



INPE – National Institute for Space Research
São José dos Campos – SP – Brazil – May 16-20, 2016

ANALYSIS OF SPATIOTEMPORAL PATTERNS OF REPORTED CASES OF AIDS AND TUBERCULOSIS IN THE CITY OF SÃO PAULO BY ADMINISTRATIVE DISTRICTS, USING BAYESIAN DISEASE MAPPING

LIZZI, EAS¹; MARTINEZ, EZ²; RUFFINO-NETO, A³; GOLUB, J⁴

¹Universidade Tecnológica Federal do Paraná, Cornélio Procopio-PR, Brazil, elisangelalizzi@utfpr.edu.br

²Universidade de São Paulo, Ribeirão Preto-SP, Brazil, e-mail: edson@fmrp.usp.br ;

³Universidade de São Paulo, Ribeirão Preto-SP, Brazil, e-mail: aruffino@fmrp.usp.br;

⁴John Hopkins University, Baltimore-MD, United States, e-mail: jgolub@jhmi.edu;

Abstract: Investigate the spatiotemporal patterns of AIDS and tuberculosis (TB) incidents cases of between the years 2006 to 2012 in São Paulo city, SP, according to its 96 Administrative Districts, as well as their associations with the characteristics of income. This is an ecological study, and the tools used to incidence rates estimation and analysis of data is Bayesian regression models that incorporate spatial and temporal effects. These models include random effects with a CAR distribution (conditional autoregressive) bivariate normal that capture the influence of adjacent fields on the number of cases reported in each region, according to sex. Estimates of the model parameters were obtained by stochastic simulation method MCMC (Monte Carlo Markov Chain). The spatiotemporal pattern shows the reverse pattern of the Income association with TB, and AIDS with TB in space in relation to incident cases in men. The results are useful to support the policy planning and health actions directed to the AIDS and TB in areas and at-risk populations in São Paulo.

keywords: epidemiology and mathematical models, stochastic models, time series analysis, spatial statistics, bayesian disease mapping.

1. INTRODUCTION

Tuberculosis (TB) remains the major problem of public health worldwide, with millions of notifications each year. To the disease is the second leading cause of death from infectious disease worldwide, behind only the human immunodeficiency virus (WHO, 2014). According to the World Health Organization (WHO), there were 9

million new TB cases in 2013, 1.5 million deaths; of these, 1.1 million in HIV-negative people and 0.4 million among HIV-positive people. TB is an infectious disease caused by *Mycobacterium tuberculosis* (Koch's bacillus), being spread through the air when people suffering from pulmonary TB bacillus, eliminate the bacilli, by coughing. The case detection and treatment is considered the most effective control measures for disease control. It is known that only 5 to 10% of people infected with Koch's bacillus develop the disease, which is more likely among people infected with HIV (Oliveira et al., 2004; WHO, 2014) and more frequent among men than women (Holmes et al, 1998; Borgdorff et al., 2000). HIV and *Mycobacterium tuberculosis* are among the most lethal human pathogens worldwide. In addition, the synergy between HIV and TB (coinfection HIV / TB) is a major threat to public health in developing countries (Espert, Beaumelle & Vergne, 2015). In areas of high HIV prevalence, TB can not be prevented and effectively treated without the prevention and treatment of HIV / AIDS. The treatment of latent tuberculosis infection, in patients infected with human immunodeficiency virus is effective but worldwide have a joint processing deficit (Martinson et al., 2011). On the other hand, the actions directed for TB control are of fundamental importance in the effectiveness of planned actions of HIV / AIDS (Jamal and Moherdaui, 2007)

2. METHODOLOGY

It is an ecological epidemiological study of spatiotemporal analysis. Where we will be studied new cases of tuberculosis and AIDS, in São Paulo, southeastern Brazil, in 96 Administrative Districts (AD), in the period 2006 to 2012. The information

relating to AIDS new cases were obtained by TABNET / DATASUS , and tuberculosis were obtained by the TB-Web. crusades were the incidence of disease information with per capita income, assuming that TB is notoriously linked to poverty (Hawker et al., 1993; Jeremy et al, 1999), and aspects of social inequality in urban conglomerates (Ruffino -Netto; 2002), this work has the interest to understand this relationship together in time, space and the diseases in question. For the statistical analysis in question Y_{ikst} consider the number of incident cases in the administrative districts i ($i = 1, \dots, 96$) and t years ($t = 2006, \dots, 2012$), s by sex ($s = 1$ if male and $s = 2$ are female) and k diseases ($k = 1$ if $k = 2$ TB to AIDS). The statistical model that considers Y_{ikst} is a random variable that follows a Poisson distribution with expected value $N_{ikst} * \theta_{ikst}$. In the case of count data, mathematically, the statistical model is written as: $Y_{ikst} | N_{ikst}, \theta_{ikst} \sim \text{Poisson}(N_{ikst} * \theta_{ikst})$ where N_{ikst} is the number of inhabitants of the i District Administrative, in year t , s by sex and k for disease, where θ_{ikst} is a parameter to be estimated by the model on the incidence rate disease for each district, year, disease and gender. It uses a link function of the logarithmic type to estimate the incidence rate, considering the space, time, disease and sex, defined as:

$$\ln(\theta_{ikst}) = + \alpha_{kt} W_{KI} + \beta_{kst}. \quad (1)$$

We use Bayesian approach with a priori distributions of uninformative type. Thus, α_{kt} is a constant intercept for each sex, and year following a multivariate normal distribution with arrays unstructured W_{KI} is a spatial random effect following conditional bivariate autoregressive distribution, which allows correlations between nearby areas in space are larger also considering the information between diseases and β_{kst} follows a normal distribution with mean 0 and variance structured according to a gamma distribution with the hyper = 0.1 and $b = 0.1$. To compose the measurement of covariate per capita income, multiply the β_{kst} the covariate of interest.

We use intensive simulation methods with the MCMC algorithm (MCMC), with the support of Openbugs program, and additional module Geobugs. Where 100,000 samples were obtained. Considered a burn-in of size 10,000, to eliminate the effect of the initial values in the algorithm, and used 10 size jumps to minimize the effects of autocorrelation between successive samples of the posterior distributions of all model parameters. It was considered percentiles of 2.5% and 97.5% for the credibility intervals (95% CI) for the parameter of interest. The convergence was verified by the usual graphic diagnosis (correlogram and trace the graph), with the support of software and choosing the best

model among many was considered ordinary predictive conditional (CPO). Thematic maps were obtained with the help of R software (version 2.14).

3. RESULTS AND DISCUSSION

By studying the crude rates incidence of AIDS and TB, during the years 2006-2012, for females and males.

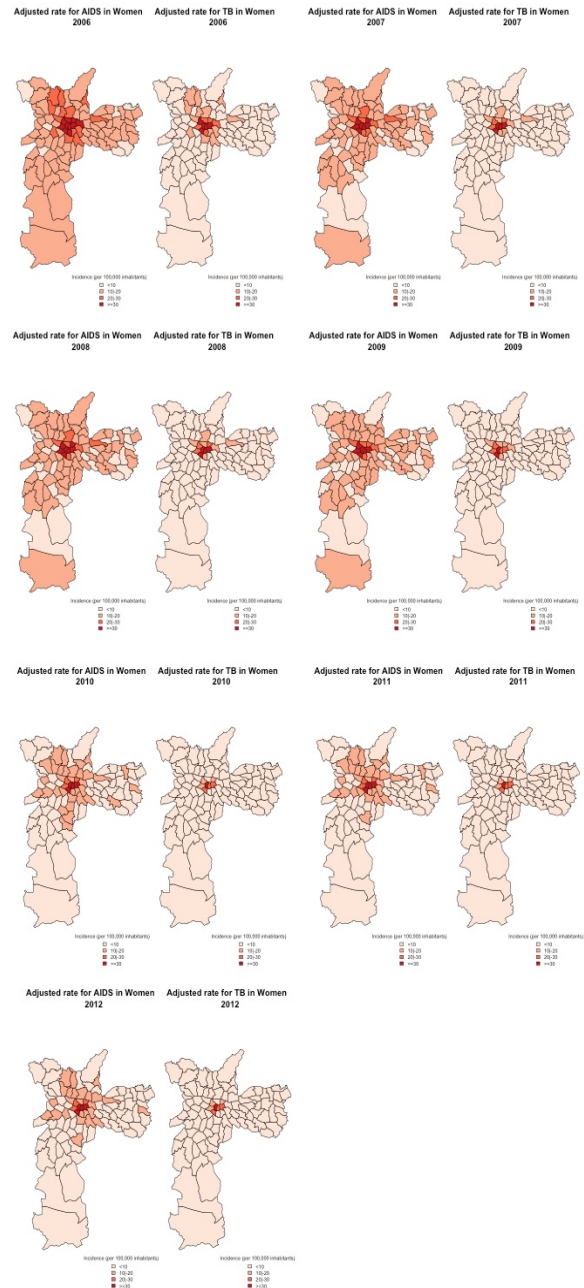


Figure 1: Adjusted rate incidence by AIDS and TB in women, São Paulo city-Brazil.

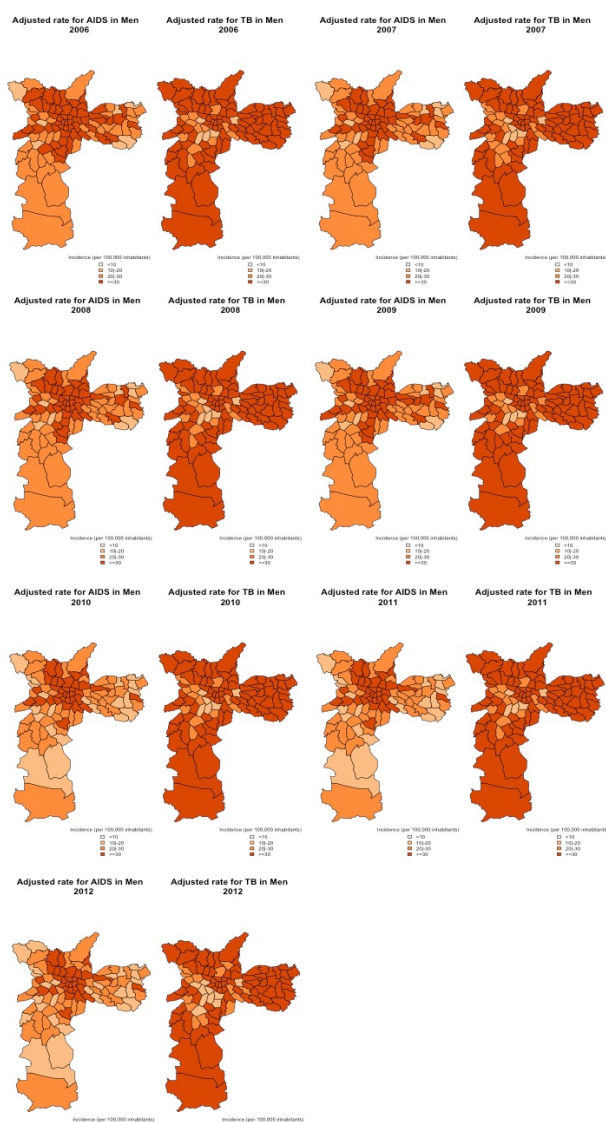


Figure 2: Adjusted rate incidence by AIDS and TB in men, São Paulo city-Brazil.

It is observed in Figure 1 and 2, that in women the highest incidence rates are concentrated in the Midwest, but with shredded information, ie without a clear spatial distribution. With respect to male the highest TB incidence rates appear in the southern peripheral regions, east and north, inversely observed in AIDS incidence rates, which are the lowest incidence rates. In other words, showing the incidence of inverse spatial pattern in space which is maintained over time with subtle changes. After adjusting the incidence rates by Bayesian spatiotemporal model, there is a smoothing of these rates.

For females, we can see that the adjusted incidence rates focus on "center" districts of the city under study, in contrast to AIDS incidence rates, describes a border around this center with the second highest

rate of incidence of disease. For males the highest AIDS incidence rates are in the central areas, and the lowest AIDS rates in peripheral areas; TB there are higher rates in the peripheral regions, indicating that the peripheral regions, supposedly with less economic power, are the most affected by TB than AIDS. The correlation between the diseases according to the spatio-temporal model is 0.41 (CI: 0.22 to 0.68), identifying the association between the disease happens moderately, so as increases AIDS incident cases also shows up an increase in TB incident cases in the period and the population studied.

Limitations of this study involve important aspects such as the quality of the data because the information comes from secondary databases available in health systems as TABNET and TB-Web. And also because it is a study of grouped information, ecological type, and can not generalize our findings to the individual level information. By comparing the information of the two diseases with per capita income, we can observe evidence of the association of income with TB cases, in inverse. That is, the districts that have the highest TB incidence rates as well have the lowest per capita income, there was no association of evidence of per capita income with AIDS incidence rates. The trend between income per capita and TB incidence rates with a curve estimated by the model, we observed an inverse relationship between the components. So we have evidence that the administrative districts with higher rates of incidence of TB has the lowest values of per capita income, showing the close link between socioeconomic status and TB, confirming issues of poverty and pauperization (Fonseca et al., 2000; Bastos and Szwarcwald, 2000). Poverty reduction would obviously be part of the actions to control the global epidemic of TB (Creswell et al 2011).

These results indicate an inverse relationship of incidence disease in gender and space, during the study time, showing the issue of feminization and pauperization of AIDS and TB (Fonseca et al., 2000; Bastos and Szwarcwald, 2000). The issue of lack of medical assistance (or disability) for coinfection, TB and AIDS, demonstrates vulnerability of disadvantaged districts with respect to these morbidities. With respect to TB treatment, the public health network in Brazil, has been decentralized to the basic level of health care, and assistance to AIDS, which is newer, focuses on secondary and tertiary levels. Treatment of coinfecting individuals (TB and HIV / AIDS) occur in different locations, making it difficult to access more expensive the same, contributing to lower adherence to treatment (Jamal et. Al 2007). The difficulty of access to health services and the inefficiency of the treatment for

coinfected patients is also found in studies conducted in South Africa (Daftary, 2012) and Europe (Mansfeld et. Al 2015).

3. CONCLUSION

Bayesian methods of disease mapping were satisfactory to understand the conjoint incidence of disease in space and time, these results allow us to present evidence of spatiotemporal patterns of the diseases in question, thus subsidizing the policy planning and public health actions directed at the combat and control them in the city in question. It emphasizes the need for service integration for both diseases and diversification in access to health services, gender by Administrative District.

ACKNOWLEDGMENTS

Thanks for the financial support of the project for *The International Clinical, Operational and Health Services Research and Training Award* (ICOHRTA) funded by the *National Institutes of Health* (NIH). Number of process U2RTW006885.

References

- [1] Bastos, FI e Szwarcwald, CL. . AIDS e pauperização: principais conceitos e evidências empíricas. **Cad. Saúde Pública**, 16(1): 65-76; 2000.
- [2] Borgdorff, M. W.; Nagelkerke, N. J. D.; Dye, C.; Nunn, P. Gender and tuberculosis: a comparison of prevalence surveys with notification data to explore sex differences in case detection. **The International Journal of Tuberculosis and Lung Disease**, 4(2):123-132; 2000.
- [3] Creswell, J.; Jaramillo E.; Lönnroth, K.; Weil, D.; Ravigliione, M. Tuberculosis and poverty: what is being done. **The International Journal of Tuberculosis and Lung Disease**. 15(4):431–432; 2011.
- [4] Daftary, A. Padayatchi, N. Social constraints to TB/HIV healthcare: accounts from coinfectd patients in South Africa. **AIDS Care**. 24(12): 1480–1486; 2012.
- [5] Espert, L. Beaumelle, B., Vergne, I. Autophagy in Mycobacterium tuberculosis and HIV infections. **Frontiers in Cellular and Infection Microbiology**. 5(49):1-8, 2015
- [6] Fonseca MG, Travassos C, Bastos FI, Silva N do V, Szwarcwald CL. Social distribution of AIDS in Brazil, according to labor market participation, occupation and socioeconomic status of cases from 1987 to 1998. **Cad Saude Publica**. 2003; 19(5):1351-63.
- [7] Jamal, LF; Moherdaul, F. Tuberculosis and HIV infection in Brazil: magnitude of the problem and strategies for control. **Rev Saúde Pública**; 41(1):104-110, 2007.
- [8] Golub, JE; Bur, S; Cronin, WA; Gange, S; Baruzh, N; Comstock, GW; Chaisson, RE. Delayed tuberculosis diagnosis and tuberculosis transmission. **International Journal of Tuberculosis Lung Disease (Union)**. 10(1):24–30; 2006
- [9] Hawker, JI; Surinder, SB; Ali, S; Farrington CP. Ecological analysis of ethnic differences in relation between tuberculosis and poverty. **BMJ** 1999; 319:1031–4
- [10] Holmes, C. B.; Hausler, H.; Nunn, P. A review of sex differences in the epidemiology of tuberculosis. **The International Journal of Tuberculosis and Lung Disease**. 2(2):96-104, 1998.
- [11] Lora et al. Evaluation of Microscopic Observation Drug Susceptibility (MODS) and the string test for rapid diagnosis of pulmonary tuberculosis in HIV/AIDS patients in Bolivia. **BMC Infectious Diseases**. 215:222; 2015.
- [12] Martinson, NA; Barnes, GL; Moulton, LH; Msandiwa, R; Hausler, H; Ram, M; McIntyre, JA; Gray, GE; Chaisson, RE. New Regimens to Prevent Tuberculosis in Adults with HIV Infection. **New England Journal of Medicine**. 365:11-20; 2011
- [13] Mansfeld, M. et. al. TB:HIV study group in EuroCoord. Major differences in organization and availability of health care and medicines for HIV/TB coinfectd patients across Europe. **HIV Medicine**. doi: 10.1111/hiv.12256; 2015.
- [14] Oliveira, HB; Marín-León, L; Cardoso, JC. Differences in mortality profile of tuberculosis patients related to tuberculosis- AIDS co-morbidity. **Revista de Saúde Pública**. 38(4): 503-510, 2004.
- [15] Ruffino-Netto, A. Tuberculose: a calamidade negligenciada. (Tuberculosis: the neglected calamity). **Revista da Sociedade Brasileira de Medicina Tropical**. 35(1): 51-58, 2002.
- [16] Spencer, DPS; Hotchiss, J; Willians, CSD; Davies, PDO. Tuberculosis and poverty, **BMJ** 1993; 307:759-61
- [17] Selik, RM; Starcher, ET; Curran, JW. Opportunistic diseases reported in AIDS patients: frequencies, associations, and trends. **AIDS**, 1:175-182, 1987.
- [18] World Health Organization. Global tuberculosis report 2014. Geneva: **World Health Organization**; 2014.