

Temporal trend and spatial distribution of gestational and congenital syphilis in the State of Espírito Santo from 2010 to 2019

Tendência temporal e distribuição espacial das sífilis gestacional e congênita no Estado do Espírito Santo entre 2010 e 2019

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ABSTRACT

Objective: To evaluate the temporal trend and spatial distribution of gestational and congenital syphilis in the State of Espírito Santo from 2010 to 2019. **Materials and Methods:** This is an ecological time series study utilizing data on gestational and congenital syphilis obtained from the National Injury Notification System (SINAN) and live births data from the Information System on Live Births (SINASC). Incidence rates of gestational and congenital syphilis were calculated, grouped according to the IBGE health macro-regions, and analyzed in biennia. **Results:** A total of 9,763 cases of gestational syphilis and 3,912 cases of congenital syphilis were reported. Gestational syphilis rates ranged from 1.46 in 2013 to 31.49 cases per 1,000 live births in 2018, while congenital syphilis rates ranged from 0.12 in 2010 to 11.51 cases per 1,000 live births in 2017. The Southern region exhibited the lowest incidence rates (2.32 cases per 1,000 live births for gestational syphilis and 0.54 per 1,000 live births for congenital syphilis), whereas the Metropolitan region displayed the highest rates (37.08 cases per 1,000 live births for gestational syphilis and 13.74 per 1,000 live births for congenital syphilis). **Conclusion:** The increase in disease cases suggests a deficiency in the quality of prenatal care.

RESUMO

Objetivo: Avaliar a tendência temporal e a distribuição espacial da sífilis gestacional e congênita no Estado do Espírito Santo entre 2010 e 2019. **Materiais e métodos:** Trata-se de um estudo ecológico de série temporal com dados sobre sífilis gestacional e congênita obtidos do Sistema Nacional de Agravos de Notificação (SINAN) e de nascidos vivos no Sistema de Informação sobre os Nascidos Vivos (SINASC). As taxas de incidência de sífilis gestacional e congênita foram calculadas a partir dos dados obtidos e agrupadas conforme as macrorregiões de saúde do IBGE, sendo analisadas em biênios. **Resultados:** Foram notificados 9.763 casos de sífilis gestacional e 3.912 casos de sífilis congênita. As taxas de sífilis gestacional variaram de 1,46 em 2013 a 31,49 casos/1.000 nascidos vivos em 2018, as taxas de sífilis congênita, por sua vez, variaram de 0,12 em 2010 a 11,51 casos/1.000 nascidos vivos em 2017. Quanto às macrorregiões, a região Sul apresentou as menores taxas de incidência (2,32 casos/1.000 nascidos vivos para sífilis gestacional e 0,54/1.000 nascidos vivos para sífilis congênita) e a região Metropolitana as maiores (37,08 casos/1.000 nascidos vivos para sífilis gestacional e 13,74/1.000 nascidos vivos para sífilis congênita). **Conclusão:** O aumento dos casos da doença sugere deficiência na qualidade do pré-natal.

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Introduction

One of the major health issues in contemporaneity is the high rate of Sexually Transmitted Infections (STIs)¹. Among these infections, syphilis holds a prominent position², caused by the spirochete bacterium *Treponema pallidum*³. It was deemed a significant health problem in remote times; however, it still constitutes a source of concern in the present day. An example of its impact nowadays is the progressive increase in both the incidence rate of congenital syphilis (from 0.4 in 2010 to 3.5 cases per 1000 live births in 2017, representing a 776% rise), and the infant mortality rate due to syphilis (from 2.3 in 2010 to 6.1 deaths per 100,000 live births in 2018) in Brazil over the past 10 years⁴.

Congenital syphilis is transmitted from the infected pregnant woman to the fetus either through transplacental transmission or direct transmission during birth canal passage⁵⁻⁷. Vertical transmission can occur during any gestational trimester and at any stage of the disease, with higher probabilities in primary and secondary syphilis (70 to 100%) compared to late-stage syphilis (late latent and tertiary) (30%)⁵⁻⁶. The consequences of the disease in the infant are diverse and

may vary based on the severity of the mother's illness, capable of causing early morbidities (such as skin and mucosal lesions, periostitis, osteocondritis), or late morbidities (such as alterations in dental, bone, joint, ocular structures, deafness, or mental retardation), or leading to spontaneous abortion, stillbirth, or perinatal death in about 40% of untreated pregnant fetuses⁸.

Given that syphilis is a preventable disease, with a relatively simple diagnosis and low-cost treatment provided by the Unified Health System (SUS)⁵, it is regarded as a sentinel event to assess Primary Health Care^{5,7,9}. Thus, a more detailed retrospective investigation of cases becomes necessary, as the persistence of failures in disease control is linked to obstacles in accessing healthcare, the use of condoms, the non-treatment of infected partners, and prenatal care^{5,7}. Studies like this one enable the generation of scientific input to propose relevant and effective measures capable of altering the current epidemiological profile, prioritizing the most underserved regions⁹. The study's objective was to describe the temporal trend and spatial distribution of gestational and congenital syphilis in the State of Espírito Santo between 2010 and 2019.

Methods

Data collect

This is an ecological study that utilized official data provided through TabNet (<https://tabnet.datasus.gov.br/>), a web application that presents a Database of the Unified Health System (DATASUS) from the Ministry of Health of Brazil. The considered at-risk population was that of live births according to the Live Births Information System (SINASC)¹⁰. The cases considered were those reported and confirmed by the National System of Notification of Diseases (SINAN)¹¹, related to cases of gestational and congenital syphilis for the State of Espírito Santo between 2010 and 2019.

For the description of the study population, information about the characteristics of mothers and newborns was collected from the SINAN website for each year. An arithmetic mean was calculated for each characteristic between the years 2010 and 2019. Analyzed maternal data included: age group, skin color, education level, timing of maternal syphilis diagnosis (primary, secondary, tertiary, and latent syphilis), and prenatal care. For the notified newborn, the variables were: age group, gender, and final disease classification (recent congenital syphilis, late congenital syphilis, syphilis-related abortion, syphilitic stillbirth).

Health indicators analyzed

The evaluated parameters were: vertical transmission rate, incidence rate for cases of gestational syphilis and congenital syphilis per 1,000 live births, and mortality rate for congenital syphilis. The mentioned rates were calculated as follows in the following paragraphs.

Vertical transmission rate, for each year of the study¹²: $(\text{Number of reported cases of congenital syphilis occurring in the State of Espírito Santo in a given period}) / (\text{Number of reported cases of gestational syphilis occurring in Espírito Santo during the same period}) \times 100$.

Incidence rate of gestational syphilis, per 1,000 live births, for each year of the study¹³: $(\text{Number of newly confirmed cases of gestational syphilis occurring in the State of Espírito Santo in a given period}) / (\text{Number of live newborns in Espírito Santo during the same period}) \times 1,000$.

Incidence rate of congenital syphilis, per 1,000 live births, for each year of the study¹³: $(\text{Number of newly confirmed cases of congenital syphilis occurring in the State of Espírito Santo in a given period}) / (\text{Number of live newborns in Espírito Santo during the same period}) \times 1,000$.

The number of deaths due to congenital syphilis is available in the Mortality Information System (SIM)¹⁴, and the case fatality rate is calculated according to the following formula¹³: $(\text{Number of confirmed deaths caused by congenital syphilis occurring in the State of Espírito Santo in a given period}) / (\text{Number of confirmed cases of congenital syphilis occurring in Espírito Santo during the same period}) \times 100$.

Analysis of spatial distribution

In order to spatially analyze the incidence rates of gestational and congenital syphilis, the health macro-regions established by the Brazilian Institute of Geography and Statistics (IBGE)¹⁵ were used as units of analysis (Figure 1). According to Resolution No. 153/220 of the Secretary of State for Health of Espírito Santo¹⁵, the Central/North region is made up of the municipalities: Água Doce do Norte, Águia Branca, Alto Rio Novo, Baixo Guandu, Barra de São Francisco, Boa Esperança, Colatina, Conceição da Barra, Ecoporanga, Governador Lindenberg, Jaguaré, Linhares, Mantenópolis, Marilândia, Montanha, Mucurici, Nova Venécia, Pancas, Pedro Canário, Pinheiros, Ponto Belo, Rio Bananal, São Domingos do Norte, São Gabriel da Palha, São Mateus, São Roque do Canaã, Sooretama, Vila Pavão and Vila Valério. The Metropolitan Region is composed of: Afonso Cláudio, Aracruz, Brejetuba, Cariacica, Conceição do Castelo, Domingos Martins, Fundão, Guarapari, Ibatiba, Ibirapuçu, Itaguaçu, Itarana, João Neiva, Laranja da Terra, Marechal Floriano, Santa Leopoldina, Santa Maria from Jetibá, Santa Teresa, Serra, Venda Nova do Imigrante, Viana, Vila Velha and Vitória. Finally, the South region covers the municipalities: Alegre, Alfredo Chaves, Anchieta, Apiacá, Atílio Vivacqua, Bom Jesus do Norte, Cachoeiro de Itapemirim, Castelo, Divino São Lourenço, Dorés do Rio Preto, Guaçuí, Ibitirama, Iconha, Irupi, Itapemirim, Iúna, Jerônimo Monteiro, Marataízes, Mimoso do Sul, Muniz Freire, Muqui, Piúma, Presidente Kennedy, Rio Novo do Sul, São José do Calçado and Vargem Alta.

Health macro-regions of the state of Espírito Santo



Figure 1. State of Espírito Santo divided into health macro-regions according to the Brazilian Institute of Geography and Statistics (IBGE). Source: Own collection.

Data were divided into biennia: 2010-2011, 2012-2013, 2014-2015, 2016-2017 and 2018-2019. This division into bienniums is important to attenuate annual

fluctuations in data^{6,16,17}. At the end of this data division, maps of the incidence rates of gestational and congenital syphilis per 1,000 live births were constructed and analyzed for each health macro-region in each biennium. The maps were generated from the Corel Draw X8¹⁸ program.

Because they are only secondary data and in the public domain, without identifying the participants, there was no need for submission and approval by the Research Ethics Committee (CEP System).

Results

Over the 10 years of analysis, 9,763 cases of gestational syphilis were reported, and 546,171 live births occurred in Espírito Santo, with 3,912 cases of congenital syphilis being reported. Regarding the characteristics of congenital syphilis cases, 70.35% of mothers were aged between 20 and 39 years, 56.13% had a mixed race skin color, and 28.78% had incomplete elementary education or were illiterate. About prenatal care, 77.53% of pregnant women received monitoring, with 57.18% of cases diagnosed during prenatal care and 35.50% during the latent phase of syphilis. In relation to newborns, the disease appeared within the first six days of life in 96.96% of cases; of these, 47.19% were female,

in 92.34% the final classification was recent congenital syphilis, and in 93.04% the cases were alive at the time of notification.

The vertical transmission rate of syphilis varied from 2.40% in 2010 to 48.59% in 2014 (**Table 1**). Furthermore, a specific underreporting of syphilis in pregnant women was identified during the study period, as in 2013 the number of reported cases of congenital syphilis (334) exceeded the number of reported cases of gestational syphilis (79).

The lowest and highest incidence rates of gestational syphilis were 1.46/1,000 live births in 2013 and 31.49/1,000 live births in 2018, respectively. The lowest incidence rate of congenital syphilis was 0.12/1,000 live births in 2010, and the highest was 11.51/1,000 live births in 2017. Overall, there is an increase in absolute syphilis incidence rates throughout the study period, with reductions mainly in the later years of analysis (2018 and 2019) (**Table 1**).

The year 2017 had the lowest disease fatality rate (0.31%), and the year 2014 had the highest (1.85%). Between 2010 and 2019, 37 newborns died due to the disease, representing 0.56% of the period's deaths (**Table 1**).

Table 1. Vertical Transmission Rate, Incidence Rate of Gestational Syphilis, Incidence Rate of Congenital Syphilis, and Congenital Syphilis Fatality Rate in the State of Espírito Santo between the years 2010 and 2019.

Year	Cases of gestational syphilis	Cases of congenital syphilis	Vertical Transmission Rate (%)	Live births	Rate Incidence of gestational syphilis ^a	Incidence rate of congenital syphilis ^a	Deaths from congenital syphilis	Lethality rate due to congenital syphilis (%)
2010	250	6	2,40	51.850	4,82	0,12	ND	–
2011	420	169	40,24	53.043	7,92	3,19	2	1,18
2012	923	273	29,58	52.825	17,47	5,17	5	1,83
2013	79	334	NA ^b	54.061	1,46	6,18	3	0,90
2014	778	378	48,59	56.548	13,76	6,68	7	1,85
2015	1089	513	47,11	56.941	19,13	9,01	3	0,58
2016	1277	599	46,91	53.412	23,91	11,21	3	0,50
2017	1516	643	42,41	55.846	27,15	11,51	2	0,31
2018	1786	561	31,41	56.720	31,49	9,89	5	0,89
2019	1642	436	26,55	54.925	29,90	7,94	7	1,61

^aPer 1,000 live births. ^bNA = Not applicable. The number of cases of gestational syphilis notified in the year was lower than the number of cases of congenital syphilis notified in the same year.

The analysis of the maps with the spatial distribution of the incidence rates of gestational syphilis and congenital syphilis for each biennium (**Figure 2**) shows an increase for both rates in all periods, with the exception of congenital syphilis between the 2016-2017 and 2018 biennia -2019.

Still referring to congenital syphilis, considering all the years of study, the South health macro-region had the lowest incidence rate (0.54 cases/1,000 live births) in 2010-2011 and the Metropolitan macro-region the highest (13.74 cases/ 1,000 live births) in the 2016-2017 biennium.

As for gestational syphilis, the South macro-region had the lowest rate (2.32 cases/1,000 live births) in 2012-2013 and the Metropolitan macro-region had the highest rate (37.08 cases/1,000 live births) in 2018-2019.

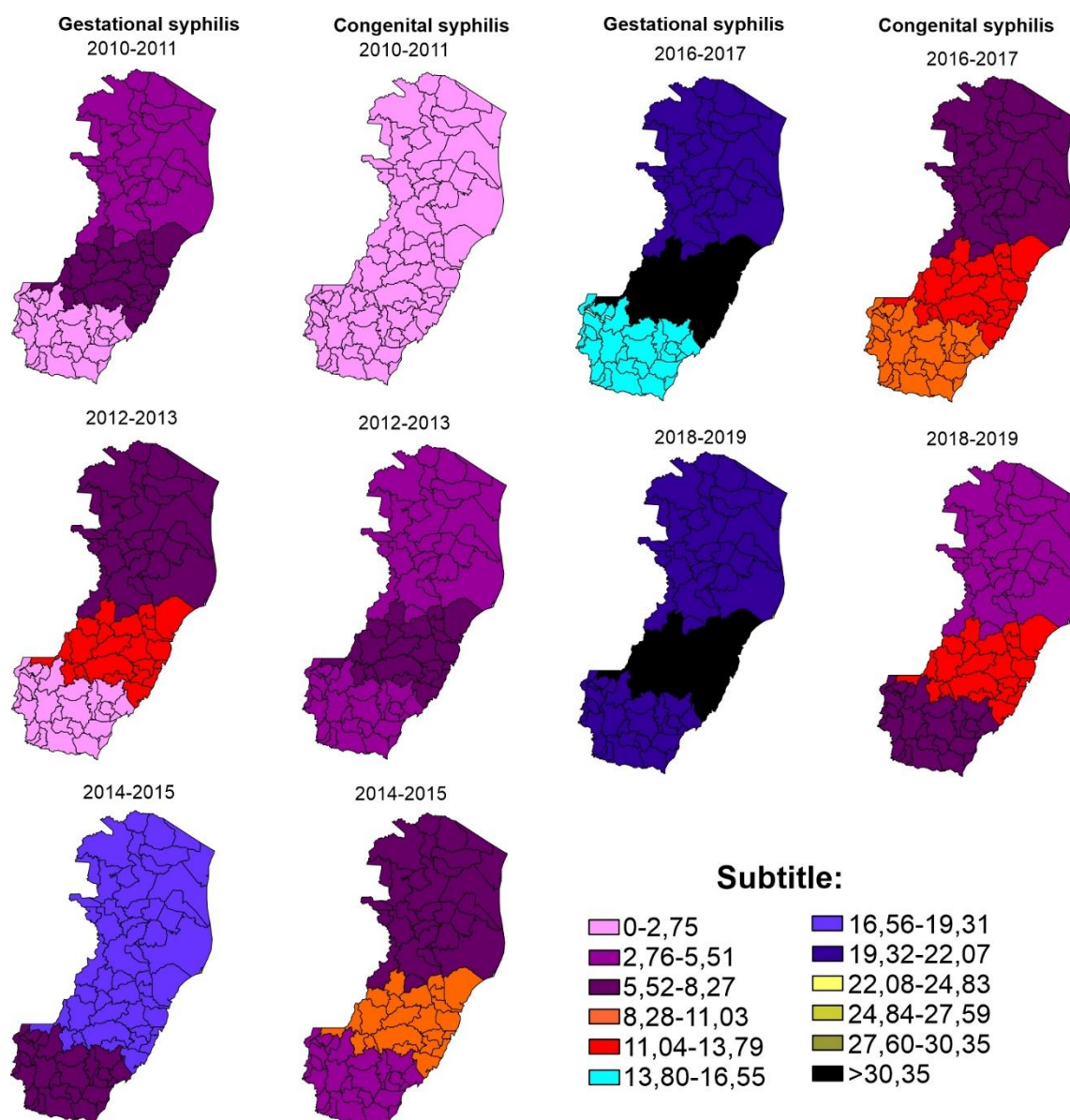


Figure 2. Biennial Spatial Distribution of Incidence Rate of Gestational Syphilis and Congenital Syphilis per 1,000 Live Births in the State of Espírito Santo during the period 2010-2019.

Discussion

STIs are a significant public health problem worldwide, as they are among the most common transmissible infections and can lead to complications during pregnancy and childbirth, fetal death, and health issues in children¹⁹.

With the exception of the recent years under analysis, cases of gestational and congenital syphilis tended to increase over time. There have been governmental strategies developed to address this increasing trend. The document "Strategy and Action Plan for the elimination of vertical transmission of HIV and congenital syphilis" was formulated in 2010, aiming to reaffirm the commitment of American countries to eliminate the vertical transmission of these diseases by 2015, with the goal of reducing the incidence of congenital syphilis to less than 0.5 case per 1,000 live

births²⁰. However, only in Espírito Santo did the rate surpass the 2012-2019 target, reaching a value of 11.51 cases per 1,000 live births in 2017. In 2016, the World Health Assembly presented a global health sector strategy for STIs, encompassing actions to reduce the impact of these infections as a public health problem by 2030, with global reduction targets for syphilis and elimination of congenital syphilis¹⁹.

However, it is worth noting that the implementation of certain programs can contribute to an increase in the detection rate of gestational and congenital syphilis due to improved diagnosis and health surveillance. An example is the "Rede Cegonha" (Stork Network) initiated by the Federal Government in 2011, where one of the strategies involves conducting rapid diagnostic tests for HIV and syphilis screening²⁰. Alongside the "Rede Cegonha," other factors that may have contributed to the

increased detection of this infection are the advancement of epidemiological surveillance, expanded prenatal coverage through the implementation of Family Health Strategy (ESF) teams, and healthcare professional training^{6,20-21}. An important episode to highlight was the irregular supply of penicillin (considered the gold standard treatment for gestational syphilis) across the country between 2015 and 2016, a period marked by a lack of raw materials for its production, leading to medication shortages in healthcare facilities nationwide^{4,22}.

In terms of national research, the rise in cases of gestational and congenital syphilis is also observed in other Brazilian states, with some even diverging from the target reduction of 0.5 cases per 1,000 live births. A study conducted in the period of 2001-2012 in Rio Grande do Sul showed that detection rates of syphilis in pregnant women varied from 0.46 in 2006 to 6.69 cases per 1,000 live births in 2012, while rates of congenital syphilis varied from 1.03 in 2001 to 5.1 cases per 1,000 live births in 2012, with an annual increase of 0.84 cases per 1,000 live births ($p < 0.01$)⁶. In another national study carried out in Goiás during the periods of 2007-2017, a rising trend was observed in the incidence rates of gestational syphilis (from 2.8 in 2007 to 14.8 cases per 1,000 live births in 2017; annual percentage change [APC] of 18.0 – 95% confidence interval [CI] from 15.3 to 20.8) and congenital syphilis (from 0.3 in 2007 to 2.9 cases per 1,000 live births in 2017; APC = 16.8 – CI 95% 20.1 to 33.8), alongside a 326% increase in the number of municipalities with a congenital syphilis incidence rate >0.5 per 1,000 live births²².

This upward trend in syphilis rates is not limited to studies involving the Brazilian population; similar trends have been observed in international research. In an ecological study conducted in Mexico from 2010 to 2019, the incidence of congenital syphilis increased by an average of 0.336 cases per 100,000 per year, with a rise in the number of cases from 62 in 2010 to 372 cases in 2019²³. In China, the national rate of congenital syphilis increased nearly 26 times, from 2.6 in 2000 to 69.9 cases per 100,000 live births in 2013²⁴.

In conclusion, the incidence of gestational and congenital syphilis found in Brazil and other countries has been steadily increasing in recent years. However, it is important to note that comparability between these studies is hindered due to the criteria used to define congenital syphilis. Some authors include stillbirths in their incidence calculations²⁵, while others exclude such cases²⁶. Similarly, the upper age limit for diagnosing recent congenital syphilis in children may vary from 18 to 24 months²⁶⁻²⁷.

While investigating vertical transmission of syphilis is important, there remain few studies in the country focusing on these rates, as most research tends to investigate other diseases, such as HIV¹². However, it is crucial to report that this study identified underreporting of gestational syphilis cases in the year 2013. Underreporting and incomplete or blank reporting of

gestational syphilis cases are issues encountered in various studies and different regions of the country^{21,28-29}. Despite having an instructional manual attached to the notification form, the clarity of the material may be hindering its correct completion²¹. Accurate completion of this notification form is essential for monitoring gestational and congenital syphilis, as well as evaluating programs and public policies. In this analysis, the decision was made not to exclude data classified as "Blank" or "Unknown" in order to prevent underestimation of the results.

Identifying health macro-regions with higher incidence rates of both gestational and congenital syphilis serves as a tool for formulating public policies and control programs for these diseases. Throughout the 10-year study period, the Metropolitan macro-region had the highest rates for both gestational and congenital syphilis, indicating a need for more focused attention from health authorities. It's important to note that this macro-region encompasses municipalities with higher Gross Domestic Products (GDP)³⁰, which could lead to higher incidence rates due to better healthcare services, improved access to diagnostic methods, and higher detection rates³¹. Similar findings were observed in a study conducted by Teixeira et al.⁶ in the Southern region of Brazil, where regions with higher Human Development Index (HDI) Municipal scores exhibited higher incidences of congenital syphilis.

As mentioned earlier, the present study has limitations since it relies on secondary data that may be underreported. Nonetheless, SINAN is an official system widely used in technical-scientific research³¹. Furthermore, public policies are based on reported data, and this study revealed a significant increase in syphilis numbers in the state of Espírito Santo. Ecological studies, which provide information on exposure and disease at a population level, cannot directly generalize information about comorbidities³¹. In summary, comparing the findings of this study with others is hindered by the scarcity of research that analyzes the temporal and spatial distribution of gestational and congenital syphilis.

Conclusion

Gestational and congenital syphilis serve as indicators of the quality of maternal and child health care due to their link with the reduced risk of transmission, timely diagnosis, and effective treatment when there is good quality of care. Therefore, the increase in incidence rates across different regions of the state may suggest deficiencies in prenatal care, despite observed efforts to improve healthcare services in recent years. The information provided in this study can contribute to the planning and monitoring of changes in the local epidemiological landscape. However, further studies will be necessary to assess the effectiveness of programs and the efficiency of healthcare.

Conflict of interests

The authors declare that there is no potential conflict of interest.

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References

- Anjos KF, Santos VC. Sífilis uma realidade prevenível. Sua erradicação, um desafio atual. *Saúde e Pesquisa* 2009;2(2):257-63.
- World Health Organization [homepage na internet]. The global elimination of congenital syphilis: rationale and strategy for action [acesso em 31 mai 2021]. Disponível em: http://apps.who.int/iris/bitstream/10665/43782/1/9789241595858_eng.pdf.
- Domingues RM, Leal MC. Incidência de sífilis congênita e fatores associados à transmissão vertical da sífilis: dados do estudo Nascer no Brasil. *Cad Saude Publica* 2016;32(6).
- BRASIL. Ministério da Saúde. Boletim Epidemiológico de Sífilis 2020. Brasil: MS; 2020. Ano VI n° 01.
- Brasil. Ministério da Saúde. Secretaria de Vigilância em Saúde. Programa Nacional de DST/AIDS. Diretrizes para controle da sífilis congênita: manual de bolso / Ministério da Saúde, Secretaria de Vigilância em Saúde, Programa Nacional de DST/Aids. – 2. ed. – Brasília: Ministério da Saúde, 2006.
- Teixeira LO, Belarmino V, Gonçalves CV, Mendoza-Sassi RA. Tendência temporal e distribuição espacial da sífilis congênita no estado do Rio Grande do Sul entre 2001 e 2012. *Ciência & Saúde Coletiva* 2018;23(8):2587-97.
- Mota ACC, Andrade CHS, Lima DC, Araújo GGF, Araújo ICV, Maia JTR, Gonçalves LO, Abraão LSO, Leite MD, Santos YA. Sífilis congênita no Pará: O panorama de uma década na região metropolitana de Belém. *Brazilian Journal of health Review* 2020;3(4):8568-80.
- Brasil. Ministério da Saúde. Secretaria de Atenção à Saúde. Departamento de Atenção Básica. Cadernos de Atenção Básica, nº 32. Atenção ao pré-natal de baixo risco / Ministério da Saúde. Secretaria de Atenção à Saúde. Departamento de Atenção Básica. – Brasília: Editora do Ministério da Saúde, 2012.
- Domingues RSM, Saraceni VS, Hartz ZMA, Leal MC. Sífilis congênita: evento sentinela da qualidade da assistência pré-natal. *Cad Saude Publica* 2013;47(1):147-57.
- Brasil. Ministério da Saúde. Departamento de Informações e Informática do Sistema Único de Saúde (Datasus). Sistema de Informação sobre os Nascidos Vivos (SINASC). Mortalidade e nascidos vivos: nascidos vivos desde 1994 – Espírito Santo [acesso em 31 mai 2021]. Disponível em: <http://tabnet.datasus.gov.br/cgi/defthtm.exe?sinasc/cnv/nves.def>.
- Brasil. Ministério da Saúde. Departamento de Informações e Informática do Sistema Único de Saúde (Datasus). Sistemas de Informação de Agravos de Notificação (SINAN). Sífilis Congênita: casos confirmados de 2007 em diante [acesso em 31 mai 2021]. Disponível em: <http://www2.datasus.gov.br/DATASUS/index.php?area=0203&id=29878153>.
- Kupek E, Oliveira JF. Transmissão vertical do HIV, da sífilis e da hepatite B no município de maior incidência de AIDS no Brasil: um estudo populacional no período de 2002 a 2007. *Rev Bras Epidemiol* 2012;15(3):478-87.
- Rede Interagencial de Informação para à saúde. Indicadores básicos para a saúde no Brasil: conceitos e aplicações. 2ª ed. – Brasília: Organização Pan-Americana da Saúde; 2008.
- Brasil. Ministério da Saúde. Departamento de Informações e Informática do Sistema Único de Saúde (Datasus). Sistema de Informações sobre Mortalidade (SIM). Estatísticas vitais. Óbitos por causas evitáveis - 0 a 4 anos – Espírito Santo [acesso em 31 mai 2021]. Disponível em: <http://tabnet.datasus.gov.br/cgi/defthtm.exe?sim/cnv/evita10es.def>.
- Governo do Estado do Espírito Santo (Brasil). Resolução nº 153/2020, de 18 de dez de 2020. Dispõe sobre a aprovação dos limites regionais instituindo no Território do Estado do Espírito Santo - ES 03(três) Regiões de Saúde: Região Central/Norte, Região Metropolitana e Região Sul. Vitória: Comissão Intergestores Bipartite 2020 [acesso em 06 mai 2022]. Disponível em: <https://saude.es.gov.br/Media/sesa/CIB/Resolu%C3%A7%C3%A3o%20CIB%20153-2020%20-%20PDR%20ES%202020.pdf>.
- Duarte-Cunha M, Souza-Santos R, Matos HJ, Oliveira MLW. Aspectos epidemiológicos da hanseníase: uma abordagem espacial. *Cad Saude Publica* 2012;28(6):1143-55.
- Martins-Melo F, Lima MS, Alencar CH, Ramos NA, Carvalho FHC, Machado MMT, Heukelbach J. Tendência temporal e distribuição espacial do aborto inseguro no Brasil, 1996-2012. *Revista de Saúde Pública* 2014; 48(3):508-20.
- CorelDRAW Graphics Suite X8, 2016.
- BRASIL. Ministério da Saúde. Boletim Epidemiológico de Sífilis 2021. Brasil: MS; 2021. Ano V n° 01.
- BRASIL. Ministério da Saúde (MS). Boletim Epidemiológico de Sífilis 2015. Brasil: MS; 2015. Ano IV n° 01.
- Costa CC, Freitas LV, Sousa DMN, Oliveira LL, Chagas ACMA, Lopes MVO, Damasceno AKC. Sífilis congênita no Ceará: análise epidemiológica de uma década. *Rev Esc Enferm USP* 2013;47(1):152-9.
- Nunes PS, Guimarães RA, Rosado LEP, Marinho TA, Aquino EC, Turchi MD. Tendência temporal e distribuição espacial da sífilis gestacional e congênita em Goiás, 2007-2017: um estudo ecológico. *Epidemiol Serv Saúde* 2021;30(1):e2019371.
- Cisneiros SG, Ortiz AH, Portugal MO, Alemán MAS. Re-emergence of syphilis in women of reproductive age and its association with the increase in congenital syphilis in Mexico during 2010–2019: an ecological study. *BMC Infect Dis* 2021;21(1):992.
- Wang Y, Wu M, Gong X, Zhao L, Zhao J, Zhu C, Gong C. Risk Factors for Congenital Syphilis Transmitted from Mother to Infant - Suzhou, China, 2011–2014. *Morbidity and Mortality Weekly Report* 2019;68(10):247-50.
- Simms I, Tookey AP, Goh TB, Lyall H, Evans B, Townsend LC, Fifer H, Ison C. The incidence of congenital syphilis in the United Kingdom: February 2010 to January 2015. *BJOG* 2016;124(1):72-7.
- Lopez NO, Diez M, Diaz O, Simon F, Diaz A. Epidemiological surveillance of congenital syphilis in Spain, 2000-2010. *The Pediatric Infectious Disease Journal* 2012;31(9):988-90.
- Hong FC, Yang YZ, Liu XL, Feng TJ, Liu JB, Zhang CL, Lan LN, Yao MZ, Zhou H. Reduction in mother-to-child transmission of syphilis for 10 years in Shenzhen, China. *Sexually Transmitted Diseases* 2014;41(3):188-93.
- Schetini J, Ferreira DC, Passos MRL, Salles EB, Santos DDG, Rapozo DCM. Estudo da prevalência de sífilis congênita em um hospital da rede SUS de Niterói – RJ. *Jornal brasileiro de doenças sexualmente transmissíveis: DST* 2005;17(1):18-23.
- Holanda MTCG, Bareto MA, Machado KMM, Pereira RC. Perfil Epidemiológico da sífilis congênita no Município de Natal, Rio Grande do Norte – 2004 a 2007. *Epidemiol Serv Saude* 2011; 20(2):203-12.
- Instituto Brasileiro de Geografia e Estatística [homepage na internet]. Panorama [acesso em 27 abr 2022]. Disponível em: <https://cidades.ibge.gov.br/brasil/es/vitoria/panorama>.
- Venâncio TS, Tuan TS, Nascimento LFC. Incidência de tuberculose em crianças no estado de São Paulo, Brasil, sob enfoque espacial. *Ciência & Saúde Coletiva* 2015;20(5):1541-7.