Pulmonary Tuberculosis and HIV/AIDS in Portugal: joint spatiotemporal clustering under an epidemiological perspective [1]

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Abstract: Since the mid-80s Tuberculosis declining trend became softer and even reversed in some countries. HIV/AIDS frequently appears as the main cause for the resurgence of Tuberculosis. This work aims at identifying critical areas for the joint occurrence of these conditions in Portugal, and at confirming the belief that HIV is not a major explanation for the slow Tuberculosis incidence decline.
Based on correlation analyses and space-time scan statistics, a weak statistical correlation between HIV and TB incidence rates were observed (0.279; $p<0.001$). For both diseases, Oporto and Lisbon Metropolitan Areas were identified as critical locals, with relative risks of, respectively, 1.77 and 1.78 for TB, and 5.66 and 3.31 for HIV. Similar areas were identified with a multivariate scan.
Keywords: Tuberculosis, HIV/AIDS, Spatiotemporal clustering,

1. Introduction

Although Tuberculosis and HIV /AIDS are presenting a decreasing trend, especially in developed countries, critical areas must be identified, to allow a global control of both diseases (Anandaiah *et al.*, 2011; de Colombani *et al*., 2004). Also, it is well known and stated in scientific literature that the particular and strong relation between these two diseases encourages joint actions (Bhagyabati Devi *et al.*, 2005; Couceiro *et al*., 2011). Some epidemiological dimensions (e.g.: risk factors) that are common to both TB and HIV lead to challenges and opportunities in surveillance, by promoting joint surveillance and control programs, including the development of TB/HIV indicators (Sanchez *et al.*, 2010). Only pulmonary cases are considered, given their outstanding role in disease transmission (Couceiro *et al*., 2011).
The goals of this study are: to identify critical areas for each disease separately, based on two independent datasets, in Portugal Mainland, per municipality and per year (2000-2009); and to identify and characterize critical areas for the joint occurrence of both diseases.

2. Materials and Methods

Data available concern the period 2000 to 2009, per municipality and were provided by three different official sources: the number of Tuberculosis notified cases - by the National Program for Tuberculosis Control; the number of HIV/AIDS notified cases - by the National Registry of HIV infected individuals (Communicable Diseases and

[1] CIMA/EU, and Lilly Portugal - Produtos Farmacêuticos, Lda. from Project: A Tuberculose em Portugal e seus determinantes.

Epidemiological Surveillance Center, INSA); and population data - by the National Statistical Institute. Constant detection rates among municipalities and in time are assumed. This study is exploratory and the interference of external relevant dimensions in the focused associations was not accounted for yet.

In a first approach, for either HIV/AIDS or Tuberculosis incidence rates, some independent exploratory data analyses were conducted. Additionally, correlation analyses pertaining to both entities were done.

In order to identify critical high incidence areas, spatiotemporal clustering analyses, based on the space-time scan statistic (Kulldorff, 1997), were applied separately for each disease. A multivariate scan with a multiple data sets process was applied, as HIV/AIDS is one of the risk factors for Tuberculosis and because both diseases have common risk factors. This method allows us to identify significant space-time joint clusters.

Space-time scan statistic is one of the most referred techniques in spatiotemporal epidemiological scientific literature, due to its appropriateness for the purpose, to its robust theoretical framework and also to the existence of free and friendly software (www.satscan.org).

3. Results

Brief descriptive analyses of Pulmonary Tuberculosis incidence rates (TBIR) and of HIV/AIDS incidence rates (HIVIR), based on incidence rates per municipality and per year (2000-2009), are presented in Tables 1 and 2 and Figure 1.

Table 1. Municipalities TBIR Descriptive Statistics (10^{-5}), global and per year.

TBIR	Global	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
Mean	20.50	24.59	22.57	23.25	21.43	20.01	20.11	18.13	16.09	20.16	18.71
Median	16.99	20.73	18.15	19.34	18.02	16.63	17.50	14.77	13.95	16.53	16.24
Std. Deviation	18.51	22.58	19.80	19.44	18.13	17.98	17.57	16.45	14.76	17.92	18.08
Maximum	155.70	144.58	109.57	92.87	103.14	112.28	90.80	77.39	68.98	95.02	155.70

A slow, hesitating and declining global trend in time was apparent for mean TBIR in the Mainland, between 2000 and 2009 (Table 1). The global mean (standard deviation) for TBIR was 20.50 (18.51).

Table 2. Municipalities HIVIR Descriptive Statistics (10^{-5}), global and per year.

HIVIR	Global	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
Mean	7.87	9.73	9.64	8.88	9.18	8.04	7.60	7.89	7.37	6.37	4.02
Median	2.57	2.39	3.98	4.43	5.42	2.36	4.03	4.22	3.06	.00	.00
Std. Deviation	12.73	18.04	14.69	13.59	12.79	12.30	11.33	11.18	11.73	10.69	7.26
Maximum	192.07	192.07	106.54	104.83	103.27	105.04	96.37	82.53	87.92	77.75	43.92

A steeper global decline of HIVIR was observed, in the same period and area (Table 2), with a global mean (standard deviation) of 7.87 (12.73).

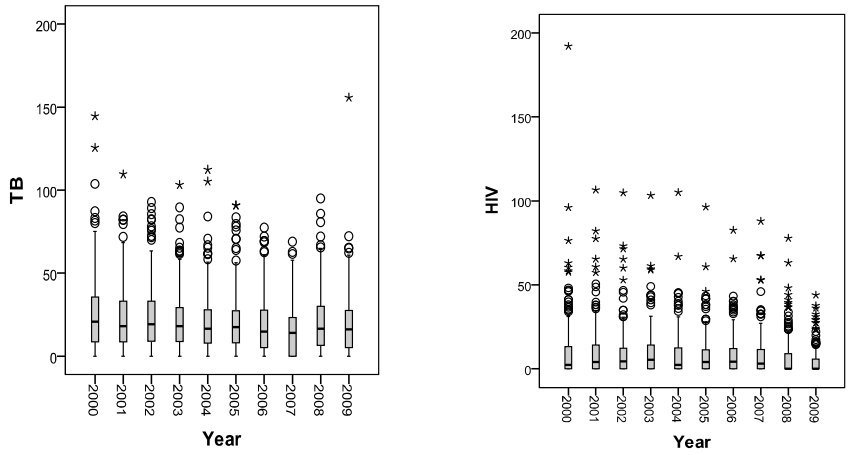


Figure 1: Boxplots of Municipalities TBIR and HIVIR, per year.

The presence of outliers, in most years, makes it difficult to interpret a global time trend for the incidence rates, regarding each disease (Figure 1).
As shown, from the minimum ("0" in all cases), the maximum and the median values, as well as from the boxplots, the data distribution was highly asymmetric for either TBIR or HIVIR, partly due to the strong presence of those outliers.

Table 3. Spearman Correlation Coefficient between TBIR and HIVIR (p<0.001).

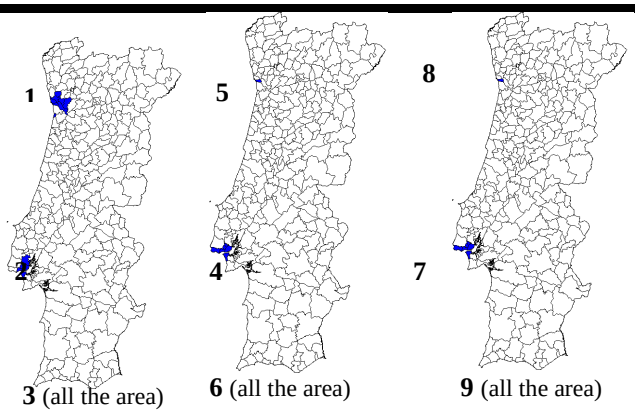
Global	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
0.279	0.294	0.342	0.308	0.341	0.204	0.280	0.313	0.281	0.213	0.202

The associations between TBIR and HIVIR, globally and per year, as expressed by Spearman correlation coefficients, seem stable but rather weak, though significant (Table 3). Correlation varied from 0.202 to 0.342 between 2000 and 2009, and it was 0.279 globally (p<0.001).

Table 4 & Figure 2. Results of TBIR(a) and HIVIR(b) spatiotemporal clustering analyses; (c) Multivariate Scan of TBIR and HIVIR (p<0.001).

Cl	Radius (km)	Time Frame	Observed/ Expected	R.R.
1	24543	2000-2009	6926/4345	1.77
2	13203	2000-2009	6563/4078	1.78
3	All	2000-2003	13561/11722	1.29
4	11591	2000-2009	6216/2467	3.31
5	0	2000-2009	2192/429	5.66
6	All	2000-2004	10692/9004	1.46
7	11591	2000-2009 2000-2009	6216/2467 6447/4029	3.31 1.77
8	0	2000-2009 2000-2009	2192/429 1668/701	5.66 2.46
9	All	2000-2004 2000-2004	10692/9004 16545/14705	1.46 1.28

Maps



a)TBIR b)HIVIR c)TBIR/HIVIR

For both diseases, Oporto and Lisbon Metropolitan Areas were identified as critical locals, based on spatiotemporal clustering analyses (Table 4 & Figure 2). Relative risks for Oporto and Lisbon were, respectively, 1.77 and 1.78 in TB study, and 5.66 and 3.31 in HIV case. Clusters 3, 6 and 9 were related to the whole area under study and only for the first years (until 2003 or 2004). This fact is concordant with the decreasing apparent trend already mentioned for both diseases.

4. Concluding remarks

The evidence of some matching between high incidence critical areas regarding both diseases is expected, in accordance with the scientific literature. Joint distributions of HIV/AIDS and Pulmonary Tuberculosis in space and time in Portugal Mainland were, in fact, not independent: very similar space-time critical areas were found, reinforcing the previous conviction that, in Portugal, HIV/AIDS may be faced as an explanatory, but not a major dimension for TB incidence. Oporto and Lisbon metropolitan areas were identified as important places for urgent Public Health interventions.

In order to improve the characterization of TB and HIV correlation, there is a need to: confirm that the detection rates are not interfering with results; explore the role of high outlier values as a source of joint variability; better understand the role of demographic and socio-cultural dimensions in the apparent associations; develop individuals-based studies, as a complement this ecological approach.

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