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Type of the Paper Article

Tuberculosis among peoples who were living on the street and used alcohol, tobacco, and illegal drugs: analysis of territories in extreme vulnerability and trends in southern Brazil

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Abstract: (1) Background: tuberculosis presents an epidemiological trend towards inequality, especially among people in social exclusion and situations of vulnerability. To analyze territories where there is a concentration of people diagnosed with tuberculosis, in a street situation, and who make chronic use of alcohol, tobacco, and illicit drugs. We will also analyze trends in this health condition in southern Brazil; (2) Methods: Ecological study, developed in the 399 municipalities of Paraná, Southern Brazil, with all tuberculosis cases in the homeless population registered in the Information System of Notifiable Diseases between 2014 to 2018. For data analysis, we used descriptive statistics, for the time series, the Prais-Winsten autoregression method, whereas for spatial analysis, we used the Getis-Ord Gi technique*; (3) Results: in total, 560 cases were reported. We found a predominance of alcohol, smoking, and illicit drugs users, with an increasing trend in the state and clusters of spatial risk in the East health macro-region; (4) Conclusions: We observed territories with critical levels of highly vulnerable people who use psychoactive substances and are in a street situation. The results highlight the importance of incorporating public policies of social protection to these individuals and resolutive health services that receive and assist in eradicating TB.

Keywords: Tuberculosis 1; Vulnerable populations 2; Homeless Persons 3; Substance-Related Disorders 4.

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1. Introduction

Tuberculosis (TB) is an infectious disease caused by Mycobacterium tuberculosis. Considered a serious public health problem, it is among the ten most common causes of preventable deaths in the world [1-3].

Historically, TB presents an epidemiological trend towards inequality, especially among people in social exclusion and situations of vulnerability [4]. Thus, homeless population, Population Deprived of Liberty (PPL), people with Human Immunodeficiency Virus (HIV), the user or addicted to psychoactive substances, alcohol, tobacco, and other drugs [5,6] are considered indicators that contribute to the spread of the disease in the territories.

In this sense, homeless population is defined as a heterogeneous population group that has in common extreme poverty, family ties interrupted or weakened and the absence of regular conventional housing, and that uses public spaces and degraded areas as a living and subsistence space, temporarily or permanently, as well as reception units for temporary accommodation or as temporary housing [7].

Thus, being homeless is an aggravating factor for the spread of TB in social exclusion groups is the form of infection of the disease since the respiratory route transmits it by inhaling the sputum droplets expelled by the infected person [6]. Given the social situation of homeless people, there may be a great spread of the disease among them since they tend to remain grouped. Specifically, among homeless population, TB has a high prevalence since the same have a close contact with a large contingent of homeless and the fluctuation between different shelters and territories [8].

In addition, most infected people do not present signs and symptoms of the disease, which are classified as carriers of Latent Infection by TB. The absence of signs and symptoms prevents the search for treatment and intensifies the spread of the disease. It is estimated that approximately 2 to 3 billion people in the world are infected by TB, and of these, about 5 to 15% will evolve to active TB during life [9,10]. Studies point out that TB among homeless population is the third largest cause of illness and has an incidence of 10 to 85 times higher to develop latent and active TB infection when compared with the general population [11].

This evidence indicates that vulnerable populations have become a major challenge for countries to develop strategies and achieve their TB elimination goals globally. In social epidemiology, there are several resources available that demonstrate the strength of the social determinants of territories in the TB progression chain, with a large number of studies using spatial analysis in the general population. However, this is not the reality of homeless population since the address is an aspect required for geoprocessing/georeferencing, which makes many studies with these approaches exclude this population.

Another gap is that vulnerability is multifaceted. Within the same context, many vulnerabilities end up countering each other, causing cases to become overly complex, requiring equally complex approaches to alleviating suffering and bringing solutions to the problem. Given the problems presented, this study is of great importance. It brings the question of territories, homeless population to TB and the relationship with alcohol, tobacco, and illicit drugs, which causes that in some regions and territories, the disease control is far away. Therefore, the study aims to analyze territories where there is a concentration of people diagnosed with tuberculosis, in a street situation, and who make chronic use of alcohol, tobacco, and illicit drugs. We will also analyze trends in this health condition in southern Brazil.

2. Materials and Methods

Study design

Ecological study [12].

Study location and population

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A study carried out in the 399 municipalities of Paraná, located in the southern region of Brazil in the geographic coordinates 24º59' S latitude and 53º56' W longitude, whose estimated population is 11.34 million inhabitants. It is the fifteenth state of Brazil with the largest national territory and the fifth one with the population number [5].

In 2020, Paraná had 2,190 TB cases, obtaining an incidence of 19 cases per 100.000 inhabitants, with 157 deaths and an incidence of 1.4 per 100.000 inhabitants and about 6.2% abandoning treatment [3].

According to the Inter-sector Committee for Monitoring and Monitoring the Population Policy in Street Situation (CIAMP Street/PR), which aims to enable and assist in the implementation and monitoring of public policies aimed at the population in a street situation, it is estimated that in 2021 the state has about 8,659 people registered at CIAMP street/PR. It is noteworthy that among this quantitative may occur an undernotification, indicating that the contingent should be higher, mainly due to the current situation in the country, as well as the high turnover of homeless people. Between 2015 to 2020, the state showed an increase of 65% TB cases in the homeless population, and in 2020, an increase in the percentage of cases of 6,8% [13].

To develop the spatial distribution, we subdivided the 399 municipalities that make up the state of Paraná into four health macro-regions (East, North, Northwest, and West), and used as a unit of geographical analysis. **Figure 1** illustrates the location of the state and its health macro-regions.

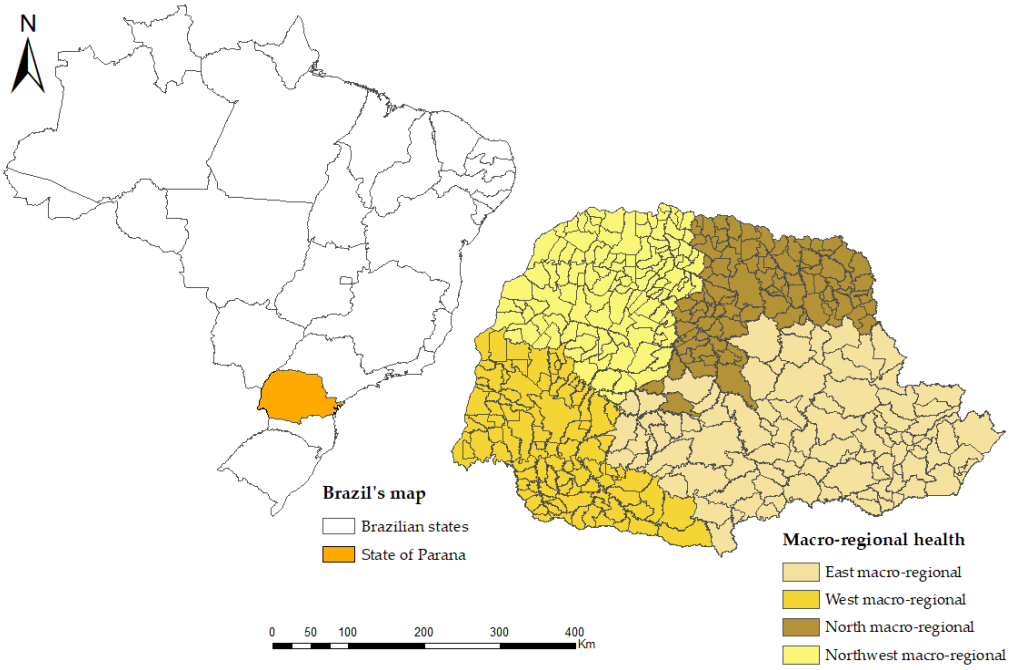

Figure 1. - Geographical location of health macro-regions according to municipalities in the state of Paraná.

Inclusion criteria

We considered all cases of TB in the homeless population obtained in the Information System of Notifiable Diseases (SINAN) from 2014 to 2018. These data were made available by the Health Department of the State of Paraná in an electronic spreadsheet in Excel.

It was adopted as inclusion criteria for people diagnosed with TB, included in the notification form as a person on the street, alcoholic, smoker, illicit drug user, and aged 18 years or older. To identify risk areas and time series, the population was subdivided

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into general TB; TB alcoholism; TB smoking, and TB users of illicit drugs. It is emphasized that an individual may belong simultaneously to one or more study groups.

Analysis plan

First, the descriptive statistics of the data were performed utilizing absolute and relative frequency, which used the following variables: alcoholism, smoking, and illicit drugs, sex, age group, race/color and schooling, TB/HIV coinfection, diabetes mellitus, mental disorder and data related to the clinical profile of TB, such as type of entry, form, radiography, sputum smear, histopathology, molecular test, and case closure. The IBM SPSS software version 25 was used to analyze the data.

Time series

Time series are characterized as observations taken sequentially over time [14]. It is worth noting that the temporal trend refers to the direction in which the time series develops according to a determined time interval, which may follow a growth, decrease, or stationary pattern [15, 16]. The month and year of notification of TB cases were used to perform the analysis.

The Prais-Winsten autoregression method [15] was performed in the STATA software, version 14, to classify the event's temporal trend as increasing, decreasing, or stationary in the study period. When the temporal trend was classified as increasing or decreasing, the percentage of monthly variation (MPC - Monthly Percent Change) and their respective 95% confidence intervals (95 CI) were calculated [14].

Next, we used the robust time series decomposition method called Seasonal-Trend by Loess (STL by Loess) [16]. This decomposition method is based on a locally weighted regression (Loess). It is the method used to estimate nonlinear relations, managing to separate the components that make up a time series: trend, seasonality, and noise [16, 17]. For the analysis, the RStudio software and the forecast package were used.

In contrast to the Prais-Winsten method where the time trend assessment is global and a constant is generated by classifying the whole period under study, the STL method allows the evaluation of the time trend over the whole period under analysis, notice its variations over time, check if the trend has always been increasing/decreasing/stationary or if there have been periods of variations with peaks and/or decreases.

Spatial analysis

The technique called Getis-Ord General G and Getis-Ord Gi* was used to identify whether clusters were formed, using the number of cases per municipality. The Getis-Ord General G technique, based on the Moran Global Index and, as in inferential statistics, the results are based on the null hypothesis that there is no spatial grouping. If p is significant, the null hypothesis can be rejected, and the z-score value becomes important, where its values of ±3 represent a 99% confidence level [18, 19]. If the z-score value is positive, the observed G-Index is higher than expected, indicating high event indices grouped in the area under study. The negative z-score value, the G-index observed is lower than the expected index, indicating that the low values are grouped in the study area [20].

The Getis-Ord Gi* technique indicates a local association, considering the values for each census tract from a neighborhood matrix. In this analysis, a z-score is generated for statistically significant municipalities, and the higher the z-score, the more intense is the grouping of high values (Hotspot). The logic is the same for the Z-negative score, i.e., the lower the z-score, the more intense the grouping of low values (cold spot) [20].

In addition to the z-score, p-value and significance level (Gi-Bin) are also provided, which identify statistically significant hot and cold spots. The values may vary between +/- 3 and reflect statistical significance with a confidence level of 99%, +/- 2 with a confidence level of 95%, and +/- 1 with a confidence level of 90%, with a zero-value corresponding to non-statistically significant areas [20].

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Ethical aspects

This study was approved by the Research Ethics Committee of the School of Nursing of the University of São Paulo, Campus Ribeirão Preto, in accordance with the Regulatory Guidelines and Norms for Research with Human Beings, Resolution nº 466/2012 of the National Health Council, under the Presentation Certificate for Ethical Appreciation nº 3,836,401 obtaining a Presentation Certificate of Ethical Appreciation number: 24963319.1.0000.5393, issued on. February 13, 2020.

3. Results

Between 2014 and 2018, 560 cases of TB were reported among the homeless population. When analyzing the consumption of psychoactive substances, homeless users were predominant (n=420; 36.30%), smokers (n=382; 33.02%), and other drugs (n=355; 30.68%).

Table 1 shows the characterization of TB cases in homeless population subdivided by type of psychoactive substances. The total sample showed higher predominance of TB in males, with age group above 40 years of white race/color, with schooling from 5th to 8th grade of elementary school and living in the urban perimeter. The sociodemographic characteristics of the homeless population of users of alcohol, tobacco, and illicit drugs are similar to that of the general homeless population. Some peculiarities were noted, such as one-third of alcohol and tobacco users having low schooling (1st to 4th grade), 43.1% (n=153) of other drug users are younger (30 to 39 years of age), when compared to alcohol users (50.2%; n=211) and tobacco (47.1%; n=180) that are in the age group of 40 years or older. Notably, 73.7% (n=412) of the general street population who has TB do not receive government benefits. Regarding the presence of chronic diseases, it is observed that the TB-AIDS coinfection was more prevalent among all variables studied, followed by the categories 'other diseases' and mental illness.

Table 1. - Sociodemographic characterization of tuberculosis cases in the homeless population of the state of Paraná, Brazil (2014-2018).

Variables	Street population using alcohol		Street population using tobacco		Street population using illicit drugs		General street population	
	n	%	n	%	n	%	n	%
Genre								
Male	362	82,3	318	83,2	281	79,2	472	84,4
Female	58	13,2	64	16,8	74	20,8	87	15,6
Age group								
18 to 29 years	61	14,5	65	17,0	77	21,7	97	17,4
30 to 39 years	148	35,2	137	35,9	153	43,1	197	35,2
40 or more	211	50,2	180	47,1	125	35,2	265	47,4
Race								
White	217	51,7	197	51,6	180	50,7	292	52,2
Black	51	12,1	47	12,3	39	11,0	61	10,9
Yellow	2	0,5	1	0,3	4	1,1	4	0,7
Brown	143	34,0	125	32,7	122	34,4	183	32,7
Indigenous	1	0,2	1	0,3	1	0,3	2	0,4
Schooling								
Illiterate	11	2,6	11	2,9	11	3,1	17	3,0
1st to 4th grade	126	30,0	111	29,1	84	23,7	149	26,7
5th to 8th grade	112	26,7	103	27,0	108	30,4	157	28,1
> 8 years of study	39	9,3	41	10,7	35	9,9	55	9,8
Housing perimeter								
Urban	367	87,4	334	87,4	323	91,0	485	86,8
Rural	16	3,8	16	4,2	10	2,8	25	4,5
Periurban	1	0,2	-	-	-	-	2	0,4
Government benefit								
Yes	22	5,2	24	6,3	24	6,8	39	7,0

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No	312	74,3	288	75,4	266	74,9	412	73,7
Alcoholism								
Yes	420	100,0	318	83,2	284	80,0	420	75,1
No	-	-	56	14,7	60	16,9	118	21,1
Smoking								
Yes	318	75,7	382	100,0	274	77,2	382	68,3
No	82	19,5	-	-	65	18,3	140	25,0
Other drugs								
Yes	284	67,6	274	71,7	355	100,0	355	63,5
No	110	26,2	94	24,6	-	-	163	29,2
HIV/AIDS								
Yes	110	26,2	106	27,7	117	33,0	153	27,4
Noo	291	69,3	258	67,5	224	63,1	378	67,6
Diabetes Mellitus								
Yes	15	3,6	14	3,7	11	3,1	19	3,4
No	389	92,6	354	92,7	331	93,2	511	91,4
Mental illness								
Yes	28	6,7	28	7,3	26	7,3	36	6,4
No	371	88,3	338	88,5	310	87,3	487	87,1
Other diseases								
Yes	50	11,9	46	12,0	41	11,5	64	11,4
No	287	68,3	263	68,8	245	69,0	389	69,6

Regarding the clinical profile of TB cases in the homeless population **(Table 2)**, in the general street population, there was a prevalence of new cases, pulmonary TB, with suspect chest radiography, positive sputum culture, not performed histopathology, HIV negative test, not performed molecular test, not informed sensitivity test and cure in TB treatment. When analyzing the clinical profile of cases associated with the type of drug, it was evidenced that the same specificities of the total population occurred, noting that, regarding the closure situation, the abandonment and death due to TB and other causes were more present among patients who used alcohol, tobacco, and other drugs.

Table 2. - Clinical profile of tuberculosis cases in the homeless population of the state of Paraná, Brazil (2014-2018).

Variables	Street population using alcohol		Street population using tobacco		Street population using illicit drugs		General street population	
	n	%	n	%	n	%	N	%
Type of entry								
New case	256	61.0	232	60.7	217	61.1	351	62.8
Recurrence	37	8.8	33	8.6	31	8.7	46	8.2
Reentry after loss to follow-up	80	19.0	73	19.1	72	20.3	102	18.2
Do not know	2	0.5	-	-	2	0.6	3	0.5
Transfer	41	9.8	41	10.7	31	8.7	51	9.1
Clinical form								
Pulmonary	378	90.0	343	89.8	313	88.2	504	90.2
Extrapulmonary	20	4.8	17	4.5	19	5.4	24	4.3
Pulmonary + extrapulmonary	22	5.2	22	5.8	23	6.5	31	5.5
Chest radiography								
Suspect	356	84.8	329	86.1	292	82.3	466	83.4
Normal	7	1.7	5	1.3	7	2.0	9	1.6
Other pathology	1	0.2	1	0.3	1	0.3	1	0.2
Unrealized	52	12.4	43	11.3	52	14.6	78	14.0
Sputum smear microscopy								
Positive	265	63.1	247	64.7	222	62.5	359	64.2
Negative	63	15.0	62	16.2	52	14.6	85	15.2
Unrealized	88	21.0	71	18.6	78	22.0	110	19.7

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Sputum culture								
Positive	168	40.0	153	40.1	145	40.8	221	39.5
Negative	80	19.0	82	21.5	77	21.7	106	19.0
In progress	15	3.6	14	3.7	11	3.1	18	3.2
Unrealized	157	37.4	133	34.8	122	34.4	214	38.3
Histopathology								
Baar positive	46	11.0	45	11.8	41	11.5	67	12.0
Suggestive of TB	12	2.9	10	2.6	9	2.5	14	2.5
Non suggestive of TB	2	0.5	3	0.8	4	1.1	4	0.7
In progress	12	2.9	9	2.4	6	1.7	13	2.3
Unrealized	343	81.7	311	81.4	291	82.0	454	81.2
HIV test								
Positive	113	26.9	107	28.0	120	33.8	156	27.9
Negative	270	64.3	247	64.7	208	58.6	352	63.0
Unrealized	36	8.6	27	7.1	27	7.6	50	8.9
Final status								
Cure	152	36.2	149	39.0	114	32.1	200	35.8
Primary abandonment	13	3.1	10	2.6	10	2.8	14	2.5
Abandonment	91	21.7	85	22.3	85	23.9	137	24.5
Death by TB	31	7.4	26	6.8	23	6.5	39	7.0
Death from other causes	44	10.5	36	9.4	39	11.0	52	9.3
Transference	68	16.2	64	16.8	67	18.9	91	16.3
TB-DR	12	2.9	10	2.6	8	2.3	13	2.3
Molecular testing								
Detectable at rifampin	112	26.7	107	28.0	108	30.4	158	28.3
Detectable rifampin resistant	9	2.1	6	1.6	8	2.3	11	2.0
Undetectable	13	3.1	13	3.4	11	3.1	14	2.5
Inconclusive	6	1.4	5	1.3	4	1.1	6	1.1
Unrealized	262	62.4	235	61.5	213	60.0	344	61.5
Uninformed	18	4.3	16	4.2	11	3.1	26	4.7
Sensitivity test								
Resistant to Isoniazid only	6	1.4	6	1.6	3	0.8	7	1.3
Resistance to rifampin only	2	0.5	1	0.3	2	0.6	3	0.5
Resistant to Isoniazid and Rifampicin	4	1.0	4	1.0	2	0.6	5	0.9
Resistant to other drugs 1st line	3	0.7	4	1.0	4	1.1	4	0.7
Sensitive	74	17.6	66	17.3	62	17.5	98	17.5
In progress	6	1.4	7	1.8	4	1.1	8	1.4
Unrealized	61	14.5	51	13.4	45	12.7	77	13.8
Uninformed	264	62.9	243	63.6	233	65.6	357	63.9

The temporal trend of TB cases in the homeless population **(Table 3)** presented an increasing scenario for all categories analyzed. For the population using alcohol, the growth was 29.71% per month (95% CI 18.03 - 42.56), tobacco 27.93% per month (95% CI 16.68 - 39.95), other drugs 30.31% per month (95% CI 18.57 - 43.21), and general drugs 38.35% (95% CI 23.31 - 55.23).

Table 3. - Temporal trend of tuberculosis incidence in the street population according to the consumption of psychoactive substances. Paraná, Brazil (2014-2018).

Variable	Coefficient (CI*95%)	Temporal trend	MPC**(CI95%)
Street population using alcohol	2.47 (1.50 – 3.54)	Crescent	29.71 (18.03 – 42.56)
Street population using tobacco	3.32 (1.39 – 3.32)	Crescent	27.93 (16.68 – 39.95)
Street population of illicit drugs	2.52 (1.54 – 3.60)	Crescente	30.31 (18.57 – 43.21)
General street population	3.19 (1.94 – 4.60)	Crescente	38.35 (23.31 – 55.23)

* Confidence Interval

** Monthly Percent Change.

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Figure 2. shows the time series decomposition technique. We found an increase in the temporal trend of TB cases in homeless population for alcohol, tobacco, other drugs, and general street population. We identified slight fluctuation of the temporal trend concerning the number of cases in the months, thus corroborating the findings presented in Table 1 referring to the analysis of Prais-Winsten.

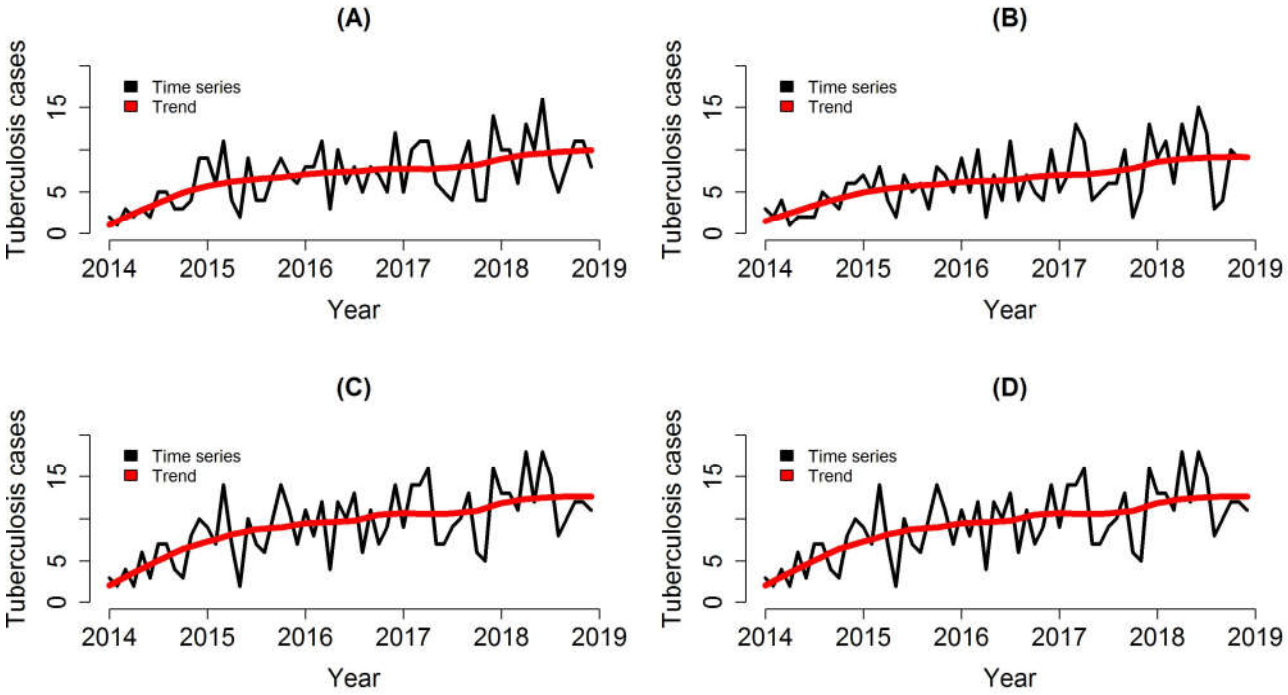

Figure 2. - Time series of the homeless population diagnosed by tuberculosis in the state of Paraná, Brazil. (2014-2018).

For the results of the global spatial association (G), we observed that the values of z-score and the pseudo-significance test confirmed the non-randomness of TB cases in the population using alcohol (z-score of 3.00 and $p < 0.00$), tobacco (z-score 3.12 and $p < 0.00$) illicit drugs (z-score 2.79 and $p < 0.00$), and general drugs (total) (z-score 3.78 and $p < 0.00$). **Figure 3** shows the local spatial association (Gi*) of TB cases, which shows hotspots in the Eastern macro-region in the metropolitan region of Curitiba for alcohol, tobacco, illicit drugs, and General street population.

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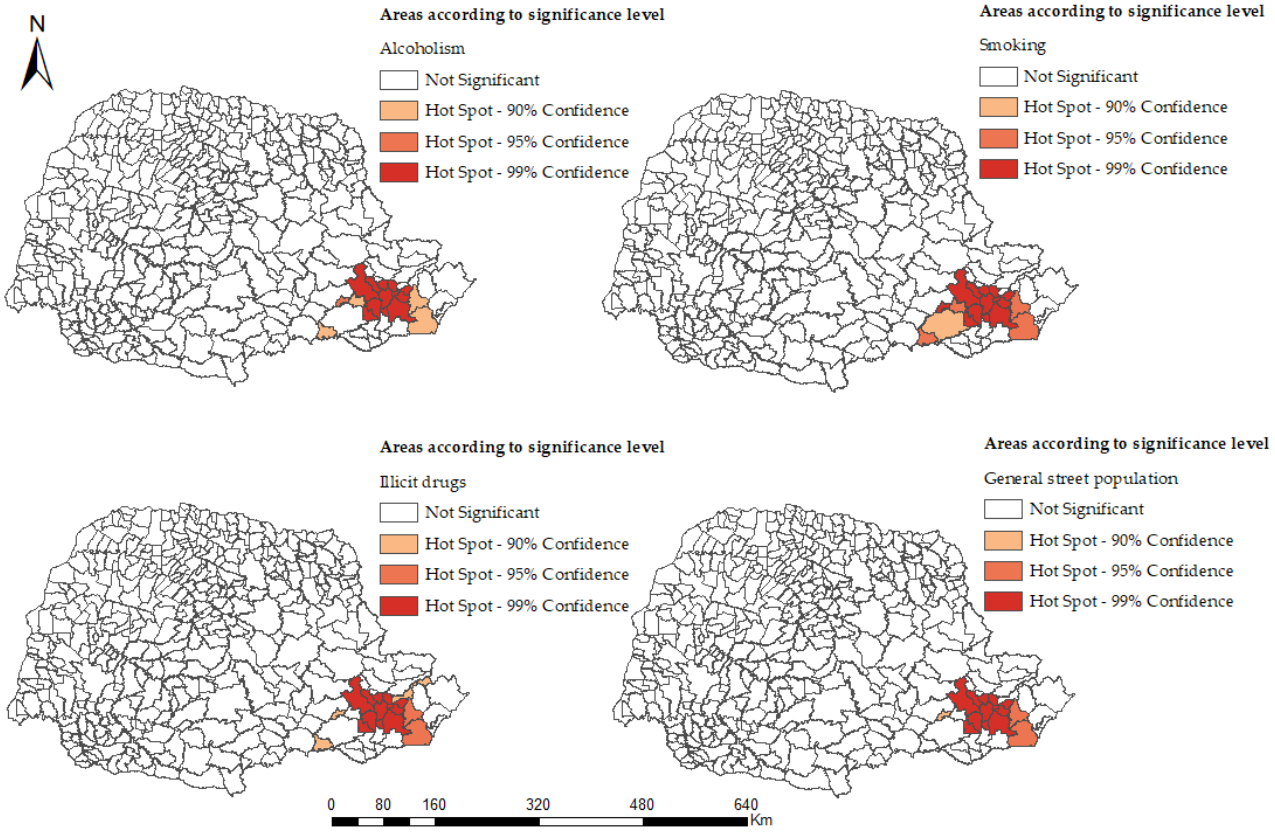

Figure 3. - High-clusters and Low-clusters for tuberculosis cases in the homeless population in the state of Paraná, Brazil. (2014-2018).

4. Discussion

We analyzed territories with a concentration of people diagnosed with tuberculosis, in homeless situation, and who make chronic use of alcohol, tobacco, and illicit drugs and trends of this health condition in southern Brazil. We observed that in the South of Brazil, despite being considered one of the most developed regions of the country, there were still clusters or areas of the population with extreme vulnerability, people diagnosed with TB, using psychoactive substances, and still on the street. And there was also a growing increase in this situation in the East Health macro-region (metropolitan region of Curitiba - state capital).

International and national studies indicate that homeless population has a high prevalence for the development of TB associated with the use of alcohol, tobacco, and illicit drugs, being a risk factor that favors the development of new cases and the maintenance of the TB transmission cycle [4,8,21]. Thus, homeless population has 48 to 67 times more chances of developing TB when compared to the general population [22].

A study conducted in the United States between 2006 and 2010 found that the annual incidence of TB among homeless population ranged from 36 to 47 cases per 100.000 inhabitants [23]. In Germany, the incidence of TB is 30 cases per 100.00 inhabitants [8], whereas, for Brazil, there are no specific data that address this population.

It is worth noting that Brazil does not have official data on the quantity of homeless population, considering that the demographic census does not include homeless residents in the investigation, since the data are collected in fixed residences, thus making it

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impossible the identification the correct quantitative of these individuals which make them invisible [23].

The high prevalence of TB in this population is related to precarious urbanization, sanitary conditions (close contact with a contingent of people and fluctuation in different shelters), social exclusion, and extreme poverty [25]. These individuals daily experience a highly vulnerable environment, which helps develop health problems and infection to different types of diseases, including TB [8]. This population also has high rates of avoidable deaths from all causes compared to the general population, which makes evident the influence of inequalities and social determinants of health in the illness process of these individuals [26].

In addition, this population has specificities that favor the development of health problems such as low schooling, which consequently generates ignorance of primary health care and the health process-disease. Moreover, commonly have difficulties in access to health services, stigma, prejudice, conflicting or nonexistent family ties, lack of life project, among other factors [4, 25].

homeless population presents a deficit in self-care concerning hygiene and eating habits, which contributes to a precarious lifestyle and a high prevalence of complications due to chronic diseases, infectious conditions, and injuries related to violence [27]. Therefore, strategic actions should be implemented for the coverage and supply of health services, social assistance, and effective housing to these individuals so that basic human needs are guaranteed.

When evaluating the spatial determinants and the conformation of the clusters when applying the Getis-Ord Gi* technique, clusters of Hotspot were identified in the East Health macro-region. It is estimated that in Brazil, there is a population of approximately 100.000 homeless and that 75% of this population lives in municipalities with more than 100.000 inhabitants [24].

Access to housing is understood as an important determinant of health, and homelessness is directly related to an increase in morbidity and mortality compared to the sheltered population, and mortality among homeless population is 3 to 11 times higher [28].

In addition, it can be highlighted that mobility among homeless people, loss of follow-up, lack of attendance to follow-up appointments and unstable housing, incarceration, fear of invasive investigations and side effects of TB treatment, transportation and location of health services, lack of flexible hours of care and problems to remember commitments and the correct use of medicines are some barriers that hinder a favorable outcome of TB treatment among homeless population users/psychoactive substances dependents [29].

It is necessary to recognize the magnitude of the public health problem present in large cities among the street population and implement public policies aimed at this heterogeneous group that is in extreme social vulnerability [30,31]. Thus, implementing policies of social support and reintegration of the street population in society is extremely important, and programs aimed at income distribution, such as the *Bolsa Familia* Program.

The Bolsa Family Program aims to provide income to families in poverty and extreme poverty. The aid seeks to overcome the situation of vulnerability and poverty, thus ensuring the right to food and access to education and health [32].

The implementation of the Bolsa Família Program provided an increase in the rate of adherence and cure of patients with TB, highlighting the need to implement policies aimed at social support [33].

Another behavior analyzed in this study was that TB is growing among alcohol, tobacco, and illicit drugs users. This result is extremely important since the higher the consumption of psychoactive substances by homeless population, the worse the prognosis of these individuals are, as well as maintenance, increased incidence, recurrence of new cases of TB and TB-DR. In addition, homeless people who use psychoactive sub-

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stances move through spaces/territories with a high number of individuals, a characteristic that contributes to a greater spread of the disease.

Therefore, the psychoactive substances is considered an aggravating and complicating factor for the containment and eradication of TB in the world. It is noteworthy that the Sustainable Development Goals of the WHO reinforce the importance of implementing prevention and treatment of disorders related to the use of alcohol and other drugs among vulnerable populations [34].

In this sense, investing in public policies, health services targeted at vulnerable populations and skilled professionals can be an effective tool for early diagnosis, correct treatment, decrease in the incidence of TB, and guarantee of access to health services, social support, and a direction for the social reintegration of these individuals who are on the streets.

Moreover, the use of psychoactive substances among vulnerable populations promotes community transmission and TB contamination since these individuals live in an environment of extreme sanitary prevarication and share objects and materials such as pipe and needles to make use of psychoactive substances. This characteristic contributes to the spread and dissemination of latent and active TB in these territories [35].

It was also observed that the worst outcomes in treatment and death are present in vulnerable populations that use or are dependent on any substance. Therefore, the vulnerable population has a high TB infectivity rate and thus makes it a strategic population for actions aimed at eradicating TB in the world. Developing public policies aimed at vulnerable populations is a way to contain the spread of the disease in these territories [30,31,36] and thus achieve the goals established through the end TB strategy.

In order to reduce the infection rate and decrease the new cases of TB or relapse, countries need to develop specific strategies aimed at vulnerable populations, especially among users of alcohol, tobacco, and other drugs, whereas by implementing health actions directed at these individuals, it is possible to ensure early detection and diagnosis of TB and consequently effective treatment [36]. It should be emphasized that countries need to act and invest in research to highlight the territories with the greatest risk for illness and, thus, identify why people get sick in some territorial regions [37].

Ensuring health services that are responsive and targeted to vulnerable populations is of utmost importance and ensuring reception and, consequently, providing a correct sequencing during treatment. However, what is observed in health services is a barrier to access and health care for vulnerable populations, which makes it an invisible population to the public health system, which contributes to the maintenance of TB and other health problems [38].

Strategies that can enhance and provide more comprehensive health care to these populations are the incorporation of health services within vulnerable territories and the implementation of street offices and health care within prisons.

The purpose of street offices is to expand the access of homeless population to health services, to provide comprehensive health care to individuals who are in vulnerable conditions or with fragile family ties [38,39].

The street office has a dynamic of work that provides the active search of people in situation of street in several places of the city, valuing the welcoming and creation of links, in order to supply the needs brought of these individuals, without judgments or social standards, guaranteeing them the right to health advocated in the constitution [40].

It is also relevant to consider the implementation in the country of networks that seek better social protection for vulnerable populations, considering that, when investing in measures that aid equity in health and poverty reduction, a reversal will occur in the context of morbidity and mortality of TB, strategy is emphasized and recommended by the WHO.

Another measure to be adopted is incorporating health policies aimed at reducing the consumption of psychoactive substances within vulnerable territories and developing actions to prevent early consumption among children and adolescents and the conscious consumption of the substance.

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Finally, the study brings significant contributions and joins the global efforts to control TB since it was possible to incorporate statistical methods that identified areas of spatial risk for TB among users dependent on alcohol, tobacco, and illicit drugs.

5. Conclusions

This section is mandatory.

6. Patents

Not applicable

Supplementary Materials: The following supporting information can be downloaded at: www.mdpi.com/xxx/s1, Figure S1: title; Table S1: title; Video S1: title.

Author Contributions: For research articles with several authors, a short paragraph specifying their individual contributions must be provided. The following statements should be used

Conceptualization: ARS, JDA and RAA.; methodology, ARS, JDA, TZB and RAA.; software, ARS and ACVR.; formal analysis, ARS, JDA, TZB, ACVR and RAA.; investigation, ARS.; data curation, ARS, JDA, TZB, ACVR and RAA.; writing—original draft preparation, ARS.; writing—review and editing, ARS, SCP, JTM, MJQG, ECM, FMD and RAA.; supervision, RAA.; project administration, ARS.; All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement: The study was approved by the Research Ethics Committee of the Escola de Enfermagem de Ribeirão Preto da Universidade de São Paulo, under CAAE (Process number: 24963319.1.0000.5393).

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The data presented in this study are available on request from the corresponding author on reasonable request.

Conflicts of Interest: The authors declare no conflict of interest.

Appendix A

The appendix is an optional section that can contain details and data supplemental to the main text—for example, explanations of experimental details that would disrupt the flow of the main text but nonetheless remain crucial to understanding and reproducing the research shown; figures of replicates for experiments of which representative data is shown in the main text can be added here if brief, or as Supplementary data. Mathematical proofs of results not central to the paper can be added as an appendix.

Appendix B

All appendix sections must be cited in the main text. In the appendices, Figures, Tables, etc. should be labeled starting with "A"—e.g., Figure A1, Figure A2, etc.

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