Syphilis in the Americas

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TTIMS Program
REDS-IV-P Brazil

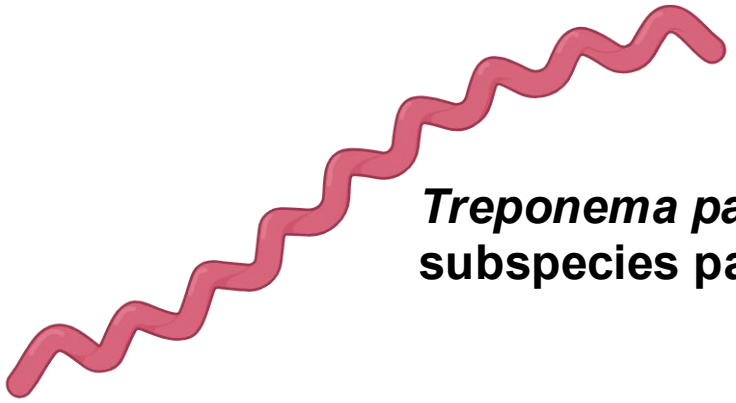


IPFA/PEI 31st International Workshop on Surveillance and Screening of Blood-borne Pathogens

14 - 15 May 2025 | Heidelberg, Germany

Overview

- Background on syphilis
- General population data
- Blood donor data
- Considerations/possible directions



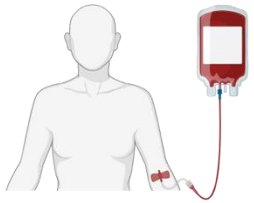
***Treponema pallidum*, subspecies pallidum**



Sexual transmission



Transplacental transmission



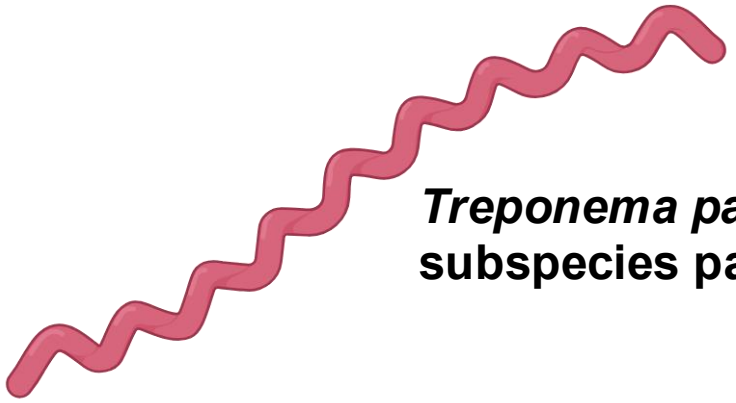
Transfusion transmission

Pinta (also known as azul, carate, empeines, lota, mal del pinto, and tina) is a human skin disease caused by infection with the spirochete ***Treponema carateum***, which is morphologically and serologically indistinguishable from the bacterium that causes syphilis and bejel.

While pinta has become extremely rare over the past several decades due to widespread antibiotic treatment, it may still exist in remote areas.[1]

[1] https://rarediseases.org/rare-diseases/pinta/

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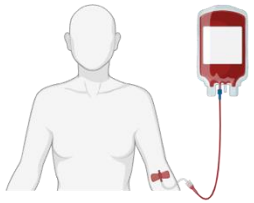
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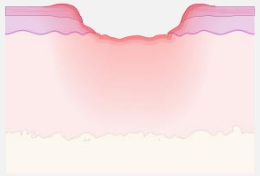
Transplacental transmission



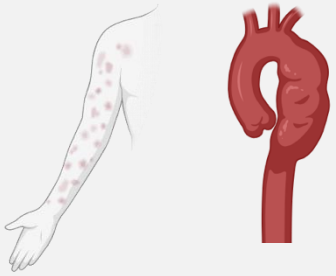
Transfusion transmission

Clinical presentation:

- Asymptomatic (latent)

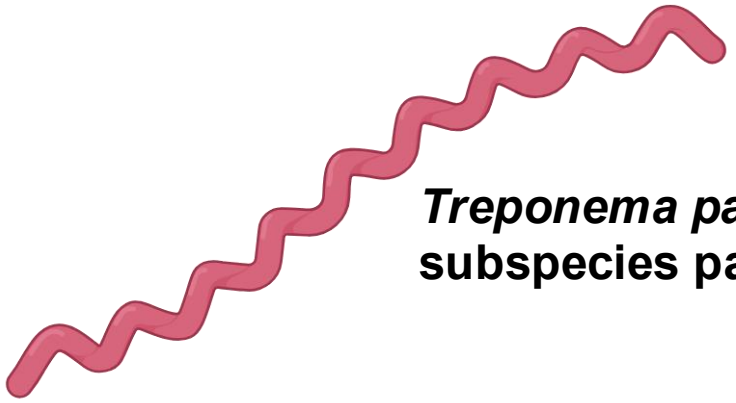


- Symptomatic
  - Primary
  - Secondary
  - Tertiary



- Congenital

Image created with www.biorender.com



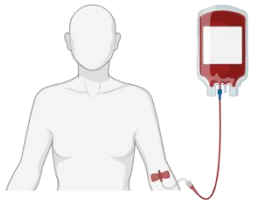
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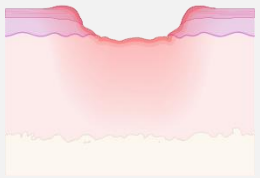
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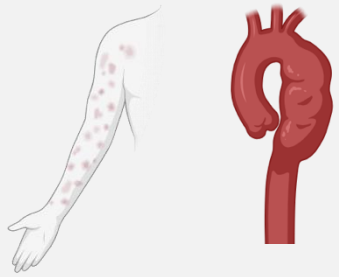


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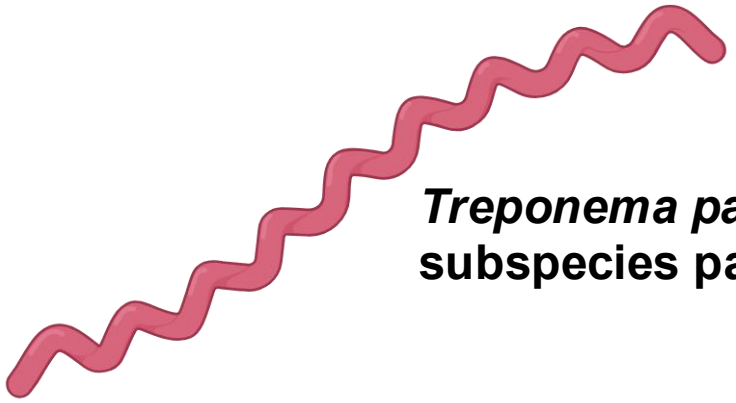




Diagnosis:

-*T. pallidum* detection in samples collected from skin/mucosal lesions (dark field microscopy; PCR)
-Serologic tests (treponemal; non-treponemal)

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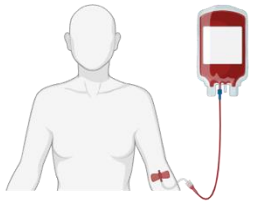
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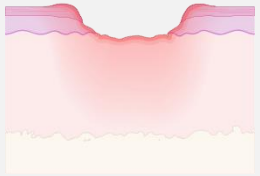
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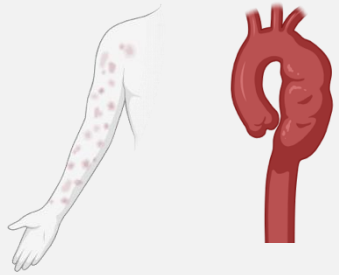


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Diagnosis:

-*T. pallidum* detection in samples collected from skin/mucosal lesions (dark field microscopy; PCR)
-Serologic tests (treponemal; non-treponemal)

Monitoring asymptomatic infections is challenging in the absence of routine testing of lower-risk populations

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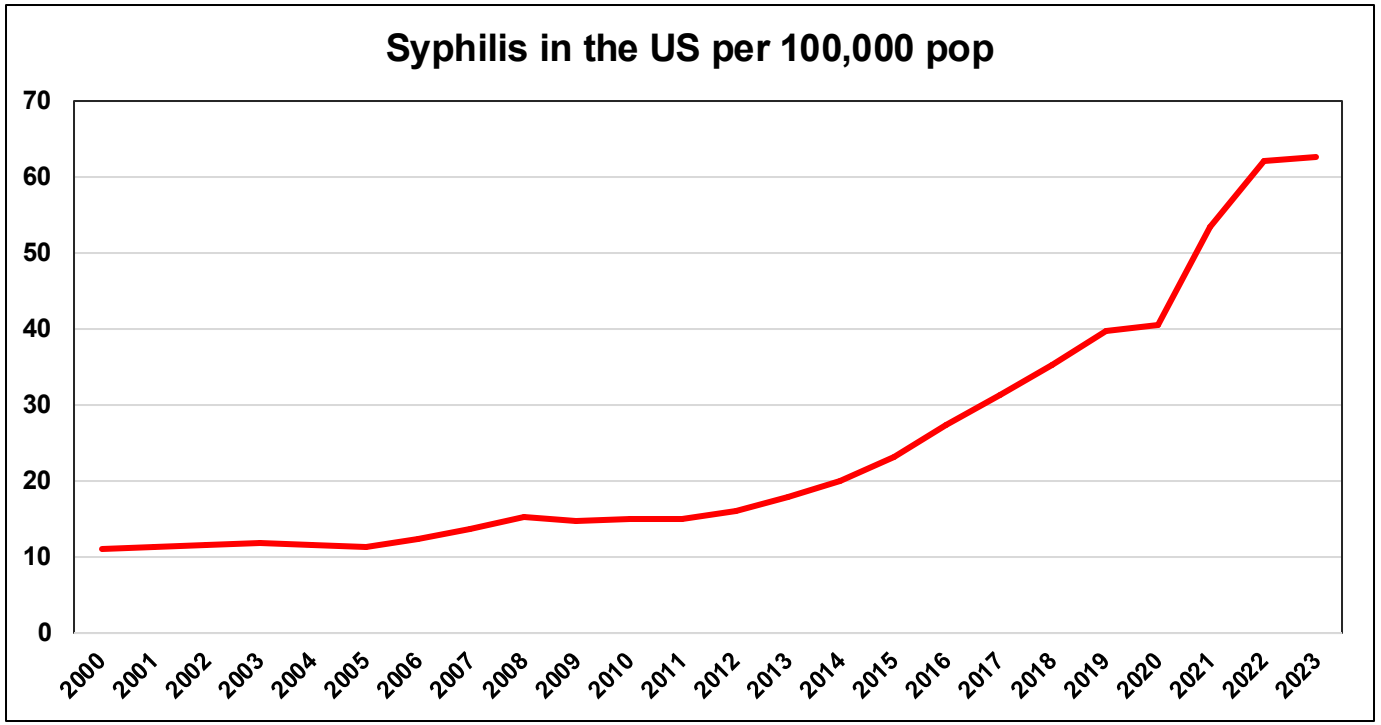
Syphilis in the general population

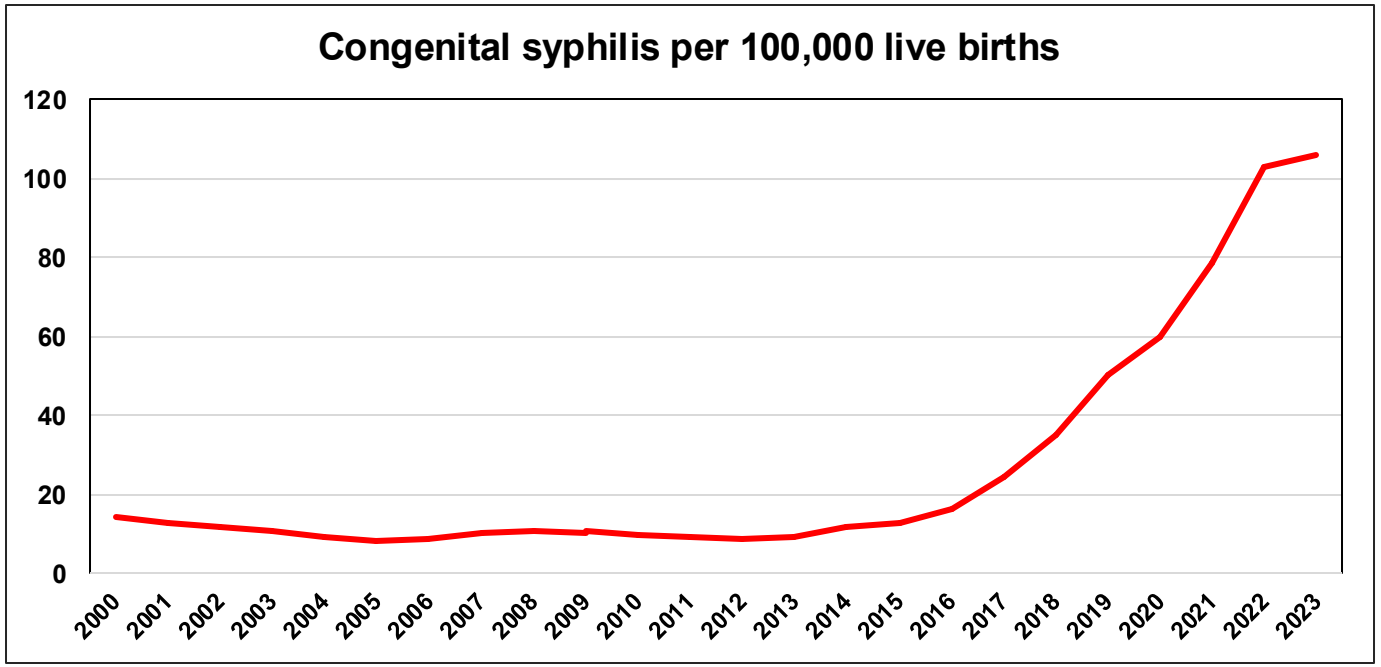


United States

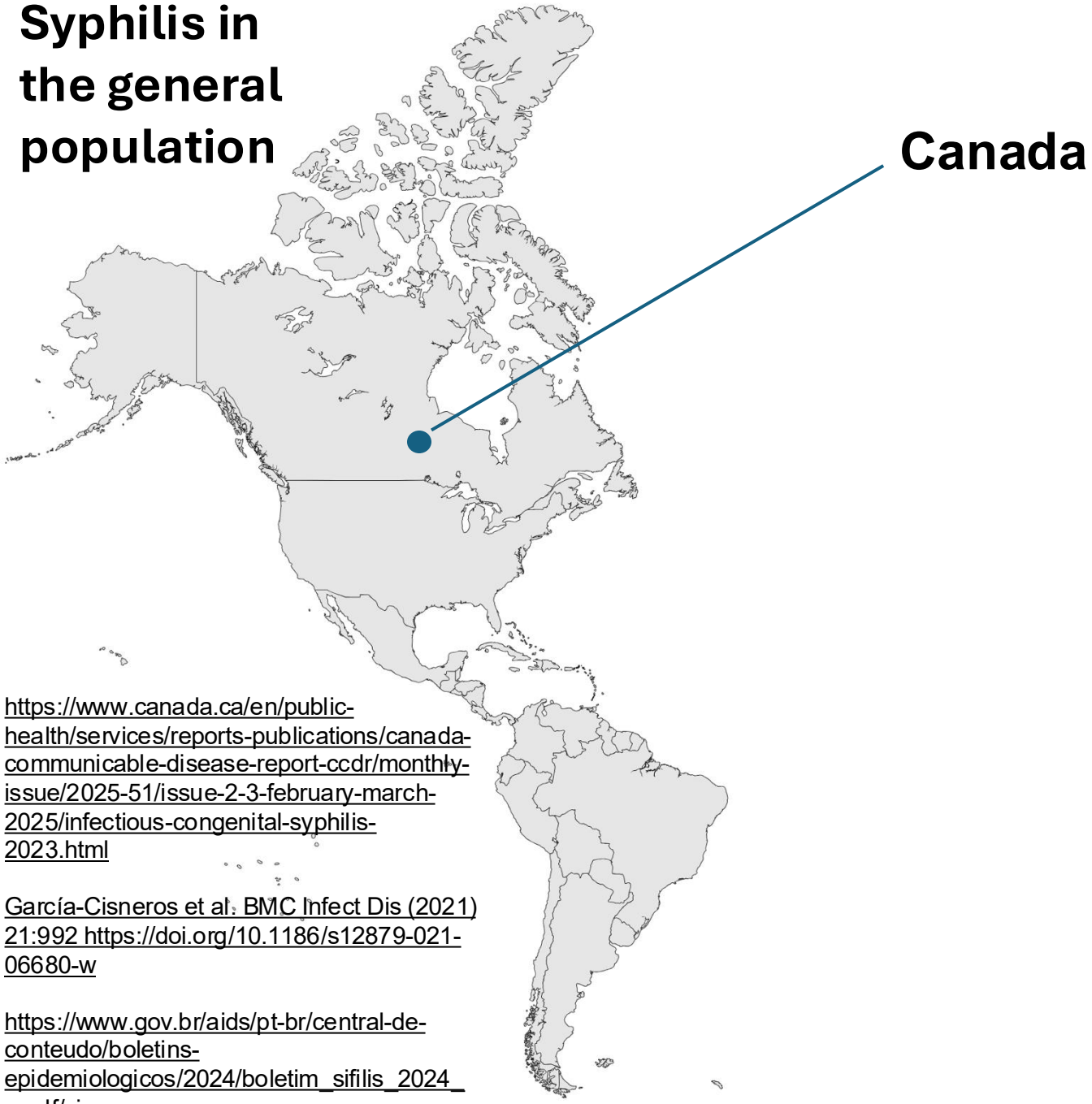
2023 rate: 62.5 per 100,000 people

https://www.cdc.gov/sti-statistics/data-vis/table-sticasesrates.html





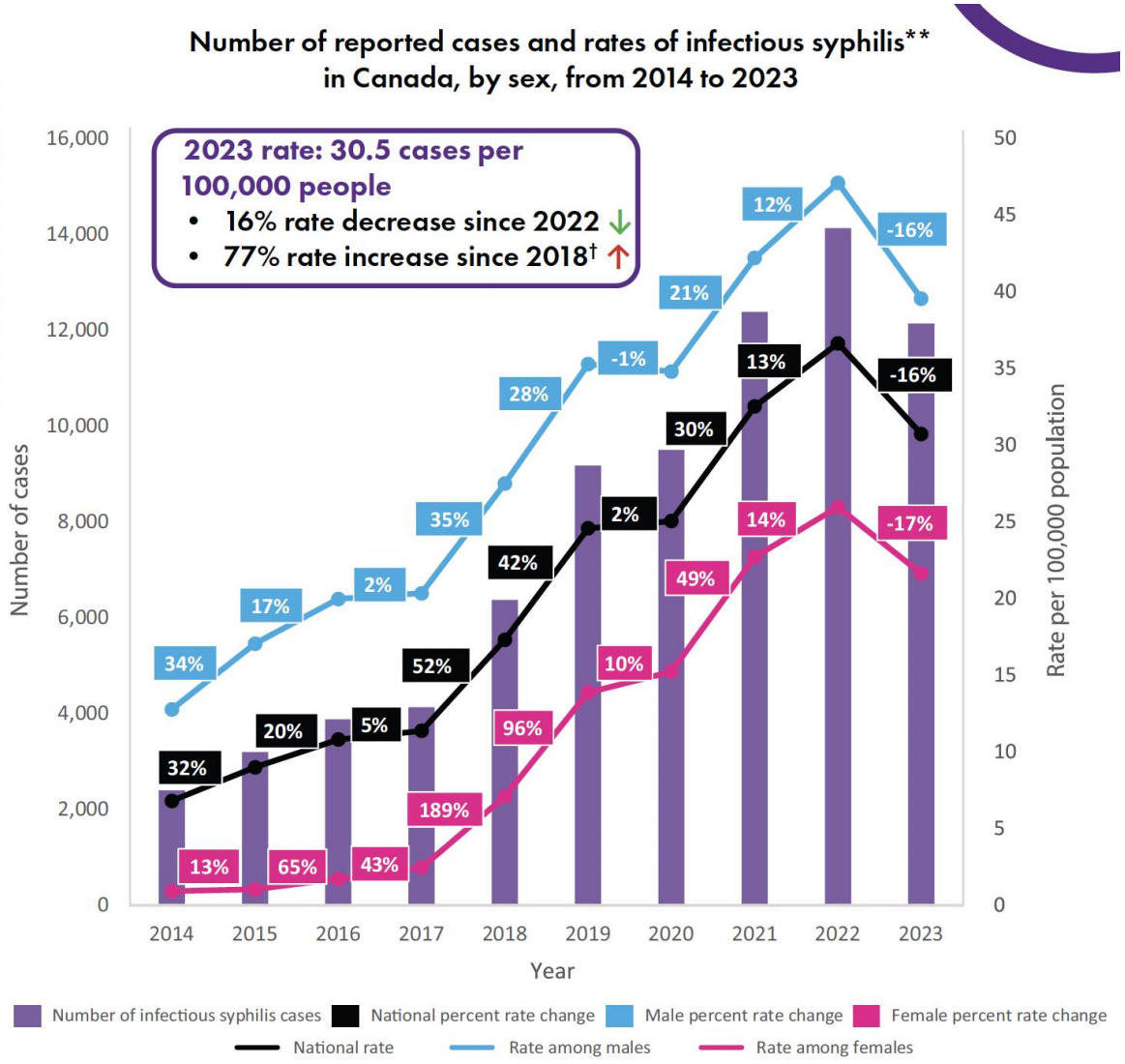
Syphilis in the general population



https://www.canada.ca/en/public-health/services/reports-publications/canada-communicable-disease-report-ccdr/monthly-issue/2025-51/issue-2-3-february-march-2025/infectious-congenital-syphilis-2023.html

García-Cisneros et al. BMC Infect Dis (2021) 21:992 https://doi.org/10.1186/s12879-021-06680-w

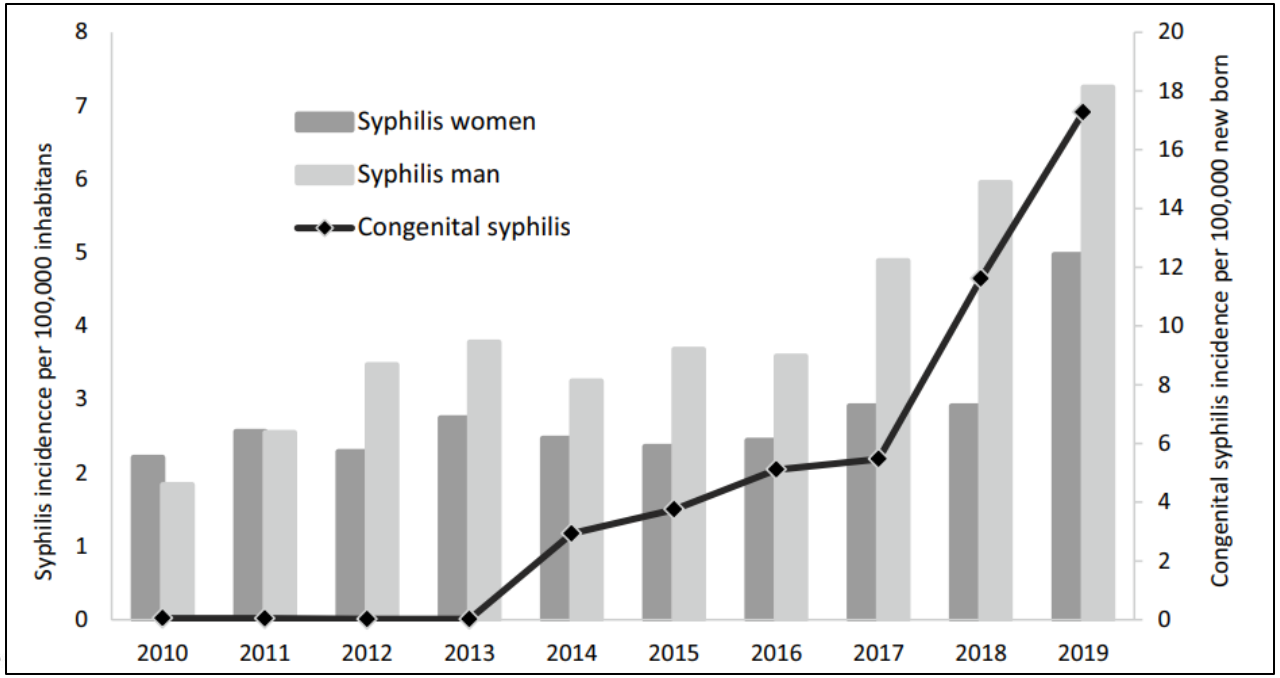
https://www.gov.br/aids/pt-br/central-de-conteudo/boletins-epidemiologicos/2024/boletim_sifilis_2024_e.pdf/view





Syphilis in the general population





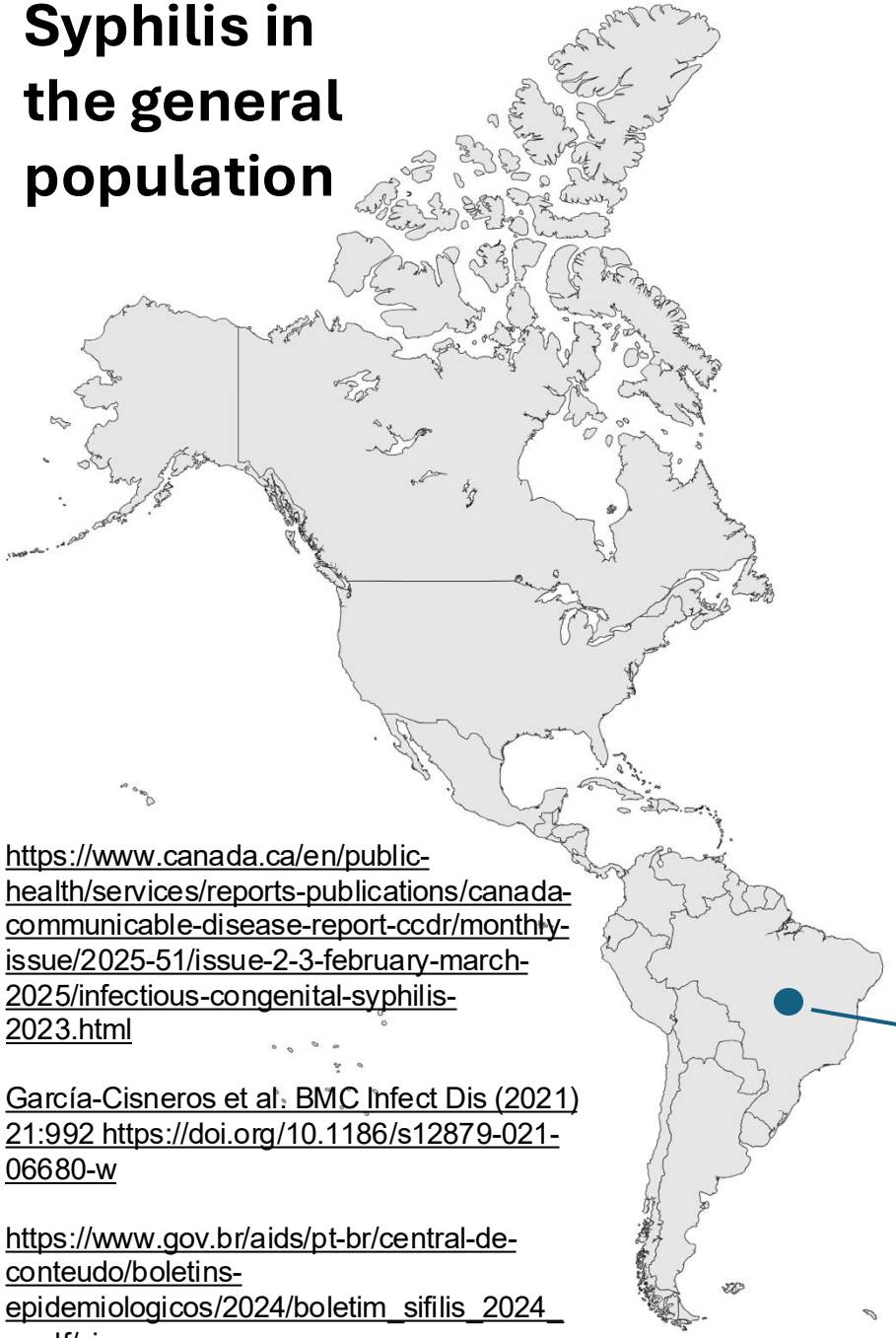
https://www.canada.ca/en/public-health/services/reports-publications/canada-communicable-disease-report-ccdr/monthly-issue/2025-51/issue-2-3-february-march-2025/infectious-congenital-syphilis-2023.html

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per 1000 births

Syphilis in the general population

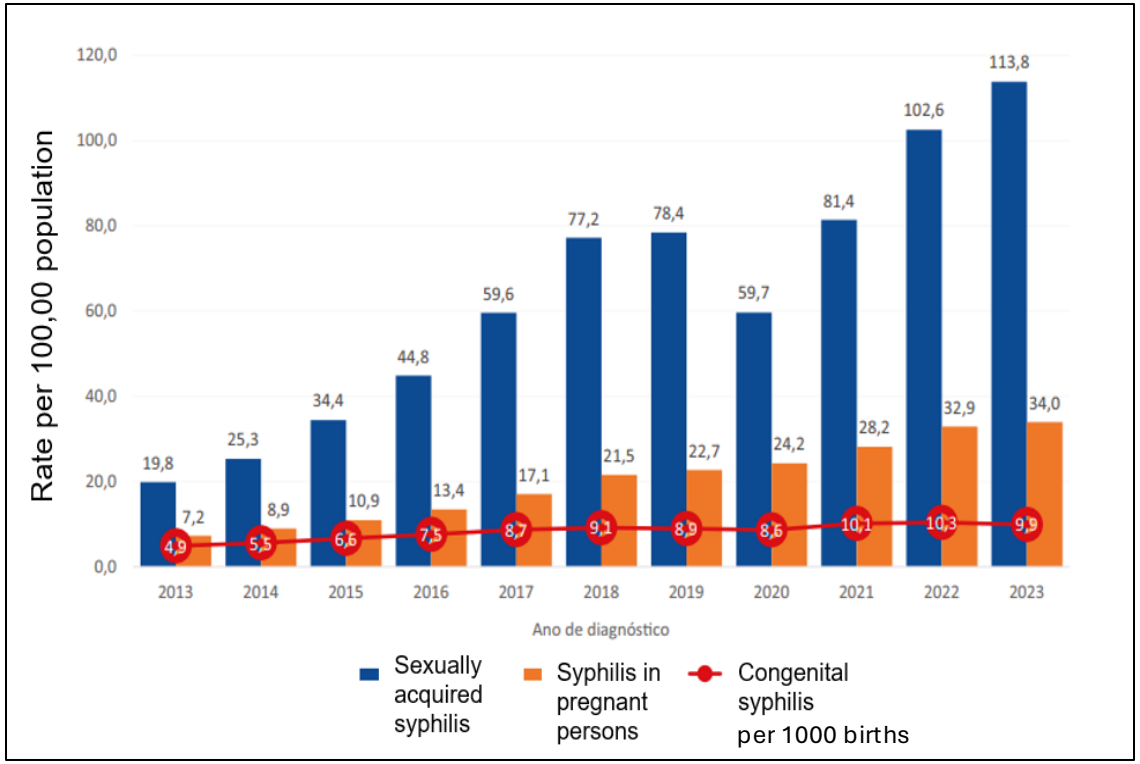


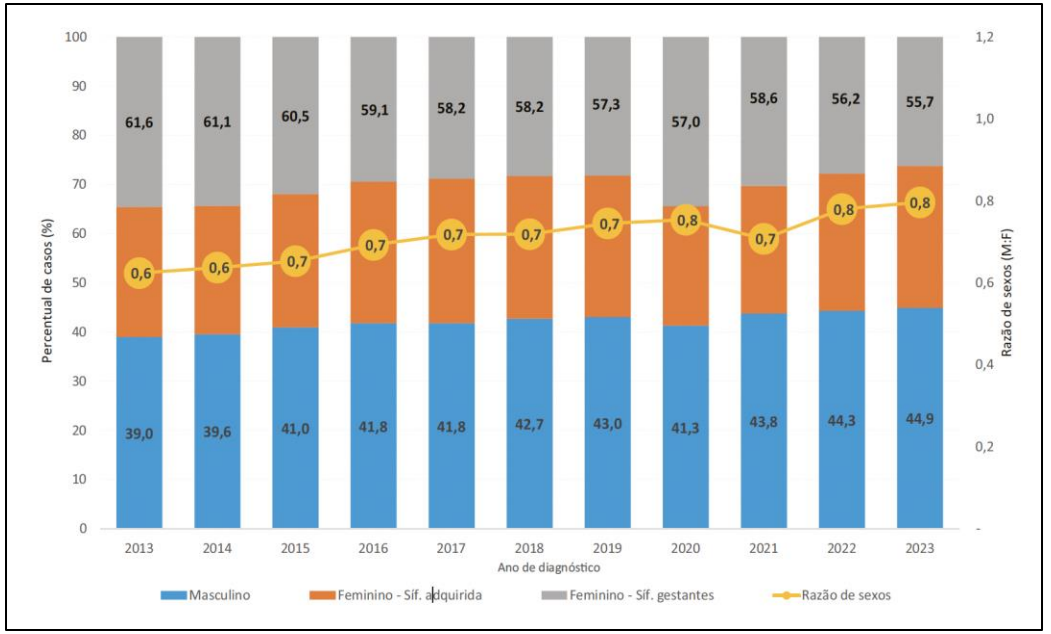
Brazil

https://www.canada.ca/en/public-health/services/reports-publications/canada-communicable-disease-report-ccdr/monthly-issue/2025-51/issue-2-3-february-march-2025/infectious-congenital-syphilis-2023.html

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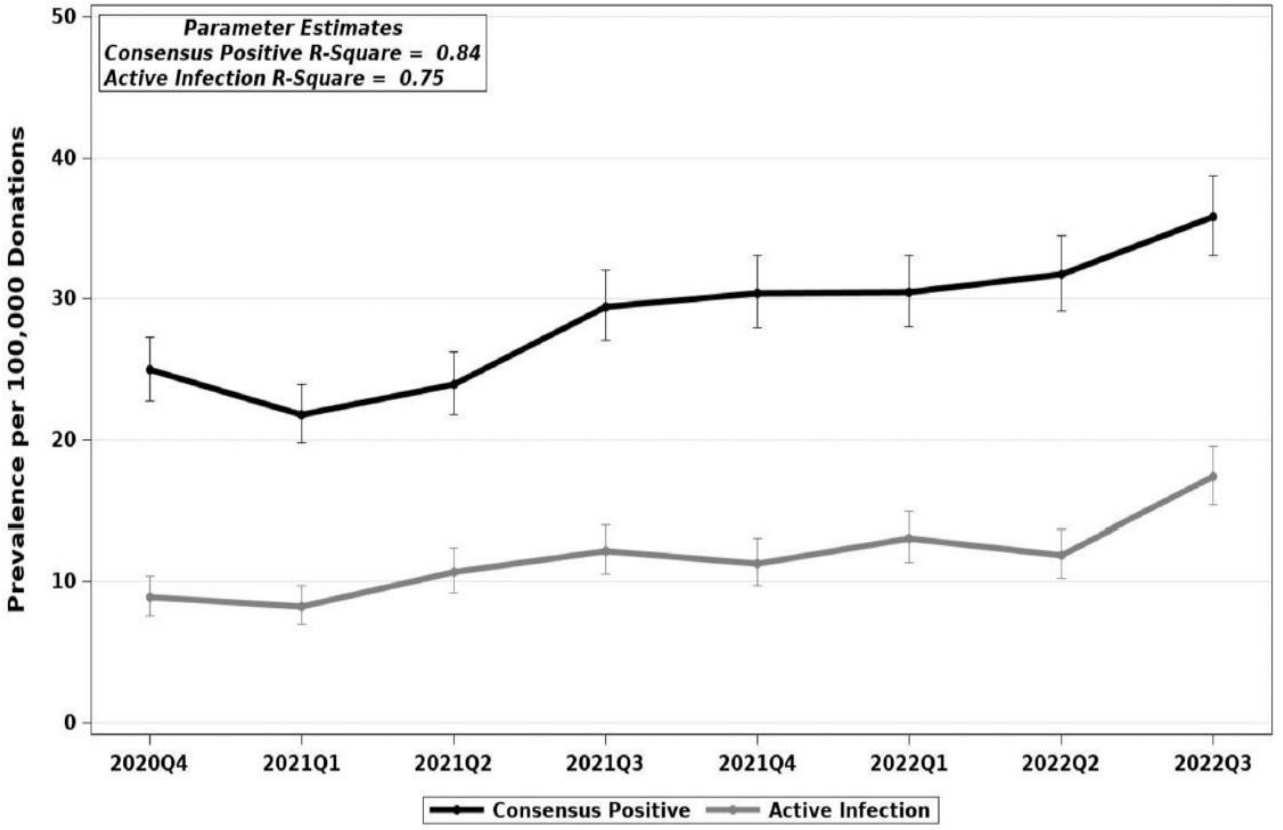




Syphilis in blood donors from the U.S.

US: Conti G. et. al, Transfusion 2024

- Transfusion-Transmissible Infections Monitoring System (TTIMS)
- 14.75 million US donations from October 2020 to September 2022
- Syphilis prevalence = 28.4/100,000 donations; significantly higher during the 2nd year compared to the 1st year
- Syphilis incidence 10.8/100,000 person-years
- Highest rates occurred among males, first-time, Black, and younger (ages 18–39) donors, and those in the South US Census region



Transfusion Transmissible Infections Monitoring System

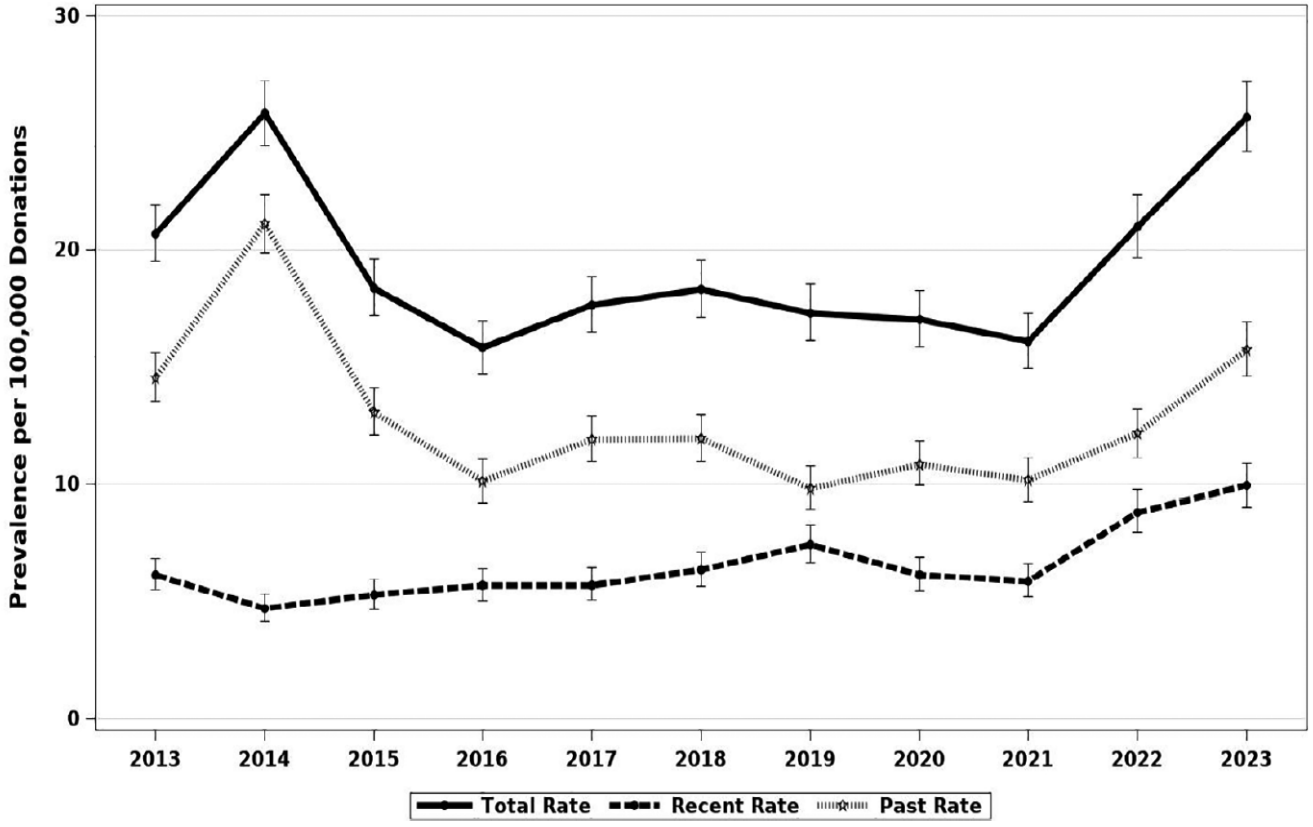
Transfusion. 2024 February ; 64(2): 325–333. doi:10.1111/trf.17707.

Syphilis in blood donors from the U.S

US: Conti G. et. al, Transfusion 2025

From 53 million tested donations from 2013 to 2023 (American Red Cross):

- 10,365 syphilis infections
  - 3463 recent (RPR-positive, 0.007%)
  - 6902 past (RPR-negative, 0.01%)
- 48,719 syphilis false-positive donations
  - 82% of all screen-positive donations
- Syphilis infections in blood donors are trending upward, paralleling US population trends



Transfusion. 2025;1–8. DOI: 10.1111/trf.18145

Syphilis in blood donors from Mexico

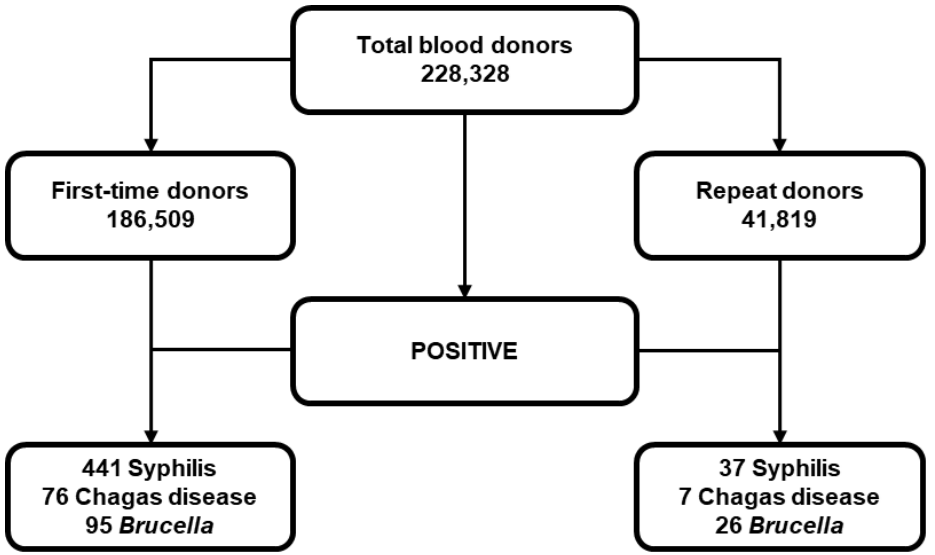
Guerrero-Garcia J. et. al, Pathogens 2024, 13, 1027

From over 225,000 donors in Guadalajara, the database included blood donors between 18 and 65 years old from August 2018 to July 2023.

- ~65% male
- ~35% female

Serological screening for anti-Treponema pallidum and anti-Trypanosoma cruzi antibodies by chemiluminescence immunoassay (CIA) platform ABBOTT Architect i4000 with Architect System Syphilis TP (specificity 99.94%, CI 95% 99.83–99.9%; sensitivity ≥ 99.9%)

Confirmatory tests for anti-Treponema pallidum by passive hemagglutination BIO-RAD TPHA (specificity 99.72%, CI 95% 99.53–99.85%; sensitivity 100%, CI 95% 99.2–100.0%)



First-Time Donors

Sex	Positive Cases (%)	Age Means (SD, CI 95%)	Prevalence (Cases/100,000)	Prevalence by Sex (Cases/100,000)	IC 95%
Men	292 (66.21)	37.12 (11.49, 35.80–38.44)	157	249	222–280
Female	149 (33.79)	34.91 (10.30, 33.24–36.58)	80	215	184–253
Total	441 (100)	36.38 (11.14, 35.34–37.42)	236	236	215–260

Repeat Donors

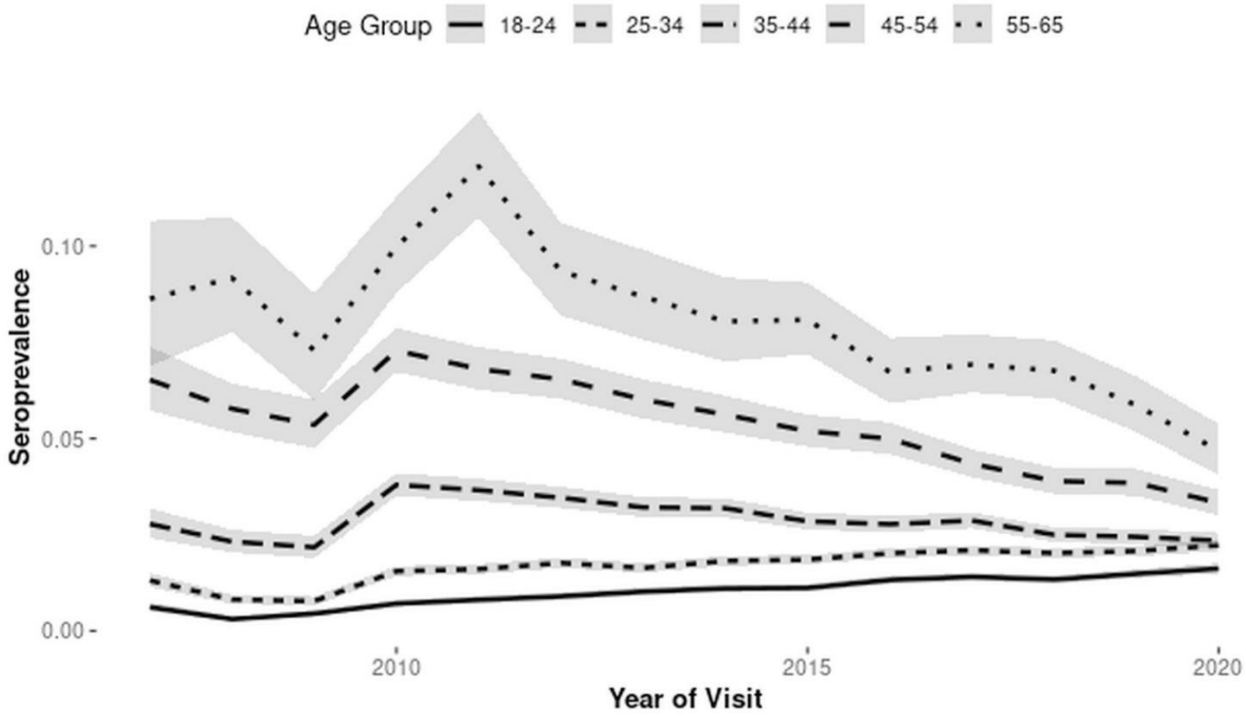
Sex	Positive Cases (%)	Age Means (SD, CI 95%)	Prevalence (Cases/1000)	Prevalence by Sex (Cases/1000)	IC 95%
Men	23 (62.16)	35.57 (10.04, 31.23–39.91)	55	78	0.52–1.17
Female	14 (37.84)	36.50 (8.97, 31.32–41.68)	33	114	0.68–1.91
Total	37 (100)	35.92 (9.53, 32.74–39.10)	88	88	0.64–1.22

Pathogens 2024. https://doi.org/10.3390/pathogens13121027

Syphilis in blood donors from Brazil

Brazil: Cortez A. et. al, Plos One 2025

- 1,424,850 donations from first-time donors at 4 Brazilian blood collection organizations, 2007-2020 (REDS-III Brazil)
- Prevalence of treponemal-positive donations: 2.19%
- Risk factors: male gender, older age, lower education level, and self-reported black or mixed skin color
- Increasing trend in syphilis seroprevalence was observed among younger donors and those born after 1990

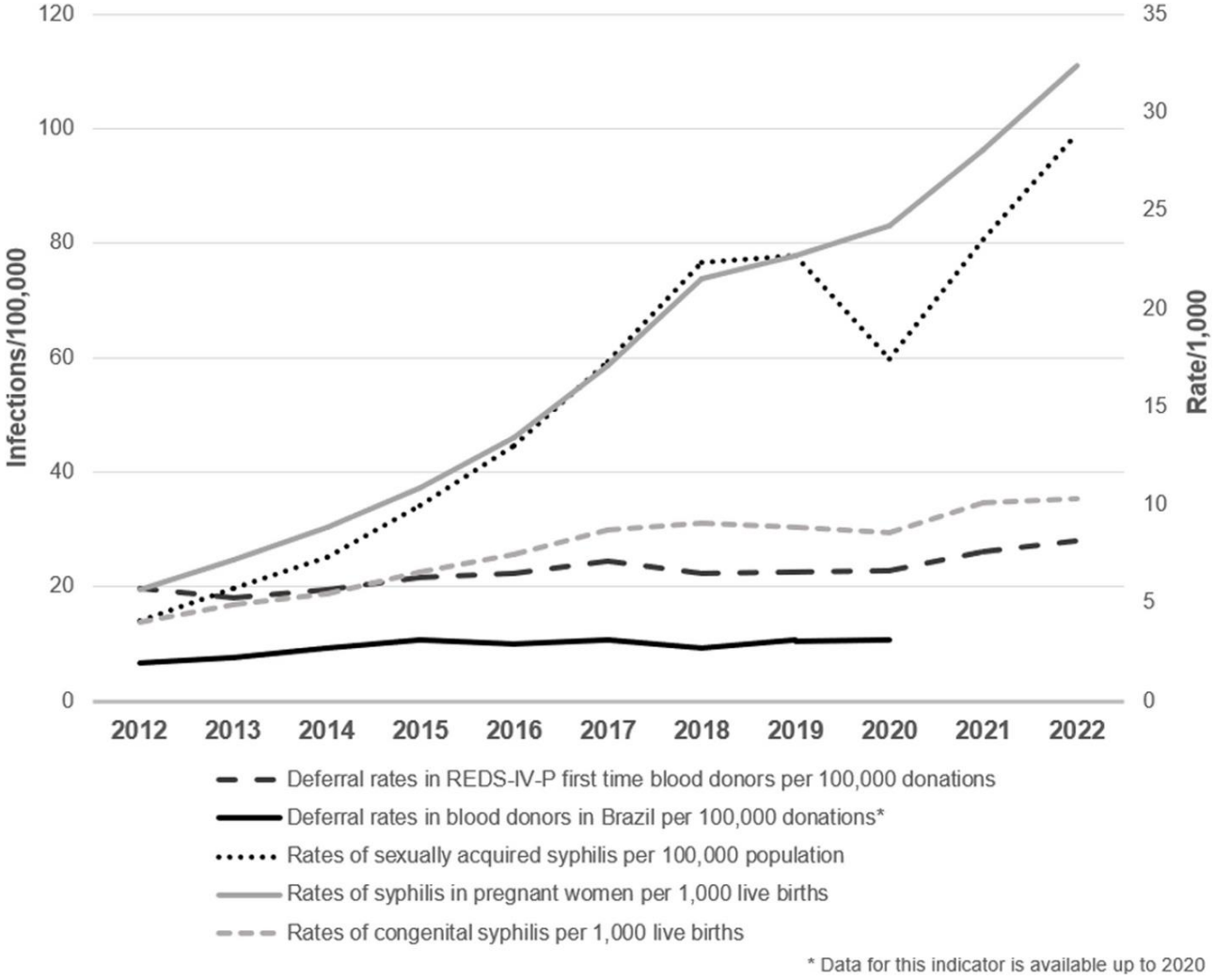


PLoS ONE 20(2): e0315933. https://doi.org/10.1371/journal.pone.0315933

Syphilis in blood donors from Brazil

Brazil: Braga N. et. al, BMC Pub Health 2025

- 862,146 donations collected between January 2020 and February 2022 at five Brazilian blood centers (REDS-IV-P)
- Screening + centralized confirmatory testing algorithm
- Syphilis prevalence (RPR-positive and RPR-negative cases): 2.5% among FTD and 0.6% among RD
- Syphilis incidence in RD: 90/100,000 person-years (95% CI 86–95)
  - Younger age, male gender, Black and Mixed race and lower education associated with incident syphilis
- Syphilis infections in blood donors are trending upward, paralleling Brazil congenital syphilis trends



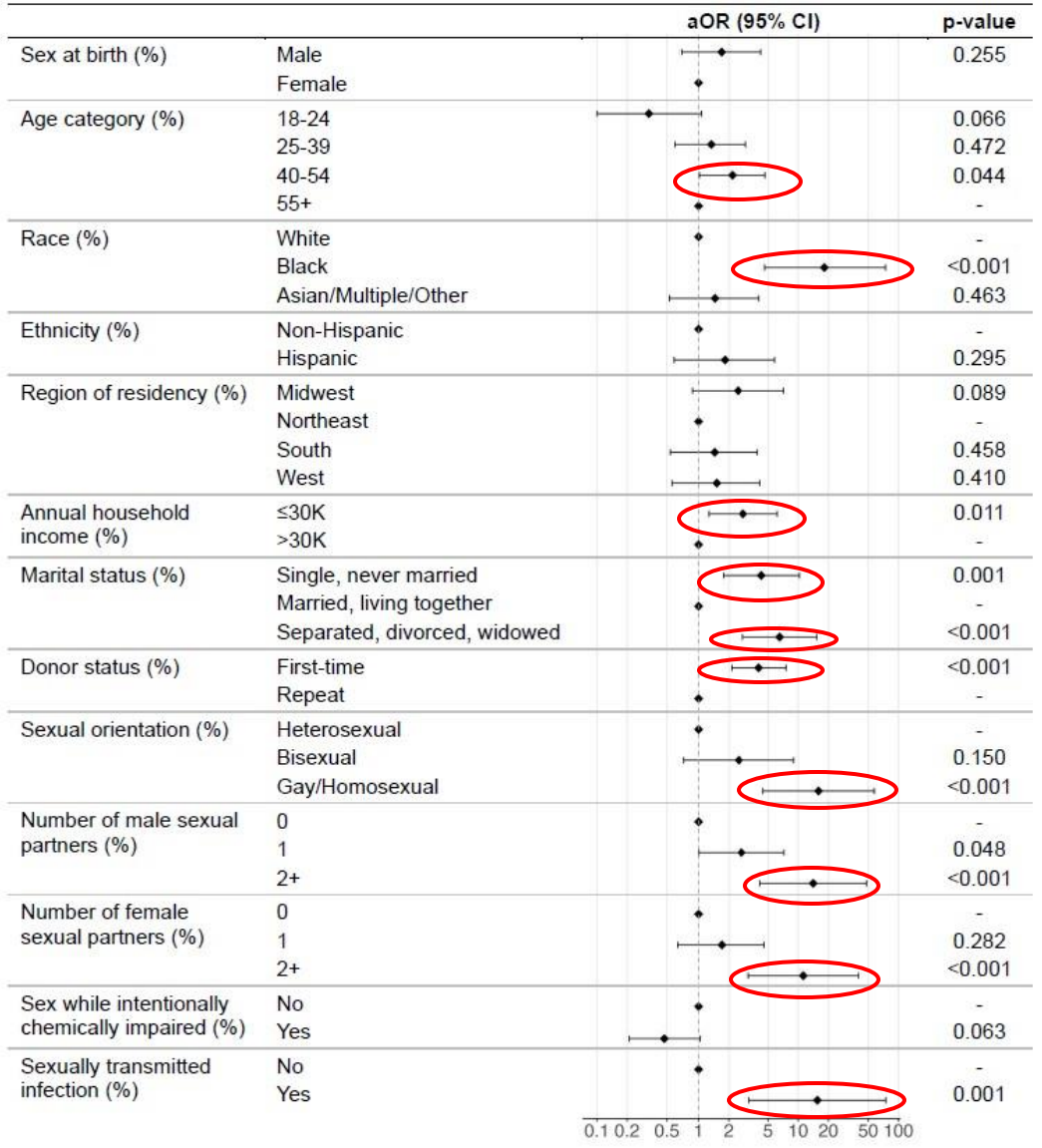
BMC Public Health (2025) 25:60. https://doi.org/10.1186/s12889-024-21114-3

Syphilis in blood donors – risk factors

Transfusion Transmissible Infections Monitoring System

US: Avelino-Silva V. et al. (*In Press*)

- Case-control study including blood donors from 4 major US blood collection organizations (TTIMS)
- 369 active syphilis infection (ASI) cases and 868 matched controls
- Risk factors for ASI investigated with a risk factors questionnaire and conditional logistic regression models
- Risk factors in the multivariable-adjusted model:
  - Age between 40 and 54 years old (compared to 55+)
  - Black race (compared to White)
  - Lower income
  - Single/never married and separated/divorced or widowed (compared to married or living together)
  - First-time donation
  - Gay/homosexual sexual orientation
  - Having ≥2 male or ≥2 female sexual partners in the past 12 months
  - History of sexually transmitted infection



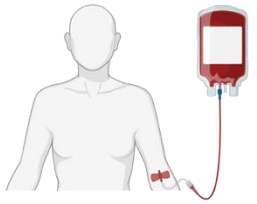
aOR, adjusted odds ratio; CI, confidence interval

Treponema pallidum,

Sexual transmission

Blood donation testing is useful for monitoring asymptomatic infections in a lower-risk population

Transplacental transmission



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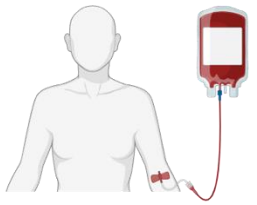
Image created with www.biorender.com

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But is syphilis still being transmitted through blood transfusion?

Transfusion transmission

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Image created with www.biorender.com

Transfusion-transmitted syphilis (TTS)

- No documented cases in the U.S. since 1966
- Current transfusion practices likely reduce the risk of TTS:
  1. Low syphilis prevalence in volunteer blood donors screened with DHQ;
  2. Reduced survival of the spirochete after storage/refrigeration;
  3. Potential impact of pathogen inactivation and leukoreduction technologies;
  4. Extensive use of antibiotics in blood recipients

- Modeling study: TTS risk=
  - 1/49.5m transfusions for universal testing
  - 1/2.8m transfusions for no testing

- Testing of donations not routinely performed in Denmark, Iceland, and Norway

Chambers RW. Transfusion. 1969 Jan 2;9(1):32–4
Orton S. Transfusion Medicine Reviews. 2001 Oct;15(4):282–92.
Drews SJ. Transfusion. 2021 Nov;61(11):3055–60.
Jayawardena T. Vox Sanguinis. 2019 Feb;114(2):107–16.

Syphilis screening tests

Non-treponemal tests:

- Detection of antibodies against cardiolipin, a lipid antigen released by damaged host cells during active syphilis infection
- Test titers can be used to identify reinfections and monitor treatment response
- Labor-intensive

Treponemal tests:

- Detection of anti-*T. pallidum*-specific IgG
- Remain reactive in resolved infections that no longer represent a TTS risk
- High-throughput instruments – have largely replaced non-treponemal tests

Syphilis screening conundrum

Situation:

- Rarely transmitted by transfusion even without any screening test
- Useful as a marker of sexual exposure risk?

Testing:

Donation screening performed using a serologic test that remains reactive in resolved infections that no longer represent a TTS risk

Consequences:

- Unnecessary discard of blood donations
- Need for additional testing with confirmatory treponemal and non-treponemal tests
- Burden to donors and donor counseling and notification

Potential solutions

- Eliminate syphilis testing of blood donations?
- Resume testing with non-treponemal assays?
  - Only in subgroups at higher risk?
- NAT testing for syphilis in blood donations to identify true active infection?
  - Major challenges in assays using blood rather than lesion/mucosal swab samples

Summary

- Syphilis epidemiology in the Americas is complex
  - Clear evidence of increase in all sectors of the general population over the last 10 years
- Donor selection procedures reduce the risk, but not to the same magnitude as for viral infections
- Transfusion transmission is exceptionally rare
- New approaches for syphilis screening are warranted

Thank you