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Short Communication

Attributable fraction of congenital syphilis due to the lack of prenatal care

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Abstract

Introduction: Although congenital syphilis is preventable, its incidence has increased in Brazil. **Methods:** In this ecological study, a Bayesian spatio-temporal model was used to estimate the attributable fraction of congenital syphilis cases due to the lack of prenatal care recorded between 2010 and 2015 in the state of São Paulo, Southeast Brazil. **Results:** For the year 2016, it was estimated that between 79.4% and 95.3% of the congenital syphilis cases among women who did not have prenatal care could have been prevented. **Conclusions:** A significant proportion of congenital syphilis cases can be prevented if prenatal care coverage is expanded.

Keywords: Congenital syphilis. Ecological studies. Attributable risk. Epidemiology. Brazil.

In 1954, congenital syphilis (CS) was described as "a disease that is rapidly decreasing in incidence, yet still exists; it is so destructive to the young and so easily prevented that its importance can hardly be overestimated"[1]. Even so, 37,436 cases of maternal syphilis and 20,474 of CS were reported in Brazil in 2016 according to the Brazilian National Disease Surveillance Data System (SINAN)[2]. Between 2010 and 2016, the rate of CS infection increased from 2.4 to 6.8 cases per 1000 live births, probably as a consequence of the increase in the detection rate of syphilis in pregnant women (from 3.7 to 12.4 cases per 1000 live births)[2]. In the State of São Paulo, 24,108 cases of CS were reported for the period from 1987 to 2015[3]. According to data from the Epidemiological Bulletin of Syphilis published in 2016, aside from the increasing incidence rates of CS in Brazil, infant mortality from this disease should be seriously considered. The incidence of CS in children under 1 year increased from 1.7 cases per 1000 live births in 2004 to 6.5 cases per 1000 live births in 2015. Infant mortality from syphilis increased from 2.4 per 1000 live births in 2005 to 7.4 per 1000 live births in 2015[3].

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The objective of this ecological study was to determine the attributable fraction of CS due to lack of prenatal care among women exposed (AFexp) in the State of São Paulo, located in the Southeastern region of Brazil. The state is one of the largest industrial centers in Latin America which has 17 Regional Health Departments (RHD) administered by local and regional public health authorities. Information on new cases of CS and on the number of live births were obtained from the SINAN and from the National Live Birth Information System (SINASC), respectively. Both health information systems can be freely accessed from the database of the Brazilian Health System (DATASUS) (http://tabnet.datasus.gov.br). The Bayesian conditional autoregressive (CAR) spatial model was used to obtain smoothed annual incidence rates for CS and the corresponding estimates of AFexp for each RHD in the State of São Paulo from the period between 2010 and 2016.

AFexp is generically defined as the proportion of cases among exposed individuals that can be attributed to a given exposure[4]. In this study, AFexp was the proportion of CS cases among women who did not have prenatal care in a given year, attributable to the lack of prenatal care. Considering all live births reported in a given region at a given period, let p_1 be the incidence rate of CS among women who did not have prenatal care and let p_2 be the incidence rate of CS among women who had prenatal care. Thus, AFexp is derived as $AFexp = (p_1 - p_2)/p_1$ (see definitions in **Table 1** of the article by Perez e Künzli[4]).

TABLE 1: Attributable fraction (AFexp) of CS due to lack of prenatal care with their corresponding Bayesian 95% credible intervals (95% CRI) for the 17 Regional Health Departments of the State of São Paulo, Southeast Brazil.

Regional Health Departments		2010		2013		2016	
		AFexp (%)	95% CRI	AFexp (%)	95% CRI	AFexp (%)	95% CRI
1.	Grande São Paulo	96.6	(95.7, 97.3)	95.6	(94.7, 96.4)	94.5	(93.3, 95.5)
2.	Araçatuba	95.2	(94.2, 96.1)	94.0	(93.0, 94.9)	92.5	(91.2, 93.5)
3.	Araraquara	92.8	(89.9, 94.9)	90.9	(87.6, 93.3)	88.5	(84.3, 91.6)
4.	Baixada Santista	92.6	(90.3, 94.3)	90.6	(88.1, 92.6)	88.2	(85.2, 90.6)
5.	Barretos	93.4	(91.7, 94.7)	91.6	(89.8, 93.1)	89.5	(87.2, 91.3)
6.	Bauru	97.0	(96.5, 97.4)	96.2	(95.8, 96.6)	95.3	(94.7, 95.7)
7.	Campinas	92.8	(91.0, 94.0)	90.7	(89.1, 92.2)	88.3	(86.4, 90.1)
8.	Franca	95.3	(93.7, 96.5)	94.1	(92.3, 95.5)	92.6	(90.4, 94.3)
9.	Marília	92.6	(90.7, 94.2)	90.7	(88.5, 92.4)	88.3	(85.7, 90.6)
10.	Piracicaba	95.3	(93.6, 96.5)	94.0	(92.1, 95.5)	92.5	(90.2, 94.4)
11.	Presidente Prudente	87.0	(78.8, 91.9)	83.6	(73.2, 89.7)	79.4	(66.8, 87.2)
12.	Registro	95.4	(94.0, 96.4)	94.2	(92.6, 95.4)	92.7	(90.8, 94.2)
13.	Ribeirão Preto	96.0	(95.0, 96.7)	94.9	(93.9, 95.7)	93.6	(92.3, 94.6)
14.	São João da Boa Vista	97.0	(96.0, 97.8)	96.2	(94.9, 97.2)	95.2	(93.6, 96.5)
15.	São José do Rio Preto	94.9	(93.8, 95.9)	93.6	(92.4, 94.7)	92.0	(90.4, 93.3)
16.	Sorocaba	94.9	(92.0, 96.7)	93.5	(89.8, 95.8)	91.9	(87.3, 94.8)
17.	Taubaté	90.0	(87.2, 92.1)	87.3	(84.3, 89.7)	84.1	(80.3, 87.2)
State of São Paulo		96.1	(95.4, 96.6)	94.8	(94.3, 95.3)	93.2	(92.5, 93.7)

In the proposed spatiotemporal statistical model, Y_{kit} denotes the observed number of new CS cases in area i and in the year t (let $t = 1$ if year 2010, $t = 2$ if year 2011, and so on). In addition, we have $k = 1$ for newborns of mothers who did not have prenatal care and $k = 2$ for newborns of mothers who had prenatal care. It was assumed that Y_{1it} and Y_{2it} were random variables following independent Poisson distributions with parameters μ_{1it} and μ_{2it}, respectively, where $\mu_{kit} = N_{kit} \times p_{kit}$. In this case p_{kit} denotes the incidence rates of CS, N_{kit} denotes the number of live births reported in area i and in the year t, and k remains as defined above.

The rates p_{kit} are related to a spatiotemporal structure considering the expression $\log(p_{kit}) = \alpha_{kt} + u_{ki} + w_i$, where α_{kt} are unknown fixed parameters; u_{ki} are spatially unstructured effects following a normal distribution; the random effects w_i was assumed to have a CAR structure that required an adjacency matrix and a weight matrix[5]. Thus, we adopted the Queen adjacency criteria (which defines a location's neighbors as those with either a shared border or vertex) with similar weights[5]. For the Bayesian estimation of parameters of the model, Markov chain Monte Carlo (MCMC) methods with non-informative priors were used[6]. Using the GeoBUGS module in OpenBUGS software, 1,000,000 samples for each parameter of interest were generated, with a burn-in of 5,000 iterations aimed at avoiding the influence of the initial values and a thinning interval of 200, aimed at avoiding correlation between successive samples. AFexp for the area i and in the year t was thus estimated by $\text{AFexp}_{it} = (p_{1it} - p_{2it})/p_{1it}$, for i = 1…,17 and k =1,2.

The maps in **Figure 1** show the smoothed incidence rates of CS obtained from the Bayesian model. For newborns of mothers who did not have prenatal care, the median incidence rates of CS in 2010 and 2016 were 26.6 cases per 1000 (range: 9.9–62.0) and 77.7 per 1000 (range: 29.2–181.3) live births, respectively. Whereas for newborns of mothers who had prenatal care, the median incidence rates of CS in 2010 and 2016 were 1.2 cases per 1000 (range: 0.5–2.4) and 5.6 per 1000 (range: 2.7–11.2) live births, respectively. The Moran's I statistic, a measure of spatial autocorrelation, was calculated to evaluate spatial autocorrelation for the smoothed incidence rates of CS. For newborns of mothers who did not have prenatal care, Moran's I values were close to −0.14 for all corresponding maps in **Figure 1** (all respective p-values were higher than 0.7). Whereas for newborns of mothers who had prenatal care, Moran's I values were close to zero for all corresponding maps in **Figure 1** (all respective p-values were approximately 0.4). These results suggest that the incidence rates of CS are homogeneously distributed across all RHD.

Table 1 shows the AFexp of CS due to lack of prenatal care, with their corresponding Bayesian 95% credible intervals (95% CRI) for the 17 RHD of the State of São Paulo. Credible intervals are the Bayesian analogs of the traditional confidence intervals. The Bayesian model estimated values for all periods,

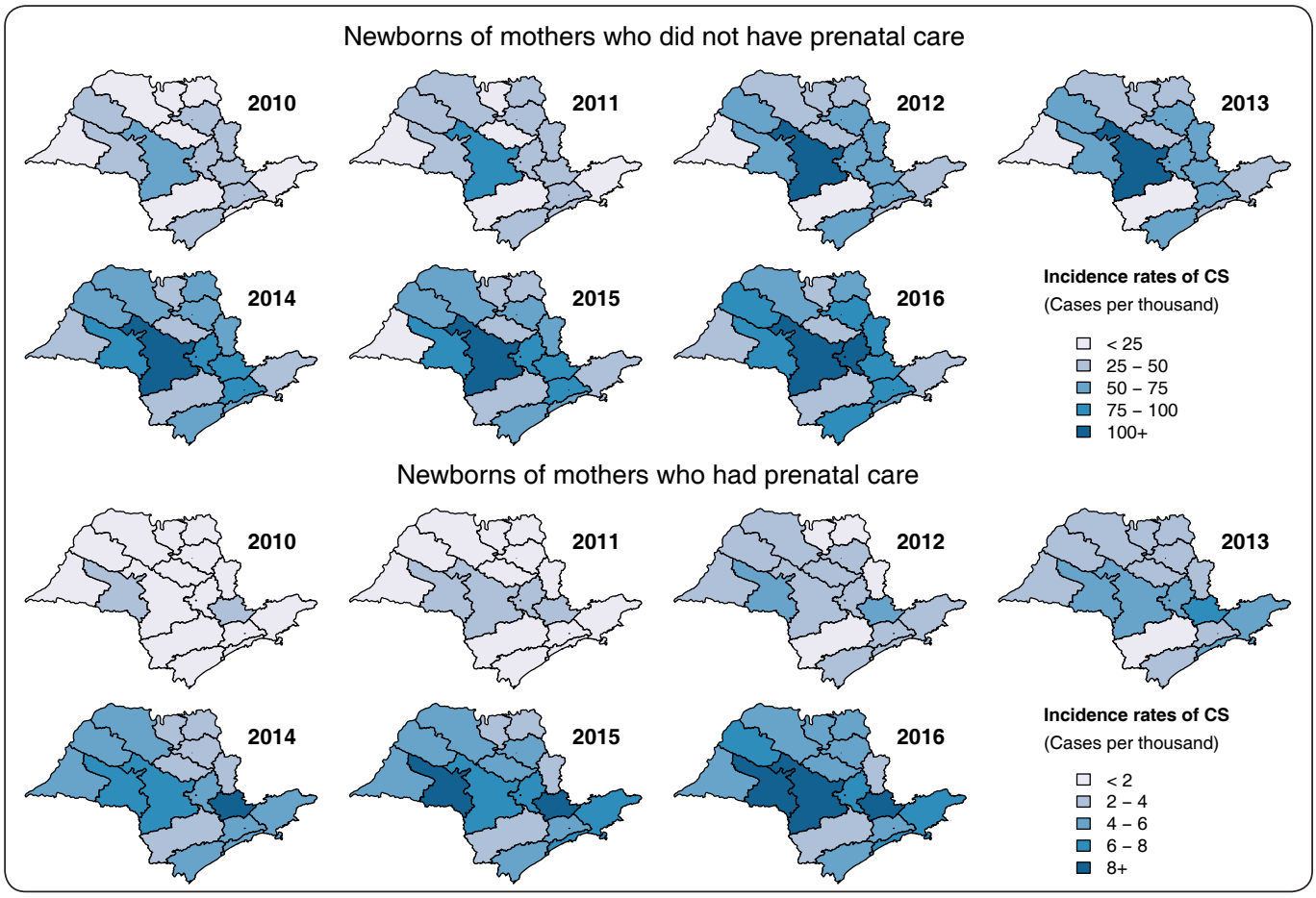

FIGURE 1: Maps of the State of São Paulo describing the smoothed incidence rate of congenital syphilis in each regional health department (new cases per 1000 live births), considering newborns of mothers who did not have prenatal care (top) and newborns of mothers who had prenatal care (bottom).

but as the results are similar, we present in **Table 1** the results for 2010, 2013, and 2016, when 598.418, 604.823, and 597.654 births, respectively, reported in the State of São Paulo. For the year 2010, 87.0%–97.0% of new CS cases were estimated to be attributable to the lack of prenatal care. For the year 2016, these values ranged from 79.4%–95.3%. Over the study period, all RHD were noted to have a slight increase in AFexp of CS due to lack of prenatal care.

This study showed very high attributable fractions of CS due to lack of prenatal care. However, based on data from the SINASC, we observed that the proportion of pregnant women who undertook at least one prenatal visit remained approximately constant throughout the study period in all RHD. For the whole State of São Paulo, these proportions were 98.9% in 2010, 98.7% in 2012, and 99.0% in 2016. In addition, the incidence rate of CS increased in both groups, among women who did or did not have prenatal care. These results suggest that other factors may be associated with the rapid increase in the disease incidence, which need to be investigated in future studies. Some authors have related the presence of CS with variables such as maternal schooling and ethnicity[7,8], but these characteristics may not be sufficient to explain the increase in incidence in recent years. Another explanation could be the increase in the report rate by health care providers[9].

According to the results of a recent research[2], the main risks for syphilis were low maternal schooling, alcohol and/or drug use, multiple sex partners, and poor access to antenatal care. In addition, regarding CS, some evidences of association were detected with lack of follow-up of the pregnant women with syphilis and lack of reporting of syphilis status in medical records or antenatal cards. According to these authors, the main barriers to syphilis eradication are still present at both the individual and public health levels, as regular antenatal care is a definitive strategy to improve detection, prevention, and treatment of CS[2,10]. In addition, some studies found a strong association between late/incomplete antenatal care and syphilis, which may be indicative of barriers to access health services, lack of interest, or low awareness of the importance of early pregnancy screening and monitoring [2,11].

Cardoso *et al*.[12] stated that the World Health Organization (WHO) and the Pan American Health Organization (PAHO) launched a proposal, adopted by the Brazilian Ministry of Health, with the global objective of eliminating CS as a public health problem to a point where incidence of at most 0.5 cases per 1000 live births would be considered acceptable. Our results indicate that the incidence rate of CS in the State of São Paulo is above the proposed value, even among mothers who had prenatal

care. Cooper and Sánchez[13] established that every CS case must be seen as a failure of the public health system to provide optimal prenatal care for pregnant women. Under this consideration, it is essential that policies be established to continuously improve the effectiveness and quality of care, including the availability of health workers, especially at the primary care level, laboratory tests for syphilis (VDRL), strategies for increasing access to health services, and educational campaigns to promote adequate number of prenatal care visits. Early identification of syphilis among pregnant women, followed by treatment of the infection, and access to sexual and reproductive health services in prenatal support programs are important strategies for CS prevention.

The main limitation of this study is the use of data from public health information systems to assess the AFexp of CS due to lack of prenatal care, based on an ecological design. The data provided by SINAN and SINASC are subject to incomplete notification forms and underreporting[14] that may lead to biased results. Data on prenatal care was dichotomized into groups of women who did or did not have prenatal care. More informative results would be obtained, taking into account the number of prenatal consultations or the trimester of gestation in which the women started prenatal care. However, the tabulations provided by SINAN did not provide these information. Despite these limitations, our results do provide an indication of current patterns of CS due to lack of adequate prenatal care in the State of São Paulo. Such findings can be useful to assist further efforts to reduce disease burden in this region.

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Conflict of Interest

The authors declare no conflict of interest.

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