults and Adolescents

Syphilis Stage	First-line Options	Effective Substitutes
Early syphilis primary, secondary and early latent syphilis of not more than two years' duration	**Benzathine penicillin G 2.4 million units** once intramuscularly.	**Procaine penicillin G 1.2 million units** 10–14 days intramuscularly. When penicillin cannot be used/not available: • **Doxycycline 100 mg** twice daily orally for 14 days OR • **Ceftriaxone 1 g** intramuscularly once daily for 10–14 days OR • In special circumstances only when local susceptibility to azithromycin is likely, **Azithromycin 2 g** once orally
Late syphilis* or unknown duration *late latent and tertiary syphilis of more than two years' duration without evidence of treponemal infection	**Benzathine penicillin G 2.4 million units** intramuscularly once weekly for 3 consecutive weeks.	**Procaine penicillin 1.2 million units** intramuscularly once daily for 20 days. When penicillin cannot be used/not available: • **Doxycycline 100 mg** twice daily orally for 30 days.

WHO Guidelines for the Treatment of Treponema pallidum (Syphilis). Geneva: World Health Organization; 2016.

WHO Treatment: Syphilis in Pregnant Women

Syphilis Stage	First-line Options for Pregnant Women	Alternative Treatments for Rare Situations
Early syphilis primary, secondary and early latent syphilis of not more than two years' duration	**Benzathine penicillin G 2.4 million units** once intramuscularly.	**Procaine penicillin 1.2 million units** intramuscularly once daily for 10 days. In rare situations when penicillin cannot be used/is not available, WHO suggests one of the following options with caution and enhanced follow-up: • Ceftriaxone 1 g intramuscularly once daily for 10–14 days; *or* • Erythromycin 500 mg orally 4 times daily for 14 days.
Late syphilis* or unknown duration *late latent and tertiary syphilis of more than two years' duration without evidence of treponemal infection	**Benzathine penicillin G 2.4 million units** intramuscularly once weekly for 3 consecutive weeks.	**Procaine penicillin 1.2 million units i**ntramuscularly once daily for 20 days. In rare situations when penicillin cannot be used/is not available, WHO suggests one of the following options with caution and enhanced follow-up: • Erythromycin 500 mg orally 4 times daily for 30 days.

Updated recommendations for the treatment of Neisseria gonorrhoeae, Chlamydia trachomatis and Treponema pallidum (syphilis), and new recommendations on syphilis testing and partner services. Geneva: World Health Organization; 2024. Licence: CC BY-NC-SA 3.0 IGO.

WHO Treatment: Syphilis in Pregnant Women

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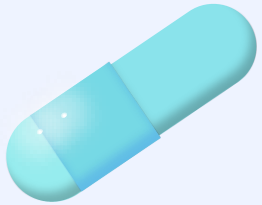
syphilis of more than two years' duration without evidence of treponemal infection	consecutive weeks.	• Erythromycin 500 mg orally 4 times daily for 30 days.

Erythromycin treats the pregnant woman. It does not cross the placental barrier completely and as a result the fetus is not treated. It is therefore necessary to treat the newborn infant soon after delivery.

Updated recommendations for the treatment of Neisseria gonorrhoeae, Chlamydia trachomatis and Treponema pallidum (syphilis), and new recommendations on syphilis testing and partner services. Geneva: World Health Organization; 2024. Licence: CC BY-NC-SA 3.0 IGO.

New Prevention Methods for Syphilis

Doxycycline Post-Exposure Prophylaxis

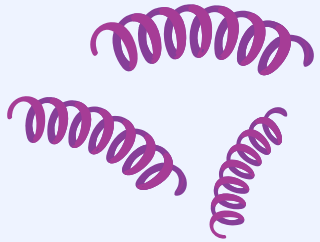


Syphilis Vaccine

Key Takeaways

1

Syphilis is an ancient infection that continues to plague us today



2

Syphilis is challenging to manage and diagnose

3

Syphilis diagnostics and treatments are limited

Thank You!

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

Pâmela Cristina Gaspar

Pâmela Cristina Gaspar is a pharmaceutical biochemist with a Master's degree in Pharmacy and a PhD in Public Health. She is currently General Coordinator for the Surveillance of Sexually Transmitted Infections at the Brazilian Ministry of Health.

She has focused for over a decade on the formulation and implementation of public health policies aimed at the prevention, diagnosis, expanded access to testing, and treatment of sexually transmitted infections. Her work also encompasses the surveillance of antimicrobial resistance in *Neisseria gonorrhoeae*, the development and revision of clinical guidelines, and strategies for the elimination of vertical transmission of HIV, syphilis, viral hepatitis, and HTLV.

Challenges and opportunities in the treatment of syphilis: Brazilian experience

Pâmela Cristina Gaspar (Pharm., Ph.D)

General Coordinator for the Surveillance of Sexually Transmitted Infections - CGIST

Department of HIV, AIDS, Tuberculosis, Viral Hepatitis, and Sexually Transmitted Infections - Dathi

Secretariat for Health and Environmental Surveillance - SVSA

Ministry of Health of Brazil - MoH

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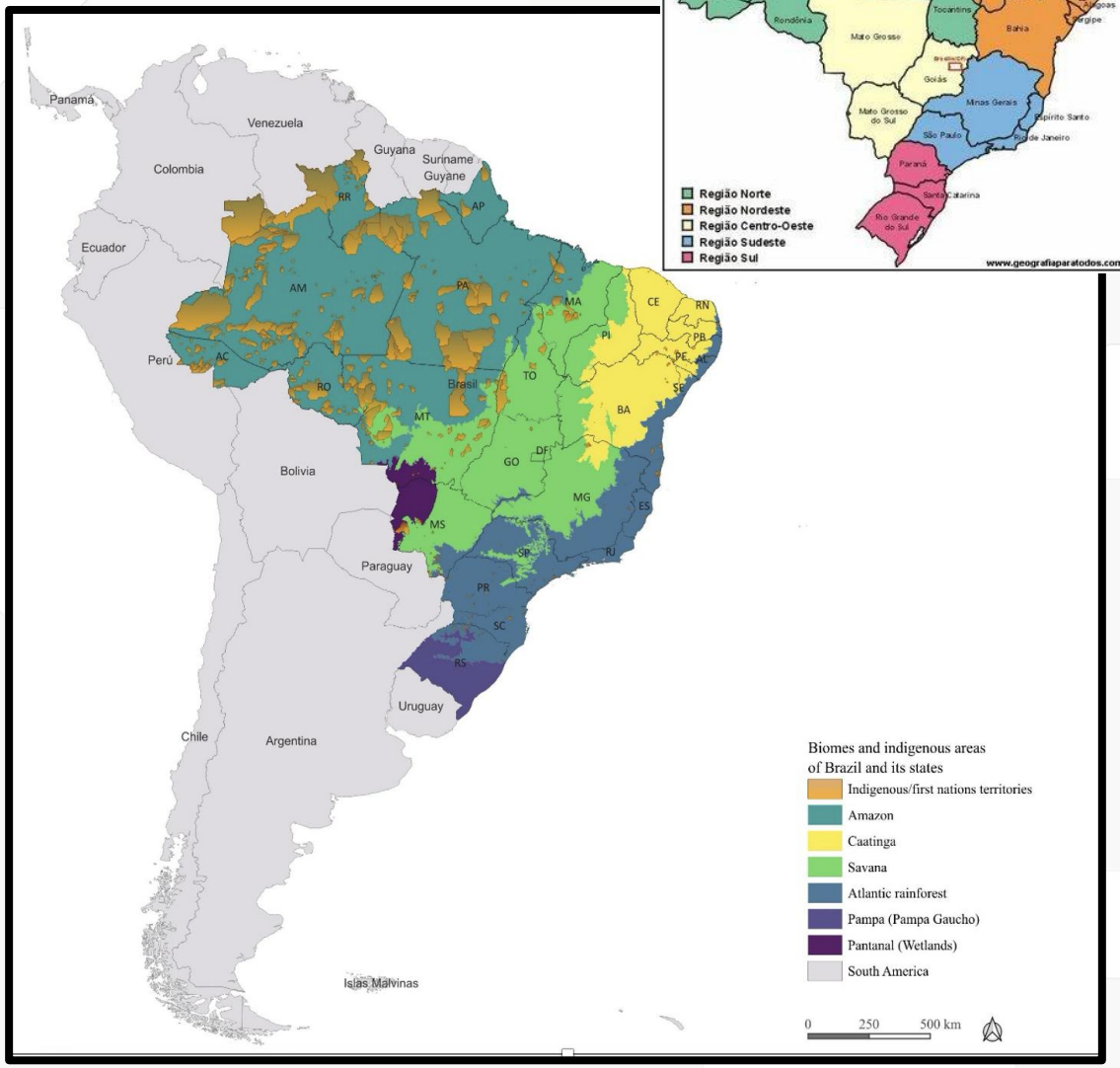
Brazil

- **Area:** 8,514,877 km2: continental country (sixth largest)
- **Population:** 212,583,750 inhabitants(seventh most populous)
- **Live Births:** 2,54 million

- **Geographical regions:** 5 / **Federal Units:** 27
- **Municipalities:** 5,571
- **Municipalities with over 100,000 inhabitants:** 327 (122,829,918 inhabitants – 58% of the population)

Regional differences in geography, income, population, and infrastructure.



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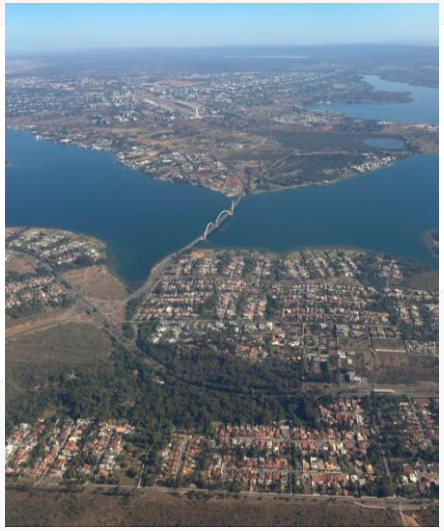
There are many Brazils within the same country



OVERVIEW OF THE UNIFIED HEALTH SYSTEM (SUS)

Created by the 1988 Federal Constitution.

Regulated by Laws No. 8,080/1990 and 8,142/1990.

Principles: universality, completeness, and equity.
Access guaranteed to all citizens.

COVERAGE OF BRAZIL'S HEALTH NETWORK

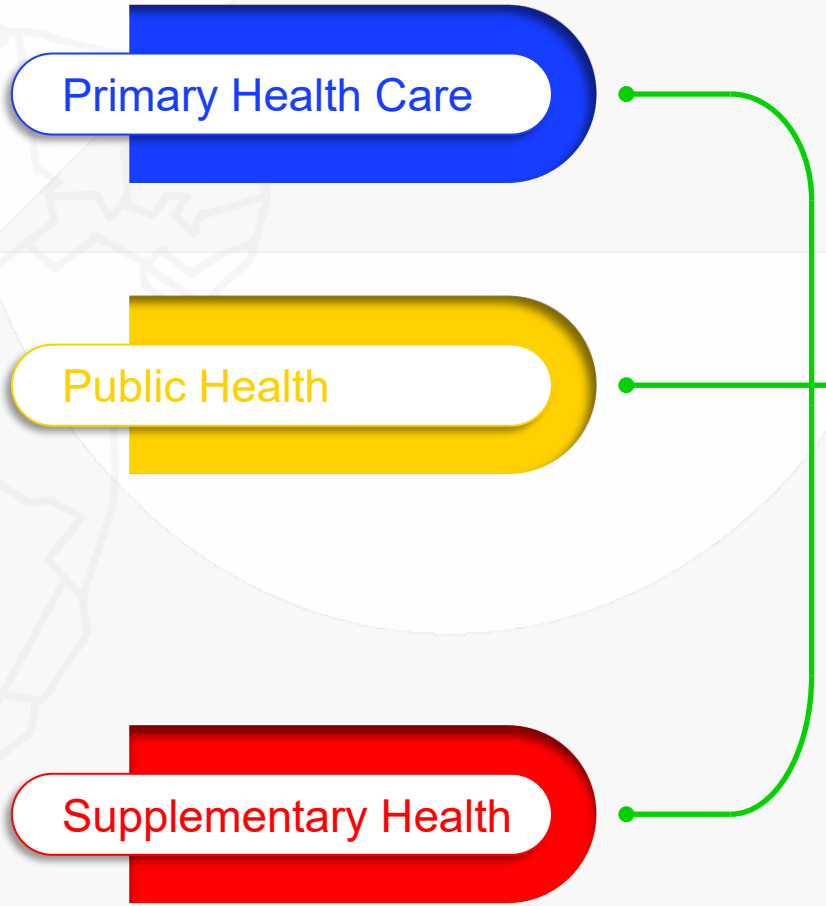
GOV.BR/SAUDE
minsaude

Primary Health Care (PHC) coverage reaches **98.16%** of the national territory;

About **71.5%** of the Brazilian population relies exclusively on the public health network — approximately 150 million people (PNS/IBGE, 2020).

Around **24.9%** of the population uses the supplementary health network, which can also access the Unified Health System (SUS) (ANS, 2023).

Regarding births in 2023, only **13.5%** were performed in the supplementary network, showing that the vast majority **(86.5%)** take place in the public health network.



Health Network Coverage and Dependence

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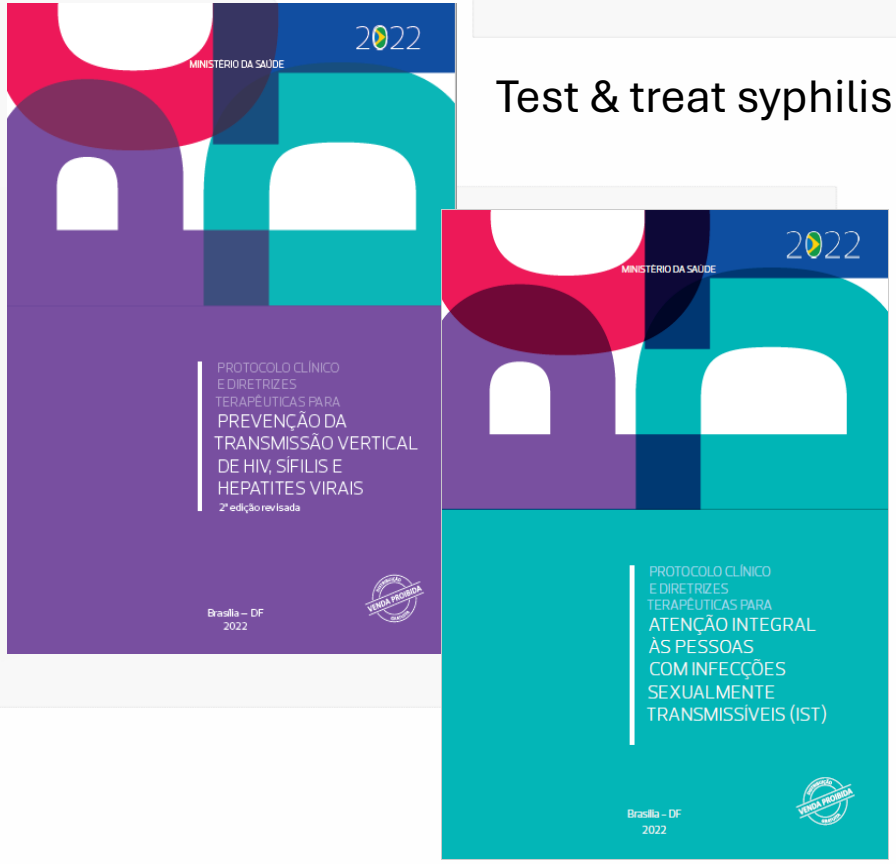
National Guidelines



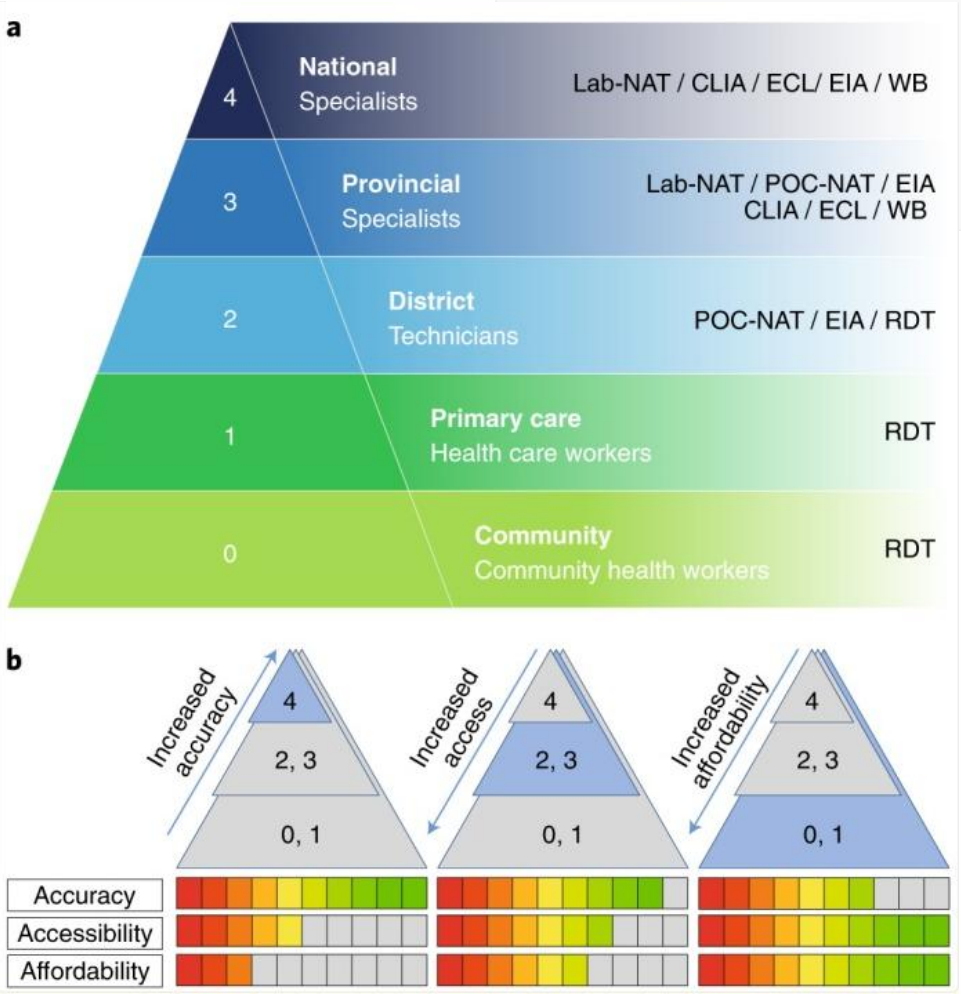
Test & treat syphilis

And HOW to test?

Algorithm with the classic approach (starting with non-treponemal test)

Algorithm with the reverse approach (starting with treponemal test)

“The right test for the right patient at the right time in the right setting”. (Prof. Rosanna Peeling)



a, Schematic showing the different levels of health care available from national to community levels, indicating the equipment and tests which are available at each level. Lab-NAT: laboratory-based nucleic acid tests; EIA, enzyme immunoassay; WB, western blot; CLIA, chemiluminescence immunoassay; ECL, electrochemiluminescence immunoassay. b, Key characteristics of diagnostics tests to reflect trade-offs between accuracy, accessibility and affordability for different levels of the health care system. Panel a adapted from ref. 14, WHO.

Ideal Test → Rapid Diagnostic Test

- **R**eal-time connectivity
- **E**ase of specimen collection
- **A**ffordability
- **S**ensitivity
- **S**pecificity
- **U**ser friendliness
- **R**apid and robust
- **E**quipment-free
- **D**eliverable to end-users

Land KJ et al. REASSURED diagnostics to inform disease control strategies, strengthen health systems and improve patient outcomes. Nat Microbiol. 2019 Jan;4(1):46-54

Definition of a logistics system for rapid POC tests

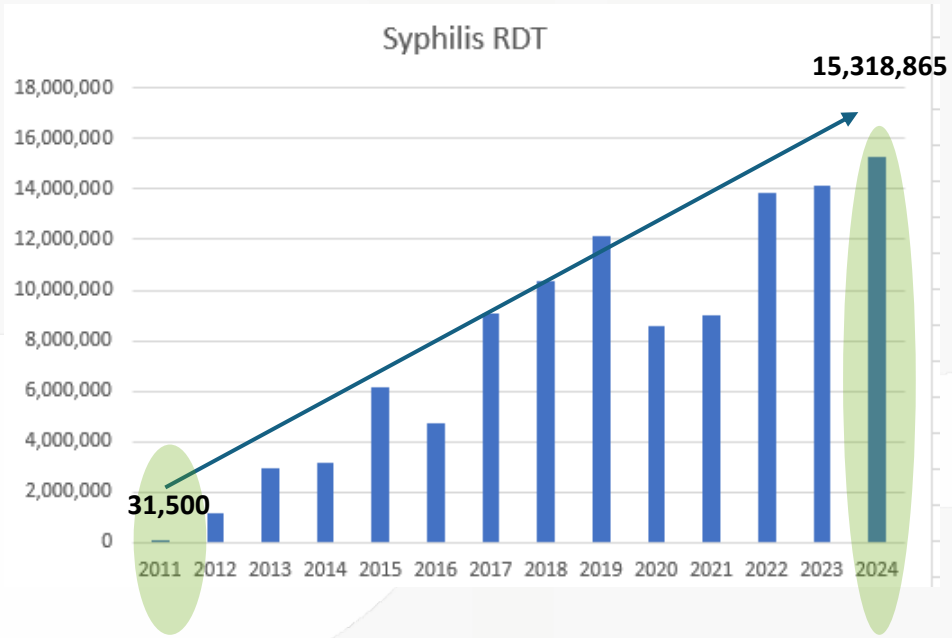
MoH

27 States

5,570 Municipalities

50,293 primary health care units
+
700 HIV/STI services (testing and treatment)
+
5,513 hospitals/maternities

Rapid diagnostic test of HIV, syphilis, Hepatitis B and C



More dangerous than a test not performed is a test performed without quality!

Brazilian MoH manages five quality tools for Rapid Diagnostic Test in public healthcare system

Prof. Maria Luiza Bazzo

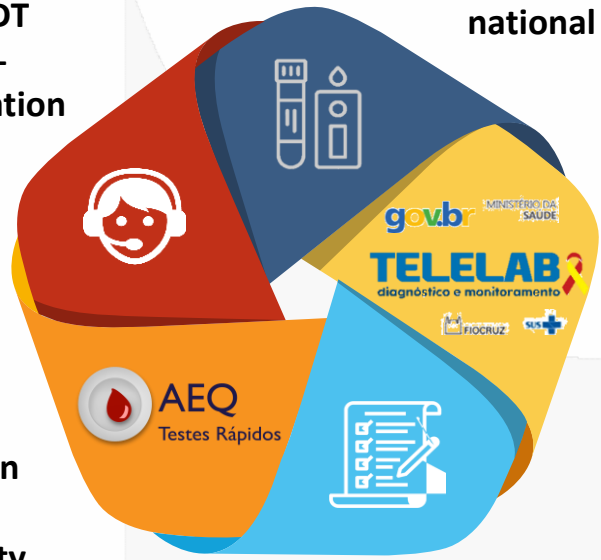
AEQ Testes Rápidos

LBMMS

Execution of rapid tests for HIV, syphilis and hepatitis C virus with dried Tube Specimen – DTS (serum or plasma samples with red dye) – Twice a year.

Customer Service (CS) registers for RDT reactive post-marketing evaluation

Technical criteria definition for RDT acquisition and national algorithms



Adherence to distance RDT training provided by MoH

Participation in Rapid RDT External Quality Assessment (EQA) program

Verification of the testing quality and performance of nationally available tests and of each lot of RDT received

In Brazil, we have the possibility to purchase tests beyond those prequalified by the WHO, as we evaluate their quality and performance in the national scenario.

National Guidelines

Test & treat syphilis

WHO to test?	When?
Adolescents and young people (≤30 years)	Annually
Pregnant women	At the first prenatal consultation (1rd trimester); At the beginning of the 3rd trimester; At the time of delivery; In case of miscarriage/stillbirth. In cases of sexual violence, at any time
Gay men and MSM (men who have sex with men)	Semiannually
Sex workers	
Transgender women and men	
People living with HIV and AIDS	
People deprived of liberty	
People engaging in receptive anal intercourse (passive) without condom use	
People who use alcohol and other drugs	
People diagnosed with other STIs	At diagnosis and 6 weeks after the STI diagnosis
People in situations of sexual violence	At initial care, then 4 to 6 weeks, and 3 months after exposure
People using PrEP	Quarterly
People using PEP	At initial care and 4 to 6 weeks after exposure

National Guidelines

- Considering the syphilis epidemic in Brazil and the sensitivity of diagnostic algorithms, it is recommended to initiate the investigation with the **treponemal test (rapid POC treponemal test).**

- For pregnant women and other special situation, **immediate treatment with benzathine benzylpenicillin is recommended** after just one reactive test for syphilis (either treponemal or non-treponemal test).

- The treatment protocol for syphilis in pregnant women for latent syphilis or syphilis of unknown duration involves administering three doses of penicillin with intervals ideally of 7 days, **but tolerating up to 9 days.**

National Guidelines

Clinical classification	Therapeutic scheme	Alternative (except for pregnant women)	Follow-up
Recent syphilis: primary, secondary, and recent latent syphilis (up to one year of evolution)	Benzathine benzylpenicillin 2.4 million international units (IU), intramuscular (IM), single-dose (1.2 million in each gluteus)	Doxycycline 100mg, 12/12 hours, oral route (OR), for 15 days	Trimestral nontreponemal test up to 12 months of follow-up (in pregnant women, monthly control)
Late syphilis: late latent syphilis (with more than one year of evolution) or latent with unknown duration and tertiary syphilis	Benzathine benzylpenicillin 2.4 million IU, IM, once/week (1,2 million in each gluteus) for three weeks[b] Total dose: 7.2 million	Doxycycline 100mg, 12/12 hours, OR, for 30 days	Trimestral nontreponemal test up to 12 months of follow-up (in pregnant women, monthly control)
Neurosyphilis	Benzylpenicillin potassium (crystalline), 3 to 4 million IU, 4/4 hours, intravenous (IV) or continuous infusion, making up 18-24 million per day, for 14 days.	Ceftriaxone 2g, IV, once/day, for 10-14 days.	Cerebrospinal fluid examination of 6/6 months up to normal

Notes: a) Benzathine benzylpenicillin is the only safe and efficient option for adequate treatment of pregnant women. Any other treatment conducted during pregnancy, for purposes of defining the case and therapeutic approach of congenital syphilis, is deemed inadequate treatment for the mother; consequently, the newborn will be notified as having congenital syphilis undergo clinical and laboratory assessment; b) The interval between doses must not be longer than 14 days. In such a case, the scheme must restart. **In pregnant women, the dosing interval should ideally be 7 days and should not exceed 9 days.**

Nursing leadership in syphilis prevention and care

The **Ministry of Health** worked together with the **Federal Nursing Council** to authorize nurses to →

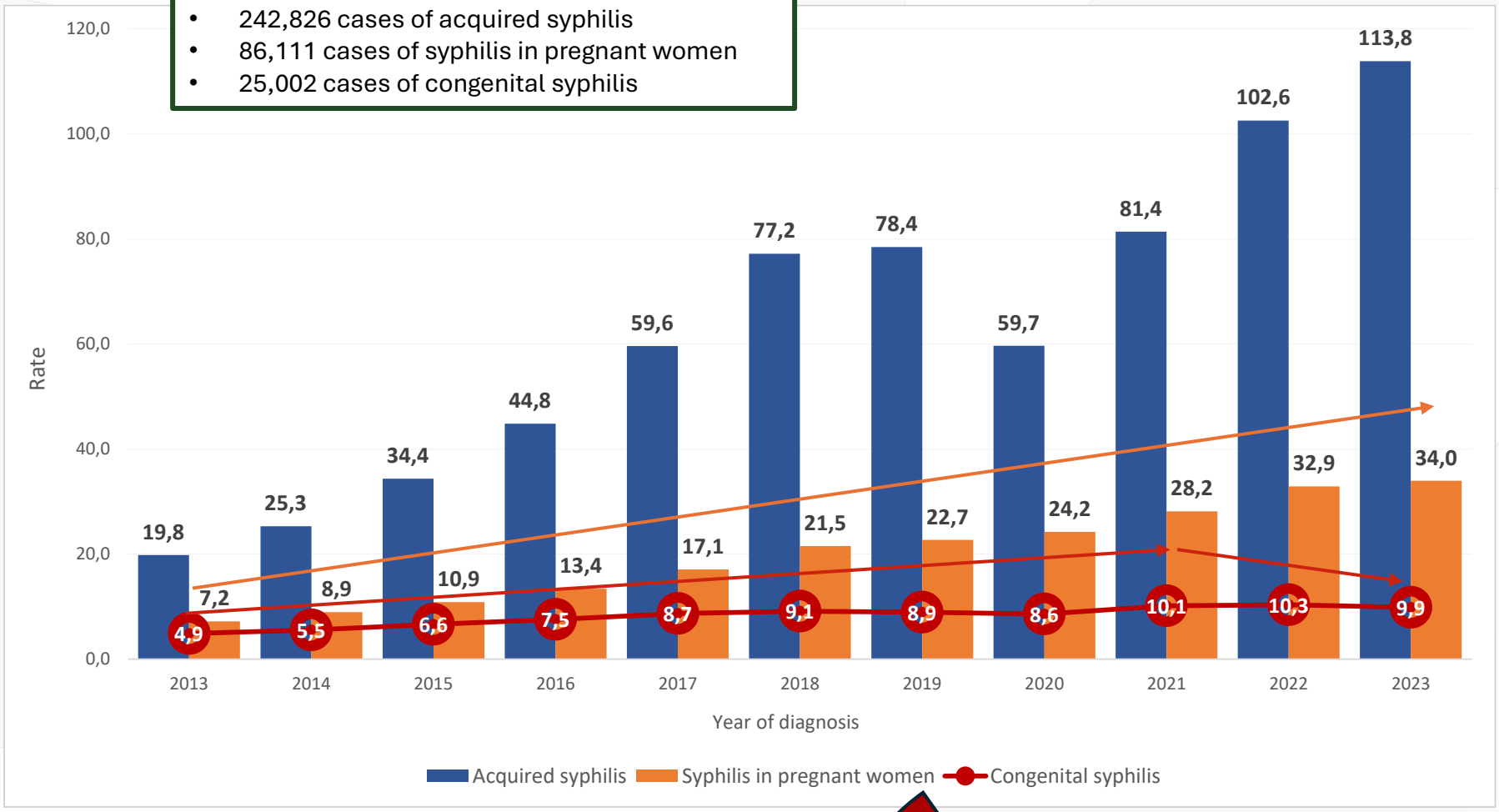
- Performs rapid tests - being responsible for issuing the test result report
- Technical supervision of professionals performing rapid tests (technical level)
- Requesting laboratory tests (e.g., VDRL, RPR)
- Prescribing treatment for syphilis
- Supervision of penicillin administration

Some national data....

- We estimate that **around 80%** of HIV, syphilis, and Hepatitis B and C **Rapid Diagnostic Tests are performed by nursing professionals**.
- In our 58 municipalities and 3 states that have obtained some subnational **certification for the elimination of congenital syphilis**, or are certified as being on the path toward elimination, there is **strong leadership from nurses.**

Detection rate of acquired syphilis (per 100,000 population), detection rate of syphilis in pregnant women, and incidence rate of congenital syphilis (per 1,000 live births), by year of diagnosis. Brazil, 2013-2023

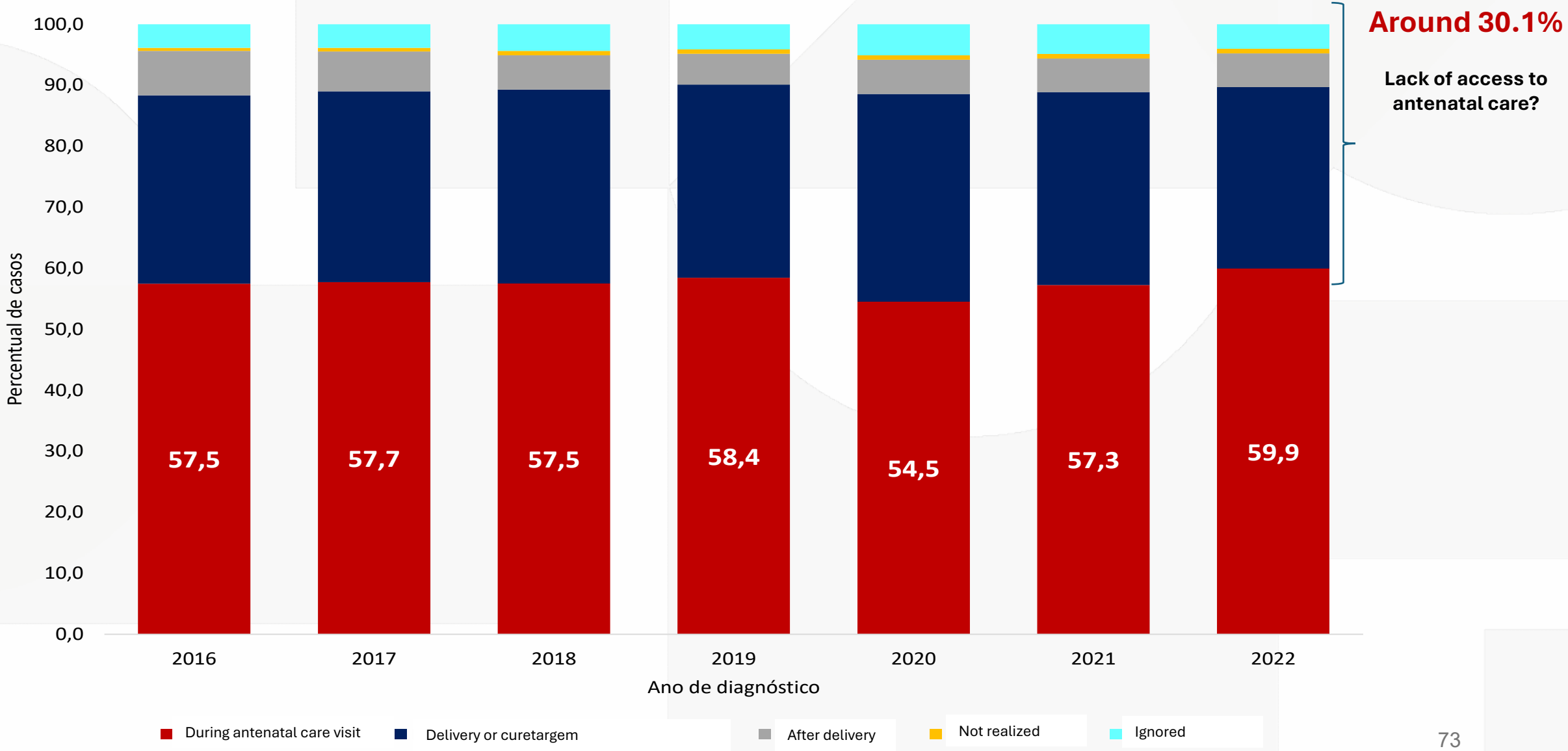
In 2023...
- 242,826 cases of acquired syphilis
- 86,111 cases of syphilis in pregnant women
- 25,002 cases of congenital syphilis



SC: 990/100,000LB

Challenges and opportunities in the treatment of syphilis

Percentage of new cases of congenital syphilis according to the timing of maternal diagnosis and year. Brazil, 2016 to 2022



Fonte: Sistema de Informação de Agravos de Notificação (Sinan), atualizado em 30/06/2023.

PROJETO SÍFILIS

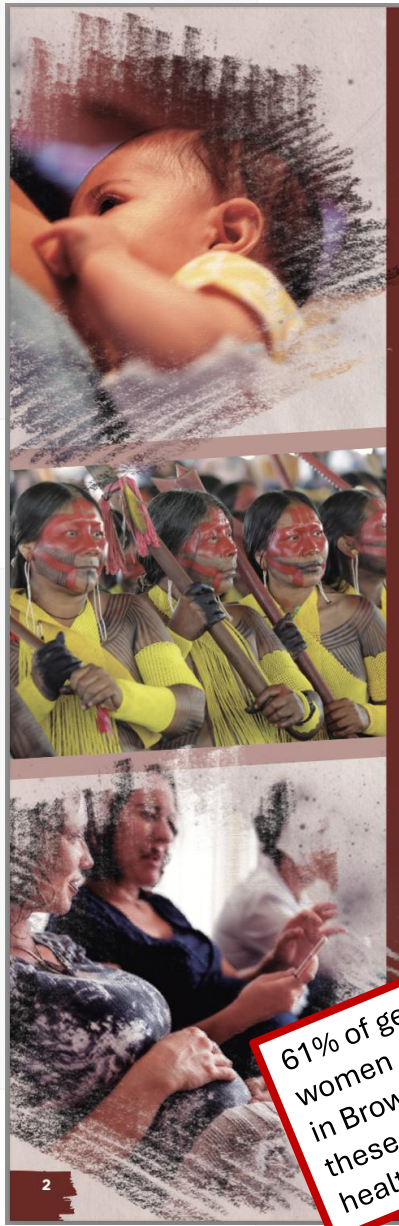
Policy Brief

Efeitos das desigualdades sociais na sífilis gestacional e congênita em mulheres e crianças

Motivados pelo aumento de casos de sífilis na última década (2010-2020) no Brasil, tanto em sua forma gestacional, quanto congênita, a equipe de pesquisadoras e pesquisadores do projeto "Avaliação dos determinantes e impacto direto e indireto de políticas sociais na sífilis gestacional e congênita e seus efeitos adversos sobre o concepto-Brasil, 2001-2018" investigou as dinâmicas sociais por trás da ocorrência da doença e como a sífilis afeta a saúde de gestantes e crianças no país.

Os resultados apontam que as desigualdades que permeiam os marcadores sociais – como racismo e baixa escolaridade - diminuem a garantia de acesso a consultas por gestantes, testes rápidos e tratamento adequado. Além disso, verificou-se que a probabilidade de morte entre crianças menores de 5 anos atingidas pela doença é 2 vezes a daquelas sem sífilis. Este cenário, somado a uma taxa de subnotificação de casos de sífilis diagnosticados durante a gestação (com uma estimativa de 13% de casos não registrados), entre 2007 e 2018, ajudam a compreender por que a sífilis é um importante problema de saúde pública no Brasil de hoje.

CNPq · SUS · Ministério da Saúde · Governo Federal Brasil União e Reconstrução · Ministério da Saúde Fiocruz Fundação Oswaldo Cruz · cidacs Centro de Integração de Dados e Conhecimentos para Saúde



Os casos de sífilis apresentaram um aumento no Brasil nas últimas décadas. Mesmo havendo tratamento e diagnóstico de baixo custo e disponível no Sistema Único de Saúde (SUS), os casos de sífilis diagnosticada na gestação (SG) aumentaram cerca de 5 vezes entre 2011 e 2021 e a ocorrência da sífilis congênita (SC) foi cerca de 20 vezes maior que a meta de 0,5 a cada 1.000 nascidos vivos recomendada pela Organização Pan-Americana da Saúde (OPAS).[1]

Para entender esse contexto, a pesquisa vinculou informações de diversas fontes de dados administrativos, como os Sistemas de Informação de Agravos de Notificação (Sinan), Nascimentos (Sinasc), Mortalidade (SIM), Internações (SIH/SUS) e as Coortes desenvolvidas pelo Cidacs/Fiocruz Bahia: a Coorte de 100 milhões de brasileiros – cuja população é proveniente do Cadastro Único (CadÚnico) - e a Coorte de Nascimentos – resultante da vinculação entre Sinasc e Coorte de 100 milhões.

Foram consideradas as informações de todas as gestantes na faixa etária de 10 a 49 anos, registradas nas bases de dados no período de 2001 a 2015, e a população de nascidos vivos relativos ao período de 2001 e 2018.

Para avaliar os determinantes sociais relacionados à infecção, a equipe [illegible] pesquisa realizou análises com [illegible] marcadores sociais de inte[illegible] quesito raça/cor e [illegible] buscou ente[illegible] associad[illegible] [illegible]edicine [illegible]úde Coletiva [illegible]e Federal da Bahia

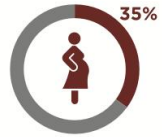
61% of gestational syphilis in Black women and 46% of gestational syphilis in Brown women could be avoided if these women had the same access to healthcare services as White women

DESIGUALDADES RACIAIS

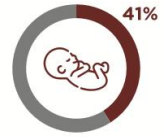
Um importante resultado do projeto é a estimativa da sífilis gestacional e congênita atribuída às desigualdades étnico-raciais. A equipe se questionou em que medida o racismo e suas manifestações é determinante para que haja diferenças nas taxas de detecção da sífilis gestacional entre mulheres pretas e mulheres pardas em comparação com as mulheres brancas.

35% de todos os casos notificados de **sífilis gestacional** e **41%** do total de casos de **sífilis congênita** seriam evitados entre mulheres negras e bebês.

CASOS NOTIFICADOS DE SÍFILIS GESTACIONAL EVITÁVEIS ENTRE MULHERES NEGRAS



CASOS NOTIFICADOS DE SÍFILIS CONGÊNITA EVITÁVEIS ENTRE CRIANÇAS DE MÃES NEGRAS



Mulheres pretas e mulheres pardas têm as maiores chances de não serem tratadas ou terem acesso a tratamento inadequado para SG quando comparada com as mulheres brancas. São elas também as que têm as maiores chances (11%) de terem acesso ao diagnóstico tardio da doença (no momento do parto ou após o mesmo) em comparação as mulheres brancas.

A proporção de SG e SC no estudo é de 0,91% e 0,5%, respectivamente. Houve também uma váriação na proporção de SG e SC de acordo com os grupos étnico-raciais, conforme os quadros a seguir."

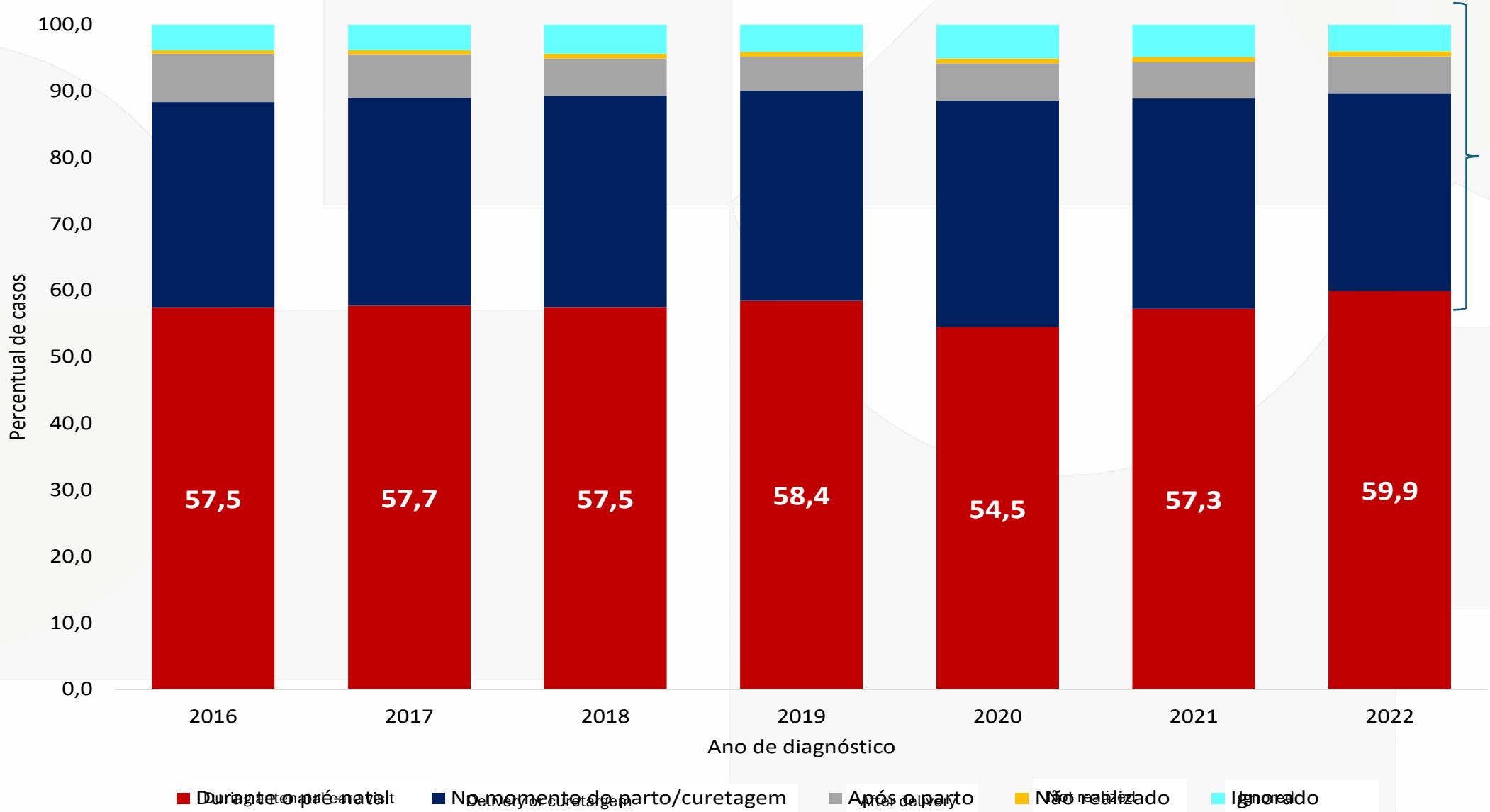
TAXA DE DETECÇÃO DE SG	
Mulheres pretas	1,71%
Mulheres pardas	1,93%
Mulheres indígenas	0,56%
Mulheres brancas	0,64%

TAXA DE DETECÇÃO DE SC	
Crianças de Mães pretas	1,02%
Crianças de Mães pardas	0,56%
Crianças de Mães indígenas	0,26%
Crianças de Mães brancas	0,31%

Fonte: Maternal and congenital syphilis attributable to ethnoracial inequalities: a national record-linkage longitudinal study of 15 million births in Brazil 2023

De acordo com a pesquisa, 61% os casos de sífilis gestacional entre as mulheres pretas e 46% dos casos entre as mulheres pardas seriam evitados se elas tivessem o mesmo acesso a serviços em saúde e tratamentos quando comparado às mulheres brancas. Quando se analisa a interseção entre os marcadores sociais raça e escolaridade, a redução de casos alcançaria quase 87% entre as mulheres negras quando comparadas às mulheres brancas com mais de 12 anos de estudo).[2]

Percentage of new cases of congenital syphilis according to the timing of maternal diagnosis and year. Brazil, 2016 to 2022



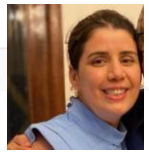
Around 30.1%

Lack of access to antenatal care?

Absence of syphilis testing during antenatal care?

Fonte: Sistema de Informação de Agravos de Notificação (Sinan), atualizado em 30/06/2023.

Innovation: Syphilis/HIV Rapid Diagnostic Test



Pilot implementation

Article *Diagnostics* **2023**, *13*(4), 810; https://doi.org/10.3390/diagnostics13040810

Assessment of the Accuracy, Usability and Acceptability of a Rapid Test for the Simultaneous Diagnosis of Syphilis and HIV Infection in a Real-Life Scenario in the Amazon Region, Brazil

by Daniela Cristina Soares [1,*], Luciano Chaves Franco Filho [1], Herald Souza dos Reis [1], Yan Corrêa Rodrigues [1], Felipe Bonfim Freitas [2], Cintya de Oliveira Souza [1], Giseli Nogueira Damacena [3], Nazle Mendonça Collaço Véras [4], Pamela Cristina Gaspar [4], Adele Schwartz Benzaken [5,6], Joana da Felicidade Ribeiro Favacho [1], Olinda Macedo [2] and Maria Luiza Bazzo [7]

(P331) Dual tests HIV/Syphilis usability and acceptance in Brazil: strategy for expanding prenatal syphilis screening

Wednesday, July 26, 2023 16:00 - 18:00 CST

Primary Presenter(s)

Adson B F Paixão
Technical consultant for diagnosis
Brazilian Ministry of Health, United States

STI & HIV 2023 WORLD CONGRESS
CHICAGO, IL USA 24-27 JULY 2023

Syphilis and HIV Among Parturient Women in Brazil: Could Duo Testing Prevent Missed Diagnoses During Pregnancy?

380

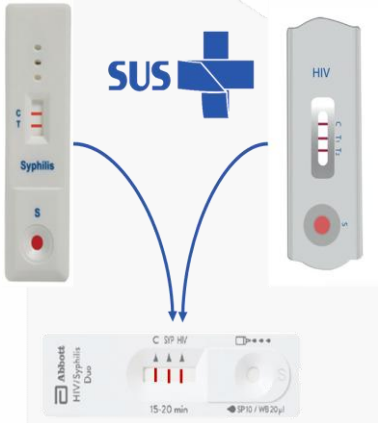
Accepted - Oral Presentation

Oral Presentation

STI&HIV2025 WORLD CONGRESS
July 26-30, 2025 · Montreal, Canada

Dr. Angelica Espinosa Miranda
Affiliations: Universidade Federal do Espírito Santo

- **E**ase of specimen collection
- **A**ffordability
- **S**ensitivity
- **S**pecificity
- **U**ser friendliness
- **R**apid and robust
- **E**quipment-free
- **D**eliverable to end-users



Implementation in SUS (Brazil)

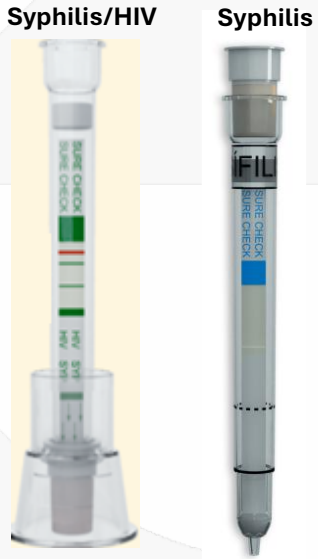
- Priority: Antenatal Care – mainly to increase rapid syphilis testing coverage (avoiding missed rapid testing opportunities)
- Pricing Challenge Overcome: From $4.00 to $0.50 per test
- 4,000,000 Bioline HIV/Syphilis Duo
- Started in May 2024
- Advocacy for expansion to other populations
- New acquisition of 6,000,000 TR DPP® HIV/Syphilis Combo – Bio-Manguinhos (Price: $0.46)
- Expansion underway for key-population testing

Innovation in progress

TR DPP® Sífilis Duo (treponemal and non-treponemal test)

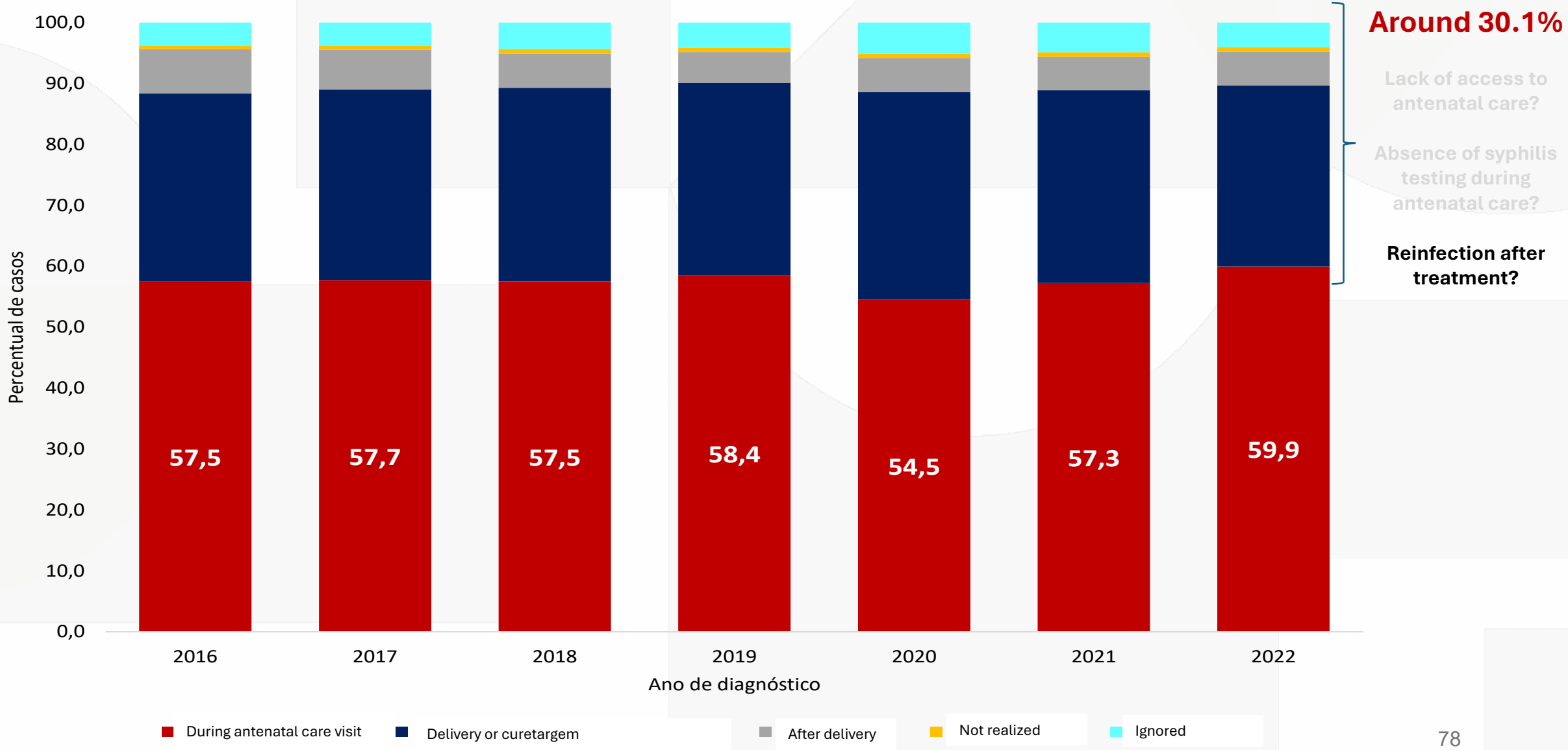
- **Laboratory analysis:** low sensitivity for non-treponemal component under 1/16 titers)
- **Real life** – how does it work? Are there change in practice comparing to treponemal rapid test + VDRL/RPR?
  - Key-population (São Paulo-SP)
  - Antenetal care (Vitória-ES)

Syphilis and HII/Syphilis self-test



- Having syphilis self-testing will help not only to increase testing access but also to **stimulate people's interest in learning more about syphilis** (demand creation on prevention, testing and treatment)
- **Usability and Acceptability Study**
- Population of the study:
  - Men who have sex with men
  - Transgender people
  - Sex workers
  - People with STIs
  - Individuals attending sexual and reproductive health clinics
  - Pregnant women and their sexual partners

Percentage of new cases of congenital syphilis according to the timing of maternal diagnosis and year. Brazil, 2016 to 2022



Fonte: Sistema de Informação de Agravos de Notificação (Sinan), atualizado em 30/06/2023.

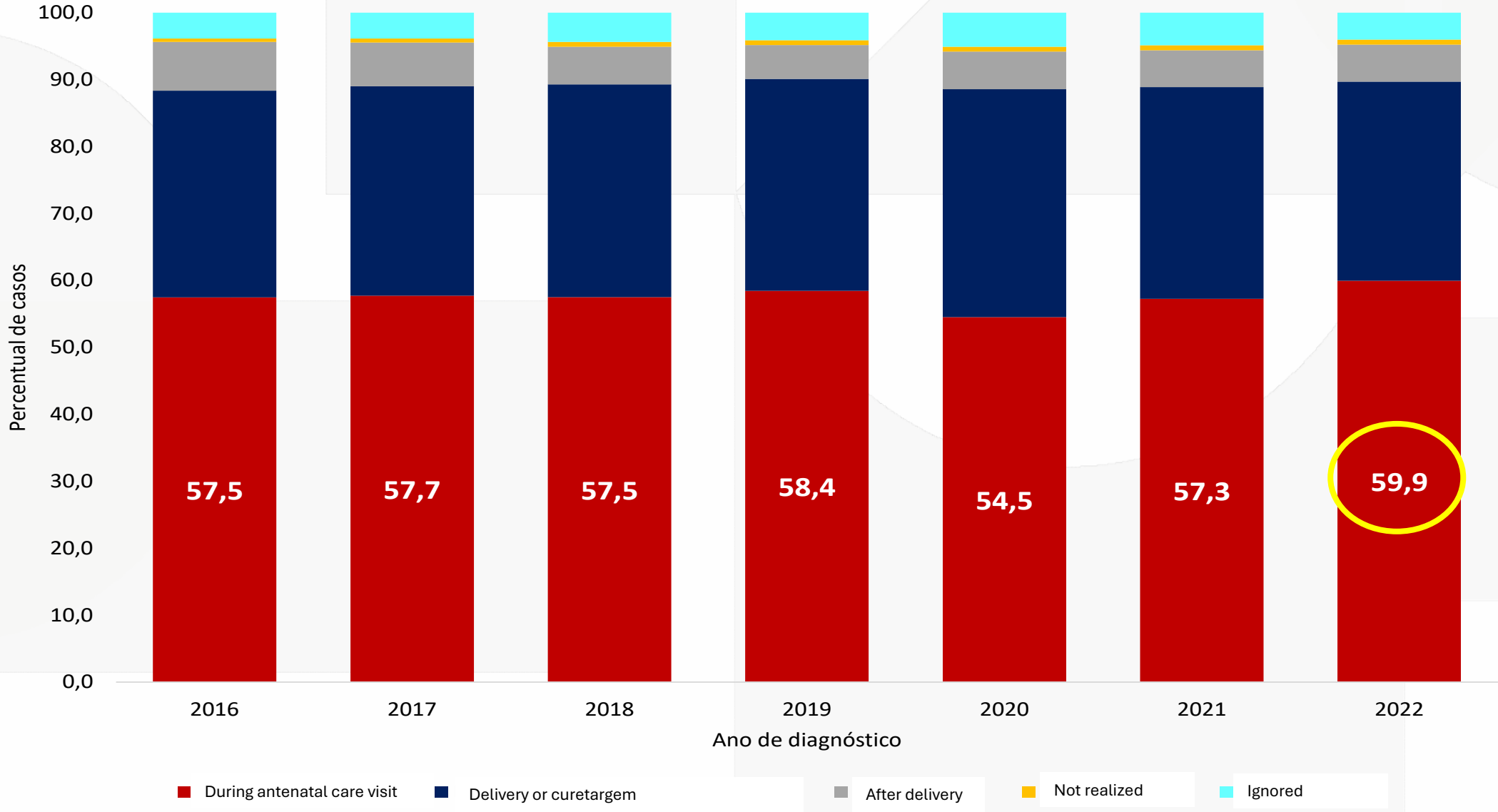
Prenatal care of the partner

Lembrete: conhecer o diagnóstico e ter acesso ao tratamento é um direito de todas as pessoas.

No que diz respeito aos exames e aos procedimentos de rotina, sugerimos os seguintes:

1. anamnese e exame físico;
2. tipagem sanguínea e fator RH (no caso da mulher ter RH negativo);
3. pesquisa de antígeno de superfície do vírus da hepatite B (HBsAg);
4. teste treponêmico e/ou não treponêmico para detecção de sífilis;
5. pesquisa de anticorpos anti-HIV;
6. pesquisa de anticorpos do vírus da hepatite C (anti-HCV);
7. em caso de sintomas presentes, testagem para covid-19;
8. hemograma;
9. lipidograma: dosagem de colesterol total, HDL e triglicerídeos;
10. dosagem de glicemia de jejum;
11. eletroforese da hemoglobina (para detecção da doença falciforme);
12. aferição de pressão arterial;
13. verificação de peso e altura para cálculo de IMC (índice de massa corporal).

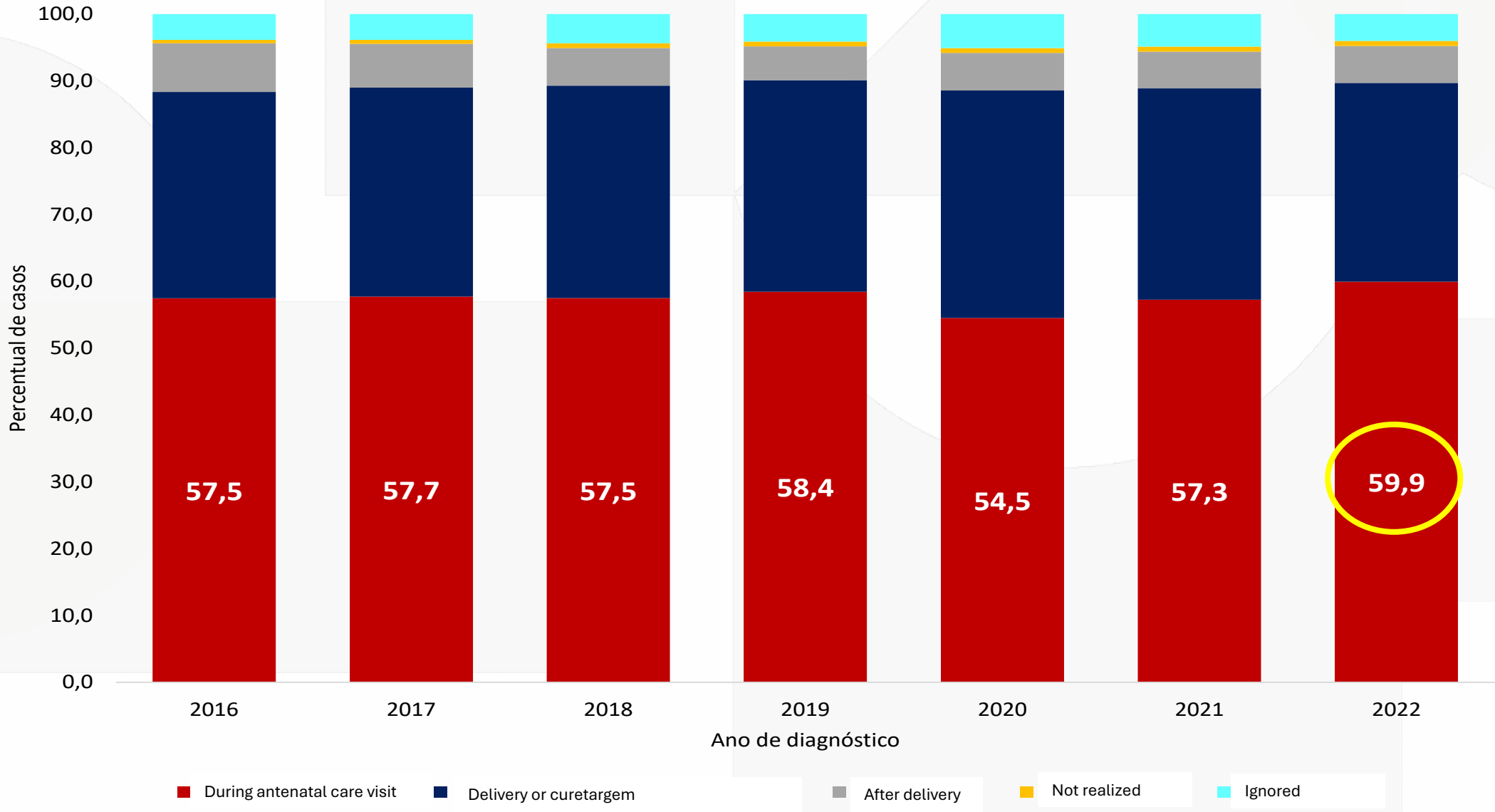
Percentage of new cases of congenital syphilis according to the timing of maternal diagnosis and year. Brazil, 2016 to 2022



15,863 cases diagnosed during antenatal care visit

Fonte: Sistema de Informação de Agravos de Notificação (Sinan), atualizado em 30/06/2023.

Percentage of new cases of congenital syphilis according to the timing of maternal diagnosis and year. Brazil, 2016 to 2022



Inadequate treatment?

Need for active follow-up to ensure treatment adherence?

Lack of case monitoring?

15,863 cases diagnosed during antenatal care visit

Fonte: Sistema de Informação de Agravos de Notificação (Sinan), atualizado em 30/06/2023.

Difficulty in defining the clinical stage for determining the treatment protocol

Resistance among professionals to administer penicillin due to the false information about a high risk of causing anaphylactic shock.

Treatment with a very painful medication

Requirement of 3 doses (6 injections) of a painful regimen, particularly in asymptomatic cases (latent syphilis).

The interval between doses must be observed; otherwise, the treatment will have to be restarted from the beginning.

Non-treponemal test for treatment monitoring, with results that may vary according to the methodology used (VDRL or RPR) and the professional conducting the test.

CeBra study

- Evaluate the efficacy of Cefixime for the treatment of non-pregnant women with active syphilis

- Evaluate the tolerance of the proposed regimen

Cefixime 400 mg PO twice daily for 10 days

Taylor et al. BMC Infectious Diseases (2020) 20:405
https://doi.org/10.1186/s12879-020-04980-1

BMC Infectious Diseases

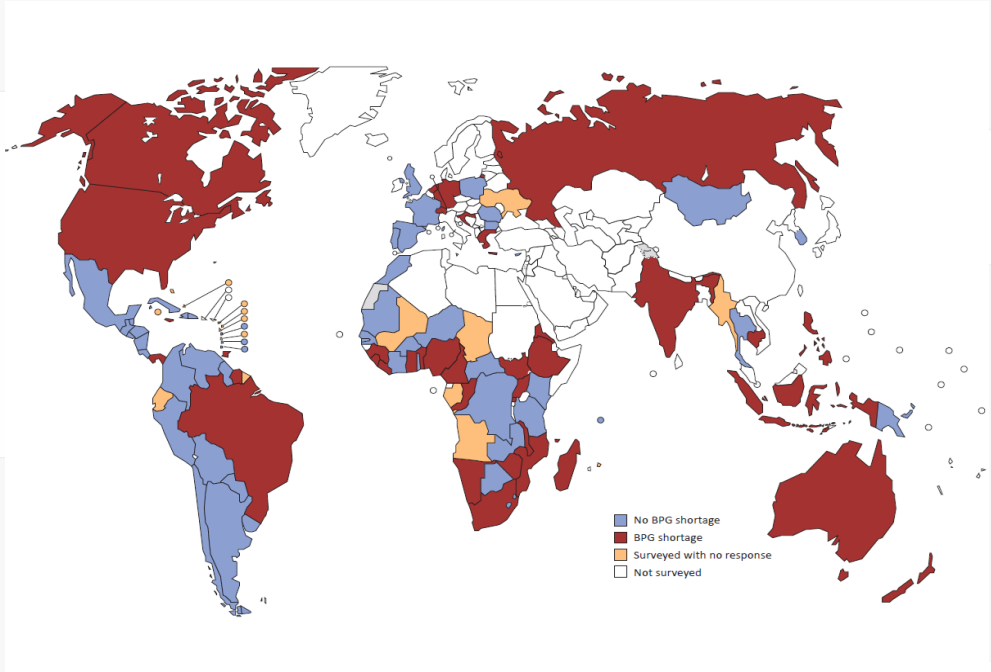
STUDY PROTOCOL Open Access

Phase II trial evaluating the clinical efficacy of cefixime for treatment of active syphilis in non-pregnant women in Brazil (CeBra)

Melanie M. Taylor[1,2*], Edna Oliveira Kara[1], Maria Alix Leite Araujo[3], Mariangela Freitas Silveira[4], Angelica Espinosa Miranda[5], Ivo Castelo Branco Coelho[6], Maria Luiza Bazzo[7], Gerson Fernando Mendes Pereira[8], Silvana Pereira Giozza[8], Ximena Pamela Díaz Bermudez[9], Maeve B. Mello[9,10], Ndema Habib[1], My Huong Nguyen[1], Soe Soe Thwin[1] and Nathalie Broutet[1]

The rationale for the Cebra study - Global situation of penicillin

- **Benzathine penicillin G (BPG) is the only medication capable of crossing the transplacental barrier to effectively treat the fetus.**
  - It is the WHO-recommended drug for the treatment of pregnant women with syphilis.
- **There is a critical need for alternative treatment options, particularly for pregnant women.**
- **Between 2014 and 2018, global shortages of penicillin were reported.**
  - As a result, many pregnant women with syphilis did not receive appropriate treatment.
  - The use of alternative therapies contributed to an estimated >500,000 cases of congenital syphilis.



Global market for penicillin

BPG is sold at a low cost

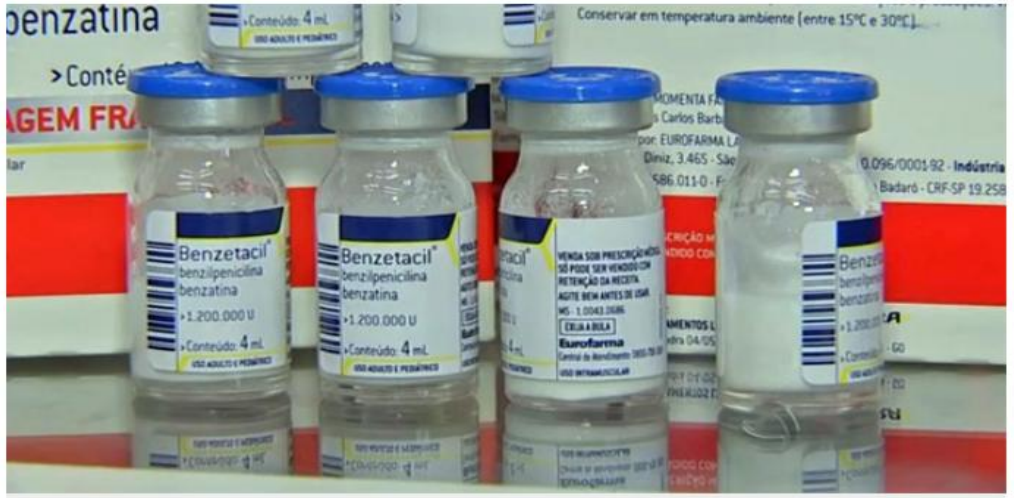
Expensive manufacturing, requiring significant financial investment in specialized infrastructure

The low market price discourages commercial manufacturers from entering or even maintaining their presence in the BPG market.

Falta de penicilina benzatina, que trata sífilis, preocupa médicos no Brasil

Crise de abastecimento foi provocada por escassez de matéria-prima. Fornecedor mundial de insumo fechou fábrica e teve que ser substituído.

Mariana Lenharo
Do G1, em São Paulo



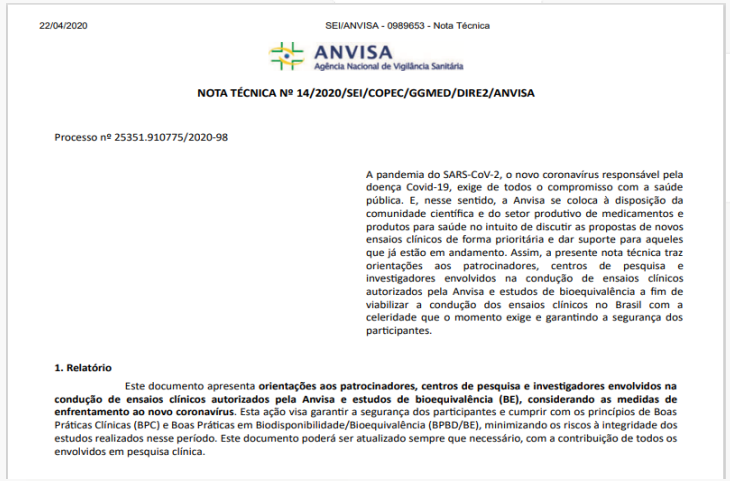
Sites of the study

Participant recruitment

- Fortaleza
- Pelotas
- Vitoria (Discontinued)

Challenges - CeBRA

Recruitment was suspended between April and November 2020.



22/04/2020 SEI/ANVISA - 0989653 - Nota Técnica

ANVISA
Agência Nacional de Vigilância Sanitária

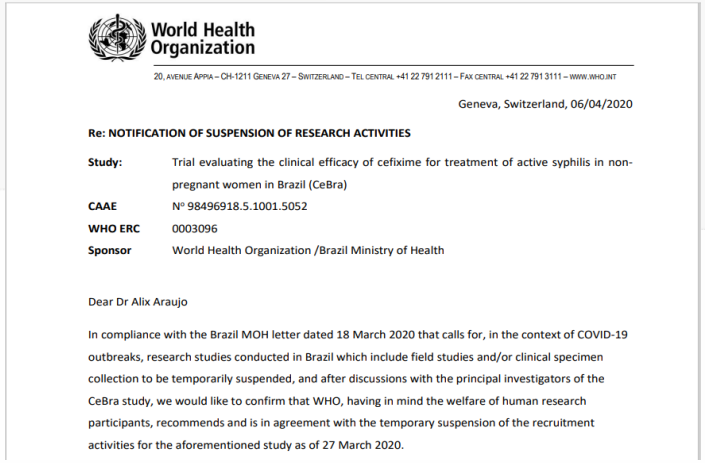
NOTA TÉCNICA Nº 14/2020/SEI/COPEC/GGMED/DIRE2/ANVISA

Processo nº 25351.910775/2020-98

A pandemia do SARS-CoV-2, o novo coronavírus responsável pela doença Covid-19, exige de todos o compromisso com a saúde pública. E, nesse sentido, a Anvisa se coloca à disposição da comunidade científica e do setor produtivo de medicamentos e produtos para saúde no intuito de discutir as propostas de novos ensaios clínicos de forma prioritária e dar suporte para aqueles que já estão em andamento. Assim, a presente nota técnica traz orientações aos patrocinadores, centros de pesquisa e investigadores envolvidos na condução de ensaios clínicos autorizados pela Anvisa e estudos de bioequivalência a fim de viabilizar a condução dos ensaios clínicos no Brasil com a celeridade que o momento exige e garantindo a segurança dos participantes.

1. Relatório

Este documento apresenta **orientações aos patrocinadores, centros de pesquisa e investigadores envolvidos na condução de ensaios clínicos autorizados pela Anvisa e estudos de bioequivalência (BE), considerando as medidas de enfrentamento ao novo coronavírus**. Esta ação visa garantir a segurança dos participantes e cumprir com os princípios de Boas Práticas Clínicas (BPC) e Boas Práticas em Biodisponibilidade/Bioequivalência (BPBD/BE), minimizando os riscos à integridade dos estudos realizados nesse período. Este documento poderá ser atualizado sempre que necessário, com a contribuição de todos os envolvidos em pesquisa clínica.



World Health Organization

20, AVENUE APPIA – CH-1211 GENEVA 27 – SWITZERLAND – TEL CENTRAL +41 22 791 2111 – FAX CENTRAL +41 22 791 3111 – WWW.WHO.INT

Geneva, Switzerland, 06/04/2020

Re: NOTIFICATION OF SUSPENSION OF RESEARCH ACTIVITIES

Study: Trial evaluating the clinical efficacy of cefixime for treatment of active syphilis in non-pregnant women in Brazil (CeBra)
CAAE Nº 98496918.5.1001.5052
WHO ERC 0003096
Sponsor World Health Organization /Brazil Ministry of Health

Dear Dr Alix Araujo

In compliance with the Brazil MOH letter dated 18 March 2020 that calls for, in the context of COVID-19 outbreaks, research studies conducted in Brazil which include field studies and/or clinical specimen collection to be temporarily suspended, and after discussions with the principal investigators of the CeBra study, we would like to confirm that WHO, having in mind the welfare of human research participants, recommends and is in agreement with the temporary suspension of the recruitment activities for the aforementioned study as of 27 March 2020.

Lockdown

- Closure of health facilities for a prolonged period.
- Suspension of rapid testing campaigns.
- Reduced patient attendance at health facilities due to fear of SARS-CoV-2 infection.

Patients presenting with low RPR titers.

Complex bureaucracy related to RPR kit importation.

- Regulatory changes.
- Requirement to contract a company specialized in import logistics.
- Importation processes lasted 4–6 months, causing delays in the study (including 2 suspensions).
- Elevated procedural costs.
- Lengthy approval timelines by ANVISA.

Increased vulnerability of the study population.

- Patients from higher socioeconomic backgrounds expressed fear of exposure when attending the study site.
- Adherence to the study protocol, requiring a 9-month follow-up, represented an additional challenge.**

Adherence to the protocol (9-month follow-up)

Collaborators

SUS

MINISTÉRIO DA SAÚDE

GOVERNO FEDERAL

BRASIL

UNIÃO E RECONSTRUÇÃO

Organização Pan-Americana da Saúde

World Health Organization

human reproduction programme hrp

research for impact

UNDP · UNFPA · UNICEF · WHO · WORLD BANK

FUNDAÇÃO EDSON QUEIROZ

UNIVERSIDADE DE FORTALEZA

ENSINANDO E APRENDENDO

UNIVERSIDADE FEDERAL DO CEARÁ

UNIVERSIDADE FEDERAL DE PELOTAS

RS - BRASIL

UNIVERSIDADE FEDERAL DO ESPÍRITO SANTO

DOCETE OMNES GENTES

UFES

UFSC

Funding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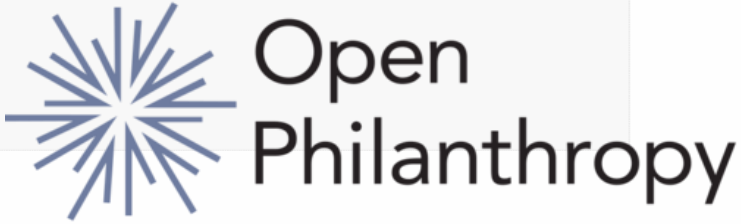
Open
Philanthropy


GATES foundation

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Maria Alix Leite Araujo

Professora do Programa de Pós-Graduação em Saúde Coletiva

Universidade de Fortaleza – UNIFOR

Contact: mleite@unifor.br

We need to talk more about syphilis!

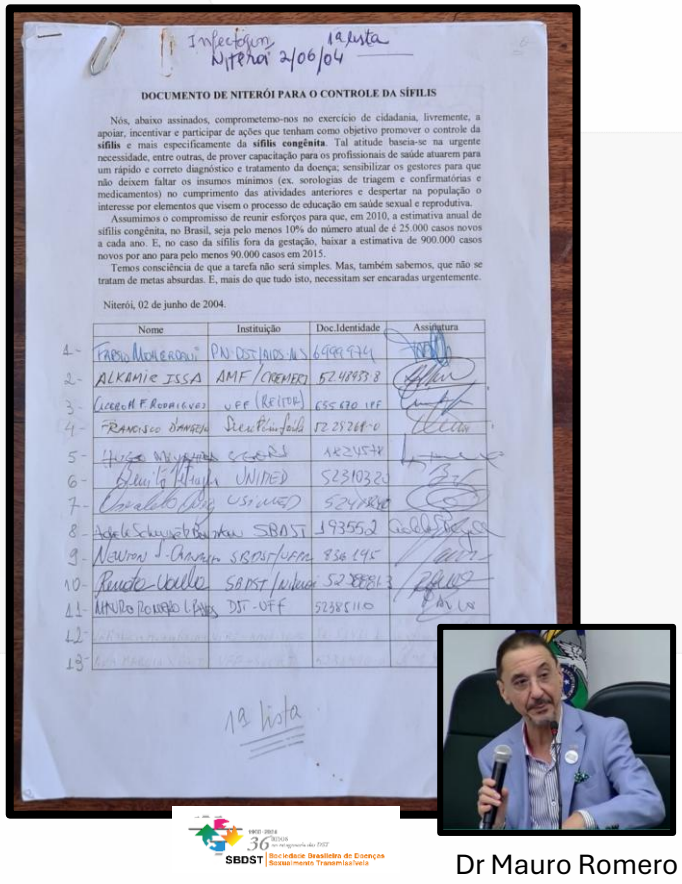
WHO?

Everyone!

Cecília Li

The National Day for the Fight Against Syphilis and Congenital Syphilis – 3rd Saturday of October

A petition promoted by the **Brazilian Society of Sexually Transmitted Diseases** in 2004, signed by healthcare professionals, public health managers, and scientists, resulted in a bill proposed in the Federal Congress requesting the establishment of Syphilis Day.



Dr Mauro Romero

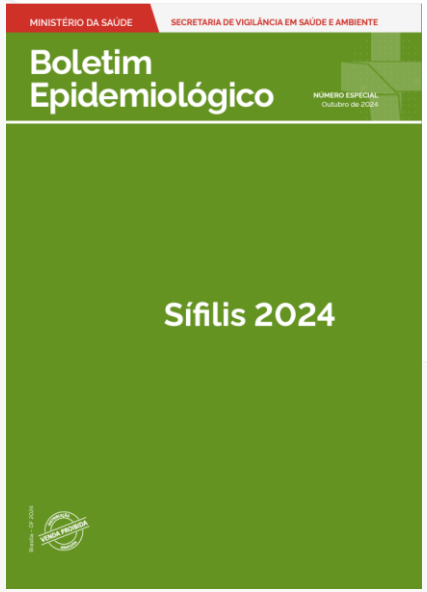
The **Ministry of Health** worked with the Chamber of Deputies to ensure the bill was voted on. After approval by the Chamber of Deputies, the National Day for the Fight Against Syphilis and Congenital Syphilis was passed in the Senate.

Law 13,430/2017

Dr Adele Benzaken

Last year (Ministry of Health)...

Epidemiological bulletin

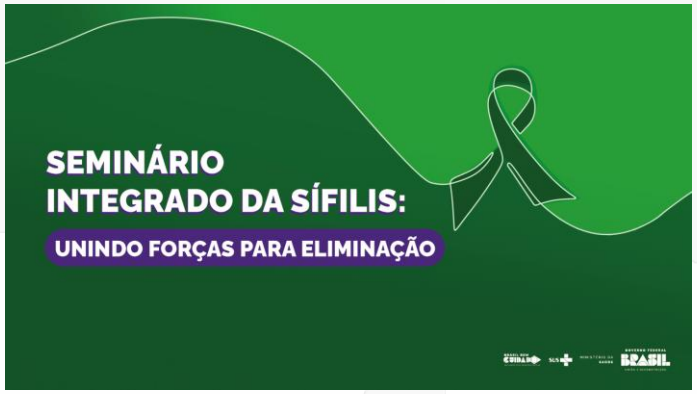


Published annually on the third Saturday of October - National Syphilis Awareness Day.

www.gov.br/saude/pt-br/centrais-de-conteudo/publicacoes/boletins/epidemiologicos/especiais/2024/boletim-epidemiologico-de-sifilis-numero-especial-out-2024.pdf

National Campaign

Integrated Seminar: Joining Forces for Elimination



Last year (states, municipalities, scientific societies)...

State of Sergipe: Prevention in the square

City of Maceió (State Alagoas)

Brazilian Society of Sexually Transmitted Diseases: Banner about syphilis and information on syphilis on the big screen at one of Brazil's biggest football matches (Fla X Flu)

Last year (states, municipalities, scientific societies)...

State of Espírito Santo: social media

Webinar of the Brazilian Society of Pediatrics

Webinar of the regional medical council of Rio de Janeiro

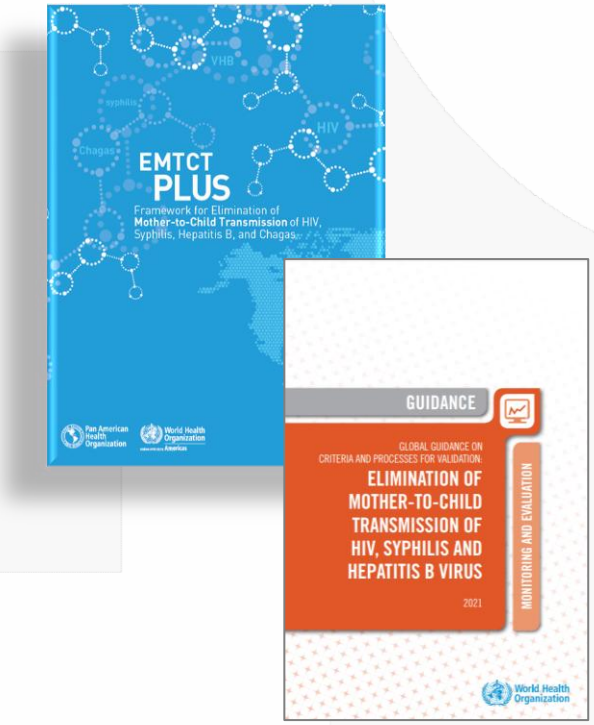
Actions not only on National Day, but also throughout the entire month – Green October!

Elimination of mother-to-child transmission: INTERNATIONAL COMMITMENTS

Pan American Health Organization

World Health Organization

Brazil is part of a group of countries, along with the **Pan American Health Organization (PAHO)** and the **World Health Organization (WHO),** that are committed to eliminating the mother-to-child transmission of HIV, syphilis, Hepatitis B, Chagas disease, and HTLV as a public health problem.



SUSTAINABLE DEVELOPMENT GOALS

3 GOOD HEALTH AND WELL-BEING

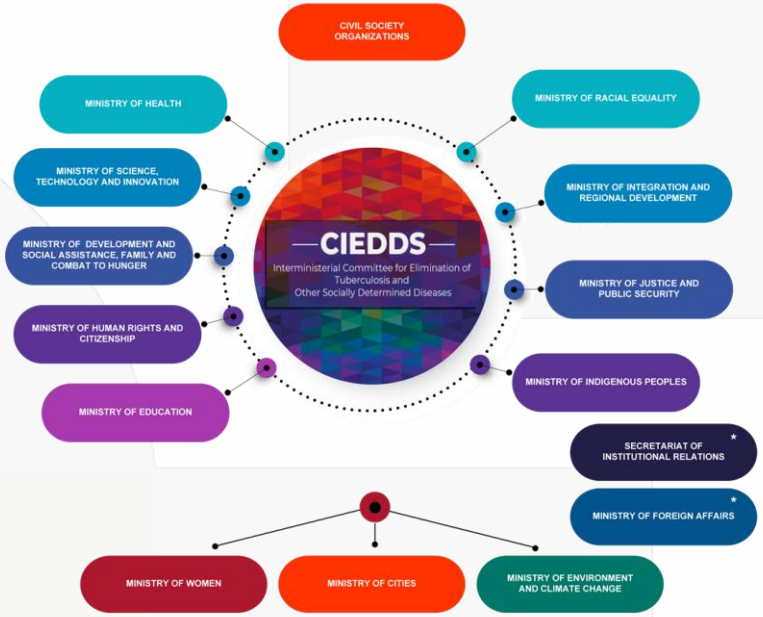
3.3 By 2030, end the epidemics of AIDS, tuberculosis, malaria and neglected tropical diseases and combat hepatitis, water-borne diseases and other communicable diseases.

ELIMINATION OF MOTHER-TO-CHILD TRANSMISSION: NATIONAL COMMITMENTS

IMPACT GOALS

- Reduce the vertical transmission rate of HIV to ≤ 2% by 2025.
- Reduce the incidence of congenital syphilis (including stillbirths) to ≤ 0.5 cases per 1,000 live births by 2030.
- Reduce the prevalence of HBsAg in children aged 4 to 6 years to ≤ 0.1% by 2030. (under revision)
- Achieve proven cure, confirmed by negative serological test after treatment, in 90% or more of children diagnosed with T. cruzi infection by 2030.
- HTLV: Indicators for MTCT elimination under development.

BRAZILIAN GOVERNMENT'S COMMITMENT



HEALTHY BRAZIL
Together to care

BRASIL SAUDÁVEL
Unir para cuidar

Diseases **expected to be eliminated as a public health problem by 2030**

- Malaria
- Geohelminthiasis
- Trachoma
- Lymphatic Filariasis
- Onchocerciasis
- Chagas Disease
- Schistosomiasis

Vertical Transmission

- Chagas Disease
- Syphilis
- Hepatitis B
- HIV
- HTLV

Diseases expected to reach the WHO and MoH **operational targets** by 2030

Tuberculosis
Incidence ≤ 10 cases per 100,000 inhabitants

Leprosy
Prevalence < 1 case per 10,000 inhabitants*

Hepatitis
Diagnose 90% of people

Treat 80% of people diagnosed

Reduce new infections by 90%

Reduce mortality by 65%

HIV
95% of people living with HIV diagnosed

95% of the people living with HIV on antiretroviral treatment

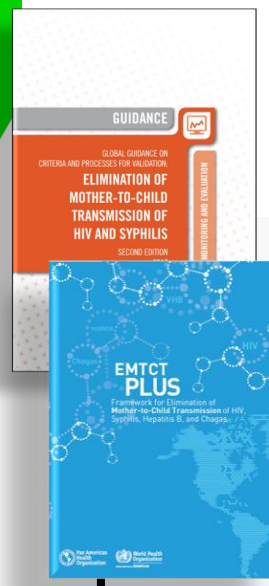
95% of people living with HIV with suppressed viral load

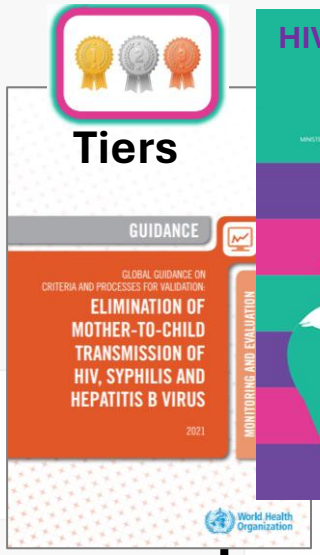
Subnational Certification of Elimination of Mother-to-Child Transmission of HIV, Syphilis, Hepatitis B, Chagas Disease, and HTLV in Brazil

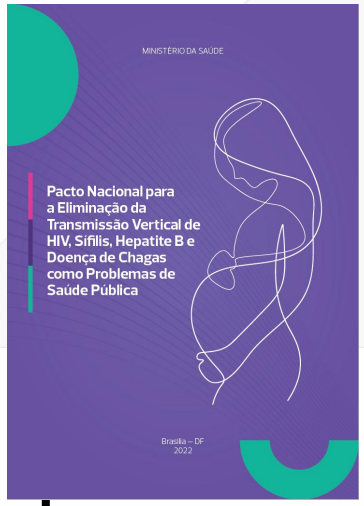
Municipalities ≥100,000 inhabitants and Federal Units, including the possibility for the bronze, silver or gold tiers certification in “the path to elimination”, encouraging gradual reduction in MTCT rates

Encourage, support, and recognize the local efforts to elimination of MTCT

Subnational certification EMTCT

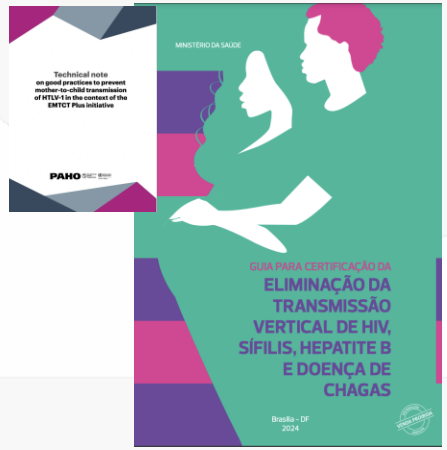






HIV, Syphilis, Hepatitis B and chagas Disease

HIV, Syphilis, Hepatitis B, Chagas disease and HTLV



2017

HIV EMTCT:
1 city
- Curitiba

2018

2019

HIV EMTCT:
2 cities
- Umuarama
- São Paulo

2021

HIV EMTCT: 28 cities
Syphilis EMTCT: 1 city
HIV MTCT tiers: 10 cities
Syphilis MTCT tiers: 21 cities
TOTAL: 43 cities

2022

2023

HIV EMTCT: 37 cities
Syphilis EMTCT: 1 city
HIV MTCT tiers: 33 cities
Syphilis MTCT tiers: 27 cities
TOTAL: 73 cities

Federal units certified:
- **HIV Silver MTCT tier:** 2 states
- **EMTCT and bronze MTCT tier for syphilis:** 2 states

2024

HIV EMTCT: 20 cities
Syphilis EMTCT: 2 cities
Hepatitis B EMTCT: 1 city
HIV MTCT tiers: 31 cities
Syphilis MTCT tiers: 25 cities
Hepatitis B MTCT tiers: 17 cities
TOTAL: 60 cities

Federal units certified:
- **HIV Silver MTCT tier:** 2 states
- **HIV EMTCT and bronze MTCT tier for syphilis:** 1 state

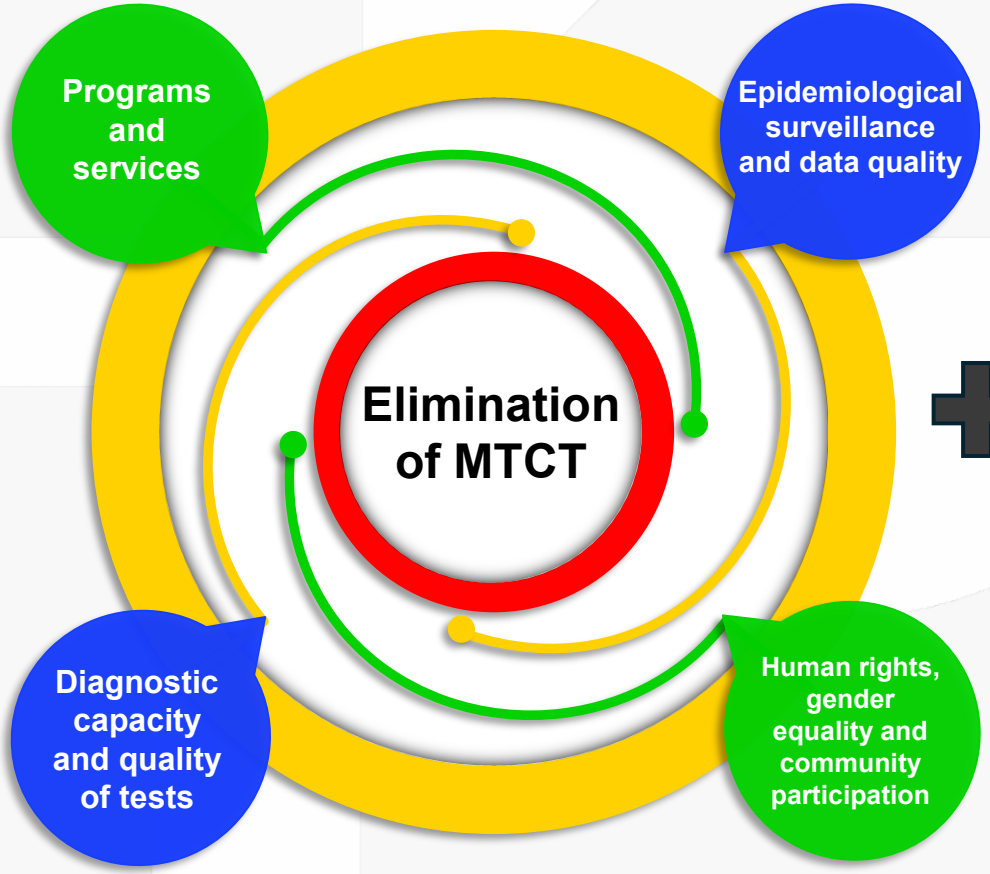
2025

HTLV

A total 151 municipalities and 7 federal states with some certification until 2025

Analyze **public health programs and services organized within the Unified Health System (SUS),** for the **prevention of mother-to-child transmission** of HIV, syphilis, Hepatitis B, and Chagas disease.

- Primary Health Care (PHC) units
- Referral services (high-risk prenatal care,
- Follow-up for exposed/infected children
- Specialized outpatient services for HIV, AIDS, and VH
- Institutions that provide childbirth services, especially in areas with greater social and individual vulnerability.



+ **Committees for MTCT investigation**

- **Adequacy of the service network for providing diagnostic tests** (rapid and/or conventional tests for HIV, syphilis, Hepatitis B, and Chagas disease) **and for monitoring pregnant women and newborns** (e.g., viral load tests and CD4+ T-cell count).
- It also evaluates whether the obtained **results are accurate and reliable**.
- It examines whether the **execution of diagnostic tests and monitoring exams meets established quality control and management standards** (laboratory quality management, the quality of diagnostic components, the competence of the team performing the tests, and the management of laboratory data)

- **Coverage of case screening, diagnosis, and treatment during prenatal** care is assessed, along with the follow-up of children exposed to or infected with HIV, syphilis, Hepatitis B, and Chagas disease.
- The **reporting and investigation of cases by health services** (public, contracted, affiliated with SUS, and private) in locations that have eliminated vertical transmission or are on the path to elimination are evaluated.

- The broader concept of health encompasses the analysis of multiple social determinants, as well as risk factors and vulnerabilities that may affect pregnant women's and newborns' access to the necessary care for preventing vertical transmission.
- The evaluation of this thematic area aims to **assess the guarantee of human rights, including gender, racial, and ethnic equality,** as well as ensuring **community participation and civil society involvement** in the development, monitoring, and evaluation of public policies.

IMPACT TARGETS (ADAPTED) – ELIMINATION AND TIERS

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Impact target	Elimination	Parameters			Assessment period
		Gold	Silver	Bronze	
1) Incidence rate of HIV-infected children due to mother-to-child transmission	≤ 0.5 case per 1,000 Live Births (LBs)	≤ 1.0 case per 1,000 LBs	≤ 1.5 cases per 1,000 LBs	≤ 2.0 cases per 1,000 LBs	At least for one year (last full year)
2) Rate of mother-to-child transmission of HIV (public and private sectors)	≤ 2%	≤ 2%	≤ 2%	≤ 2%	
3) Incidence rate of congenital syphilis	≤ 0.5 case per 1,000 LBs	≤ 2.5 cases per 1,000 LBs	≤ 5.0 cases per 1,000 LBs	≤ 7.5 cases per 1,000 LBs	
4) Hepatitis B surface antigen (HBsAg) prevalence in children ≤5 years old	≤ 1.0 case per 1,000 ≤5-year-old birth	≤ 1.0 case per 1,000 ≤5-year-old birth	≤ 2.0 cases per 1,000 ≤5-year-old birth	≤ 3.0 cases per 1,000 ≤5-year-old birth	
5) Coverage of etiological treatment for children aged 0 to 3 years diagnosed with *T. cruzi* infection	≥ 90%	≥ 90%	≥70%	15% increase in coverage compared to the previous baseline year	At least for two years (last two full years)
6) Incidence rate of acute Chagas disease among women in child-bearing age	≤ 0.5 case per 100,000 women in child-bearing age	≤ 1.0 case per 100,000 women in child-bearing age	≤ 1.5 cases per 100,000 women in child-bearing age	≤ 2.0 cases per 100,000 women in child-bearing age	

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SUS
MINISTÉRIO DA SAÚDE
GOVERNO FEDERAL BRASIL UNIÃO E RECONSTRUÇÃO

IMPACT TARGETS (ADAPTED) – ELIMINATION AND TIERS

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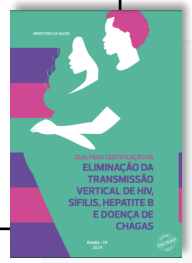
Process target	Elimination	Parameters			Assessment period
		Gold	Silver	Bronze	
1) Minimum coverage of 4 (four) prenatal care visits	≥ 95%	≥ 95%	≥ 90%	≥ 90%	At least for two years (last two full years)
2) Coverage for pregnant women who underwent at least one HIV test during prenatal care					
3) Coverage for pregnant women living with HIV using antiretroviral therapy during prenatal care					
4) Coverage for pregnant women who underwent at least one syphilis test during prenatal care					
5) Coverage for pregnant women adequately treated for syphilis during prenatal care					
6) Coverage for Hepatitis B vaccine in children (up to 30 days after birth)		≥ 90%	≥ 85%	≥ 80%	
7) Coverage for three doses of Hepatitis B vaccine (infant vaccination)					
8) Coverage for pregnant women who underwent at least one HBV test during prenatal care	≥ 90%	≥ 85%	≥ 80%	≥ 70%	
9) Coverage for pregnant women who underwent at least one Chagas disease test during prenatal care			≥ 70%	15% increase in coverage compared to the previous baseline year	
10) Coverage for testing diagnosis for children ≤ 1 year old exposed to *T. cruzi* through vertical transmission					
11) Coverage of etiological treatment for Chagas disease among women in child-bearing age					



IN SUMMARY: CERTIFICATION OF FEDERATED STATES AND MUNICIPALITIES WITH ≥100,000 INHABITANTS

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- **In total, 151 municipalities and 7 states obtained some form of certification or seal, with certain locations holding more than one (one for each infection), amounting to 228 active municipal certifications.**
  - HIV vertical transmission certifications (139): 72 elimination certifications; 67 silver seals.
  - Syphilis vertical transmission certifications (58): 3 elimination certifications; 10 gold seals; 45 silver seals; 13 bronze seals.
  - Hepatitis B vertical transmission certifications (18): 1 elimination certification; 3 gold seals; 6 silver seals; 8 bronze seals.

- **At the state level, 10 certifications were awarded across 7 states:**
  - Elimination certification for HIV vertical transmission and bronze seal towards syphilis vertical transmission elimination: São Paulo, Paraná, and Santa Catarina.
  - *Silver seals towards elimination of HIV vertical transmission:* Goiás, Federal District, Sergipe, and Minas Gerais.

EMTCT CERTIFICATION CEREMONY

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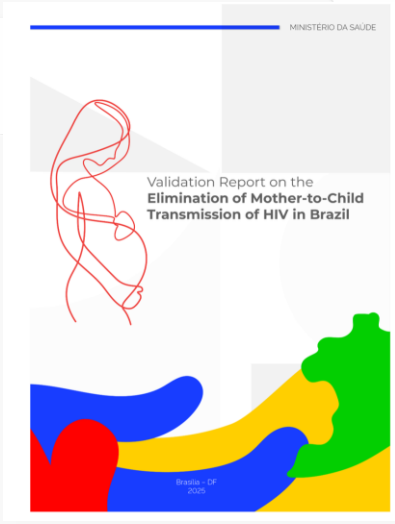


Forty years ago, it seemed impossible….

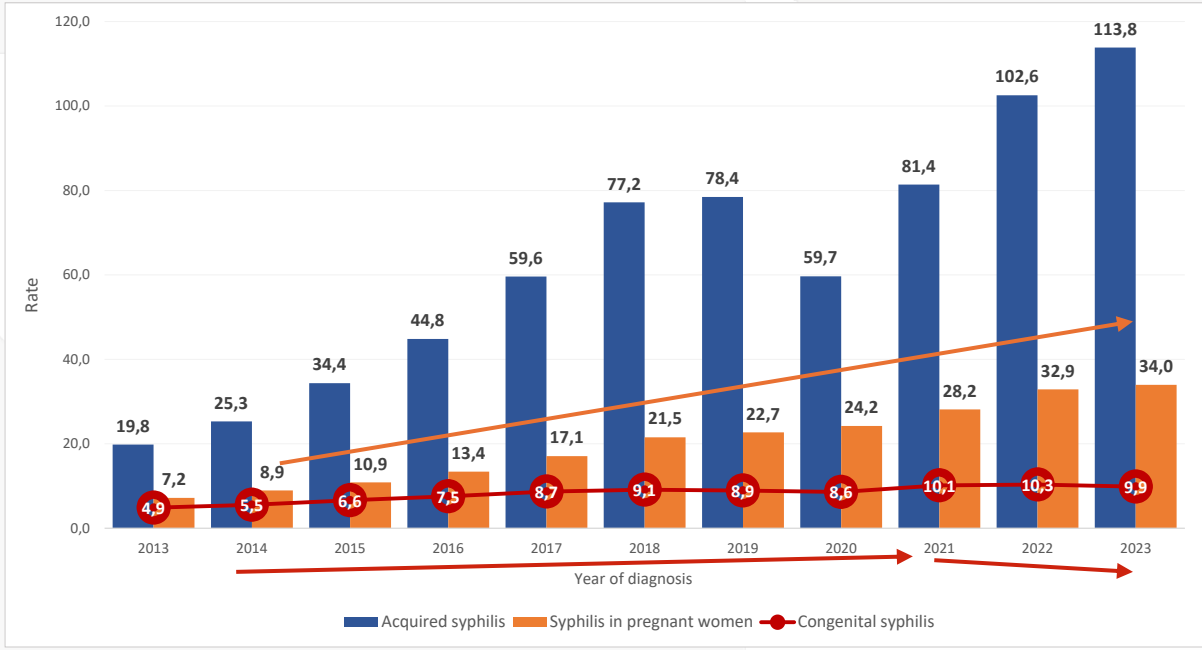
And today, it is a reality!

Request for CERTIFICATION of the Elimination of Mother-to-child Transmission of HIV in Brazil for PAHO/WHO in June/2025

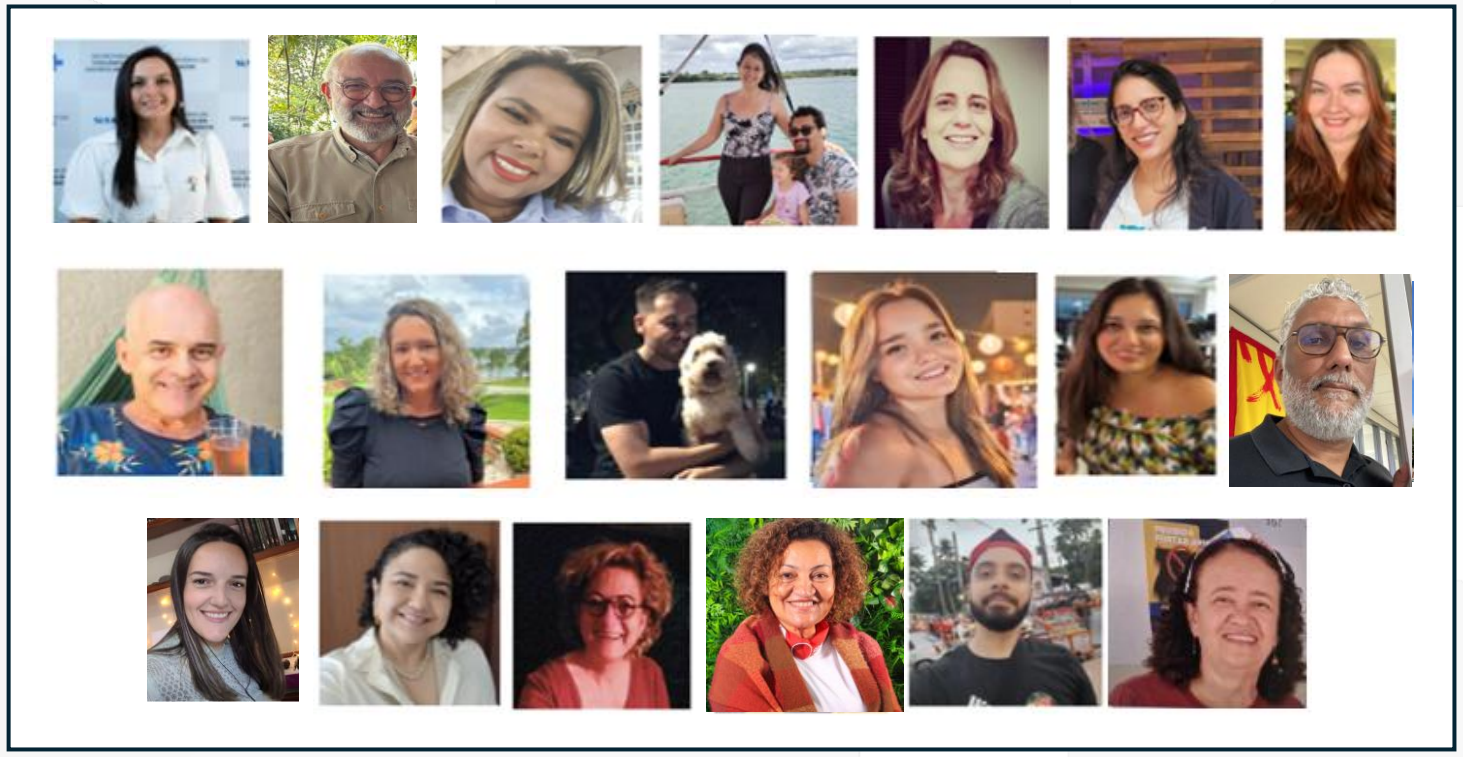
The **HIV Rapid Diagnostic Test** has played a central role in increasing access and preventing HIV vertical transmission…

…and it is also proving **essential** in the fight against **syphilis.**

Detection rate of acquired syphilis (per 100,000 population), detection rate of syphilis in pregnant women, and incidence rate of congenital syphilis (per 1,000 live births), by year of diagnosis. Brazil, 2013-2023



We have finally managed to **reverse the upward trend of congenital syphilis**, and we continue moving forward toward **elimination.**



On behalf of the

General Coordination for the Surveillance of Sexually Transmitted Infections –

CGIST and Dathi

Thank you!

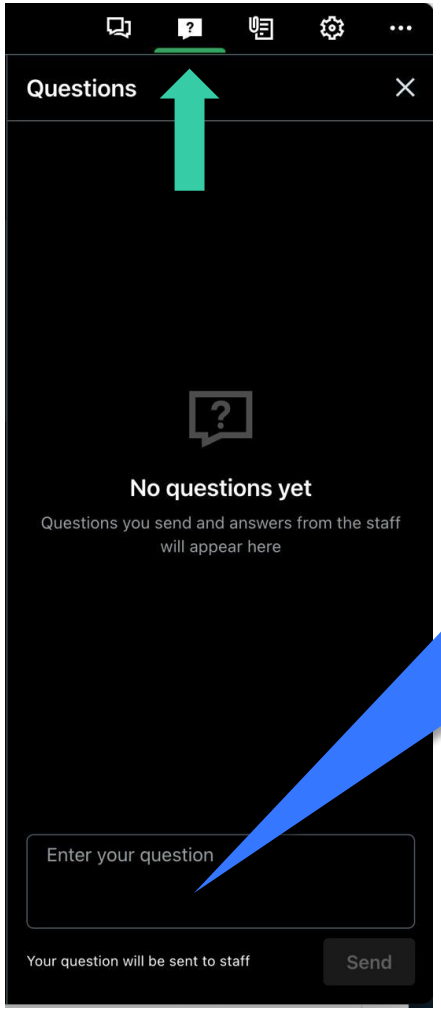
Obrigada!

pamela.gaspar@aids.gov.br
cgist@aids.gov.br

How to submit your questions

REVIVE by GARDP

If your question is addressed to a specific speaker, please include their name when submitting the question.



Please submit your questions through the box provided after clicking the ‘questions’ button. We will review all questions and respond to as many as possible after the presentation.

Today's speakers

REVIVE by GARDP

Challenges and opportunities in the treatment of syphilis

Moderator:
Esther Bettiol
GARDP,
Switzerland

Laura Hinkle Bachmann
Centers for Disease Control and Prevention, USA

Pâmela Cristina Gaspar
Ministry of Health, Brazil

Upcoming webinars

REVIVE by GARDP

Overcoming challenges of tuberculosis drug discovery and development

- With Jeremy Rock, Dirk Schnappinger & Laura Cleghorn
- 9 September 2025, 15:30-17:00 CEST

Introducing the REVIVE journal club

REVIVE by GARDP

- Authors of the latest publications in antimicrobial R&D will discuss their findings.
- Please share your pick of recently published articles within antimicrobial R&D
- Publication dates from 1 Oct 2024 up to today are eligible.

Thank you for joining us