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SYPHILIS RESURGENCE IN THE 21ST CENTURY: GLOBAL EPIDEMIOLOGICAL SHIFTS, CONGENITAL BURDEN, AND IMPLICATIONS FOR PREVENTION

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ABSTRACT

Background. Syphilis is not a disease we fail to cure; it is a disease we fail to prevent. Caused by Treponema pallidum and fully susceptible to penicillin, it should not be resurging. Yet over the past decade, syphilis has re-established itself as a global public health threat, with rising incidence and a striking resurgence of congenital syphilis- an outcome that exposes systemic gaps in maternal care and surveillance.
Aim. This review interprets recent global shifts in syphilis epidemiology and evaluates advances in preclinical syphilis vaccine development to clarify the prospects for future prevention.
Material and methods. A narrative review was conducted using PubMed, Scopus, and MDPI databases (2015-2025), and supplemented by surveillance reports from the official websites of international agencies, including the World Health Organization (WHO), the Centers for Disease Control and Prevention (CDC), and the European Centre for Disease Prevention and Control (ECDC). Sources were selected for epidemiological relevance or substantive contributions to vaccine research.
Results. Across regions, evidence consistently demonstrates sustained increase in syphilis and congenital syphilis rates. Preclinical vaccine studies have yielded promising immunogenicity and partial protection in animal models; however, no candidate has entered human trials, as key antigenic and translational barriers persist.
Conclusions. The contemporary rise of syphilis reflects health-system fragility rather than therapeutic limitation. While vaccines may eventually augment prevention efforts, immediate progress depends on strengthening surveillance, ensuring universal antenatal screening, and closing the structural gaps that allow a curable infection to continue to spread.

KEYWORDS

Syphilis, Congenital Syphilis, Vaccine Development, Sexually Transmitted Infections

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1. Background

There are infectious diseases that medicine still struggles to cure, but syphilis has never been one of them. Caused by Treponema pallidum subspecies pallidum, syphilis has persisted for centuries despite being fully treatable and readily preventable through established screening strategies and penicillin-based therapy (Peeling et al., 2017; Benzaken et al., 2022). Although transmission is rooted in intimate sexual networks, the ability of T. pallidum to cross the placenta extends its consequences far beyond adult populations. Congenital syphilis (CS), therefore, functions as a sentinel indicator of maternal health-system performance; its resurgence reflects not therapeutic failure but systemic breakdowns, exposing gaps in access, surveillance, and timely prenatal care (Kamb et al., 2019; Bowen et al., 2021; World Health Organization [WHO], 2017, 2022).

More than seven million new syphilis infections occur globally each year, with a growing proportion affecting women of reproductive age (Rowley et al., 2019; WHO, 2022). Enhanced surveillance over the past decade has revealed a sustained epidemiological shift in which syphilis increasingly extends beyond historically defined high-risk groups into heterosexual networks, younger adults, and pregnant populations (Peeling et al., 2017; Bowen et al., 2021; Kojima & Klausner, 2018; Tsuboi et al., 2023). The parallel rise in congenital infections—an outcome almost entirely preventable through early antenatal screening and prompt treatment—illustrates persistent failures in diagnosis, continuity of care, and engagement with maternal health services (Taylor et al., 2021; WHO, 2022).

Congenital syphilis remains a major global cause of fetal loss, stillbirth, neonatal death, and infant morbidity. In 2022, the World Health Organization estimated more than 700,000 cases of congenital syphilis worldwide, resulting in approximately 390,000 adverse birth outcomes, underscoring both the scale and urgency of the problem (Rowley et al., 2019; WHO, 2022). These figures reflect not only biological

transmission but also structural determinants of health, including delayed entry into antenatal care, limited health-system reach, and socioeconomic inequities that shape access to preventive services. Recent increases in adult and congenital syphilis reported in countries such as the United States, Australia, Brazil, Canada, and Japan demonstrate that these vulnerabilities persist even in settings with long-standing availability of effective diagnostics and treatment (Bowen et al., 2021; Tsuboi et al., 2023; Public Health Agency of Canada, 2023; Ministério da Saúde, 2023).

The COVID-19 pandemic further amplified these weaknesses. Widespread clinic closures, disrupted diagnostic capacity, and interruptions in antenatal services delayed detection and treatment, disproportionately affecting vulnerable populations (Mackintosh et al., 2023; Natale et al., 2023). While the pandemic did not initiate the resurgence of syphilis, it accelerated pre-existing trends already driven by structural and health-system fragility.

Against this backdrop, growing scientific interest in syphilis vaccine development necessitates careful contextualization within contemporary epidemiology. This review synthesizes global trends in syphilis and congenital syphilis from 2015 to 2025, examines the cost-effectiveness of established prevention strategies, and evaluates recent advances in preclinical vaccine research to clarify priorities for future prevention efforts.

2.Methods

This narrative review synthesizes contemporary evidence on global trends in syphilis and congenital syphilis and examines recent advances in preclinical vaccine development. The literature search covered publications from January 2015 to November 2025. Sources were identified through PubMed, Scopus, and MDPI using a structured combination of free-text terms and controlled vocabulary related to syphilis epidemiology, congenital infection, maternal screening, sexual health systems, and syphilis vaccine research. Only English-language publications were included.

To complement peer-reviewed literature, official surveillance data were obtained from the World Health Organization (WHO), the United States Centers for Disease Control and Prevention (CDC), the European Centre for Disease Prevention and Control (ECDC), and national infectious disease institutes, including Japan's National Institute of Infectious Diseases. Additional reports from ministries of health in high-burden regions were reviewed to capture local epidemiological shifts.

The review prioritized population-level studies, including national and regional surveillance reports, observational epidemiological analyses, modeling studies, and public health evaluations. Research on maternal syphilis screening and congenital syphilis prevention was included where it contributed to understanding health-system performance. Preclinical vaccine studies were included if they provided substantive insight into antigen design, immunogenicity, or protective efficacy in animal models. Case reports or purely microbiological investigations were excluded unless they offered mechanistic relevance to vaccine development or transmission dynamics.

Approximately two hundred abstracts were screened, yielding around eighty full-text sources for inclusion. Although not a systematic review, this work followed transparent eligibility criteria and incorporated evidence from diverse geographical and methodological contexts. Generative AI tools were used exclusively for linguistic refinement; all literature selection, appraisal, and scientific interpretation were conducted manually by the authors. The review adhered to SANRA standards to ensure clarity of scope, transparency in literature selection, and methodological consistency throughout.

2.1. AI

Artificial intelligence–assisted language tools were used to support manuscript editing, particularly in stylistic refinement. All scientific content, data interpretation, and final editorial decisions were performed by the authors manually.

3.Main body

3.1. Global Epidemiological Landscape of Syphilis, 2015–2025

Syphilis has re-emerged across diverse regions over the past decade, with more than seven million new infections reported annually worldwide (Korenromp et al., 2019; Peeling et al., 2023; World Health Organization [WHO], 2020). Countries including the United States, Japan, Australia, and the United Kingdom now report incidence rates not observed for several decades, while many middle- and low-income regions continue to experience persistently high prevalence or renewed increases (Centers for Disease Control and Prevention [CDC], 2024; Espinoza & Trung, 2025; European Centre for Disease Prevention and Control [ECDC], 2025; Australian Centre for Disease Control, 2025). These patterns do not represent a singular epidemiological shift but rather a sustained reconfiguration shaped by evolving sexual networks, delayed engagement with care, and heterogeneous public health capacity across regions (Peeling et al., 2023; Gilmour & Walls, 2023; Espinoza & Trung, 2025).

3.1.1 Changing Sexual Networks

Transmission patterns have expanded beyond their earlier concentration in men who have sex with men to include younger heterosexual adults, particularly those less engaged with routine sexual health services (Anand et al., 2024; Peeling et al., 2023; Glikas et al., 2025). Digital platforms have broadened partner networks, often accompanied by reduced condom use and changing perceptions of risk in the context of HIV prevention tools, including pre-exposure prophylaxis (Peeling et al., 2023; Espinoza & Trung, 2025; Welc et al., 2025). Rising incidence among women of reproductive age is especially consequential, reflecting the influence of socioeconomic vulnerability, limited access to primary care, and structural inequities that shape who receives timely screening and treatment (Anand et al., 2024; Duarte et al., 2024; Gilmour & Walls, 2023).

3.1.2. Surveillance Gaps and Health-System Fragility

Syphilis surveillance remains uneven worldwide. Variations in diagnostic algorithms, case definitions, and reporting infrastructure contribute to inconsistent data quality across regions. Even in well-resourced settings, sexual health services frequently experience underfunding, staffing shortages, and weak integration with primary care (Gilmour & Walls, 2023; Espinoza & Trung, 2025). The COVID-19 pandemic magnified these vulnerabilities by interrupting clinical services, delaying diagnostics, and reducing access to antenatal and sexually transmitted infection screening (Cunha-Oliveira et al., 2023; Nazir et al., 2022; Liu et al., 2023; Welc et al., 2025). These disruptions obscured transmission trends and delayed detection, allowing cases to accumulate undiagnosed.

Congenital syphilis is among the most sensitive indicators of maternal healthcare performance, as vertical transmission is almost entirely preventable through early antenatal screening and timely benzathine penicillin treatment (Korenromp et al., 2019; Moseley et al., 2024; WHO, 2021).

3.2 Congenital Syphilis Incidence and Geographic Heterogeneity

Between 2018 and 2023, congenital syphilis incidence demonstrated pronounced geographic variation (Table 1). Brazil reported the highest burden throughout the study period, with incidence persistently exceeding 700 cases per 100,000 live births and surpassing 1,000 per 100,000 in 2023 (Gazeta & Pereira, 2023; Epidemiological Review of Syphilis in the Americas, 2022). Argentina exhibited a marked resurgence, with incidence increasing from approximately 114 per 100,000 live births in 2020 to over 220 per 100,000 by 2023 (Epidemiological Review of Syphilis in the Americas, 2022).

In North America, the United States experienced a steep and sustained increase, with congenital syphilis incidence rising from approximately 35 per 100,000 live births in 2018 to over 100 per 100,000 by 2022–2023 (CDC, 2024; Anand et al., 2024). Canada showed a similar upward trajectory, with rates increasing from 4.3 per 100,000 live births in 2018 to approximately 30 per 100,000 by 2022, although substantial interprovincial variation was observed (CCDR, 2023).

European countries generally reported lower absolute incidence; however, several demonstrated emerging upward trends. Portugal and Hungary showed increases into the range of 10–20 cases per 100,000 live births during 2021–2023, suggesting early deterioration in maternal screening effectiveness (ECDC, 2025). Poland and Italy maintained low incidence throughout the period, typically below 2 cases per 100,000 live births (ECDC, 2025). Japan reported comparatively low but steadily increasing rates, rising from approximately 1.8 per 100,000 live births in 2018 to over 6 per 100,000 in 2023 (Espinoza & Trung, 2025). Scandinavian countries, including Sweden, Norway, and Finland, sustained near-zero incidence across the study period.

Marked differences in congenital syphilis incidence corresponded closely to antenatal screening program performance (Table 2). Countries reporting incidence well above the WHO elimination of mother-to-child transmission (EMTCT) benchmark—such as Brazil (>1,000 per 100,000 live births), Argentina (>200), and the United States (>100)—were characterized by delayed antenatal engagement, inconsistent repeat screening, or variable coverage despite formal universal screening policies (Korenromp et al., 2019; Moseley et al., 2024; WHO, 2021). In contrast, countries sustaining very low incidence, including Italy, Poland, Japan, and Scandinavian nations with near-zero incidence, consistently implemented early first-trimester screening within highly integrated maternal health systems. These findings underscore that congenital syphilis incidence functions as a sensitive quantitative indicator of health-system performance rather than policy intent alone.

Table 1. Congenital syphilis incidence per 100 000 live births, 2018–2023.

Country	2018	2019	2020	2021	2022	2023
Brazil	896.83	846.92	774.44	989.65	—	1033,78
Canada	4.27	13.12	15.23	27.39	31.70	14.53
Poland	0.52	0.80	0.84	0.30	0.33	0.73
Portugal	4.60	15.02	8.29	18.85	16.73	16.34
United States	35.00	50.20	59.80	78.50	102.50	105.80
Argentina	157.72	136.71	113.84	131.37	—	221.31
Italy	1.59	0.95	0.25	0.25	0.51	1.58
Hungary	5.35	3.22	3.20	12.77	8.92	14.83

Note. Incidence values represent confirmed congenital syphilis cases per 100,000 live births as reported through national surveillance systems in Brazil, the United States, Canada, Argentina, Japan, Portugal, Italy, Hungary, and Poland. A dash (—) indicates years for which national data were not reported or were not publicly available. These data illustrate substantial geographic variation and a rising incidence in several regions despite the well-established preventability of vertical transmission through timely antenatal screening and treatment (Peeling et al., 2017; Kamb et al., 2019; World Health Organization, 2022).

3.2.1 Clinical Impact of Congenital Syphilis

Congenital syphilis encompasses a broad clinical spectrum. Early disease frequently manifests with hepatosplenomegaly, anemia, thrombocytopenia, jaundice, mucocutaneous lesions, rhinitis, and skeletal abnormalities, while severe cases may present with sepsis-like illness, hydrops fetalis, or respiratory distress (Peeling et al., 2023; Gilmour & Walls, 2023; Moseley et al., 2024). Untreated maternal infection is strongly associated with stillbirth, neonatal death, prematurity, and low birth weight (Korenromp et al., 2019; Wozniak et al., 2023).

Late congenital syphilis is associated with irreversible sequelae, including sensorineural hearing loss, dental abnormalities, interstitial keratitis, skeletal deformities, and neurodevelopmental impairment (Peeling et al., 2023; Gilmour & Walls, 2023). Importantly, a substantial proportion of infected neonates are asymptomatic at birth, reinforcing the inadequacy of symptom-based detection and underscoring the necessity of universal antenatal screening (Korenromp et al., 2019; WHO, 2021).

3.2.2 Antenatal Screening Programs

Marked differences in congenital syphilis incidence corresponded closely to antenatal screening program characteristics (Table 2). Countries reporting incidence far above the WHO EMTCT validation threshold of fewer than 50 cases per 100,000 live births—including Brazil, Argentina, the United States, and Canada—were characterized by delayed antenatal entry, inconsistent repeat screening, or variable coverage despite formal universal screening policies (Brandenburger & Ambrosino, 2021; Huntington et al., 2020; WHO, 2021).

By contrast, countries sustaining low incidence, including Italy, Poland, Japan, and Scandinavian nations, consistently implemented early first-trimester screening embedded within integrated maternal health systems and reported high coverage (ECDC, 2025; Espinoza & Trung, 2025). Scandinavian countries, which met EMTCT benchmarks throughout the study period, functioned as elimination exemplars, demonstrating that near-elimination is achievable when early screening is reliably delivered and linked to timely treatment.

Taken together, these findings indicate that congenital syphilis incidence functions as a sensitive sentinel marker of antenatal screening performance, capturing cross-national variation in maternal healthcare delivery despite broadly similar policy frameworks.

Table 2. Antenatal syphilis screening policies and congenital syphilis incidence in selected countries.

Country	Screening policy	Timing of routine screening	Repeat screening	Testing modality	Reported Coverage	CS incidence (per 100 000 live births)
United States	Universal screening mandated	First prenatal visit	Third semester and at delivery in high-risk states	Laboratory serology (RPR and treponemal)	>95% at first visit	100 (2022-2023)
Canada	Universal screening	First prenatal visit	Third semester and at delivery in high-risk provinces	Laboratory serology (RPR and treponemal)	>95%	30 (2022)
Brazil	Universal screening	First trimester	Third trimester recommended	Point of care + laboratory	Variable 70-85%	>1 000 (2023)
Argentina	Universal screening	First prenatal visit	Inconsistent	Laboratory serology	Incomplete	>200 (2023)
Portugal	Universal screening	First trimester	Variable	Laboratory serology	High (>90%)	15-20 (2021-2023)
Italy	Universal screening	First trimester	Not routine	Laboratory serology	>95%	<2 (2018-2023)
Poland	Universal screening	First trimester	Not routine	Laboratory serology	>95%	<1 (2018-2023)
Japan	Universal screening	First prenatal visit	Not routine	Laboratory serology	>95%	5-6 (2023)
Sweden	Universal screening	Early firrst semester	Not routine	Laboratory serology	99%	0 (2023)
Norway	Universal screening	Early firrst semester	Not routine	Laboratory serology	99%	0 (2023)
Finland	Universal screening	Early firrst semester	Not routine	Laboratory serology	99%	0 (2023)

Note. The table summarizes national antenatal syphilis screening strategies alongside approximate congenital syphilis incidence per 100,000 live births, based on the most recent publicly available surveillance data. Incidence values are presented as ranges or rounded estimates to facilitate cross-country comparison and interpretation relative to the World Health Organization elimination of mother-to-child transmission (EMTCT) benchmark of <50 cases per 100,000 live births. Scandinavian countries are included as elimination exemplars, reflecting sustained programmatic coverage and early-pregnancy screening adherence (World Health Organization, 2017, 2022; Taylor et al., 2021).

3.2.3. Congenital Syphilis as a Sentinel Indicator of Health-System Performance

Congenital syphilis incidence functioned as a highly sensitive sentinel indicator of antenatal screening effectiveness across countries during the study period (Table 2). Countries reporting the highest congenital syphilis burden—including Brazil, Argentina, the United States, and Canada—consistently exceeded the World Health Organization elimination of mother-to-child transmission (EMTCT) benchmark of fewer than 50 cases per 100,000 live births, in some settings by more than an order of magnitude (Korenromp et al., 2019; WHO, 2021; Moseley et al., 2024). In contrast, countries maintaining low incidence, including Italy, Poland, Japan, and Scandinavian nations, remained below or close to EMTCT thresholds throughout most or all of the observed period, reflecting sustained effectiveness of antenatal screening and referral pathways (ECDC, 2025; Espinoza & Trung, 2025).

Notably, substantial heterogeneity was observed among countries operating under formally similar universal screening policies. Despite comparable policy commitments, congenital syphilis incidence varied by more than two orders of magnitude across settings. Scandinavian countries sustained near-zero incidence across consecutive years, whereas several countries in the Americas experienced persistently elevated or rapidly increasing rates. European countries generally reported lower absolute incidence, but emerging upward trends in some settings suggested early strain within maternal health systems rather than outright policy failure.

Across regions, rising congenital syphilis incidence closely aligned with differences in the timing of antenatal entry, repeat testing practices during pregnancy, and effective screening coverage (Table 2). These findings underscore the value of congenital syphilis surveillance as a quantitative, outcome-based marker of antenatal care performance, capturing real-world health-system functionality beyond the presence of universal screening policies alone.

Taken together, these findings indicate that congenital syphilis incidence functions as a sensitive sentinel marker of antenatal screening performance, capturing cross-national variation in maternal healthcare delivery despite broadly similar policy frameworks.

3.2.4 Cost-Effectiveness of Screening and Timely Intervention

Universal syphilis screening during pregnancy remains among the most cost-effective public health interventions currently available. Economic evaluations and systematic reviews consistently demonstrate that the societal and healthcare costs associated with a single case of congenital syphilis far exceed the costs of screening large antenatal populations and providing timely treatment to seropositive pregnant women (Brandenburger & Ambrosino, 2021; Huntington et al., 2020; Zhang et al., 2024). Across diverse epidemiological and healthcare settings, early antenatal screening has been shown to substantially reduce adverse pregnancy outcomes, including stillbirth, neonatal death, and long-term infant morbidity (Korenromp et al., 2019; Moseley et al., 2024).

These findings underscore that the principal barrier to effective syphilis prevention is not the complexity or affordability of interventions, but rather their inconsistent implementation within health systems. Missed opportunities for screening, delayed antenatal entry, and fragmented follow-up pathways continue to undermine otherwise highly cost-effective prevention strategies (Brandenburger & Ambrosino, 2021; Zhang et al., 2024).

3.3. Advances in Syphilis Vaccine Development

The persistence of Treponema pallidum is rooted in its distinctive immunobiology. The organism possesses a sparse outer membrane with a limited number of surface-exposed antigens, employs antigenic variation—particularly within the TprK protein—to evade host immune recognition, and elicits a delayed immune response that permits widespread dissemination prior to clinical detection (Peeling et al., 2023; Cameron, 2018; Lithgow & Cameron, 2017). Natural infection does not confer durable protective immunity, and reinfections are common, creating a pathogen for which population-level immunity alone offers limited protection against sustained transmission (Ramchandani et al., 2023; Peeling et al., 2023).

Recent scientific advances have reinvigorated syphilis vaccine research. Recombinant outer membrane proteins, including full-length TprC variants and multivalent constructs combining TprC, TprK, and Tp0751, have demonstrated meaningful immunogenicity and partial protective efficacy in rabbit models, with reductions in lesion severity and treponemal burden following challenge (Lukehart et al., 2022; Liu et al., 2024; Kojima et al., 2022). Adhesins such as Tp0954 have also shown encouraging immune responses, further expanding the pool of viable antigen candidates (He et al., 2023). Concurrent advances in structural biology and immunoinformatics continue to refine antigen selection and epitope targeting strategies (Ávila-Nieto et al., 2023; Waugh & Cameron, 2024).

Despite this progress, substantial challenges remain. Sterilizing immunity has not yet been achieved in preclinical models, and antigenic variability continues to complicate the development of broadly protective vaccines (Cameron, 2018; Lithgow & Cameron, 2017). Emerging platforms—including outer membrane vesicles, virus-like particles, and mRNA-based approaches—offer promising conceptual avenues but remain at early stages of development and have yet to be validated in translational or clinical settings (Ávila-Nieto et al., 2023; Kojima et al., 2022). Nonetheless, the current trajectory represents the most sustained momentum in syphilis vaccine development in more than half a century (Peeling et al., 2023; Liu et al., 2024).

4. Discussion

Although Treponema pallidum remains uniformly susceptible to benzathine penicillin, syphilis transmission persists where access to timely sexual health services, antenatal screening, and consistent follow-up is uneven. The expanding demographic profile of affected populations—including younger heterosexual adults and women of reproductive age—reflects changing risk environments shaped by socioeconomic vulnerability, digital partner-seeking networks, and declining engagement with routine sexually transmitted infection care (Peeling et al., 2023; Anand et al., 2024; Espinoza & Trung, 2025).

Congenital syphilis provides the clearest expression of these systemic vulnerabilities. Because vertical transmission is almost entirely preventable through early antenatal screening and timely treatment, rising congenital syphilis incidence exposes delays in antenatal entry, fragmented referral pathways, and structural inequities that influence access to adequate prenatal care (Korenromp et al., 2019; Gilmour & Walls, 2023; Moseley et al., 2024). Countries reporting the steepest increases—including Brazil, Argentina, the United States, and Canada—exhibit patterns consistent with weakened maternal health infrastructures, whereas nations maintaining universal early screening and strong primary care integration continue to sustain near-elimination (WHO, 2021; Moseley et al., 2024).

Beyond acute neonatal morbidity, congenital syphilis carries substantial long-term health consequences that extend across the life course. Survivors of early disease may develop irreversible sequelae, including sensorineural hearing loss, neurodevelopmental delay, visual impairment due to interstitial keratitis, and musculoskeletal deformities that impair growth and mobility (Peeling et al., 2023; Gilmour & Walls, 2023). Neurosyphilis may occur at any stage of congenital infection and can present with seizures, cognitive impairment, or behavioral abnormalities, but may also remain clinically silent in early life without targeted evaluation (Peeling et al., 2023; Ramchandani et al., 2023). These outcomes frequently necessitate prolonged medical follow-up and specialized supportive care, underscoring that the burden of congenital syphilis is not fully captured by neonatal case counts alone but includes long-term disability and sustained healthcare utilization (Korenromp et al., 2019; Wozniak et al., 2023).

Current epidemiological trends diverge substantially from the World Health Organization elimination of mother-to-child transmission (EMTCT) framework, which requires congenital syphilis incidence below 50 cases per 100,000 live births and at least 95% coverage of antenatal screening and treatment of seropositive pregnant women (WHO, 2021). The incidence levels observed globally—including values exceeding 1,000 per 100,000 live births in Brazil and rapidly increasing rates in North America and parts of Europe—demonstrate the extent to which many health systems have drifted from EMTCT validation criteria. Even historically low-burden countries, such as Japan, now show gradual increases, suggesting early strain within antenatal care pathways (Espinoza & Trung, 2025; Moseley et al., 2024).

The COVID-19 pandemic further exacerbated existing health-system fragilities. Temporary clinic closures, reduced diagnostic capacity, and interruptions in routine antenatal visits contributed to missed screening opportunities, delayed treatment, and the accumulation of undiagnosed infections (Cunha-Oliveira et al., 2023; Nazir et al., 2022; Welc et al., 2025). Although these disruptions were transient, they amplified pre-existing structural weaknesses and accelerated transmission in already vulnerable populations.

The biological characteristics of T. pallidum compound these systemic challenges. The organism's sparse outer membrane, limited repertoire of surface-exposed antigens, substantial antigenic variation, and absence of durable natural immunity facilitate reinfection and sustained transmission (Cameron, 2018; Lithgow & Cameron, 2017; Peeling et al., 2023). While recent advances in vaccine research have generated cautious optimism, including partial protection in preclinical models, significant translational barriers remain. To date, no vaccine candidate has achieved sterilizing immunity or progressed to human clinical trials, underscoring that vaccination, if realized, will complement rather than replace established screening and treatment strategies (Ávila-Nieto et al., 2023; Liu et al., 2024).

This review has limitations, including its narrative design, potential selection bias, and reliance on heterogeneous surveillance systems. Nevertheless, the consistency of epidemiological trends across regions supports several robust conclusions. Mitigating the resurgence of syphilis—particularly congenital syphilis—will require strengthening maternal healthcare pathways, ensuring uninterrupted availability of benzathine penicillin, restoring comprehensive sexual health services, and improving national and regional surveillance capacity. Without renewed and coordinated investment across these domains, progress toward EMTCT benchmarks is unlikely to be sustained.

5. Conclusions

Syphilis has resurged not because its biology has changed, but because health systems have struggled to provide consistent, equitable prevention and care. Rising adult incidence and increasing congenital infections reveal gaps in timely screening, fragmented service delivery, and persistent structural inequities. Despite promising advances in antigen discovery and preclinical vaccine research, no candidate has yet entered clinical trials, and substantial scientific barriers remain.

Immediate progress depends on strengthening surveillance, ensuring universal antenatal syphilis screening, and securing reliable access to benzathine penicillin. These interventions are simple, cost-effective, and proven—but they require functional systems to achieve their potential. A future vaccine may ultimately contribute to long-term control, yet the foundations of prevention remain unchanged: early detection, timely treatment, and resilient health systems capable of reaching those most at risk.

Syphilis remains a curable infection. Its persistence reflects not therapeutic limitation but the broader social and structural forces that shape health. Addressing these vulnerabilities is essential for sustainable control today and for integrating future vaccine strategies effectively.

Supplementary Materials

Table 1. Congenital syphilis incidence per 100 000 live births, 2018–2023.

Country	2018	2019	2020	2021	2022	2023
Brazil	896.83	846.92	774.44	989.65	—	1033,78
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Poland	0.52	0.80	0.84	0.30	0.33	0.73
Portugal	4.60	15.02	8.29	18.85	16.73	16.34
United States	35.00	50.20	59.80	78.50	102.50	105.80
Argentina	157.72	136.71	113.84	131.37	—	221.31
Italy	1.59	0.95	0.25	0.25	0.51	1.58
Hungary	5.35	3.22	3.20	12.77	8.92	14.83

Incidence values represent confirmed congenital syphilis cases per 100 000 live births reported through national surveillance systems in Brazil, the United States, Canada, Argentina, Japan, Portugal, Italy, Hungary, and Poland. "—" indicates years in which national data were not reported or not publicly available. These data illustrate substantial geographic variation and rising incidence in several regions despite the preventability of vertical transmission.

References 7-10, 14–23, 26

Table 2. Antenatal syphilis screening policies and congenital syphilis incidence in selected countries.

Country	Screening policy	Timing of routine screening	Repeat screening	Testing modality	Reported Coverage	CS incidence (per 100 000 live births)
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Brazil	Universal screening	First trimester	Third trimester recommended	Point of care + laboratory	Variable 70-85%	>1 000 (2023)
Argentina	Universal screening	First prenatal visit	Inconsistent	Laboratory serology	Incomplete	>200 (2023)
Portugal	Universal screening	First trimester	Variable	Laboratory serology	High (>90%)	15-20 (2021-2023)
Italy	Universal screening	First trimester	Not routine	Laboratory serology	>95%	<2 (2018-2023)
Poland	Universal screening	First trimester	Not routine	Laboratory serology	>95%	<1 (2018-2023)
Japan	Universal screening	First prenatal visit	Not routine	Laboratory serology	>95%	5-6 (2023)
Sweden	Universal screening	Early firrst semester	Not routine	Laboratory serology	99%	0
Norway	Universal screening	Early firrst semester	Not routine	Laboratory serology	99%	0
Finland	Universal screening	Early firrst semester	Not routine	Laboratory serology	99%	0

Note. The table summarizes national antenatal syphilis screening strategies alongside approximate congenital syphilis incidence per 100,000 live births, based on the most recent publicly available surveillance data. Incidence values are presented as ranges or rounded estimates to facilitate cross-country comparison and interpretation relative to the World Health Organization elimination of mother-to-child transmission (EMTCT) benchmark of <50 cases per 100,000 live births. Scandinavian countries are included as elimination exemplars, reflecting sustained programmatic coverage and early-pregnancy screening adherence (World Health Organization, 2017, 2022; Taylor et al., 2021).

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REFERENCES

1. Anand, P., Learner, E. R., Barbee, L. A., & Jackson, D. A. (2024). Trends in syphilis case rates among women of reproductive age—United States, 2013–2022. *Sexually Transmitted Diseases, 52*(7), 392–394. https://doi.org/10.1097/OLQ.0000000000002127
2. Ávila-Nieto, C., Pedreño-López, N., Mitjà, O., Clotet, B., Blanco, J., & Carrillo, J. (2023). Syphilis vaccine: Challenges, controversies and opportunities. *Frontiers in Immunology, 14*, 1126170. https://doi.org/10.3389/fimmu.2023.1126170
3. Brandenburger, D., & Ambrosino, E. (2021). The impact of antenatal syphilis point of care testing on pregnancy outcomes: A systematic review. *PLOS ONE, 16*(3), e0247649. https://doi.org/10.1371/journal.pone.0247649
4. Cameron, C. E. (2018). Syphilis vaccine development: Requirements, challenges and opportunities. *Sexually Transmitted Diseases, 45*(9), S17–S19. https://doi.org/10.1097/OLQ.0000000000000831
5. Castillo-Laborde, C., Gajardo, P., Nájera-De Ferrari, M., Matute, I., Hirmas-Adauy, M., Aguirre, P., Ramírez, H., Ramírez, D., & Aguilera, X. (2021). Modelling cost-effectiveness of syphilis detection strategies in prisoners: Exploratory exercise in a Chilean male prison. *Cost Effectiveness and Resource Allocation, 19*(1). https://doi.org/10.1186/s12962-021-00257-9
6. CCDR. (2023). Infectious syphilis and congenital syphilis in Canada, 2023. *Canada Communicable Disease Report, 51*(2/3). 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
7. Centers for Disease Control and Prevention. (2024, November 12). *Sexually transmitted infections surveillance, 2023*. https://www.cdc.gov/sti-statistics/annual/index.html
8. Cunha-Oliveira, A., de Brito Pinto, T. K., Pereira Afonso, M. R., de Almeida Peres, M. A., Pina Queirós, P. J., Santos, D. G., & Gómez-Cantarino, M. S. (2023). Perspective on two major pandemics: Syphilis and COVID-19, a scoping review. *Sustainability, 15*(7), 6073. https://doi.org/10.3390/su15076073
9. Day, S., Carter, A., Lloyd, A., Seña, A. C., Radolf, J. D., & Tucker, J. D. (2024). Barriers and facilitators of participation in syphilis vaccine trials: A qualitative analysis to inform trial design and community engagement in the United States. *Sexual and Reproductive Health Matters, 32*(1), 2473199. https://doi.org/10.1080/26410397.2025.2473199
10. Duarte, G., Melli, P. P. dos S., Miranda, A. E., Milanez, H. M. B. P. M., Menezes, M. L., Travassos, A. G., & Kreitchmann, R. (2024). Syphilis and pregnancy. *Revista Brasileira de Ginecologia e Obstetrícia, 46*, e-FPS09. https://doi.org/10.61622/rbgo/2024FPS09
11. Pan American Health Organization. (2022). *Epidemiological review of syphilis in the Americas, December 2021*. https://iris.paho.org/handle/10665.2/56085
12. Espinoza, J. L., & Trung, L. Q. (2025). Resurgent syphilis across the globe: A public health perspective on bridging surveillance and strategy. *Pathogens, 14*(11), 1148. https://doi.org/10.3390/pathogens14111148
13. Australian Centre for Disease Control. (2025, December 12). *National syphilis monitoring reports*. https://www.cdc.gov.au/resources/collections/national-syphilis-monitoring-reports

14. Gazeta, R. E., & Pereira, M. D. P. (2023). Perfil epidemiológico da sífilis congênita e fatores de risco associados na Rede Regional de Atenção à Saúde 3, São Paulo, Brasil. *BEPA: Boletim Epidemiológico Paulista, 20*, 1–20. https://doi.org/10.57148/bepa.2023.v.20.39359
15. Gilmour, L. S., & Walls, T. (2023). Congenital syphilis: A review of global epidemiology. *Clinical Microbiology Reviews, 36*(2). https://doi.org/10.1128/cmr.00126-22
16. Glikas, M. W., Day, M., & Toon, M. (2025). The resurgence of syphilis: A critical public health concern. *Journal of Pediatric Health Care, 39*(3), 479–488. https://doi.org/10.1016/j.pedhc.2024.09.003
17. He, Y., Chen, D., Fu, Y., Huo, X., Zhao, F., Yao, L., Zhou, X., Qi, P., Yin, H., Cao, L., Ling, H., & Zeng, T. (2023). Immunization with Tp0954, an adhesin of *Treponema pallidum*, provides protective efficacy in the rabbit model of experimental syphilis. *Frontiers in Immunology, 14*, 1130593. https://doi.org/10.3389/fimmu.2023.1130593
18. Huntington, S., Weston, G., Seedat, F., Marshall, J., Bailey, H., Tebruegge, M., Ahmed, I., Turner, K., & Adams, E. (2020). Repeat screening for syphilis in pregnancy as an alternative screening strategy in the UK: A cost-effectiveness analysis. *BMJ Open, 10*(11), e038505. https://doi.org/10.1136/bmjopen-2020-038505
19. World Health Organization. (2021). *Global guidance on criteria and processes for validation: Elimination of mother-to-child transmission of HIV, syphilis and hepatitis B*. https://www.who.int/publications/i/item/9789240039369
20. Kojima, N., Konda, K. A., & Klausner, J. D. (2022). Notes on syphilis vaccine development. *Frontiers in Immunology, 13*, 952284. https://doi.org/10.3389/fimmu.2022.952284
21. Korenromp, E. L., Rowley, J., Alonso, M., Mello, M. B., Wijesooriya, N. S., Mahiané, S. G., Ishikawa, N., Le, L.-V., Newman-Owiredu, M., Nagelkerke, N., Newman, L., Kamb, M., Broutet, N., & Taylor, M. M. (2019). Global burden of maternal and congenital syphilis and associated adverse birth outcomes—Estimates for 2016 and progress since 2012. *PLOS ONE, 14*(2), e0211720. https://doi.org/10.1371/journal.pone.0211720
22. Lai, H., Fairley, C. K., Li, R., Chen, M. Y., Chow, E. P. F., Donovan, B., Callander, D., Guy, R., Tran, J., Aung, E. T., Shen, M., & Zhang, L. (2025). Impact and cost-effectiveness of regular self-digital anorectal examination on syphilis among gay, bisexual, and other men who have sex with men: A mathematical modeling study. *The Journal of Infectious Diseases, 232*(3), e393–e402. https://doi.org/10.1093/infdis/jiaf310
23. Lithgow, K. V., & Cameron, C. E. (2017). Vaccine development for syphilis. *Expert Review of Vaccines, 16*(1), 37–44. https://doi.org/10.1080/14760584.2016.1203262
24. Liu, A., Giacani, L., Hawley, K. L., Cameron, C. E., Seña, A., Konda, K., Radolf, J. D., & Klausner, J. D. (2024). New pathways in syphilis vaccine development. *Sexually Transmitted Diseases, 51*(11), e49–e53. https://doi.org/10.1097/OLQ.0000000000002050
25. Liu, M., Zhou, J., Lan, Y., Zhang, H., Wu, M., Zhang, X., Leng, L., Mi, X., & Li, J. (2023). A neglected narrative in the COVID-19 pandemic: Epidemiological and clinical impacts of the COVID-19 outbreak on syphilis. *Clinical, Cosmetic and Investigational Dermatology, 16*, 2485–2496. https://doi.org/10.2147/CCID.S417522
26. Lukehart, S. A., Molini, B., Gomez, A., Godornes, C., Hof, R., Fernandez, M. C., Pitner, R. A., Gray, S. A., Carter, D., Giacani, L., & Cameron, C. E. (2022). Immunization with a tri-antigen syphilis vaccine significantly attenuates chancre development, reduces bacterial load, and inhibits dissemination of *Treponema pallidum*. *Vaccine, 40*(52), 7676–7692. https://doi.org/10.1016/j.vaccine.2022.11.002
27. Moseley, P., Bamford, A., Eisen, S., Lyall, H., Kingston, M., Thorne, C., Piñera, C., Rabie, H., Prendergast, A. J., & Kadambari, S. (2024). Resurgence of congenital syphilis: New strategies against an old foe. *The Lancet Infectious Diseases, 24*(1), e24–e35. https://doi.org/10.1016/S1473-3099(23)00314-6
28. Nazir, A., Masood, W., Ahmad, S., Nair, A. M., Aborode, A. T., Khan, H. D., Farid, S., Raza, M. A., & Audah, K. A. (2022). Rise of syphilis surge amidst COVID-19 pandemic in the USA: A neglected concern. *Annals of Medicine and Surgery, 80*, 104239. https://doi.org/10.1016/j.amsu.2022.104239
29. Peeling, R. W., Mabey, D., Chen, X.-S., & Garcia, P. J. (2023). Syphilis. *The Lancet, 402*(10398), 336–346. https://doi.org/10.1016/S0140-6736(22)02348-0
30. European Centre for Disease Prevention and Control. (2025, February 10). *Syphilis: Annual epidemiological report for 2023*. https://www.ecdc.europa.eu/en/publications-data/syphilis-annual-epidemiological-report-2023
31. Ramchandani, M. S., Cannon, C. A., & Marra, C. M. (2023). Syphilis. *Infectious Disease Clinics of North America, 37*(2), 195–222. https://doi.org/10.1016/j.idc.2023.02.006
32. Saldarriaga, E. M., Pollock, E. D., Jackson, D. A., Gift, T. L., Barbee, L. A., Bachmann, L. H., & Spicknall, I. H. (2025). Cost effectiveness of the reverse sequence algorithm compared with the traditional algorithm for syphilis screening among pregnant women. *Obstetrics & Gynecology*. https://doi.org/10.1097/AOG.0000000000006019
33. Waugh, S., & Cameron, C. E. (2024). Syphilis vaccine development: Aligning vaccine design with manufacturing requirements. *Human Vaccines & Immunotherapeutics, 20*(1), 2399915. https://doi.org/10.1080/21645515.2024.2399915
34. Welc, N., Frącz, W., Olejniczak, R., Żaba, R., & Kavanagh, K. (2025). Analysis of the effect of the COVID-19 pandemic on syphilis in susceptible populations: Men who have sex with men, people living with HIV, and patients with gestational and congenital syphilis—A narrative review. *Microorganisms, 13*(6), 1205. https://doi.org/10.3390/microorganisms13061205

35. World Health Organization. (2020). *Global Health Observatory*. https://www.who.int/data/gho
36. World Health Organization. (2025, May 29). *Sexually transmitted infections (STIs)*. https://www.who.int/news-room/fact-sheets/detail/sexually-transmitted-infections-(stis)
37. Wijesooriya, N. S., Rochat, R. W., Kamb, M. L., Turlapati, P., Temmerman, M., Broutet, N., & Newman, L. M. (2016). Global burden of maternal and congenital syphilis in 2008 and 2012: A health systems modelling study. *The Lancet Global Health, 4*(8), e525–e533. https://doi.org/10.1016/S2214-109X(16)30135-8
38. Wozniak, P. S., Cantey, J. B., Zeray, F., Leos, N. K., Michelow, I. C., Sheffield, J. S., Wendel, G. D., & Sánchez, P. J. (2023). The mortality of congenital syphilis. *The Journal of Pediatrics, 263*, 113650. https://doi.org/10.1016/j.jpeds.2023.113650
39. Zhang, M., Zhang, H., Hui, X., Qu, H., Xia, J., Xu, F., Shi, C., He, J., Cao, Y., & Hu, M. (2024). The cost-effectiveness of syphilis screening in pregnant women: A systematic literature review. *Frontiers in Public Health, 12*, 1268653. https://doi.org/10.3389/fpubh.2024.1268653