REVIEW ARTICLE

COMPREHENSIVE REVIEW OF SPATIAL AND SPATIO-TEMPORAL ANALYSIS TECHNOLOGIES FOR SYPHILIS AS A POTENTIAL TOOL FOR PUBLIC HEALTH ACTIONS

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Highlights: (1) Spatial analysis strengthens health surveillance and decision-making. (2)Social determinants influence the spatial distribution of syphilis. (3)There are gaps in the use of multivariate spatial analyses regarding syphilis.

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ABSTRACT

Objective: To summarize the types of spatial and spatiotemporal analysis technologies used to study syphilis in the context of public health. **Methods:** This is an integrative literature review that used the PICo strategy to formulate the guiding question: Which scientific studies use spatial and/or spatiotemporal analysis technologies to examine the distribution of syphilis cases? Searches were conducted in the information sources PubMed®, SCOPUS, and Web of Science, as well as in the Virtual Health Library (VHL) on January 16, 2024, using Boolean operators combined with the following keywords: "Syphilis," "Spatial analysis," "Spatio-Temporal Analysis," "Public Health." The selection was performed using the Systematic Review Support (AReS) *software*, and studies were included regardless of language or time period, provided they employed an ecological study design. **Results:** Sixteen articles published since 2010 were analyzed. All used secondary data with an ecological design. Data analysis techniques included area analysis, Bayesian analysis, global and local Moran's I, sweep statistics, the Prais-Winsten model, and kernel density estimation, with a focus on incidence and prevalence rates, particularly in Brazil. **Conclusion:** It became evident in the studies that syphilis is not limited to the occurrence of cases alone but is also related to socio-spatial factors that influence its occurrence in time and space, such as socioeconomic inequalities, social vulnerabilities, and access to health services.

Keywords: syphilis, spatiotemporal analysis, spatial analysis, public health.

INTRODUCTION

Considered an ancient disease transmitted sexually and vertically, with its etiological agent, *Treponema pallidum*, discovered in 1905 and treated since the early 20th century, syphilis was expected to be controlled and eliminated; however, the current situation has shown that the disease involves more complex aspects than the mere availability of treatment. The growing number of reported syphilis cases reflects the fragility of the public health system and the numerous challenges in controlling the disease, such as limited access to Primary Health Care (PHC) services, low testing rates among pregnant women and their partners, inadequate treatment, long latency periods, and stigma and discrimination against vulnerable populations[1].

According to recent global estimates, syphilis continues to spread worldwide, with the annual number of new cases rising from approximately 6 million in 2015 to an estimated 9 million by 2025, highlighting the persistence and resurgence of the disease in various epidemiological contexts[2]. The 74th World Health Assembly, held in 2021, endorsed the need for new response strategies for 2022–2030 to finally achieve the *Sustainable Development Goals* in the area of health and well-being[3].

Given this scenario, it is indisputable that syphilis remains a public health problem worldwide; information on spatial and spatiotemporal distribution allows for an understanding of the dynamics of transmission and the epidemiological persistence of the disease, as it highlights susceptible areas and trends, as well as possible associations with local characteristics, such as social determinants, which, together with the cultural and environmental conditions of the population, lead to the stratification of health risks across population groups[4].

Furthermore, ecological studies provide scientific support to health professionals and managers as a health management tool for formulating public policies to map the needs of each region and identify priority areas for the development of

surveillance and control measures[5].

Given this scenario, it is indisputable that syphilis remains a global public health problem. The scientific literature has highlighted that using information on the spatial and spatiotemporal distribution of the disease, facilitated by various analytical and informational technologies, enables the identification of susceptible areas, epidemiological trends, and potential associations with local characteristics, including social, cultural, and environmental determinants. These elements, as described in the studies, contribute to the stratification of risks across different population groups[4].

Furthermore, evidence from scientific research indicates that technologies employed in studies with a territorial approach have been described as tools to support health professionals and managers, informing health planning and decision-making processes[5].

With the rise and use of various spatial and spatiotemporal analysis techniques applied to public health in recent years, it is worth noting that their application remains relatively limited across epidemiological contexts[5]. In this regard, this integrative review aims to synthesize the types of spatial and spatiotemporal analysis technologies used for syphilis in the context of public health.

METHODS

This is an integrative review consisting of six stages: (1) formulation of the guiding question; (2) sampling and/or literature search; (3) categorization of studies; (4) evaluation of studies included in the review; (5) interpretation of results; (6) synthesis and presentation of results[6].

The PICo strategy was used, an acronym where “P” stands for population or problem; “I” for intervention or phenomenon of interest; and “Co” for context[7]. For this study, “P” was used for syphilis, “I” for spatial and spatiotemporal analyses, and “Co” for public health. Thus, to begin the Integrative Literature Review, the following

research question was used: Which scientific studies use spatial and/or spatio-temporal analysis technologies to map the distribution of syphilis cases?

The following terms were selected from the Medical Subject Headings (MeSH) and the Descriptors in Health Sciences (DeCS): “Syphilis,” “Spatial Analysis,” “Spatio-Temporal Analysis,” “Public Health.” These were combined using two search strategies, employing the Boolean operator “AND”: the first search strategy was “Syphilis” AND “Spatio-Temporal Analysis” AND “Public Health,” and the second search strategy was “Syphilis” AND “Spatial analysis” AND “Public Health”, consulted in the Virtual Health Library and in the information sources PubMed®, Scopus, and Web of Science.

Data collection took place on February 16, 2024; there was no restriction on the publication period due to the need to identify the largest number of studies on the topic, to better elucidate the knowledge gap, and because no other integrative review with similarities to this review question was identified in the literature. After applying the search strategy, the titles and abstracts were reviewed to select articles relevant to the topic, which were then read in full.

The inclusion criteria were articles available in open-access electronic format that addressed the study’s themes and the clinical stage of the disease and answered the question related to syphilis, regardless of the type of infection (acquired, gestational, or congenital syphilis). In addition, studies with an ecological design were considered, regardless of type.

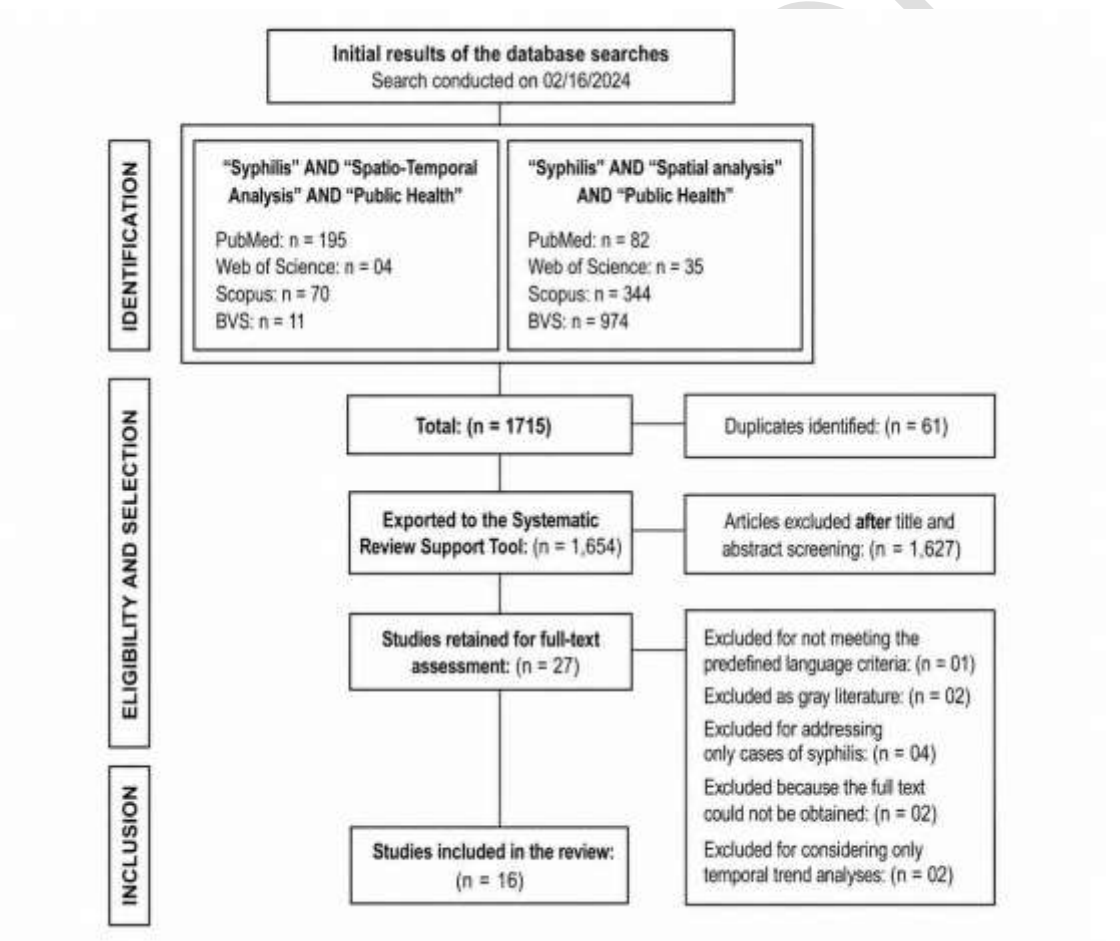
Information sources were accessed through CAFe, which provides access to the subscription-based content of the CAPES Journal Portal, ensuring consultation of the largest possible number of scientific publications.

For the initial analysis of the studies, the Systematic Review Support (AReS) tool (version 1.0), available online and free of charge[8], was used. In this stage, the title and abstract were carefully reviewed to verify compliance with the inclusion and

exclusion criteria. Of the 1,654 articles exported, 16 studies were selected for this research, as shown in the PRISMA *Flow Diagram*[9]– Figure 1.

To extract the results, a tool was created in **Excel®** (version 2309) to characterize the studies and relate them to the review's objective and research question.

Figure 1: PRISMA diagram regarding the study selection process. São Carlos, Brasil

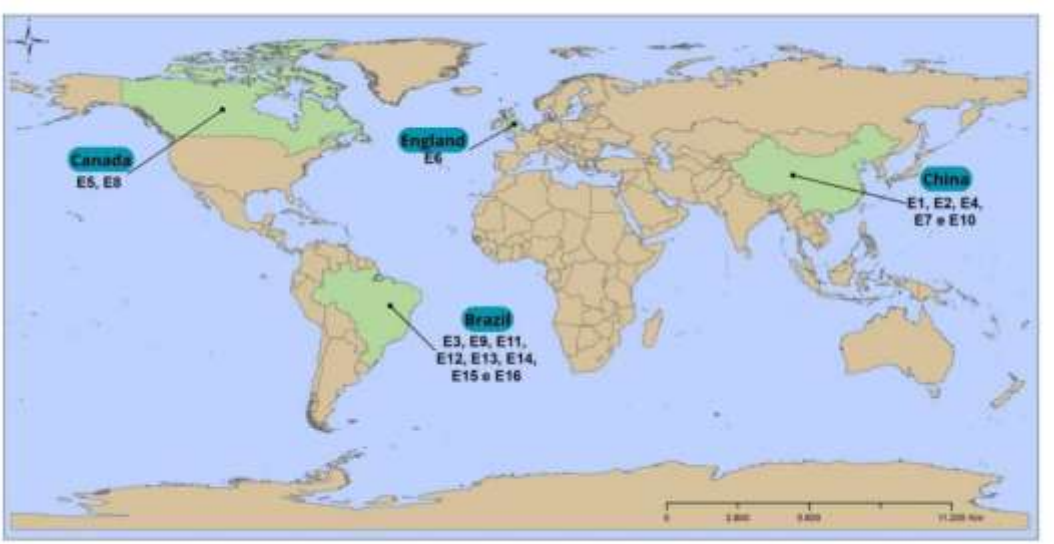


Source: Authors' own work (Adapted PRISMA)

RESULTS

Sixteen articles were selected, published since 2010, with a focus on the years 2022—4 articles (25.00%) and 2021—3 articles (18.75%), which had the highest number of publications. All studies were published in English; no publications in Spanish or Portuguese were identified. Regarding the setting, 8 (50%) of the eligible articles were published in Brazil, followed by 5 (31.00%) in China, 2 (12.50%) in Canada, and 1 (6.50%) in England (Figure 2).

Figure 2: Locations of the works considered according to country of origin.



Source: Authors' own

The data sources for the studies were derived from secondary data from various Health Information Systems specific to each country: in China (China Disease Prevention and Control Information System, National Notifiable Infectious Diseases Reporting System, China Statistical Yearbook of Health and Family Planning), in Brazil (Notifiable Diseases Information System – SINAN, Sexually Transmitted Infections (STIs) and HIV/AIDS Program of São Paulo), in Canada

(*Toronto Public Health and British Columbia Centre for Disease Control (BCCDC) Public Health Laboratory*), and finally, England (*Genitourinary Medicine Clinic Activity Dataset – GUMCAD*).

All studies had an ecological design, accompanied by a description and/or analysis of the sociodemographic characteristics of the cases. Among the main e y analysis techniques explored in the studies, the following stood out: area data analysis with spatial distribution of incidence and prevalence in 16 (100%) of the studies, spatial autocorrelation analysis (global and local Moran's I) in 8 (50.00%), Bayesian analysis in 6 (43.75%), spatiotemporal sweep analysis in 8 (50.00%), temporal trend analysis (Prais-Winsten model) in 2 (12.50%), and kernel density estimation in 2 (12.50%). Table 1 presents the distribution of articles by author/year, objectives, data source, analysis, model and/or technique used, and main findings.

Table 1: Instrument developed by the reviewers for the characterization of the studies.

Author/ Year	Objectives	Data source	Analysis, model, and/or technique used	Main findings	Limitations of the studies according to the authors
ZHU, X *et al*., 2022.	To identify epidemiological trends, priority areas, and factors related to the spatiotemporal analysis of syphilis incidence in Zhejiang Province from 2005 to 2018.	China Disease Prevention and Control Information System.	Spatial autocorrelation analysis; Global and local Moran's index; Spatio-temporal scanning analysis; Bayesian model	High prevalence of syphilis in Zhejiang Province. Case prevalence was higher among females, sex workers, farmers, the unemployed, and migrants.	Underreporting of cases due to the stigma surrounding syphilis.
WANG *et al*., 2022	To analyze the characteristics of the spatiotemporal distribution of syphilis in Ningxia, northwestern	National Notifiable Infectious Disease Reporting System	Spatial autocorrelation analysis (global and local Moran's I); and Spatio-temporal scanning	The spatiotemporal analysis from 2004 to 2017 showed that the incidence of syphilis in Ningxia increased from 3.78/100,000 in 2004 to 54.69/100,000 in 2017, with	No detailed analysis of the different stages of syphilis due to limited data.

	China, and its potential environmental influencing factors.		analysis	significant spatial heterogeneity.	
MEDEIROS *et al*., 2022	To estimate the incidence of syphilis in pregnant women and congenital syphilis in municipalities in the state of São Paulo, and to assess its relationship with socioeconomic, demographic, and healthcare variables.	Notifiable Diseases Information System (SINAN) and STI and HIV/AIDS Program	Bayesian Model	A continuous increase in the temporal RR of syphilis in pregnant women from 2007 to 2018, and congenital syphilis from 2007 to 2017. The incidence of syphilis in pregnant women and congenital syphilis increased 8.6-fold and 6.6-fold, respectively. The increase occurred simultaneously in almost all municipalities in São Paulo.	Secondary data with the possibility of underreported cases and the inability to consider variables indicative of programmatic vulnerability due to the lack of free access to this type of data.

TANG *et al*., 2021	To describe the spatial and temporal distribution of primary and secondary syphilis in Guangdong Province from 2005 to 2017, and to investigate the sociodemographic and socioeconomic factors associated with syphilis incidence.	National Notifiable Infectious Disease Reporting System.	Spatial autocorrelation analysis, Global Moran's index, Spatio-temporal scan analysis	Economically underdeveloped cities showed an initial increase in syphilis incidence during 2005–2013, followed by a decrease.	Possibility of underreporting cases.
SALWAY *et al*., 2019	To conduct a spatiotemporal epidemiological analysis of reported cases of infectious syphilis in British Columbia over 12 years.	Centre for Disease Control (BCCDC) Public Health Laboratory.	Bayesian model	Between 2007 and 2016, rates were 18 times higher for those living in downtown Vancouver compared to those living outside the cluster. In West Central Vancouver, 20% of adult men self-identified as gay and bisexual, and in East Central Vancouver, 5.1% to 20% of adult men	23% of cases had addresses that were unsuitable for inclusion in the geospatial analyses.

				self-identified as gay and bisexual.	
PETERSEN *et al.*, 2016	Spatial clusters and variations in the trajectory of local epidemics were explored in relation to sexual orientation, demographic factors, and stage of syphilis.	Genitourinary Medicine Clinic Activity Dataset (GUMCAD)	Spatio-temporal scan analysis;	Between 2009 and 2013, 12,521 cases were reported, of which 6,082 (49%) were reported in London. The incidence in London was five times higher than in the rest of England. The clusters had diagnostics ranging below 10 cases per month.	Lack of denominator data for men who have sex with men in London, Manchester, Brighton, and Blackpool.

HU *et al*., 2010	Identifying clusters of primary and secondary syphilis in Shenzhen in recent years using spatial and spatiotemporal statistics.	China Disease Prevention and Control Information System.	Spatio-temporal scan analysis.	A total of 9,126 cases of primary and secondary syphilis were reported between 2005 and 2008, in 5,173 men and 3,953 women. In 2005, there were twelve statistically significant clusters and two minor significant clusters, while the numbers were eight and seven in 2006, ten and five in 2007, and nine and four in 2008, respectively.	The number of cases of primary and secondary syphilis is very low, which can cause high variability in rates and introduce errors in calculations.

GESINK *et al*., 2014	To obtain information on the syphilis epidemic in Toronto by examining the spatial pattern and spread of syphilis over time.	Toronto Public Health	Spatio-temporal scan analysis; Bayesian model.	The relative rate of syphilis was 12.2 times higher in the central area than outside the central area, and 2 to 3 times higher within outbreak areas compared to outside outbreak areas. The epidemic curves indicate that the number of syphilis cases with risky sexual behaviors is higher in non-core and central areas and lower in outbreak areas.	SatScan has its limitations. Specifically, clusters within clusters cannot be detected, meaning that outbreaks in central areas cannot be determined. Furthermore, during spatiotemporal analyses, the cluster size is fixed; therefore, it is not possible to see how clusters change over time .

FALAVINA *et al*., 2019	Analyze the trend and spatial distribution of certain notifiable diseases in pregnant women.	SINAN.	Spatial scan Analysis and Temporal trend (Prais-Winsten model).	The syphilis rate increased annually by an average of 30.8%. In the North and Northwest, syphilis rates increased annually by an average of 40.7% and 38%, respectively. The incidence of syphilis was 141.1 per 10,000 live births, with an upward trend	Secondary data that may be influenced both by the possibility of underreporting of infectious disease cases in pregnant women and by the quality and reliability of the information contained in SINAN.
ZHU, B *et al.*, 2018	To analyze the spatial distribution patterns of 12 Class B notifiable infectious diseases that remain active throughout China.	China Statistical Yearbook on Health and Family Planning.	Spatial Autocorrelation Analysis: Global and Local Moran's Index	The third most common infectious disease is syphilis, with a proportion and number of cases of 14.25% and 433,974, respectively. Syphilis did not show significant positive global spatial autocorrelation	Risk of ecological fallacy.

LINO *et al*., 2021	To assess the epidemiological profile, spatial distribution, and time series of cases of acquired syphilis, syphilis in pregnant women, and congenital syphilis in a Brazilian municipality.	SINAN.	Kernel and Temporal trend (Prais-Winsten model)	Concentration of cases in regions with lower monthly income, showing an upward trend. There was an increase in detection rates for acquired syphilis and syphilis in pregnant women, as well as in the incidence rate of congenital syphilis. Spatial distribution showed a concentration of acquired syphilis cases in the Central and South- n regions, while reports of syphilis in pregnant women and congenital syphilis were concentrated in the Eastern region	Use of secondary data, which limited the availability of some information and led to underreporting. Inadequately reported cases of acquired syphilis; restricting information on the epidemiological profile and case investigation.

OLIVEIRA, *et al*., 2023	Estimate the level of underreporting and correct the incidence rates of congenital syphilis in the 557 Brazilian micro-regions.	SINAN.	Bayesian model	Brazilian micro-regions and states in the North and Northeast regions had the highest rates of underreporting, while the South region had the lowest rates of underreported cases. This highlights regional disparities in the incidence rate of syphilis and in the quality of prenatal care, as well as emphasizing the need to improve the quality of information recorded in SINAN, given the importance of disease surveillance nationwide	The percentages of underreported cases were calculated for the entire study period, which did not allow for an analysis of possible improvements or setbacks in the quality of information over time.

SOARES *et al*., 2023	To analyze the spatial distribution of syphilis in pregnant women from 2008 to 2018 in Brazil and identify correlations with socioeconomic and health factors.	SINAN.	Spatial autocorrelation analysis: Global and local Moran's I	The spatial analysis of SG in Brazil revealed high-high clusters of detection rates in the South and Midwest. In contrast, the central region of the Northeast exhibited low-low clusters. The Human Development Index and the Human Development Index indicated the influence of socioeconomic factors in various regions of the country	Use of secondary data from Brazilian information systems, and possible Underreporting.

RAIMUNDO *et al*., 2021	To analyze the spatial distribution of congenital syphilis cases in a state in northeastern Brazil.	SINAN.	Spatio-temporal scan analysis; Bayesian model, Spatial autocorrelation analysis; Global and local Moran's I.	The 1st, 3rd, and 7th Health Regions, with a spatial grouping encompassing the 3rd , 5th (e) and 7th Regions, were the most affected by the disease, with an increased risk of congenital syphilis of up to 2.65 times.	Use of secondary data, as this may be related to incomplete reporting information and the possibility of underreporting, contributes to an underestimation of the actual epidemiological situation of congenital syphilis in the state analyzed.

SEABRA *et al*., 2022	To analyze the epidemiological landscape of congenital syphilis in Brazil using spatial analysis techniques.	SINAN.	Spatio-temporal scan analysis, spatial autocorrelation analysis, global and local Moran's index, Kernel.	Considering that CS is a preventable disease, the recent change in federal funding for Primary Care in Brazil may improve maternal and child health indicators; the Brazilian Ministry of Health launched the Previne Brasil policy, which transfers funds to municipalities based on their health indicators.	Underreporting of congenital syphilis cases due to the use of secondary data, which may imply that the incidence rate of congenital syphilis could be higher than those presented.

SOARES *et al*., 2020	To analyze the spatial distribution of syphilis in pregnant women and congenital syphilis in the state of Espírito Santo, Brazil, from 2011 to 2018.	SINAN	Bayesian model, spatial autocorrelation, global Moran's index.	Approximately 30 municipalities with the highest incidence of the outcomes were identified, and approximately 14 municipalities with a high proportion of congenital syphilis and a low proportion in pregnant women.	This includes inference in data analysis, as the variables must be interpreted in a grouped manner. Another limitation of the study lies in the possibility of fluctuation in crude incidence rates in small and medium-sized municipalities or those with small populations.

DISCUSSION

After reviewing the articles, it was possible to identify the profile and behavior of syphilis, with clusters correlating with socio-spatial markers[10-8] and epidemiological profiles[10,13,14,15,16,19,20], characterized by high population density[21-4], inadequate prenatal care[15,16,17,18,21,22,25], and migration to developed and/or developing areas[13,16,21,22].

Regarding the landscape, it is highly relevant to highlight the countries with the highest number of published studies on the topic, especially considering the dichotomy between countries. In China, one of the world's major powers, syphilis remains a public health problem; the increase in syphilis cases is directly linked to the resurgence of the infection in the country in recent years, after it had been eradicated in the 1960s [19,24]. Brazil, on the other hand, is considered an emerging country that faces various challenges in its health system due to its vast territory, with disparities in access to health services across different regions and among vulnerable populations, socioeconomic problems, and underreporting of cases[16-8].

Therefore, the discussion of the content was divided into the following categories of analysis: Sociodemographic and epidemiological approaches to syphilis**;** Data mapping and analysis strategy; Challenges of epidemiological studies using secondary data.

Sociodemographic and epidemiological approaches to syphilis

The selected studies that addressed spatiotemporal analysis technologies demonstrate that syphilis has a high and rising prevalence among vulnerable populations. Among the studies that addressed these issues, sociodemographic characteristics revealed a profile of men who have sex with men [11–3], a higher prevalence of the disease among women [(16,21, 23)], particularly those of mixed-race or Black descent [10], sex workers [(21)], and those with low levels of education [14].

Studies addressing the infection in men who have sex with men indicate a certain vulnerability of this population to the disease[11-3]. Among these studies, one conducted in Toronto, Canada, from 2006 to 2010, showed that 79% of all male patients with syphilis reported having had sex with other men, suggesting that men living in areas with syphilis outbreaks migrate to the city center in search of sexual partners[13].

Regarding racial aspects related to syphilis, only two studies addressed the topic; one conducted in London, where primary syphilis was more prevalent among white men[12]; and another, conducted in the 645 municipalities of the state of São Paulo, Brazil [10], which identified a shift in the ethnic/racial profile of women diagnosed with syphilis: in 2007, the majority of reported cases were among white women, whereas in 2018, the majority were among Black or mixed-race women.

These findings reflect the historical pattern of existing structural racism and highlight a public health problem, as the social and economic inequality experienced by the Black population has driven the development of risk factors such as substance abuse, disease stigma, domestic violence, risky sexual behavior, and unstable housing, which increases the rate of migration to other locations[26].

Given this scenario, it is worth highlighting the inhumane and racist Tuskegee Experiment conducted in the United States from 1932 to 1972, which aimed to observe the progression of syphilis in Black men without any treatment, thereby fostering distrust among the Black population toward the medical community and increasing the stigma surrounding the disease due to negative stereotypes experienced[27].

A considerable number of studies conducted in Chinese provinces were identified[15,20-3], which can be explained by the prevention plan established in 2010 to reduce the incidence of primary and secondary syphilis in the country[22], by the rise in infectious diseases, and by the difficulty in controlling them due to high population density combined with the country's high migration rate[15].

Recent data indicate that the incidence of syphilis in China maintained a growth trend of 11.55% from 2002 to 2021[28]. Thus, the increase in the number of cases in the

country may have led to a rise in the number of studies seeking to analyze this public health problem[21-2].

In Brazil, syphilis subpopulations are well-defined in studies[10-8,25]. Since acquired, gestational, and congenital syphilis were classified as notifiable diseases in 2010, 2005, and 1986, respectively, the inclusion of these data enabled a significant improvement in epidemiological diagnoses in specific geographic areas, given that there is standardization and a definition criterion for each condition, as recommended by health information systems[29].

A study conducted in Paraná, a state in southern Brazil, analyzed the trend and spatial distribution of six notifiable diseases among pregnant women from 2013 to 2016; and of these, syphilis had the highest incidence rate, accounting for 30.8% of the diseases analyzed, and the second-highest detection rate with 141.7 cases per 10,000 live births, second only to dengue[19]. Nevertheless, in a study conducted in the same country from 2013 to 2017, among reported cases of pregnant women with syphilis, 50% received inadequate treatment, and 32.1% of partners were not treated, which increases the risk to the pregnant woman and of congenital syphilis[14].

Differentiating the epidemiological patterns of syphilis is essential to understanding how this infection manifests in different population groups and geographic regions, considering variations in disease incidence, the most affected age groups, the affected subpopulation, predominant risk factors, and characteristics of associated lesions[17] .

Finally, to elucidate the management of syphilis cases in relation to all aspects mentioned above, it was observed—in addition to the research objectives—that of the total 16 selected studies, 4 (25.00%) of the studies had acquired syphilis cases as their study population, 6 (37.50%) cases of syphilis in pregnant women, 5 (31.25%) cases of congenital syphilis, and 5 (31.25%) articles did not specify subpopulations, mentioning only the general context of syphilis. To clarify, some studies addressed two conditions.

Data mapping and analysis strategy

Early prevention of syphilis is an effective strategy for interrupting the chain of transmission of the disease; it involves identifying areas and regions with a high risk of syphilis incidence and potential links to socioeconomic factors and health resources[30]. The selected articles highlight the use of spatial and spatiotemporal distribution as a strategic and effective option for the syphilis health surveillance process. Notable geographic factors contributing to higher syphilis incidence include areas with large population clusters[17-8,21] and countries with developing economies[22-3] due to high migration rates to these locations.

Visualizing the geographic distribution of health events on maps, along with analyses of related factors, provides a valuable tool for understanding, preventing, and controlling diseases and health problems in a specific area. This not only aids in the efficient allocation of resources and efforts but also contributes to a more precise and targeted approach to the population's health needs[31].

In the context of spatial analysis technologies, another widely used analytical methodology in the research studies was the Global Moran's Index, which consists of fundamental exploratory spatial analysis for characterizing spatial dependence by relating the observed values of an attribute in a region to whether they depend on the values of that same variable in neighboring locations, to identify spatial autocorrelation[31].

Spatial autocorrelation methods were used to analyze the spatial distribution characteristics of syphilis incidence in the studies[16-8,21-5]; the Global Moran's I showed positive autocorrelation for syphilis incidence. The Local Indicator of Spatial Association (LISA), on the other hand, was used to identify spatial clusters and their statistical significance[16-8,21,22,24].

In summary, and also more recently compared to the other techniques mentioned above, it is worth mentioning the analytical potential of the Bayesian model,

which can be used in mapping diseases and their risks, testing hypotheses, establishing correlations between variables to identify areas of higher risk, aiding in health decision-making, interpreting the implementation of existing interventions, and intervening to reduce morbidity through prevention programs in health systems[32].

This method was used in studies conducted in China[21], Canada[13], and Brazil[15] using *Markov Chain Monte Carlo* (MCMC) estimation[33], and in Brazil[10] and in Canada[23], which used parameter estimation via the *Integrated Nested Laplace Approximation* (INLA) method[34].

These studies sought to relate social and economic determinants to increased syphilis incidence rates, such as per capita Gross Domestic Product (GDP), people over 60 years of age, the number of health professionals per 10,000 inhabitants, and the average annual temperature of a region[21], municipalities with large populations, teenage pregnancy, the presence of comorbidities such as Acquired Immunodeficiency Syndrome (AIDS)[10], low-income households[11,16,25], and increased residential instability[13,25]. Thus, social and economic determinants had a major influence on the rising number of syphilis cases.

Another key finding identified by the analytical strategy used in the Canadian study was unequal access to STI testing; it was found that syphilis testing rates gradually decrease as people move further from the city center, highlighting the importance of expanding testing and prevention initiatives in more suburban areas of the city where the most vulnerable populations reside[11].

In the context of congenital syphilis, in studies that addressed the spatial distribution of cases [17,18,20,25], spatial analysis has contributed to effective public health actions within the health system, focused on case finding, case reporting, health education, and the optimization of epidemiological surveillance—with the capacity to generate high-quality health data and information, thereby enhancing the effectiveness of primary health care (PHC) interventions.

Still on the topic of data mapping strategies, kernel density estimation was used

to map statistically significant hotspots in two studies[15,18]. Its application was demonstrated in an analysis conducted in Brazil addressing acquired, pregnant, and congenital syphilis, where the georeferencing of reported cases identified that the incidence of syphilis was concentrated in regions with greater social vulnerability and, consequently, among people with lower household income[14].

In another study of the congenital syphilis population in Brazil[18], the Kernel density estimate showed a spread of the disease across the country, and an improvement in case detection rates within the notification system during the study period from 2015 to 2018, due to health initiatives implemented, such as the Strategic Action Agenda for the Reduction of Congenital Syphilis in 2016. More recently, these strategies have been restructured and expanded through the Alyne Network, created in 2024, which strengthens the organization of prenatal care, childbirth, and neonatal care within the Unified Health System (SUS)[35].

Another technique that relates to population size—in this case, the at-risk population—is the spatial and spatiotemporal scanning proposed by Kulldorff to identify the location of spatial and spatiotemporal clusters. This method has been used worldwide to detect disease clusters and to determine how a given disease is distributed across a territory, whether uniformly or heterogeneously, by identifying clusters of protection or risk, with calculation of the Risk Ratio (RR) with statistical significance for a specific disease and/or health condition[36].

It should be noted that the RR is defined as the ratio of the risk of developing the conditions in an area relative to the risk of developing them outside that area. Identifying the RR of clusters allows for comparison of information across dissimilar areas, as the effects of different populations are disregarded, thereby revealing the intensity of occurrence of the phenomenon under analysis across the entire study area[37].

The application of spatial and spatiotemporal scanning techniques in the studies[12-3,16,18,20-3] detected the dynamics of syphilis evolution in high-risk regions located in areas of rapid industrial development and urbanization with increased

migration due to developed or developing economies[21-2] with greater allocation of resources to health, employment opportunities, and improved quality of life, which was accompanied by an increase in the number of syphilis cases[23,17].

However, these factors directly impact STI control, since disease surveillance is compromised by high population mobility[21], unfavorable socioeconomic conditions, and psychological issues, which also encourage unprotected sexual behavior due to low-risk perception, resulting in greater exposure to syphilis infection[19]. For illustrative purposes, in China, diseases are categorized based on their severity, ease of transmission, and impact on public health, grouping them into classes A, B, or C. Syphilis ranks third among the most common Class B notifiable infections, accounting for 14.25% of all diseases and 433,974 reported cases in 2015[24].

In a study conducted in all Brazilian state capitals[18], spatiotemporal analysis indicated that the Brazilian state capitals of Recife, Campo Grande, Rio de Janeiro, Porto Alegre, and Manaus are the cities with the highest spatial and spatiotemporal risk of congenital syphilis.

Furthermore, spatiotemporal analysis technology revealed that the high number of syphilis cases over several months may indicate recent sexual contacts, which require effective management through partner notification strategies to be rapidly controlled and the chain of transmission eliminated[12].

Finally, based on the evidence found, it is possible to state that spatial and spatiotemporal analysis techniques constitute an important tool for planning health interventions with a local focus, using the identification of areas of concentration and the movement of cases over time[23], thereby also facilitating resource optimization and the development of actions that help reduce morbidity through prevention programs. Furthermore, several of these analyses utilize neighborhood relationships that mitigate the random fluctuations that might be present in scenarios with underreported population and/or case records[10].

Challenges of studies using secondary data

The studies analyzed have some limitations mentioned even by the authors themselves, which were mainly related to the use of secondary data (collected from public-domain databases and websites or electronic patient records), in which some information is limited and comes from different information systems, affecting the quality of local surveillance services, lack of reporting on the type of syphilis[14,19,21-3] and unrecorded clinical characteristics.

In addition to these points, it is worth noting that the use of secondary data must take into account the possibility of underreporting, which, incidentally, was present in most studies [10–2, 14–8, 20, 23], as well as the limited availability of detailed information, which is common in surveillance data and epidemiological studies; due to stigma or even lack of knowledge about the disease, some individuals were afraid to provide their addresses, directly impacting the geolocation of cases, control, screening, and treatment of syphilis[11,13].

Furthermore, although we recognize the potential of ecological studies, particularly due to the ability to measure a large population sample within a defined geographic area, serving as an alternative in scenarios where individual data is unavailable, insufficient, or difficult to access[4] it is worth noting a bias that is quite prevalent in this type of study: the ecological fallacy[38-9]. Only one study addressed this risk in its limitations[21], which directly affects the interpretation of the data and does not necessarily indicate that individuals exposed in the studies are at greater risk of contracting syphilis than those who were not exposed, since the population sample is not completely homogeneous in terms of exposure.

In summary, it is important to note that the ecological relationship identified in a population group or at an aggregate level cannot necessarily be used to explain relationships at the individual level; in some cases, a correlation at one level may disappear completely at another level, or may even be reversed, requiring caution when

analyzing the data and associations present in the studies[40].

Similarly, it is worth noting that the use of secondary and aggregated data sources aids and enhances the cost-benefit ratio of a study, particularly when physical, financial, and temporal resources are limited, which elevates the potential of spatiotemporal technologies as a tool with global impact for public health[4]. However, it is necessary to expand and improve the quality of the data source, as studies conducted in Brazil[10,39] have pointed out a lack of access to variables indicative of programmatic vulnerability, such as the availability of penicillin, which in 2014 faced a global shortage of raw materials, as well as testing coverage for syphilis screening, information that could be indispensable for understanding the factors related to the persistence of syphilis cases, a disease with a history spanning millennia.

Finally, as with any research study, this one also has limitations that must be noted, such as the search for *open-access*, full-text publications; such criteria may have excluded other studies that could have contributed to the discussion of the topic.

CONCLUSION

Through this study, it was possible to observe the importance of using spatial and spatiotemporal analysis technologies in epidemiological studies to identify risk areas and factors associated with syphilis. This tool is used only partially worldwide, with studies reported in Brazil, China, Canada, and England; furthermore, no evidence or reports were found indicating that such analyses have been incorporated as a management tool by health authorities.

Furthermore, it became evident in the studies that syphilis is not limited solely to the occurrence of cases but is also related to social, demographic, economic, and cultural factors, access to services, and care models related to health surveillance as a driving force behind health needs, since several studies did not distinguish between populations affected by the disease—such as the general population, reflecting the context of acquired syphilis, and pregnant women and children in cases of congenital

syphilis.

In summary, despite the rapid advancement of knowledge and spatial and spatiotemporal analysis tools—made possible in part by the application of robust methods such as Bayesian modeling—it became evident that, among the selected studies, there was no application of multivariate spatial methods or analysis of spatial variation trends, particularly considering the subpopulations affected by syphilis (acquired, in pregnant women, and congenital), and that future studies could provide such contributions.

In terms of contributions to education, the need to strengthen training in spatial epidemiology and data analysis is emphasized. In research, the importance of expanding the use of more robust analytical methods and approaches that consider social determinants is highlighted. In healthcare, these tools facilitate the identification of priority areas and the improvement of prevention and surveillance efforts. In management, they contribute to planning and the more equitable allocation of resources, strengthening evidence-based decision-making.

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