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ORIGINAL ARTICLE

Geographic patterns and hotspots of pediatric tuberculosis: the role of socioeconomic determinants

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ABSTRACT

Objective: Children are an important demographic group for understanding overall tuberculosis epidemiology, and monitoring of childhood tuberculosis is essential for appropriate prevention. The present study sought to characterize the spatial distribution of childhood tuberculosis notification rates in continental Portugal; identify high-risk areas; and evaluate the association between childhood tuberculosis notification rates and socioeconomic deprivation. **Methods:** Using hierarchical Bayesian spatial models, we analyzed the geographic distribution of pediatric tuberculosis notification rates across 278 municipalities between 2016 and 2020 and determined high-risk and low-risk areas. We used the Portuguese version of the European Deprivation Index to estimate the association between childhood tuberculosis and area-level socioeconomic deprivation. **Results:** Notification rates ranged from 1.8 to 13.15 per 100,000 children under 5 years of age. We identified seven high-risk areas, the relative risk of which was significantly above the study area average. All seven high-risk areas were located in the metropolitan area of Porto or Lisbon. There was a significant relationship between socioeconomic deprivation and pediatric tuberculosis notification rates (relative risk = 1.16; Bayesian credible interval, 1.05-1.29). **Conclusions:** Identified high-risk and socioeconomically deprived areas should constitute target areas for tuberculosis control, and these data should be integrated with other risk factors to define more precise criteria for BCG vaccination.

Keywords: Child; Poverty; Vaccination; Mycobacterium bovis.

INTRODUCTION

Tuberculosis still has a significant burden worldwide: 10.6 million people fell ill with tuberculosis in 2021, 11% of whom were children.[1] The number of tuberculosis deaths in 2020 was approximately 1.5 million; of those, 140,000 occurred among children.[2] Despite advances in tuberculosis control, tuberculosis continues to play a significant role in mortality worldwide and is expected to rank second among the leading causes of death from a single infectious agent in 2020, after COVID-19.[3]

Regarding tuberculosis infection in children and adolescents, treatment is critical to avoid progression to tuberculosis disease and to prevent them from becoming the future reservoir for tuberculosis transmission.[4] It might be more complex to determine the precise extent of tuberculosis in children than in adults because of the lack of a standard case definition and because of diagnostic challenges such as the difficulty of bacteriological confirmation, the low specificity of clinical signs and symptoms, the high frequency of extrapulmonary disease, and underreporting.[3] Most children are infected by household members or other close contacts with tuberculosis disease, particularly parents or other caregivers, and represent a missed opportunity by the health care system to prevent the disease.[5] Children under five years of age represent an important demographic group for understanding the epidemiology of tuberculosis because it frequently progresses rapidly from primary or latent tuberculosis infection to tuberculosis disease, and severe disease manifestations are more common in this age group.[4] Therefore, these children serve as sentinel

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cases, indicating recent and/or ongoing transmission in the community.[5]

In Portugal, there has been a reduction in the incidence of tuberculosis in recent years; in 2014 Portugal reached the threshold value (of < 20/100,000 population) to be considered a low-incidence country.[3,6] Simultaneously, other criteria for adequate tuberculosis control recommended by the WHO were fulfilled: the existence of an effective surveillance system and an annual incidence of tuberculous meningitis in children below 1/10,000,000 population in the last five years.[6,7] Thus, in 2016, in line with what was already being done in other countries with low tuberculosis incidence, the strategy of selective vaccination of children under 6 years of age belonging to risk groups was adopted by the Directorate-General of Health of Portugal.[8]

The association between higher rates of tuberculosis and socioeconomic deprivation has been established in several countries, particularly in those with low income, high crowding, less education, and high unemployment.[9-12] One study evaluated the relationship between tuberculosis notification and socioeconomic deprivation across municipalities in Portugal.[13] Although the tuberculosis notification rate was not significantly associated with the Portuguese version of the European Deprivation Index (EDI-PT), it was significantly associated with some of the EDI-PT components, namely, the proportion of manual workers and the unemployment rate.[13] The EDI-PT has been positively and significantly associated with multidrug-resistant tuberculosis and non-multidrug-resistant tuberculosis notification rates in the metropolitan area of Lisbon, Portugal.[14] Although less is known about the influence of socioeconomic deprivation on childhood tuberculosis, children might be particularly vulnerable to the socioeconomic features of the community. Factors known to have an impact include the level of education of the adult population, because educated parents/adults are more likely to recognize symptoms and seek medical care,[15] and housing conditions such as overcrowding, because children are more likely to share spaces with other children and adults.[16,17] Therefore, it is plausible that composite area-level measures of socioeconomic deprivation, such as the EDI-PT, are significantly associated with childhood tuberculosis.

The epidemiological characterization of childhood tuberculosis contributes to a better diagnostic approach to tuberculosis in the overall population, and monitoring and follow-up of childhood tuberculosis cases are essential for appropriate prevention and treatment. Thus, we sought to characterize the spatial distribution of childhood tuberculosis notification rates in Portugal; identify high-risk areas; and determine whether there is an association between childhood tuberculosis notification rates and area-level socioeconomic deprivation. To our knowledge, this is the first study in Portugal to evaluate these aspects of childhood tuberculosis.

METHODS

Data collection and study area

In Portugal, tuberculosis notification is mandatory. The data were collected from the Portuguese National Tuberculosis Surveillance System. We evaluated the notification rates of childhood tuberculosis per municipality in continental Portugal (n = 278) between January of 2016 and December of 2020. We included all tuberculosis cases in children under six years of age. Archipelagos were excluded because only two cases were notified in a single municipality (Ribeira Grande, on the Azores Islands), and this would have yielded highly unstable notification rates.

Population data were extracted from the Statistics Portugal website (https://www.ine.pt/), and we used population estimates by municipality for the study period (age group, 0-5 years).

Socioeconomic deprivation

The EDI-PT was used in order to assess socioeconomic deprivation across municipalities in continental Portugal. The EDI-PT comprises eight census variables and was calculated on the basis of the equation presented in Chart 1.[18]

Statistical analysis

We used hierarchical Bayesian spatial models to estimate the relative risk (RR) and notification rates for each area and to determine high-risk and low-risk areas. We assumed that the response variable (tuberculosis cases in each area) followed a Poisson distribution where E_i is the expected number of cases and θ_i is the RR (equation 1). We used the tuberculosis notification rates for the entire country as a reference to compute the expected number of cases. The expected number of cases was obtained by summing the product of the notification rates for the reference population (i.e., the population in continental Portugal) by the population of each municipality (n = 278).

$$O_i \sim Poisson\ (E_i, \theta_i) \quad \text{(Equation 1)}$$

$$Log\ (\theta_i) = \alpha + S_i \quad \text{(Equation 2.1)}$$

where α is an intercept quantifying the mean number of tuberculosis cases in the 278 municipalities. The area-specific effect S_i was modeled on the basis of a Besag-York-Mollié model[19] with a parameterization suggested by Dean et al. (equation 2.2.).[20]

$$S_i = \tau\ (\sqrt{\varphi} * \upsilon_i + \sqrt{1-\varphi} * \nu_i) \quad \text{(Equation 2.2)}$$

where υ_i is the structured effect and ν_i is the unstructured effect. The effect was scaled to render the model more intuitive and interpretable,[21] so that φ expresses the proportion of the spatial effect caused by the structured part and $1/\tau$ is the marginal variance of S_i.

Additionally, we used the function excursions to determine high-risk and low-risk areas.[13,14,22] High-risk areas are those whose RR is significantly above 1 (i.e., above the study area average), whereas low-risk areas are those whose RR is significantly below 1 (i.e.,

Chart 1. Equation used in order to calculate the European Deprivation Index for Portugal.

Variables
EDI-PT = % non-owned households × 1.191 + % households without indoor flushing × 1.729 + % household with 5 rooms or less × 0.964 + % blue-collars × 0.370 + % residents with low education level × 0.511 + % non-employers × 0.620 + % unemployed looking for a job × 0.268 + % foreign residents × 1.038

EDI-PT: Portuguese version of the European Deprivation Index. Adapted from Ribeiro et al.[18]

below the study area average). This method uses the posterior joint distribution computed from the Integrated Nested Laplace Approximations (INLA). It considers the dependence structure, allowing accurate identification of areas where the RR is greater than 1. To facilitate interpretation, RR was converted into rates per 100,000 population in the 0- to 5-year age bracket.

We also used the aforementioned models to evaluate the association between pediatric tuberculosis and area-level socioeconomic deprivation. The association was expressed in RR, which represents the risk increment per unit increase in the socioeconomic deprivation score. An RR was considered significantly higher or lower if Bayesian credible intervals did not include the value 1. RRs and Bayesian credible intervals were derived from their posterior means and quintiles. Posterior distributions were obtained using the INLA, which was implemented in the R INLA library.[23] RR, high-risk areas, and low-risk areas were mapped with the free, open-source geographic information system QGIS, version 3.16.

Ethical considerations

Ethical approval and informed consent were not required, because all patient data, collected for an official Portuguese national surveillance system, were anonymized in accordance with the ethical research guidelines in Portugal.

RESULTS

Between 2016 and 2020, 152 childhood tuberculosis cases were notified in Portugal (number of cases per year: 19 in 2016, 31 in 2017, 34 in 2018, 43 in 2019, and 25 in 2020). This corresponds to a crude childhood tuberculosis notification rate of 5.48 notifications per 100,000 children in the 0- to 5-year age bracket. Notification rates of childhood tuberculosis ranged from 1.88 notifications (in Portimão, in the Algarve) to 13.15 notifications (in Loures, in the metropolitan area of Lisbon) per 100,000 children in the 0- to 5-year age bracket. In the study period, annual live births ranged from 84,530 to 87,126; in 2016, there were 9,277 children vaccinated with BCG (10.6%).[24,25] With regard to severe forms of tuberculosis (disseminated tuberculosis, meningeal tuberculosis, or a combination of the two), 4 cases were reported in 2018 (all 4 were unvaccinated children, and 3 with met the eligibility criteria for BCG vaccination), and 7 cases were reported in 2019 (5 were unvaccinated children, and 1 met the eligibility criteria for BCG vaccination).[6] In 2020, seven of the 25 notified children with tuberculosis (28.0%) had been vaccinated with BCG.[24]

The spatial distribution of the notification rates of pediatric tuberculosis is portrayed in Figure 1A, and the delimitation of high-risk and low-risk areas is shown in Figure 1B. As can be seen in Figure 1B, there are seven high-risk areas for pediatric tuberculosis in Portugal (Lisbon, Loures, Sintra, Amadora, Odivelas, Matosinhos, and Vila Nova de Gaia), all of which are located in the metropolitan area of Porto or Lisbon.

A significant positive association was found between the EDI-PT and the pediatric tuberculosis notification rates (RR = 1.16; Bayesian credible interval, 1.05-1.29). Thus, for each unit increase in the deprivation index, the notification rate of childhood tuberculosis increased by 16%.

DISCUSSION

In this study, we characterized the geographic distribution of the pediatric tuberculosis notification rates in Portugal during the five years following the transition from a universal to a selective BCG vaccination strategy.

Given that Portugal is a country with a low incidence of tuberculosis, the most appropriate prevention strategy in children, without increasing the risk to public health, is early screening of exposed children, preventive treatment, and vaccination of children in risk groups, because they are the ones who individually benefit the most from vaccination. It is therefore recommended that the risk in unvaccinated children < 6 years of age be reassessed every time there is a contact with the health services, because the individual risk situation can change.[26] However, in recent years there have been severe forms of tuberculosis in children who are unvaccinated but meet the criteria for BCG vaccination. This highlights the importance of identifying and vaccinating cases eligible for vaccination.

Considering this detailed spatial distribution at the municipality level, we identified high-risk and low-risk areas for childhood tuberculosis across Portugal. As previously reported in studies of spatial analysis of tuberculosis in general at the national level[13,27] and at the international level,[28] we also found a highly heterogeneous spatial distribution of childhood tuberculosis.

Because there was no predefined cutoff for determining the childhood tuberculosis incidence rate, we used as a criterion an RR significantly above the study area average. Seven high-risk areas were thus identified, all of which are located in the metropolitan area of Porto or Lisbon. While this concentration of tuberculosis in the metropolitan areas has been reported in other spatial analysis studies, high-risk areas for adult tuberculosis in Portugal can also be found in

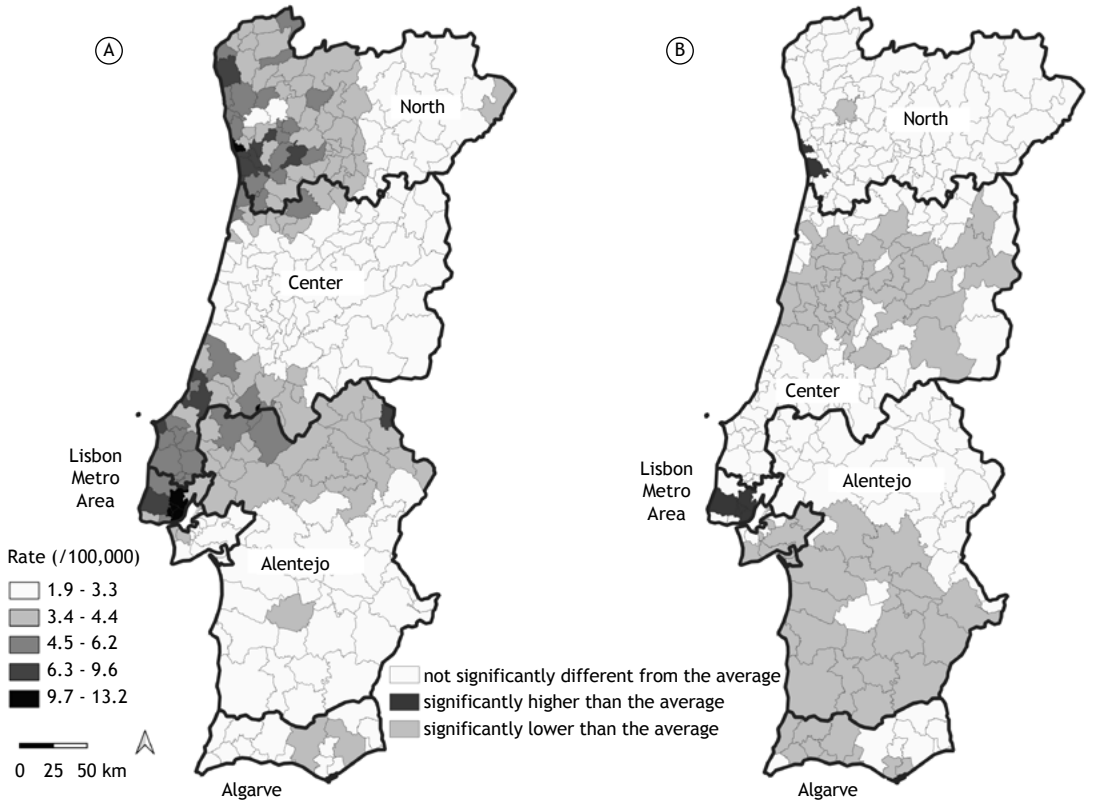

Figure 1. Spatial distribution of the notification rates of pediatric tuberculosis (in A) and corresponding delimitation of high-risk and low-risk areas (in B). High-risk areas are those whose relative risk (RR) is significantly above 1 (i.e., above the study area average), whereas low-risk areas are those whose RR is significantly below 1 (i.e., below the study area average).

peripheral and industrial regions of the metropolitan area of Porto; on the Alentejo coast; and in the Algarve.[27,29,30] To our knowledge, this type of spatial analysis of childhood tuberculosis in Portugal had never been performed. Given its unique approach, adult data should not be extrapolated to the pediatric population. Several studies have assessed the spatial distribution of tuberculosis and its association with socioeconomic deprivation; however, less is known about childhood tuberculosis. The relationship between a variety of socioeconomic factors and pediatric tuberculosis has been demonstrated in some regions: lower access to health care in the Philippines,[21] higher population density in Indonesia,[31] and higher poverty in Spain.[32] We demonstrated a significant positive association between childhood tuberculosis notification rates and socioeconomic deprivation in Portugal. For each unit increase in the EDI-PT, the notification rate of childhood tuberculosis increased by 16%, this effect being greater than that for adult tuberculosis, the percent increase for which is 5% only (unpublished results). Our results suggest that socioeconomic deprivation is a risk factor for childhood tuberculosis. These findings are not supported by a previous study conducted in Portugal, in which the composite EDI-PT was not related to the tuberculosis notification rate.[13] However, in that study,[13] a different version of the EDI-PT was used. Instead, we used an updated version. In addition, the aforementioned study[13] evaluated the overall tuberculosis notification rate, whereas, in our study, the focus was on childhood tuberculosis, reflecting epidemiological differences between tuberculosis in adults and in children. Therefore, this might be a relevant criterion when selecting candidates for BCG vaccination and the risk groups already defined by the Directorate-General of Health of Portugal for selective vaccination.[8]

One of the strengths of this study is the robust statistical methods used in order to describe the geographic distribution of childhood tuberculosis cases, which led to the identification of risk areas for childhood tuberculosis. The use of an updated socioeconomic deprivation score such as the EDI-PT, validated for use in the Portuguese population, is another strength of the present study. Some of the limitations of our study are its retrospective nature and the use of data from the Portuguese national notification system, which do not allow a more detailed characterization of the study population. As previously shown, there are numerous other recognized risk factors for childhood tuberculosis, such as malnutrition, illiteracy, overcrowded housing, immunosuppression (including HIV infection), and smoking status.[33-35] Therefore, we believe that it would be relevant to analyze other risk factors in this

population in order to gain a better understanding of the pathways behind the association between socioeconomic deprivation and adult tuberculosis.

In conclusion, we found a heterogeneous geographic distribution in childhood tuberculosis notification rates and identified high-risk areas across municipalities in Portugal. Thus, priority should be given to these areas in order to raise awareness for disease prevention in cases with known risk factors, as well as early identification and treatment of tuberculosis disease cases in adults and children. In addition, we established that socioeconomic deprivation is significantly associated with childhood tuberculosis notification rates, playing a stronger role than it does in adult tuberculosis. Furthermore, the EDI-PT was found to be a sensitive measure to capture tuberculosis-related inequalities, which might also be an important factor to consider when identifying cases eligible for vaccination. These findings should be integrated with other possible risk factors in order to define more accurate criteria for BCG vaccination and be used in order to inform public health policies related to tuberculosis disease control.

AUTHOR CONTRIBUTIONS

RD: study conception and design. SD and SC: database organization, drafting of the manuscript (both contributed equally). AIR and ETK: statistical analysis. AIR: drafting sections of the manuscript. All authors contributed to manuscript revision and approved the submitted version.

CONFLICTS OF INTEREST

None declared.

REFERENCES

1. World Health Organization. Global Tuberculosis Report 2022. Geneva: World Health Organization; 2022.
2. World Health Organization. Global Tuberculosis Report 2015. Geneva: World Health Organization; 2015.
3. World Health Organization. Global Tuberculosis Report 2021. Geneva: World Health Organization; 2021
4. Jaganath D, Beaudry J, Salazar-Austin N. Tuberculosis in Children. Infect Dis Clin North Am. 2022;36(1):49-71. https://doi.org/10.1016/j.idc.2021.11.008
5. World Health Organization. Roadmap for Childhood Tuberculosis. Geneva: World Health Organization; 2013.
6. Portugal. Direção-Geral da Saúde. Programa Nacional para a Tuberculose. Relatório da Vigilância e Monitorização da Tuberculose em Portugal - Dados definitivos 2020. Lisboa: Direção-Geral da Saúde; 2020.
7. World Health Organization. BCG vaccine: WHO position paper, February 2018 - Recommendations. Vaccine. 2018;36(24):3408-3410. https://doi.org/10.1016/j.vaccine.2018.03.009
8. Portugal. Direção-Geral de Saúde. Estratégia de vacinação contra a tuberculose com a vacina BCG. Norma no. 006/2016 (29/06/2016). Lisboa: Direção-Geral da Saúde; 2016.
9. Olson NA, Davidow AL, Winston CA, Chen MP, Gazmararian JA, Katz DJ. A national study of socioeconomic status and tuberculosis rates by country of birth, United States, 1996-2005. BMC Public Health. 2012;12:365. https://doi.org/10.1186/1471-2458-12-365
10. Lima SVMA, Dos Santos AD, Duque AM, de Oliveira Goes MA, da Silva Peixoto MV, da Conceição Araújo D, et al. Spatial and temporal analysis of tuberculosis in an area of social inequality in Northeast Brazil. BMC Public Health. 2019;19(1):873. https://doi.org/10.1186/s12889-019-7224-0
11. Nguipdop-Djomo P, Rodrigues LC, Abubakar I, Mangtani P. Small-area level socio-economic deprivation and tuberculosis rates in England: An ecological analysis of tuberculosis notifications between 2008 and 2012. PLoS One. 2020;15(10):e0240879. https://doi.org/10.1371/journal.pone.0240879
12. Nordholm AC, Andersen AB, Wejse C, Norman A, Ekstrøm CT, Andersen PH, et al. Social determinants of tuberculosis: a nationwide case-control study, Denmark, 1990-2018. Int J Epidemiol. 2022;51(5):1446-1456. https://doi.org/10.1093/ije/dyac109
13. Apolinário D, Ribeiro AI, Krainski E, Sousa P, Abranches M, Duarte R. Tuberculosis inequalities and socio-economic deprivation in Portugal. Int J Tuberc Lung Dis. 2017;21(7):784-789. https://doi.org/10.5588/ijtld.16.0907
14. Oliveira O, Ribeiro AI, Duarte R, Correia-Neves M, Rito T. Intra-urban variation in tuberculosis and community socioeconomic deprivation in Lisbon metropolitan area: a Bayesian approach. Infect Dis Poverty. 2022;11(1):24. https://doi.org/10.1186/s40249-022-00949-1
15. van Rie A, Beyers N, Gie RP, Kunneke M, Zietsman L, Donald PR. Childhood tuberculosis in an urban population in South Africa: burden and risk factor. Arch Dis Child. 1999;80(5):433-437. https://doi.org/10.1136/adc.80.5.433
16. Lopoo LM, London AS. Household Crowding During Childhood and Long-Term Education Outcomes. Demography. 2016;53(3):699-721. https://doi.org/10.1007/s13524-016-0467-9
17. Massey University. Environmental Health Intelligence New Zealand (ehinz) [homepage on the Internet]. Wellington, New Zealand: ehinz; c2018. [cited 2023 Apr 15]. Household crowding (children aged 0-14 years). Available from: https://www.ehinz.ac.nz/indicators/indoor-environment/household-crowding/
18. Ribeiro AI, Launay L, Guillaume E, Launoy G, Barros H. The Portuguese version of the European Deprivation Index: Development and association with all-cause mortality. PLoS One. 2018;13(12):e0208320. https://doi.org/10.1371/journal.pone.0208320
19. Besag J, York J, Molli A. Bayesian image restoration, with two applications in spatial statistics. Ann Inst Stat Math. 1991;43(1):1-20. https://doi.org/10.1007/BF00116466
20. Dean CB, Ugarte MD, Militino AF. Detecting interaction between random region and fixed age effects in disease mapping. Biometrics. 2001;57(1):197-202. https://doi.org/10.1111/j.0006-341X.2001.00197.x
21. Riebler A, Sørbye SH, Simpson D, Rue H. An intuitive Bayesian spatial model for disease mapping that accounts for scaling. Stat Methods Med Res. 2016;25(4):1145-1165. https://doi.org/10.1177/0962280216660421
22. Ribeiro AI, Krainski ET, Carvalho MS, Pina Mde F. Where do people live longer and shorter lives? An ecological study of old-age survival across 4404 small areas from 18 European countries. J Epidemiol Community Health. 2016;70(6):561-568. https://doi.org/10.1136/jech-2015-206827
23. Rue H, Martino S, Lindgren F. INLA: Functions which allow to perform a full Bayesian analysis of structured additive models using Integrated Nested Laplace Approximation. R package version 0.0-1404466487; 2009.
24. Portugal. Direção Geral da Saúde. Programa Nacional para a Tuberculose. Relatório da Vigilância e Monitorização da Tuberculose em Portugal - Dados definitivos 2021. Lisboa: Direção Geral da Saúde; 2021.
25. Fundação Francisco Manuel dos Santos. PORDATA [homepage on the Internet]. Lisboa: Fundação Francisco Manuel dos Santos; [cited 2023 Apr 15]. Nados-vivos de mães residentes em Portugal: total e fora do casamento. Available from: https://www.pordata.pt/portugal/nados+vivos+de+maes+residentes+em+portugal+total+e+fora+do+casamento-14
26. Portugal. Direção-Geral da Saúde. Estratégia de vacinação contra a tuberculose com a vacina BCG. Norma 006/2016 (24/03/2023). Lisboa: Direção-Geral da Saúde; 2023.

27. Couceiro L, Santana P, Nunes C. Pulmonary tuberculosis and risk factors in Portugal: a spatial analysis. Int J Tuberc Lung Dis. 2011;15(11):1445-i. https://doi.org/10.5588/ijtld.10.0302
28. Shaweno D, Karmakar M, Alene KA, Ragonnet R, Clements AC, Trauer JM, et al. Methods used in the spatial analysis of tuberculosis epidemiology: a systematic review. BMC Med. 2018;16(1):193. https://doi.org/10.1186/s12916-018-1178-4
29. Nelson LJ, Wells CD. Global epidemiology of childhood tuberculosis. Int J Tuberc Lung Dis. 2004 May;8(5):636-47. PMID: 15137548.
30. Oliveira O, Ribeiro AI, Krainski ET, Rito T, Duarte R, Correia-Neves M. Using Bayesian spatial models to map and to identify geographical hotspots of multidrug-resistant tuberculosis in Portugal between 2000 and 2016. Sci Rep. 2020;10(1):16646. https://doi.org/10.1038/s41598-020-73759-w
31. Wulan D, Rengganis S, Wahono EP. Spatial Analysis of Childhood Tuberculosis and Social Determinants in Bandar Lampung. E3S Web Conf. 2020;202(12006):1-6. https://doi.org/10.1051/e3sconf/202020212006
32. Carrilero N, Dalmau-Bueno A, García-Altés A. Socioeconomic inequalities in 29 childhood diseases: evidence from a 1,500,000 children population retrospective study. BMC Public Health. 2021;21(1):1150. https://doi.org/10.1186/s12889-021-11230-9
33. GOV.UK [homepage on the Internet]. London: UK Health Security Agency [updated 2018 Aug 3; cited 2023 Apr 15]. Immunisation Against Infectious Disease Greenbook. Chapter 32 - Tuberculosis. Available from: https://www.gov.uk/government/publications/tuberculosis-the-green-book-chapter-32
34. Singh M, Mynak ML, Kumar L, Mathew JL, Jindal SK. Prevalence and risk factors for transmission of infection among children in household contact with adults having pulmonary tuberculosis. Arch Dis Child. 2005;90(6):624-628. https://doi.org/10.1136/adc.2003.044255
35. Attah CJ, Oguche S, Egah D, Ishaya TN, Banwat M, Adgidzi AG. Risk factors associated with paediatric tuberculosis in an endemic setting. Alexandria J Med. 2018;54(4):403-409. https://doi.org/10.1016/j.ajme.2018.05.002