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# Tuberculosis mortality trend in the state of Paraná, Brazil – 1998-2012

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**Abstract** *The objective was to analyze the trend in tuberculosis mortality in Paraná from 1998 to 2012, according to healthcare macro-regional, gender and age. Ecological study of time series data with the system of the Unified System Mortality Information Health (SIM/SUS). Trend analysis of standardized mortality rates was performed by linear regression segmented identifying the points with the change trend. There were 847 deaths of residents in Paraná in the period. The trend was initially declining to state, with subsequent significant increase only for the macro-regional East. Mortality from tuberculosis showed growing trend for the age groups 20-39 years and 40-49 years and for males. The growing trend in tuberculosis mortality was observed from 2010 is a warning to managers honing the service at different levels of health care.*

**Key words** *Tuberculosis, Mortality, Health evaluation, Time series study*

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## Introduction

Tuberculosis remains as the most important cause of morbidity and mortality among infectious diseases worldwide. It accounts for a quarter of preventable deaths in developing countries, with emphasis on adults generally and men aged 45-59 years old[1,2]. It is known as the "neglected calamity" not yet resolved in this century[3]. Neglected diseases are prevalent in the Brazilian context due to social inequality, since the living conditions of a certain population configure a determining factor for tuberculosis[4].

Despite prevention and control measures adopted by health services across the country, the mortality rate of tuberculosis is still high. Control measures do not reach the entire population equitably, especially with regard to funding, which is often insufficient, in addition to little political involvement in this matter[3]. Moreover, deaths from tuberculosis may be related to factors such as HIV/Tb co-infection, advanced age, the male sex, drug resistance, history of noncompliance with treatment, alcoholism, as well as delay to diagnose the disease and start the treatment[4].

The mortality rate of tuberculosis in the world showed a decline of 40% between 1990 and 2010, with highlight to the 70.7% drop in the Americas[3]. It is considered that Brazil has significantly contributed to such reduction, although it still concentrates many of the global cases of the disease. It is believed that the less pronounced decline in the world mortality can be attributed to the existence of pockets of poverty in the African continent and densely populated countries such as China, India and Russia[3].

Brazil currently occupies the 16$^{th}$ position among the 22 countries with more cases of tuberculosis, which the World Health Organization prioritizes because, together, they account for 80% of all cases of the disease in the world[5]. To face this situation, the Brazilian Ministry of Health incorporated into its routine in 2003 the assessment of control strategies and the National Program for Tuberculosis Control in order to ensure free distribution of medicines and supplies and promote preventive and control actions[5].

Despite the magnitude and epidemiological importance of tuberculosis in the Brazilian morbimortality profile, it is possible to observe a lack of studies on the performance of the National Program for Tuberculosis Control[5], especially focusing on states and municipalities. It is also noteworthy that the form of organization of the Brazilian Unified Health System requires this assessment because such information can be used to guide and contribute to decision-making and to the turning of efforts towards areas subject to higher risk and those where the operational situation of the program is beneath the established goals.

Thus, it is appropriate and necessary to assess strategies for tuberculosis control through studies that describe its epidemiological situation. In the face of this, the following question arose: what is the trend of tuberculosis death rates in the state of Paraná? This question allowed defining as objective the analysis of tuberculosis mortality trend in the state of Paraná from 1998 to 2012, by health macro-regions, sex and age group.

## Method

This is an ecological time-series study that analyzes the trend of tuberculosis mortality rate among residents in the state of Paraná. Paraná has 399 municipalities distributed in 22 Health Regions, which are administrative bodies of the State Department of Health; they are grouped into six Health Macro-Regions: Eastern, Campos Gerais, South Central, Western, Northwestern and Northern.

Death records were obtained from the Mortality Information System [*Sistema de Informações de Mortalidade*] (SIM) of the Brazilian Unified Health System [*Sistema Único de Saúde*] (SUS); deaths with underlying cause encoded as A15 to A19, according to the International Classification of Diseases, 10$^{th}$ review[6], were selected. Age group standardization was adopted according to data available on Datasus[7]. For being data available on official databases of free access, the absence of ethical appraisal is justified.

Mortality rates were calculated from the number of deaths of residents in each health macro-region divided by the year population, according to sex and age group. The rates were standardized taking as reference Paraná's standard population in 2010.

The trend analysis, known as Joinpoint[8], was conducted by the Joinpoint Regression software of the National Cancer Institute[9], of free access. It was developed according to the segmented linear regression method, with estimation of inflection points. The software tests if one or more points should be added to the model, by means of the Monte Carlo permutation method. In the final model, each inflection point indicates a change in the trend. Another test was based on the cal-

culation of the line segment slope or Annual Percentage Change (APC), with a 95% confidence interval (CI) (negative values indicate decreasing trend, and positive values, increasing trend). In order to avoid autocorrelation between the terms of the regression equation, this study carried out the transformation of the (X) calendar-year independent variable in the centralized-year variable with the mortality rates considered as dependent variable (Y). A 5% significance level was adopted to test the null hypothesis that APC is zero.

## Results

From 1998 to 2012 there were fluctuations in tuberculosis mortality rates for residents in the state of Paraná and in the Eastern health macro-region. The mortality patterns for this macro-region showed a statistically significant downward trend between 2006 and 2010, and increase as of 2010. Regarding the other macro-regions, only the South Central showed significant drop throughout the period. For the state of Paraná there was a trend of significant decline in mortality between 2005 and 2010; however, though not significant, there is an increase in rates in subsequent years (Table 1).

Regarding the tuberculosis mortality trend by sex, despite the fluctuations and an evident growth for males from 2010, the joinpoint regression analysis showed no significant trend for either sex. Among females a downward trend remained throughout the period studied, with no statistical significance. There was a statistically significant declining trend only for the age group from 40 to 59 years old until 2010, and 60 years or over throughout the period (Table 2).

## Discussion

The significant overall trend found for the state of Paraná was decreasing from 2005 to 2010 and stable after this period, and is partly consistent with the findings of a study conducted in São Paulo, SP[10], which observed an increase in the number of deaths from tuberculosis as of 2005, but found later decrease and an increase forecast as of 2011. In its turn, a study with similar method developed in Santa Catarina pointed a significant reduction of 3.7% in the overall tuberculosis mortality[11].

Thus, the increase in tuberculosis mortality rate in the state of Paraná contradicts other studies that point a decline in these rates[1,4]. In this sense, from 1990 to 2010 tuberculosis mortality dropped by 8.6% worldwide, indicating a global reduction trend[11].

Only in 2010 Paraná registered 2,145 new cases and 125 deaths from the disease, with the fatality rate reaching 9%. This data is alarming as it points to difficulties in controlling the disease on the part of the state[12]. Although few analyzed rates have shown significant growth trend, having occurred only for the Eastern health macro-region between 2010 and 2012, the findings of this study are still worrying in view of the fluctuation/stability shown in the other rates or their increase, though not significant, since the ideal would be them presenting downward trend.

This may be related to the difficulty for health services to organize themselves and incorporate in their activities the responsibility for diagnosis, treatment and disease prevention actions[13]. In this way, it is worth emphasizing that an increase in mortality from tuberculosis, even if not significant, may indicate a mismatch between epidemiological surveillance - which should identify new

**Table 1.** Trends of tuberculosis mortality rates in Paraná's health micro-regions, 1998-2002.

| Region | Trend 1 | | Trend 2 | | Trend 3 | |
|---|---|---|---|---|---|---|
| | Year | APC (IC) | Year | APC (IC) | Year | APC (IC) |
| Eastern | 1998-2006 | -0.8 (-6,.3;5.0) | 2006-2010 | -25.6*(-42.8;-3.4) | 2010-2012 | 73.7*(2.9;193.1) |
| C. Gerais | 1998-2012 | -5.2 (-11.3;1.5) | - | - | - | - |
| South Central | 1998-2012 | -39.2*(57.9;-12.2) | - | - | - | - |
| Western | 1998-2012 | 4.1 (-18,.2;32.7) | - | - | - | - |
| Northeastern | 1998-2000 | -54.7(-83.1;21.8) | 2000-2012 | 3.6 (-2.3;9.8) | - | - |
| Northern | 1998-2012 | -5.1 (-10.7;0.8) | - | - | - | - |
| Paraná | 1998-2005 | -1.3 (-8.1;6.0) | 2005-2010 | -18.4*(-31.1;-3.4) | 2010-2012 | 58.5(-7.1;170.3) |

* APC is significantly different from zero ($p < 0.05$).

**Table 2.** Trends of tuberculosis mortality rates by sex and age group, Paraná, 1998-2012.

| | Trend 1 | | Trend 2 | | Trend 3 | |
|---|---|---|---|---|---|---|
| | **Year** | **APC (IC)** | **Year** | **APC (IC)** | **Year** | **APC (IC)** |
| Sex | | | | | | |
| Male | 1998-2006 | -3.7(-9.4;2.4) | 2006-2010 | -22.4(-41.4;2.8) | 2010-2012 | 67.8(-4.4;194.4) |
| Female | 1998-2012 | -3.0(-7.3;1.4) | - | - | - | - |
| Age Group (years) | | | | | | |
| Younger than 1 | 1998-2012 | -2.8(-44.5;70.4) | - | - | - | - |
| 1 to 19 | 1998-2012 | -3.4(-28.4;30.5) | - | - | - | - |
| 20 to 39 | 1998-2006 | -1.6(-0.8;5.2) | 2006-2009 | -32.4(-63.5;25.4) | 2009-2012 | 22.6(-10.0;66.9) |
| 40 to 59 | 1998-2010 | -10.0*(-14.0;-5.8) | 2010-2012 | 65.5(-23.6;258.7) | - | - |
| 60 or over | 1998-2012 | -5.1*(-9.2;-0.8) | - | - | - | - |

* APC is significantly different from zero ($p < 0.05$).

cases, guide measures for controlling the disease and evaluate the results of health actions - and the assistance provided, especially in primary care, suggesting that the former has low coverage and that the latter has not effected the strategy[14].

Despite advances obtained with the Brazilian Unified Health System, tuberculosis remains as an important public health issue, with cure and noncompliance rates distant from what the World Health Organization recommends[15]. Nevertheless, in spite of the increase in resistance rates found in surveys conducted in the country[11], they remain at levels considered low compared to those of other countries such as India, China and Russia, which account for nearly 60% of cases of multidrug-resistant tuberculosis in the world[16].

A national study that assessed the performance of primary health care[17] characterized tuberculosis as a preventable cause and indicator of the effectiveness of this level of care. Thus, it found that, though obtaining the highest mortality rates in this category, the incidence of new cases dropped from 42.8% to 38.4% between 2001 and 2009, respectively.

Furthermore, being configured as a preventable disease and indicator of the effectiveness of the assistance provided, tuberculosis was included in all national lists of conditions sensitive to primary care and in four of the eight lists used internationaly[18]. In this way, it is considered that cases of hospitalizations and deaths resulting from this disease have an inverse relationship with the quality of access to outpatient services. Consequently, when high, they evidence high population vulnerability, ineffective organization of the health system, as well as flaws in the prevention and early diagnosis of cases[19]. In this sense, studies about tuberculosis are worth highlight, given that it is a disease with diagnosis and treatment available in primary care.

In Paraná, although the number of deaths from tuberculosis is relatively small compared to that of the country[20], there is still a need for the establishment and implementation of new strategies for its control, since Brazil is still one of the 22 countries prioritized by the World Health Organization for concentrating, together, 80% of all cases of tuberculosis in the world[12,21].

A study developed with Rio de Janeiro, RJ, residents revealed that tuberculosis is the main cause of death for approximately 25% of patients reported with the disease two years after the diagnosis, and the main reasons include discontinuation of treatment, which increases the number of deaths and persists as a problem in the country[22]. With regard to the analysis by sex, no statistical significance was found; however, it is noteworthy that the mortality rates found evidence a decline among females and growth among males. This finding contradicts other similar studies which point reduction in mortality for both sexes[3,11,23].

Corroborating the findings of this study, researches[24,25] have been showing that the high prevalence of mortality from tuberculosis for males is commonly related to increased exposure to the bacillus in work activities and greater frequency of risk behaviors. However, there is evidence that women are more susceptible to the progression of the disease, from infection to the active disease, and, probably, there are differences in immune response according to sex[26]. Women neglect the disease and face barriers in the access to health services, indicating a possible bias in

known statistics on the disease in different countries[26].

Though having presented lower rates, it is valid to point out that, despite the disease being appearing among younger men, the female group has been showing greater risk, with a progression rate higher than that of males, resulting in a higher fatality rate among females[25].

Age group is another factor of impact in mortality from tuberculosis. In the ranges analyzed, it was possible to find a significant downward trend only in individuals aged over 40 years old. However, there is an increase in the rates referring to people aged 20-39 years old; among those aged 40-59 years old, after a period of significant decline, there is an increase as of 2010. These findings confirm those of other studies which have pointed high mortality from tuberculosis in adults at the ages of 20-49 years old[27,28], generating economic impact on family and society.

Nevertheless, the high mortality among individuals aged 60 or more, though it shows a downward trend, is worth highlighting, since the higher incidence among the elderly may be due to exposure in the past, with late manifestation of the disease and likely functional impairment related to the aging process[20].

It is worth stressing that noncompliance with the treatment is one of the main factors that lead to death[14], given that it encompasses aspects referring to the individual himself/herself and health services. Individual aspects include failure to perceive the severity of the disease and the benefits of the treatment, which can be changed through interaction with healthcare professionals and satisfaction with the care provided[14].

With respect to aspects concerning health services, the more complex the health care organization, the greater the chance of positive effects on clinical management and its outcomes. In this sense, there is also agreement in that a better Family Health Strategy coverage is linked to fewer cases of death from tuberculosis, as shown in a study conducted in Mato Grosso do Sul[19], in which tuberculosis was the only condition sensitive to primary care in the group of preventable diseases that showed significant correlation with the evolution of the Family Health Strategy.

Thus, some measures still need to be adopted so that the goals set by the World Health Organization are achieved in Brazil[3]. For such a purpose, the National Program for Tuberculosis Control was reorganized in 2004, having as main objective prevention, diagnosis and treatment[1,4]; state and city managers agreed on the need to detect at least 70% of cases of tubercle bacilli, as well as to raise the cure rate to at least 85%[29]. The program also preconizes that actions and guidelines established for tuberculosis control should be decentralized[1].

The decentralization of tuberculosis control actions for primary care aims to strengthen and consolidate the program through the systematic search for detection of cases, accompanied by early diagnosis, treatment and prevention and health education actions[11]. Thus, to achieve the goals, the assistance should be permeated by an active search for the ill and for the implementation of the Directly Observed Treatment Short-Course (DOTS)[13], which, since its implementation in Brazil in 1999 until 2007, contributed to a 32% reduction in mortality[11].

In the face of the relevance of this type of treatment, one of the main lines of research on tuberculosis seeks to check the efficacy of therapeutic interventions and the effectiveness of the DOTS strategy. So this strategy has the impact expected, the Program for Tuberculosis Control needs to be linked to the Family Health Strategy and incorporated into a regionalized network of actions that is complete and decentralized for all municipalities in the state towards improving the diagnosis process and expanding the access to tuberculosis treatment[15].

In this sense, a study developed in Carapicuíba, SP,[29] investigated the compliance with the treatment before and after the implementation of such strategy, finding improvements in compliance and greater likelihood of discharge for cure or complete treatment among patients under the DOTS strategy compared to those under self-administered treatment. This study showed that the DOTS can be successfully performed by basic health units, even with populations with a high load of bacilli, low income and residing in big urban centers[29].

In addition to these factors which are relevant to health services, death from tuberculosis can reveal the individual's great fragility due to his/her low economic, occupational and environmental status, the negative impact of epidemiological changes in the country, or also adverse health conditions such as trouble accessing services[19]. Currently, India is the country that concentrates the largest number of cases of tuberculosis in the world, that is, 21% of all new cases. For being a country with extreme differences, it is clear that socio-economic determinants amplify inequities in health, affecting mainly vulnerable groups[30].

Moreover, it should be noted that the HIV/Tb

co-infection has great influence on deaths, since it is preconized that all patients diagnosed with tuberculosis should undergo HIV testing, which does not happen during most of the services provided. The articulation between the two programs is essential so as to enable better resource management, diagnosis and disease control[13]. In addition, data pointed 4,981 deaths from tuberculosis as the underlying cause in 2004; however, if deaths from tuberculosis as associated cause or due to sequels caused by tuberculosis had been included this figure would raise to 50%[11].

Thus, the findings of this study allow concluding that tuberculosis still stands as one of the main public health problems, emphasizing the need to adopt and implement control strategies. The DOTS strategy proposed by the World Health Organization has helped reduce infections and noncompliance rates; however, it is evident that, in order to achieve the control goals intended, there should be commitment from primary care professionals as well as the restructuration of health systems, with integration of services and decentralized assistance for a better compliance with the treatment, which will consequently contribute to the decline in mortality rates[17].

There is also a need to implement systematic assessments as to the effectiveness of these programs which are carried out in an isolated manner by the health sector. Handling such complex situations requires the organization and integration of all equipment available in the municipality as a means to face the health-disease production process[10].

The study of mortality by trend analysis can be a useful tool to assess an aggravation, as it provides information to support decision-making and helps assess the impact of actions implemented for disease control. The limitations of this study are primarily related to information systems which, despite all progress, still present restrictions, especially when it comes to the quality and the standard way of filling death certificates - which are not adequate-, and the filling and feeding of all cases in the system. Moreover, it is worth pointing out that the cases diagnosed and notified by health services may represent only a portion of the actual number of cases of tuberculosis[3].

## Collaborations

HPM Cecilio, AL Santos, SS Marcon have contributed to the conception and development of the research, analysis and data interpretation, relevant critical review of the intellectual content and approval of the final version to be published. MRDO Latorre, TAF Mathias has contributed to data interpretation, relevant critical review of the intellectual content and approval of the final version to be published. RM Rossi has contributed to data analysis and interpretation and approval of the final version to be published.

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