

## Mortality, TB/HIV co-infection, and treatment dropout: predictors of tuberculosis prognosis in Recife, Pernambuco State, Brazil

Mortalidade, co-infecção por HIV/AIDS e abandono do tratamento como fatores prognósticos para tuberculose em Recife, Pernambuco, Brasil

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### Abstract

*This non-concurrent cohort study aims to identify predictors of tuberculosis mortality in a large population database in Brazil. Tuberculosis, death, and TB/HIV cases were validated respectively from the tuberculosis surveillance (SINAN/TB), mortality (SIM), and SINAN/AIDS databases for a five-year period. Analysis included proportional hazard models with relative risk estimates. Out of 5,451 individuals reported with tuberculosis, 320 (5.9%) died (incidence and mortality rates of 98.6 and 12.2/100 thousand inhabitants, respectively). After adjustment, relative risk of dying from tuberculosis was 9.8 for individuals > 50 years of age; 9.0 for TB/HIV co-infection; 3.0 for mixed TB clinical presentation; and 2.0 for treatment dropout. In the multivariate model, using cases with HIV/AIDS, all adjusted predictors lost significance except mixed clinical presentation (RR 1.9; 1.1-3.1). TB/HIV co-infection is an important predictor of TB mortality. However, among individuals without HIV/AIDS, mortality is still highly associated with older age, mixed clinical forms, and treatment dropout.*

*Tuberculosis; Survivorship; Mortality; Patient Dropouts*

### Introduction

Tuberculosis is an important cause of death worldwide. Estimates indicate 8.8 million new cases of the disease and 1.6 million deaths per year<sup>1,2</sup>. With 6% of all deaths worldwide attributed to TB, the disease is the fifth most common cause of death, next to cardiovascular diseases, respiratory infections, cancer, and diarrheal diseases<sup>3,4</sup>.

Despite advances in knowledge on TB and available technology for its control, socioeconomic inequalities affecting vast sectors of the population, deterioration of the health infrastructure (aggravating problems with access to care), and the interface with the HIV epidemic suggest the need for a specific TB alert. This scenario is particularly severe in the developing countries<sup>5,6,7</sup>.

Brazil occupies 14<sup>th</sup> place among the 23 countries that account for 80% of TB cases in the world. According to estimates, Brazil's incidence rate is 58 cases per 100 thousand inhabitants, with a total of 50 million infected individuals and 111 thousand new cases of the disease and six thousand deaths per year<sup>1</sup>. In Recife, one of the country's ten largest State capitals, TB is one of the most serious public health problems. In addition to the high incidence rate (113.95/100 thousand), Recife also has one of the country's highest tuberculosis mortality rates (9.91/100 thousand)<sup>8</sup>. The Brazilian government thus

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considers the city a priority for implementing TB control measures<sup>8,9</sup>.

This non-concurrent cohort study aims to evaluate the impact of demographic and clinical/epidemiological factors on the survival of TB patients residing in Recife and reported to the official TB surveillance system.

## Population and methods

Tuberculosis cases were identified in the Tuberculosis Reporting Data Base (SINAN/TB) under the Pernambuco State Health Department, which is the official system for mandatory reporting of diseases and health problems implemented in the State in 1993. TB reporting is mandatory nationwide for new cases, relapses, and reentries after treatment dropout<sup>7</sup>.

All patients reported from January 1, 1996, to December 31, 2000, and residing in Recife were selected for inclusion in the study. The information was located, retrieved, confirmed, or corrected in order to identify each individual, thereby eliminating multiple records. Patients with multiple entries due to dropout, hospitalization, or other factors were reorganized to comprise a single entry. Date of initial diagnosis was defined as the first report at which individuals received the TB diagnosis and specific treatment was initiated.

Data on death from tuberculosis and TB/HIV co-infection were confirmed and/or retrieved from databases in the national Mortality Information System (SIM) and SINAN/AIDS, through a systematic search, including previous and subsequent calendar years in relation to the study period (1993 to 2001 for HIV/AIDS and 1996 to 2001 for death from TB or AIDS). Death from TB was only considered when confirmed as primary cause of death in the mortality database, and TB/HIV co-infection when confirmed in the AIDS database. The censoring date for both events in the study was June 31, 2001.

The analysis excluded TB cases with reporting dates that coincided with or postdated death. The study also excluded cases with no information on follow-up and outcome in the SINAN/TB database and that were not found in the mortality database (SIM) or the SINAN/AIDS database after a systematic and exhaustive search, including the entire study period, i.e., until the censoring date.

The response variable was survival time, defined as time in months transpired from the date of initial diagnosis to death or, in the case of individuals who did not die, the last follow-

up recorded by the health service. Individuals who died were considered failures and those who remained alive until the end of the study were considered censored.

The independent variables were: (a) socio-demographic: age, gender, and years of schooling; (b) clinical/epidemiological: TB clinical presentation, i.e., pulmonary, extrapulmonary, and mixed; TB/HIV co-infection; association with AIDS-defining disease; entry into the surveillance system, including new cases, relapses, and treatment dropouts; (c) temporal: calendar year (1996 to 2000); date of diagnosis; date of death from TB; closing date for reporting.

Descriptive analyses used Student's *t*-test and Pearson's chi-square test. The Kaplan-Meier method and log-rank test were used to estimate the probability of survival and compare the survival curves between the various categories in the same variable, respectively<sup>10</sup>.

The independent effects of each covariable were measured using the Cox proportional risk model<sup>11</sup> and the hazard ratio was estimated as relative risk (RR). The importance of each covariable in the model was evaluated with the Wald test<sup>10</sup>, and the hypotheses concerning the estimated parameters were tested according to the likelihood ratio statistic<sup>11,12,13,14</sup>. Risk proportionality and goodness-of-fit were verified in the final models using graphic inspection and Martingale and Deviance residue analyses<sup>11,13</sup>.

In order to verify whether the predictive covariables for TB survival were similar, two models were constructed according to the presence or absence of HIV co-infection. The first model considered all cases of TB and the second those associated with HIV/AIDS. In all the analyses, the significance level for rejecting the null hypothesis was  $p \leq 0.05$ .

To estimate the impact of predictive factors for death from tuberculosis in the population, the proportions of population attributable risk (PAR%) were calculated using the formula by Levin<sup>15</sup> ( $PAR\% = p(RR-1)/p(RR-1)+1$ ) for each variable that presented statistical significance in the final model.

The data were analyzed with Epi Info version 6.0 (Centers for Disease Control and Prevention, Atlanta, USA) and SPSS version 11.5 (SPSS Inc., Chicago, USA).

Access to the data was authorized by the Pernambuco State Health Department and approved by the Research Ethics Committee of the Universidade Federal de Minas Gerais [Federal University in Minas Gerais] (project 120/02), where the study was conducted.

## Results

During the five years studied, 7,399 individuals residing in Recife were identified in the SINAN/TB database: 6,780 (91.6%) new cases, 280 (3.1%) relapses, 351 (4.7%) reentries due to prior treatment dropout, and 10 cases (0.1%) transferred from other municipalities or States. During the same period, 837 individuals (12.2%) died from TB. The mean incidence and mortality rates, respectively, were 98.6 and 12.2 per 100 thousand inhabitants, with a mean case-fatality rate of 12.3%.

Survival analysis excluded the following patients: 441 (6%) reported after death; 28 (0.4%) who presented change of diagnosis; 139 (1.9%) with diagnosis date on or later than the closing of reporting; 38 (0.5%) due to transfers; and 104 (1.4%) for having died of a cause unrelated to TB.

A total of 1,198 (16.2%) lacked any record of the last observation within the study period and were thus considered lost to follow-up. Individuals excluded or lost to follow-up did not show any statistically significant differences from those who remained in the study in relation to age, gender, HIV co-infection, form of entry, or calendar year ( $p \geq 0.05$ ).

The survival study thus included 5,451 (73.7%) individuals whose characteristics are summarized in Table 1. Mean and median ages were 37.2 ( $\pm 18.3$ ) and 36 years. The cohort was mostly male (3,466; 63.9%), and the male/female ratio was 1.7:1. Information on schooling was recorded in 3,466 cases (62.9%), of whom 58.6% had up to three years of schooling; 16.2% had no schooling; and only 3% had 12 or more years of schooling.

As for clinical presentation, the most frequent manifestation was the isolated pulmonary form, with 4,675 of cases (85.8%). Of the 639 patients (11.7%) with the isolated extrapulmonary clinical form and 137 (2.5%) with the combined clinical form, 25 (3.2%) had miliary tuberculosis and 36 (4.6%) had tuberculous meningitis.

A total of 861 patients (15.8%) had undergone HIV serological testing. Of these, 234 (27.2%) were recorded as HIV-positive, of whom 210 (89.7%) presented a diagnosis of AIDS-defining illness.

Death occurred in 320 cases (5.9%) in the cohort. Median survival for the entire cohort was 51.5 months (95%CI: 48.06-55.00), while the probability of surviving for 12, 36, and 50 or more months after TB diagnosis was 93%, 69%, and 37%, respectively.

All the variables were significantly associated with survival except for year of diagnosis, which was not associated, and schooling, which showed borderline association (Table 1).

Lower median survival times were observed in the 40-49-year age bracket and in males (45.4 and 51.5 months, respectively). Survival time was visibly reduced among patients with no schooling (41.6 months); extrapulmonary and mixed clinical presentation (39.6 and 22.2 months, respectively); treatment dropout (45.4 months); HIV+ serology (15.1 months); and AIDS co-morbidity (11.9 months), as shown in the penultimate column in Table 1.

In constructing the models, the variables HIV+ serology and AIDS comorbidity were combined in a single covariable (HIV/AIDS co-infection), due to the overlapping of information for positive and unknown cases, with a 89% concordance between these categories.

Compared to the references, univariate analysis (Table 2) showed that the RR of dying from TB increased significantly with age in a dose-response gradient (from 4.7 to 10.5); male gender (1.6); mixed clinical form (6.2); HIV/AIDS co-infection (10.2); and reentry into the information system after a report of previous treatment dropout (2.6). Higher schooling showed a positive but non-significant association. Entry as relapse and calendar year were also not significantly associated with mortality.

In the final multivariate model, considering the entire group, only the covariables age, gender, clinical presentation, mode of entry into the system, and HIV/AIDS co-infection remained statistically significant (Table 2). HIV/AIDS co-infection was one of the most important predictive factors for mortality in this cohort, accounting for 203 (63.4%) of the 320 deaths. Accumulated mortality for this group of patients was 86.8% (203/234) with an RR of 9.0 (95%CI: 7.0-11.8) as compared to patients without TB/HIV/AIDS co-infection. However, death from TB in patients who reentered the surveillance system after known previous treatment dropout also remained significant (RR = 2.0; 95%CI: 1.5-2.7).

Separate analysis of the models for patient groups with and without TB/HIV/AIDS (Table 3) showed a profound change in the estimators. In the model without HIV/AIDS co-infection, with the exception of male gender, which lost statistical significance, all the factors that previously predicted death remained significant. However, important changes in the magnitude of risks were observed for age, history of treatment dropout, and mixed clinical presentation.

In the model with TB/HIV/AIDS co-infection, mixed clinical presentation was the only factor that remained statistically associated with death, with a relative risk of death of 1.9 (95%CI: 1.1-3.1) when compared with pulmonary pre-

Table 1

Descriptive characteristics of TB patients living in Recife, Pernambuco State, Brazil, reported from 1996 to 2000.

Characteristics	Cases	Deaths		p value *	Median survival time	p value **
		n	%			
Age bracket (years)				< 0.001		
< 20	647	5	0.8			< 0.001
20-29	1,321	51	3.9		51.5	
30-39	1,213	93	7.7		53.6	
40-49	1,016	72	7.1		45.4	
≥ 50	1,247	98	7.9		50.0	
Gender				< 0.001		
Female	1,985	81	4.1		52.1	< 0.001
Male	3,466	239	6.9		51.5	
Schooling (years)				0.063		
≥ 12	102	9	8.8			0.058
8-11	164	8	4.9			
4-7	478	21	4.4		55.2	
1-3	2,010	123	6.1		50.0	
None	554	46	8.3		41.6	
Unknown	122	4	3.3			
Clinical presentation				< 0.001		
Pulmonary	4,691	249	5.3		52.1	< 0.001
Extrapulmonary	639	37	5.8		39.8	
Mixed	116	34	29.3		22.2	
Mode of entry				< 0.001		
New case	4,907	247	5.0		52.1	< 0.001
Relapse	211	15	7.1			
Dropout	333	58	17.4		45.4	
AIDS				< 0.001		
No	5,241	203	3.9		.	< 0.001
Yes	210	117	55.7		11.9	
HIV/AIDS				< 0.001		
No ***	5,217	117	2.2			
Yes	234	203	86.8		15.1	< 0.001
Calendar year				0.352		
1996	1,471	95	6.5		53.6	0.519
1997	1,126	73	6.5		42.3	
1998	1,090	61	5.6			
1999	992	56	5.6		24.9	
2000	772	35	4.5			

\* Comparison of proportions;

\*\* Log-rank test;

\*\*\* Serology results were confirmed in 478 patients and unavailable in 149; in 4,590 patients the test was not ordered.

sentation alone, after adjusting for age, gender, and mode of entry.

Residual analysis of all the multivariate models showed good adequacy and fit for the final models <sup>13,15</sup>.

For the entire cohort, PAR% for previous treatment dropout was 5.7%, independently of

age, gender, clinical form, and TB/HIV/AIDS co-infection (Table 4). However, for the group without TB/HIV/AIDS co-infection, PAR% for dropout increased, meaning that independently of other factors, in patients without HIV/AIDS, if dropout were eliminated, death from TB would be reduced by 11.5%.

Table 2

Cox proportional models (univariate and multivariate \*) for death from TB among 5,451 patients living in Recife, Pernambuco State, Brazil, reported from 1996 to 2000.

Characteristics	Univariate model RR (95%CI)	p value	Adjusted model RR (95%CI)	p value
Age bracket (years)				
< 20	1.00	< 0.001		< 0.001
20-29	4.67 (1.86-11.70)	< 0.001	3.21(1.28-8.08)	0.013
30-39	8.42 (3.42-20.73)	0.001	4.45 (1.79-11.05)	0.001
40-49	8.38 (3.39-20.76)	< 0.001	5.69 (2.29-14. 17)	< 0.001
≥ 50	10.53 (4.29-25.87)	< 0.001	9.76 (3.96-24.01)	< 0.001
Gender				
Female	1.00			
Male	1.58 (1.23-2.04)	< 0.001	1.41 (1.09-1.82)	0.008
Schooling (years)				
≥ 12	1.00	0.064		
8-11	0.76 (0.29-1.97)	0.568		
4-7	0.56 (0.26-1.23)	0.149		
1-3	0.76 (0.38-1.49)	0.417		
None	1.14 (0.56-1.48)	0.726		
Unknown	0.45 (0.14-1.48)	0.189		
Clinical presentation				
Pulmonary	1.00	< 0.001	1.00	< 0.001
Extrapulmonary	1.20 (0.85-1.69)	0.312	0.95 (0.67-1.35)	0.771
Mixed	6.21 (4.33-8.90)	< 0.001	2.98 (2.02-4.40)	< 0.001
Co-infection with HIV/AIDS				
No	1.00		1.00	
Yes	10.21 (8.06-12.93)	< 0.001	9.03 (6.95-11.75)	< 0.001
Mode of entry				
New case	1.00	< 0.001	1.00	< 0.001
Relapse	0.97 (0.57-1.63)	0.897	1.04 (0.61-1.76)	0.900
Dropout	2.60 (1.94-3.48)	< 0.001	2.03 (1.50-2.74)	< 0.001
Calendar year				
1996	1.00	0.521		
1997	1.26 (0.92-1.72)	0.147		
1998	1.12 (0.81-1.56)	0.493		
1999	1.31 (0.93-1.85)	0.122		
2000	1.15 (0.77-1.72)	0.499		

\* In the overall multivariate model (with all the variables), 3,428 cases were analyzed (211 deaths and 3,217 survivors). The model presented here, containing the significant variables from the univariate model, analyzed 5,444 cases (319 deaths and 5,125 survivors).

## Discussion

This study showed high TB incidence and mortality rates in patients residing in a State capital in Northeast Brazil. Age greater than 20 years, male gender, mixed clinical presentation, TB/HIV/AIDS co-infection, and treatment dropout were the significant and independent predictive factors associated with shorter survival time.

Various studies have indicated that the risk of dying from TB increases with the patient's

age. However, mortality from TB in older individuals can be attributed not only to age per se and the presence of co-morbidities, but also to difficulties in accessing diagnosis in this group of patients, thereby delaying the onset of treatment<sup>16</sup>. In our study, in both the univariate and multivariate analysis, the relative risk of dying from TB increased in a dose-response gradient with age, i.e., the older the patient, the greater the risk of dying. Similar results have been reported in other studies<sup>17,18,19</sup>. The correlation

Table 3

Cox proportional model for death from TB among patients with and without HIV/AIDS living in Recife, Pernambuco State, Brazil, reported from 1996 to 2000.

Characteristics	Patients without HIV/AIDS (n = 5,217)		Patients with HIV/AIDS (n = 234)	
	RR (95%CI)	p value	RR (95%CI)	p value
Age bracket (years)				
< 20	1.00		1.00	
20-29	2.50 (0.86-7.27)	0.093	3.15 (0.42-23.55)	0.263
30-39	5.31 (1.90-14.82)	0.001	3.07 (0.41-22.77)	0.272
40-49	5.60 (2.00-15.71)	0.001	4.25 (0.57-31.96)	0.159
≥50	11.88 (4.35-32.49)	< 0.001	3.15 (0.39-25.23)	0.279
Gender				
Female	1.00		1.00	
Male	1.21 (0.89-1.66)	0.225	1.46 (0.92-2.33)	0.113
Clinical presentation				
Pulmonary	1.00		1.00	
Extrapulmonary	0.92 (0.54-1.58)	0.773	0.99 (0.62-1.61)	0.981
Mixed	5.31 (3.00-9.40)	< 0.001	1.87 (1.12-3.13)	0.017
Mode of entry				
New case	1.00		1.00	
Relapse	0.99 (0.56-1.77)	0.983	0.99 (0.24-4.18)	0.990
Dropout	3.16 (2.21-4.51)	< 0.001	0.99 (0.57-1.72)	0.974

between age and TB mortality reinforces the importance of early diagnosis in elderly patients, since treatment efficacy is the same as in younger individuals<sup>20</sup>.

The fact that the majority of deaths were in males (239/320) is also consistent with the literature<sup>21,22</sup>. However, although the relative risk for males was significant in the final adjusted model, it lost significance in the model stratified by TB/HIV/AIDS co-infection. This finding is corroborated by reports of patients with TB and HIV/AIDS in New York (USA)<sup>17</sup>, Tanzania<sup>19</sup>, and Spain<sup>23</sup>, in which the observed effect of male gender on mortality was not significant.

Some studies confirm that persons with isolated pulmonary TB survive longer than those with the extrapulmonary and mixed forms<sup>16,23,24,25</sup>. In our study, patients with other forms combined with the pulmonary presentation showed half the median survival time and a threefold risk of death from TB as compared to cases with the isolated pulmonary form. Of the deaths in patients with mixed forms, 19.7% had HIV co-infection or AIDS. In fact, in the model for the group classified as TB/HIV/AIDS co-infection, the mixed pulmonary/extrapulmonary form was the only factor independently associated with death, while in the group without TB/HIV/AIDS diagnosis, age at diagnosis, mixed pulmonary/extrapulmonary form, and previous

treatment dropout remained significantly associated with risk of death from TB.

The results found here are consistent with the various reports in the literature<sup>25,26,27,28</sup> that the HIV epidemic has changed the prognosis for TB patients, and that HIV has a stronger impact on TB mortality than on incidence of the disease. TB/HIV/AIDS co-infection had a striking effect on risk of death, especially given the magnitude of risk of dying from TB, some 9.0 for patients with TB/HIV/AIDS co-infection as compared to those without. These results were quite similar to those of other authors<sup>17,18</sup>, suggesting the external validity of our study.

Incomplete treatment has been reported as another important risk factor for death from TB<sup>17,19,29,30</sup>. In fact, among the patients who died in this study, 18.2% had a history of previous treatment dropout. In this group of patients, in the absence of TB/HIV/AIDS co-infection, the relative risk of dying was 3.2 times greater than for patients who entered as new cases. However, in the presence of TB/HIV/AIDS co-infection, previous treatment dropout did not remain as a significant variable for risk of death.

It is possible that incomplete treatment (evaluated here by proxy with the variable "treatment dropout") may merely be a marker for other confounding variables, like worse health status, adverse drug effects, or difficult access to health<sup>16</sup>.

Table 4

Population attributable risk (PAR%) and predictive factors for death from TB among patients living in Recife, Pernambuco State, Brazil, reported from 1996 to 2000.

Characteristics	All tuberculosis cases (n = 5,451)				
	Deaths (n = 320)	Survivors (n = 5,131)	Prevalence *	Adjusted RR **	PAR% ***
20-29	51	1,270	0.242	3.2	34.8
30-39	93	1,120	0.223	4.5	43.8
40-49	72	944	0.186	5.7	46.7
≥ 50	98	1,149	0.229	9.8	66.8
Male gender	239	3,227	0.636	1.4	20.3
Mixed clinical presentation #	34	82	0.021	3.0	4.1
Dropout	58	275	0.061	2.0	5.8
HIV/AIDS	117	117	0.043	9.0	25.6

  

Characteristics	Tuberculosis cases with HIV/AIDS (n = 5,217)				
	Deaths (n = 203)	Survivors (n = 5,014)	Prevalence *	Adjusted RR **	PAR% ***
30-39	45	1,076	0.215	5.3	48.0
40-49	42	925	0.185	5.6	46.0
≥ 50	89	1,134	0.234	11.9	71.9
Mixed clinical presentation #	14	68	0.016	5.3	6.3
Dropout	42	266	0.059	3.2	11.5

\* Prevalence of predictor in the population (exposed and unexposed);

\*\* Adjusted relative risk in the final multivariate model;

\*\*\* Population attributable risk %  $\rightarrow p (RR-1)/(p (RR-1) + 1)$ , where p is prevalence of the predictor in the population (deaths + survivors/population) and RR is the relative risk;

# Combined clinical form: pulmonary + extrapulmonary.

In this study, PAR% for treatment dropout in patients without HIV/AIDS was less than that reported by Garcia-Garcia et al.<sup>30</sup>. However, since treatment dropout is the only factor associated with death that can be controlled directly by health services, our results corroborate the findings of other studies<sup>19,31</sup> and strengthen the position that complete treatment increases patient survival. It is important to emphasize the high efficacy of the directly observed treatment strategy (DOTS), even in patients with TB/HIV/AIDS co-infection<sup>30,31</sup>.

Since the database used in this study aims at epidemiological surveillance, the results are limited by the absence of important variables described in the literature<sup>23,24,30</sup>, generating possibilities for residual confounding. Particularly important are those related to TB/HIV/AIDS co-infection, like exposure categories, T-lymphocyte count, and viral load; those related to treatment dropout like social characteristics, alcohol abuse, housing conditions, occupation, illicit drug use, and associated diseases; and those related to health services access.

Other relevant limitations that should be mentioned include the incompleteness of some information, especially on schooling; some decisions made in case classification, mainly for TB/HIV/AIDS co-infection; and the exclusion of cases from the analysis. The loss of some 30% of information on schooling certainly reflects a deficiency in the capacity to evaluate the real significance of this variable, considered lacking, and thus not included in some analyses. Although this variable may admittedly be an important marker for socioeconomic status, and although the lack of this information for a large share of cases limits its interpretation, we chose to emphasize this deficiency in order to encourage discussion on the need to improve the quality of these databases. National studies in Brazil<sup>32</sup> that also used secondary databases similar to this and other events have reported the same problems, although they do not rule out other types of analysis.

In relation to the categorization of the presence or absence of TB/HIV/AIDS co-infection, the decision was based on the TB treatment protocol for health services in Brazil in the absence

of HIV serology. In other words, given the absence of a routine protocol for ordering HIV serology for all patients with a TB diagnosis, added to the difficulties with laboratory confirmation and the fact that ordering HIV serology is based on clinical suspicion, health services consider patients without HIV serology as not presenting TB/HIV co-infection, adopting the standard regimen and treatment schedule prevailing at the time<sup>33</sup>. Although we cannot rule out classification errors, i.e., including patients with HIV/AIDS in our group without co-infection, such errors might lead to underestimation rather than overestimation of our parameters.

As for internal validity, two questions can be discussed pertaining to cases excluded from the analyses. The first involves cases whose closing and outcome information was not found, even after an exhaustive search in the SINAN/TB database for possible reentries, followed by searches in the SINAN/AIDS and SIM databases for other outcomes. The confirmation and retrieval of information from other databases (SIM and AIDS)

allowed improvement of the data, but did not ensure total quality of information.

Other cases died from causes unrelated to TB. In both situations, the excluded cases did not differ significantly from those that remained in the study, in relation to the principal target variables.

Despite the above-mentioned limitations, the study highlights the importance of TB and related death in a city where the disease is highly endemic. It also points to the need for improved data quality, heightened surveillance, and better diagnosis in patients older than 50 years, with a relevant risk of dying. Equally urgent is the need for specific strategies to reduce treatment drop-out.

Since Brazil practices important public policies for free distribution of antiretroviral drugs to all HIV+ patients, more detailed studies are needed to elucidate the real impact of the HIV epidemic on TB mortality, including research on the contribution of ordering HIV serology in patients with TB diagnosis.

## Resumo

*Este estudo de coorte não concorrente objetivou identificar fatores associados ao óbito por tuberculose em pacientes notificados ao sistema de vigilância de tuberculose (SINAN/TB), residentes em Recife, Pernambuco, Brasil, de 1996-2000. Óbito por tuberculose e co-infecção HIV/AIDS foram validados nos Sistemas de Mortalidade (SIM) e SINAN/AIDS. Análise de sobrevida modelos de riscos proporcionais de Cox foram utilizados. Dos 5.451 indivíduos diagnosticados (coeficiente de incidência de 98,6/100 mil habitantes), 320 (5,9%) foram ao óbito por tuberculose (coeficiente de mortalidade de 12,2/100 mil habitantes). O risco relativo ajustado de morrer foi de 9,8 para maiores de 50 anos, 9,0 para indivíduos com co-infecção HIV/AIDS, 3,0 para aqueles com apresentação mista e 2,0 para pacientes que abandonaram o tratamento. Quando se estratificou a população em dois grupos: pacientes com e sem co-infecção HIV/AIDS, os estimadores estudados (faixa etária, modo de entrada e apresentação clínica) mantiveram o poder de associação no grupo sem a co-infecção. Entretanto, na presença da co-infecção, apenas apresentação mista manteve-se associada ao óbito (RR = 1,9). Neste estudo, apesar da relevância do HIV/AIDS, idade acima de cinqüenta anos, apresentação mista e abandono de tratamento foram importantes preditores de óbito em pacientes com tuberculose.*

*Tuberculose; Sobrevida; Mortalidade; Desistência do Paciente*

## Contributors

M. P. Domingos was in charge of elaborating the article (analyses, drafting, and review). W. T. Caiaffa participated actively in the elaboration of the article, from its conception to the final review. E. A. Colosimo contributed with the statistical analyses and discussion.



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