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Tuberculosis Burden and Determinants of Treatment Outcomes According to Age in Brazil: A Nationwide Ecological Study of 896,314 Cases Reported Between 2010 and 2019

Beatriz Barreto-Duarte[1,2,3,4*], Mariana Araújo-Pereira[1,2,5*], Betânia M. F. Nogueira[1,2,6,7], Luciana Sobral[8,9], Moreno M. S. Rodrigues[10], Artur T. L. Queiroz[2,11], Michael S. Rocha[2,6], Vanessa Nascimento[2,6,9], Alexandra B. Souza[12,13], Marcelo Cordeiro-Santos[12,13,14], Afrânio L. Kritski[4,15], Timothy R. Sterling[16], María B. Arriaga[1,2,5*], Bruno B. Andrade[1,2,3,4,5,7,8,9,16*]

[1]Laboratório de Inflamação e Biomarcadores, Instituto Gonçalo Moniz, Fundação Oswaldo Cruz, Salvador, Brazil
[2]Multinational Organization Network Sponsoring Translational and Epidemiological Research (MONSTER) Initiative, Salvador, Brazil
[3]Curso de Medicina, Universidade Salvador (UNIFACS), Laureate Universities, Salvador, Brazil
[4]Programa de Pós-Graduação em Clínica Médica, Universidade Federal do Rio de Janeiro, Rio de Janeiro, Braz
[5]Faculdade de Medicina, Universidade Federal da Bahia, Salvador, Brazil
[6]Instituto Brasileiro para Investigação da Tuberculose, Fundação José Silveira, Salvador, Brazil
[7] Programa de Pós-graduação em Ciências da Saúde, Faculdade de Medicina da Bahia, Universidade Federal da Bahia, Salvador, Bahia, Brazil.
[8] Curso de Medicina, Centro Universitário Faculdade de Tecnologia e Ciências (UniFTC), Salvador, Brazil
[9] Escola Bahiana de Medicina e Saúde Pública (EBMSP), Salvador, Brazil
[10] Laboratório de Análise e Visualização de Dados, Fundação Oswaldo Cruz, Porto Velho, Brazil
[11]Center of Data and Knowledge Integration for Health (CIDACS), Instituto Gonçalo Moniz, Fundação Oswaldo Cruz, Salvador, Brazil
[12]Fundação Medicina Tropical Doutor Heitor Vieira Dourado, Manaus, Brazil
[13]Programa de Pós-Graduação em Medicina Tropical, Universidade do Estado do Amazonas, Manaus, Brazil
[14]Universidade Nilton Lins, Manaus, Brazil
[15]Programa Acadêmico de Tuberculose da Faculdade de Medicina, Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil
[16]Division of Infectious Diseases, Department of Medicine, Vanderbilt University School of Medicine, Nashville, Tennessee, USA.

*Equally contributed to the work.

***Correspondent author:**
Bruno Bezerril Andrade
bruno.andrade@fiocruz.br

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Summary

Background: Approximately 1·4 million people die annually worldwide from tuberculosis. Large epidemiologic studies can identify determinants of unfavorable clinical outcomes according to age, which can guide implementation of public health policies and clinical management to improve outcomes.

Methods: We obtained data from the national tuberculosis case registry: cases reported to the Brazilian National Program (SINAN) between 2010-2019. Clinical and epidemiologic variables were compared between age groups (child:<10 years, young:10-24years, adult:25-64years and elderly:≥65years). Univariate comparisons were performed together with *second-generation p*-values. We applied a backward stepwise multivariable logistic regression model to identify characteristics in each age group associated with unfavorable TB treatment outcomes.

Findings: There were 896,314 tuberculosis cases reported during the period. The tuberculosis incidence was highest among adult males, but the young males presented the highest growth rate between the period. Directly observed therapy (DOT) was associated with protection against unfavorable outcomes in all age groups. The use of alcohol, illicit drugs, and smoking, as well as occurrence of comorbidities were significantly different between age groups. Lack of DOT, previous tuberculosis, race, location of tuberculosis disease, and HIV infection were independent risk factors for unfavorable outcome depending on the age group.

Interpretation: The clinical and epidemiological risk factors for unfavorable tuberculosis treatment outcomes varied according to age in Brazil. DOT was associated with improved outcomes in all age groups. Incidence according to the age and sex identified adults and young males as the groups that need prevention efforts. This supports implementation of DOT in all population to improve tuberculosis outcomes.

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Introduction

Tuberculosis (TB) remains a major public health problem worldwide, accounting for 10 million new cases and 1·4 million deaths in 2019 according to the World Health Organization (WHO) [1]. Brazil is among the 22 high TB burden countries identified by the WHO, which account for 82% of TB cases worldwide [1]. Previous studies have assessed the dynamics of age on TB epidemiology in different settings around the world[2,3] and also in Brazil[4]. Recently, an investigation of a national database identified important associations between adolescence and TB notification over several years in South Africa [5]. Additional studies using nationwide datasets in TB-endemic countries can help delineate strategies focused on age groups to identify interventions that could improve outcomes.

The Brazilian National Plan to Control Tuberculosis (PNCT) was implemented in 1999. Following WHO recommendations, the program set goals of a cure rate >85% and loss to follow-up rate <5%[6]. In addition, the PNCT employed in 2003 implemented the directly observed therapy (DOT), which is a tool proposed by the WHO for supervising and documenting the intake of anti-TB medication [7], to reduce the incidence of TB drug resistance and increase the likelihood of successful treatment outcomes. However, non-research settings, DOT has not been uniformly implemented among all persons treated for TB in Brazil. TB control at the population level requires a better understanding of the clinical and epidemiological characteristics of the people affected by TB. This was facilitated by the Information System for Notifiable Diseases (SINAN) - a health information platform created in 1993 and maintained by the Ministry of Health of Brazil [8]. SINAN collects standardized data, from diagnosis to treatment outcome, to inform and guide health professionals and policymakers about TB epidemiology in Brazil, as well as measuring the impact of the policies implemented [6].

Through the SINAN database, there is valuable information for TB control in Brazil, such as clinical and demographic characteristics, proven risk factors for TB treatment outcomes, and the actual outcomes. Moreover, it is feasible to analyze such characteristics over time, enabling the understanding of TB epidemiology nationwide over several years. In the present study, SINAN data from a 10-year period (2010-2019) were analyzed to assess temporal changes in incidence, TB clinical manifestations, and clinical outcomes, in individuals stratified by age group and biological sex.

Methods

The materials and methods used in this article are described in detail in the appendix (pp 2–3).

Results

Population characteristics over time

Overall, there were 896,314 TB cases reported in Brazil between 2010-2019. Most TB patients were male (66·9-70%) and the age group most affected was 25-64 years (70·9-75·93%). Most of the patients self-reported their race as *pardo* (41·2-49·1%) and 44·1-56·1% were literate. The percentage of patients co-infected with HIV declined over time (χ2trend p<0·001), being significantly lower in 2019. Over time, the frequency of patients who reported alcohol consumption, of those diagnosed with DM, and with smear-positive TB remained similar (Table 1). The proportion of *Mycobacterium tuberculosis* (Mtb) positive cultures increased over time (13·1-22·1, χ2trend p=0·03) while abnormal findings on chest x-rays became less frequent (χ2trend p=0·01) (Table 1). The incidence of TB remained stable over time in men (MK-trend p=0·808) and women (MK-trend p=0·709) (Figure 1A). However, within each sex, changes in TB incidence according to age group differed over the study period (Figure 1B). The incidence in adult (MK-trend p=0·12), elderly (MK-trend p=0·121), young (MK-trend p=0·751) and child females (MK-trend p=0·779) remained stable. In young men, TB incidence increased significantly over the study period (MK-trend p=0·0007), while the incidence in elderly (MK-trend p=0·004) and adult men (MK-trend p=0·004) decreased. The TB incidence in male children did not change significantly (Figure 1B).

In all the years evaluated, the proportion of cases that were new exceeded 80% (80-82·8%), while the proportion treated with DOT decreased over time (χ2trend p<0·001), even when we did not take 2019 into account (whose patients were still being treated, χ2trend p=0·015) (Table 1). The most frequent form of TB was pulmonary (PTB) (82·9-84·6%), followed by extrapulmonary TB (EPTB) (12·3-13·5%) and, finally, combined PTB-EPTB disease (2·78-3·54%). The most frequent comorbidity in all years was hypertension (9-10·5%), followed by DM (5·85-7·92%). Between 2010 and 2018 the cure rate of patients undergoing TB treatment was over 60% (63·3-68·7%), while the death rate ranged between 7·61 and 7·27%. Many patients diagnosed in 2019 were likely still in treatment when data were collected, and therefore there were missing values for this variable. Of note, we found a large number of missing and poorly filled variables in the data.

Analysis by age group

Approximately 70% (n=632,211) of TB diagnoses in Brazil during the study period were made in people 25-64 years old (Table 2). This was the age group that had the highest proportion of people reporting at least one previous episode of TB (20·5%, χ 2 trend p<0·008) among the four age groups evaluated in this study, as well as a higher proportion of persons living with HIV (PLWH)(13·9%, χ2trend p<0·003), alcohol consumption (20·7%, χ2trend p<0·001), and smoking (13·9%, χ2trend p<0·001) (Figure 2A). As expected, the frequency of literate people was significantly different between subgroups, given that the first subgroup consisted of children mainly of preschool age (χ2trend p<0·008)(Table 2). Children also had the lowest percentage of PTB (68·3%, χ2trend p<0·004) and the highest proportion of EPTB among the age groups of the study (27·3%) (appendix p 5). Consistent with this result, children also had a higher percentage of chest X-rays considered clinically normal (14·8%, χ2trend p=0·012), in addition to a higher frequency of negative sputum smears (19·1%, χ2trend p<0·001), negative TB culture (6·87%, χ2trend p<0·001) and lower detection of DM (0·31%, χ2trend p<0·001, Figure 2B). Children also had a higher proportion of cure after treatment (69·22%, χ2trend p<0·001, Figure 2C). Young people more frequently reported illicit drug use (11%, χ2trend p<0·001, Figure 2A), while elderly individuals were more likely diagnosed with DM (16·7%, χ2trend

p <0·001), hypertension (65·6%, χ2trend p<0·001) and also had a higher mortality rate (18·6%, χ2trend p<0·001) (Figure 2B and 2C).

Anti-TB treatment outcomes over time

Over time, the proportion of treatment outcomes did not differ substantially (Table 1), but there was some variability according to age group (Figure 2C, χ2trend p<0·001). Younger patients had a higher proportion of cure. Among unfavorable outcomes (non-cure), loss to follow-up was more frequent in young and adults, while death was more frequent in the elderly. (Table 2, Figure 2C). These outcomes were grouped as favorable and unfavorable (Table 3, appendix p6). Except for children, the other groups of patients with non-cure had a higher percentage of HIV co-infection (Figure 2D). The most affected group was adults (p=0·013, pδ=0), followed by young (p=0·05, pδ=0) and elderly people (p=0·006, pδ=0) (Figure 2D). Adults and young people with an unfavorable outcome also had higher frequencies of prior TB cases (Figure 2E), both with p=0·007 and pδ=0. In all age groups, the use of DOT was more frequent in patients with a favorable outcome (Figure 2F).

TB in Children

Children diagnosed with TB between the years 2010 and 2019 maintained a similiar proportion of sex distribution over the years (Table1), as well as the incidence per 100 thousand inhabitants, did not change significantly (Figure 1B). As in other age groups, the most common form of TB in children was PTB, but the frequency of EPTB was relatively high, representing 27·3% of cases (appendix p 5). Children also had a low smear-positive rate (35·8%) being diagnosed by this method (appendix p 5). A binomial logistic regression analysis was performed to test independent associations between the parameters analyzed and treatment outcomes in children (Figure 3). We found that the unfavorable outcomes were increased in patients with prior TB (adjusted odds ratio [aOR]: 4·83, 95% confidence interval [CI]: 2·17-10·76, p<0·001), in those who did not undergo DOT (aOR: 3·38, 95% CI: 1·88-6·08, p<0·001) and in those who presented with simultaneously PTB-EPTB(aOR: 3·45, 95% CI: 1·3-9·14, p=0·013).

TB in the Young

Young patients diagnosed with TB between 2010 and 2019 showed a significant change (χ2trend p-value=0·048) in the distribution by sex over the years (Table 1 and Figure 1B). This change was characterized by a significant increase in TB incidence in men over the study period (MK-trend p=0·0007), while the TB incidence in women remained relatively stable (MK-trend p=0·751) (Figure 1B). The most common (86·4%) form of TB in young patients was PTB, (appendix p 5) and a high positive smear rate was observed (76·9%, appendix p 5). Binomial logistic regression analysis showed results similar those in children, with prior TB (aOR: 3·17, 95%CI: 2·90-3·47, p<0·001) and no DOT indication (aOR:2·96, 95% CI: 2·76-3·17, p<0·001) independently associated with unfavorable treatment outcome (Figure 4). Additional factors associated with unfavorable outcomes were male(aOR: 1·18, 95%CI:1·10-1·27, p<0·001), illiteracy (aOR: 1·49, 95%CI:1·31-1·69, p<0·001), HIV infection (aOR: 2·69, 95%CI: 2·35-3·08, p<0·001), illicit drug use (aOR: 1·99, 95%CI:1·82-2·17, p<0·001), smoking (aOR: 1·50, 95% CI: 1·36-1·65, p<0·001), and kidney disease (aOR: 9·89, 95%CI: 1·66-59·11, p=0·012).

TB in Adults

Adults diagnosed with TB showed a similar proportion of men and women between 2010 to 2019 (Table 1), but in terms of incidence, there was a significant decrease only in male sex (women MK-trend p=0·12; men MK-trend p=0·004) during the 10-year study period (Figure 1B). Similar to the rest of the population, the most common type of TB was pulmonary (86·5%, appendix p 5). In adults, the proportion of positive sputum was slightly lower than that found in young people, corresponding to 70·5% of the TB adult population (appendix p 5). The binomial logistic regression analysis showed

similar results to children and young patients, with prior TB (aOR: 2·35, 95% CI: 2·26-2·44, p<0·001) and no DOT (aOR: 2·29, 95% CI: 2·60-2·79, p<0·001) independently associated with unfavorable outcome (Figure 5). As seen among children, the presence of both PTB-EPTB was associated with unfavorable outcomes (aOR: 1·17, 95%CI: 1·07-1·28, p<0·001) and as in young people, the following factors were also associated with unfavorable outcomes: HIV infection (aOR: 2·42, 95%CI: 2·31-2·53, p<0·001), illicit drug use (aOR: 1·94, 95%CI: 1·86-2·03, p<0·001) smoking (aOR: 1·19, 95%CI: 1·14-1·24, p<0·001), and kidney disease (aOR: 3·11, 95%CI: 1·37-7·07, p=0·007). Being male (aOR: 1·08, 95%CI: 1·04-1·13, p<0·001), white (aOR: 0·64, 95%CI: 0·53-0·77, p<0·001) black (aOR:0·79, 95%CI: 0·64-0·97, p=0·027), Asian (aOR: 0·62, 95%CI: 0·46-0·84, p=0·002), *pardo* (aOR : 0·69, 95%CI: 0·56-0·85, p=0·001), alcohol consumption (aOR: 1·41, 95%CI: 1·36-1·47, p<0·001), illiteracy (aOR: 1·18, 95%CI: 1·13-1·24, p<0·001), abnormal chest x-ray (aOR:1·15, 95%CI: 1·05-1·15 ,p=0·002), cancer (aOR: 1·33, 95%CI: 1·09-1·64, p=0·006) or COPD (aOR: 1·78, 95%CI: 1·05-3·02, p=0·032) were also significantly associated in this subpopulation.

TB in Elderly

The changes concerning biological sex affected by TB in the elderly population between the years 2010 and 2019 showed a pattern similar to that found in the adult population, with little change in frequencies over the years (Table 1) but showed a significant decrease only in male sex with regard to TB incidence per 100 thousand population (women MK-trend p=0·121; men MK-trend p=0·004, Figure 1B). The frequency of PTB in this population was very close to that found in young people and adults (84·4%, appendix p 5), but the proportion with smear-positive disease was considerably lower, at 62% (appendix p 5). Unlike other sub-populations, ethnicity was not associated with unfavorable outcome in elderly (Figure 6). However, factors such as prior TB (aOR: 1·60, 95%CI: 1·38-1·85, p<0·001), HIV infection (aOR: 2·69, 95%CI: 1·99-3·64, p<0·001), alcohol consumption (aOR: 1·22, 95%CI: 1·04-1·44, p=0·015), illicit drugs use (aOR: 2·01, 95%CI:1·31-3·08, p<0·001) and smoking (aOR: 1·57, 95%CI: 1·38-1·79, p<0·001), in addition to cancer (aOR: 1·69, 95%CI: 1·69-2·47, p=0·007), COPD (aOR: 1·98, 95%CI: 1·28-3·05, p=0·002), other comorbidities (aOR: 1·72, 95%CI: 1·34-2·19, p<0·001) and no DOT (aOR:1·80, 95%CI:1·62-2·00, p<0·001) were associated with unfavorable outcome.

Discussion

In the present study, we investigated the epidemiologic characteristics of TB in the Brazilian population between 2010 and 2019 through data from SINAN. We assessed favorable and unfavorable outcomes as well as the factors associated with each. We focused on identifying the specific risk factors for unfavorable outcomes in each age group, aiming to provide more detailed information for targeted interventions in each group. Our results highlight the importance of DOT for success of TB treatment and encourages the amplification of this strategy in the country, as has been recommend by WHO since 1993. DOT was associated with a considerable increase in favorable outcomes in all studied age groups.

We evaluated the population characteristics of TB cases over a 10-year period. The TB incidence rate in Brazil remained high, and of the cases reported between 2010-2019 most were male (2:1), adults, and self-reported as *pardo*. This profile is similar to that observed in previous years in Brazil [9]. The decrease in the incidence reported between the years 2011-2016 suggests that there was a positive impact of the expansion of public policies leading to an economic incentive, since patients who received cash transfer from governmental programs were about 7% more likely to have a favorable TB treatment outcome [10]. In addition, the increase in incidence recorded between the years 2017-2018 corresponds to the end of the implementation of GeneXpert, resulting in a greater use of this as a TB diagnosis strategy, which was between 2013-2017, thus being an effective strategy for the optimizing diagnosis even when sputum smear is negative.

As also found in previous years, substance use (alcohol, tobacco, and illicit drugs) was commonly reported in the studied population, but there was a significant increase throughout the years. The increase in the prevalence of tobacco smoking in this population is a surprising finding, as it is in the opposite direction of the general population in Brazil [11]. Conversely, illicit drug use seemed to follow the national trend of increasing over the years. Although there is no information about which specific drugs were responsible for our findings, national surveys have demonstrated an increase in the use of marijuana and cocaine in the Brazilian population in the past decade. The use of these drugs is particularly prevalent and growing in young males, which is compatible with the findings of the present study [12-14]. This is an important finding in the young population, particularly since we also found that substance use was significantly associated with unfavorable TB treatment outcomes. Moreover, previous studies have shown that the use of these substances are also risk factors for developing TB [11,15,16].

Another interesting finding was that the prevalence of DM in our population was similar to the general population.[17] Although there has been an increase in DM prevalence in Brazil in recent years, the increase was not statistically significant in our study population.[18,19] One of the reasons for the relatively low prevalence of DM in our study could be the fact that many cases of DM reported in SINAN are self-reported. A systematic review of DM prevalence in Brazil has shown that studies that used complex diagnoses (self-reported and laboratory investigation) of DM have found a much higher prevalence than studies that relied solely on self-report. Of note, Brazilian TB treatment guidelines suggest but do not mandate DM testing in TB patients (as with HIV testing, following WHO recommendation) [6]. Emphasis on the importance of detecting DM is important to reduce the underdiagnosis of DM.

The proportion of TB cases with positive cultures increased over time. This may be due to greater access to the test and to technical improvements. As an example, a study performed in a state reference laboratory found an increase of 61·5% in the positive results for Mtb after the implementation of a semi-automated procedure[20]. It is possible that health professionals may be more aware of the

importance of performing cultures for all TB cases. Another hypothesis pertains to the recommendation to perform universal culture and DST on all presumed TB cases, made by WHO and followed by the Brazilian MoH after 2015. It is worth noting that, despite the improvement, the access to Mtb culture in Brazil is still far from ideal. In 2019, only 24% of patients with new cases of TB had cultures performed, [21] which likely means that many patients treated for TB did not have TB. As expected, our analysis found that the number of positive cultures in children was low compared to the other age groups, which is likely due to the difficulty in collecting sputum [22], and that children often have paucibacillary disease, with a higher percentage of nodular lesions and fewer cavitary lung lesions. Another important observation was that children had a higher frequency of EPTB and a higher frequency of both PTB and EPTB, possibly due to immunological immaturity, which can contribute to the hematogenous spread of the disease in children.

TB is one of the most common opportunistic infections in persons living with HIV (PLWH) and the main cause of death in this population [23] . The prevalence of HIV/TB co-infection has declined between 2010 and 2019 worldwide, with rates of co-infection decreasing from 1·7 million to about 900 thousand people [1]. In Brazil, the Ministry of Health (MoH) has reported an increase in HIV diagnosis, but a reduction in the number of AIDS cases and deaths related to HIV. Our study also found a significant reduction in the cases of HIV/TB co-infection, but HIV infection was significantly associated with a greater number of unfavorable outcomes in all age groups, except for children.

The decline of HIV/TB follows the reduction in AIDS cases in Brazil, which is a reflection of the expansion in HIV diagnosis, as well as access to treatment. Since 2013, ART has been offered to all PLWH, regardless of CD4 count [24].In 2017, Brazil began providing dolutegravir (DTG), a very effective antiretroviral with fewer side effects, as part of the first line scheme. As a result, in 2018, 86% of PLWH knew their status, 67% were on ART and 60% were virally suppressed [24]. The reduction in HIV/TB cases and the higher proportion of people on ART are important factors explaining the decrease in TB mortality rate noted in our analysis and reinforces the essential role of HIV care policies in the control of TB.

Interestingly there was no difference in treatment outcomes among the age groups, but there were risk factors for unfavorable outcomes specific for each age group; knowing them is essential to guide public health interventions[4]. For example, it was noted in our analysis that, in disagreement with all the other curves evaluated by age that showed a reduction or stabilization, the number of young men with TB significantly increased over recent years. This subpopulation has a social risk behavior associated with a higher prevalence of illicit drug use, and once diagnosed with TB, young people have difficulty staying in care. Thus, the young age group is an important target for public health measures and knowing detailed information about them is key.

Finally, we have evaluated patient characteristics according to treatment outcomes. Along the years studied there was an increase in unfavorable outcomes, mainly caused by higher rates of treatment failure. After adjustment for confounders alcohol consumption, illicit drug use, tobacco smoking, HIV infection, kidney disease, prior TB and having PTB-EPTB were associated with unfavorable outcomes. First, our results highlight the already known strong connection of TB and social factors, such as race and substance use [25,26]. It is not within the scope of this work to detail the reasons why these characteristics affect TB outcome, but factors such as adherence to therapy, access to care and time to diagnosis may be related and need to be further investigated. Comorbidities like HIV [27] and kidney disease have previously been shown to be associated with worse outcomes [28,29] . Surprisingly, DM was not found to affect treatment outcomes, and our hypothesis for this was discussed earlier. Having PTB-EPTB and previous episodes have previously been shown to be associated with worse outcomes [30].

The first may be due to the greater difficulty of treatment [30] as well as disease severity, while the second could be due to patient non-adherence, or an increased risk of drug resistance in TB relapse cases.

This study had some limitations. It is unclear whether reporting of information was uniform throughout the country. There was a high level of under-reporting for several variables in the questionnaire. In addition, when assessing patient outcomes, 2019 was incomplete since some patients were still in follow-up. It is important to know that, with exception of name, ethnicity, age, HIV-infection, and more "clinical" variables, other fields such as consumption habits and literacy presented a considerable number of missing data.

With the above limitations noted, a study of this magnitude is extremely important to provide a national view of TB in Brazil over the past decade. This allowed us to investigate not only how public policies applied during that time period influenced the rates and treatment outcomes of TB patients in the country, but also to identify interventions that might improve TB treatment outcomes. Increased implementation of DOT in Brazil across all age groups would likely improve TB treatment outcomes in the country.

Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Author Contributions

BB-D, MA-P, MA, LS, MR, VN, AS and BA contributed to conception and design of the study. BB-D, MA-P, MA, MR, AQ, TS, and BA performed the data curation. BB-D, MA-P, and MA, processed and analyzed the data, and worked on data visualization. BB-D, MA-P, MA, BN, TS and BA wrote the first draft of the manuscript. MC-S and AK revised and contributed to the structuring of the article. TS and BA supervised the research. All authors contributed to manuscript revision, read, and approved the submitted version of the manuscript.

Data sharing

This modelling study used published or publicly available data. The data used and the sources are described in this Article and the appendix. No primary data were collected for this study.

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Research in context

Evidence before this study

We searched PubMed in 2020, for studies comparing the age and the treatment outcome in notified TB cases in Brazilian population using the terms “Tuberculosis”, “age”, “treatment”, AND “Brazil”. We did not find any studies reporting the TB burden and determinants of treatment outcomes according to age in Brazil.

Added value of this study

To our knowledge, this is the first ecological study with TB cases notified in Brazilian population stratifying patients according to the age and treatment outcome. Also, the study count with 896,314 cases notified by the Brazilian National tuberculosis program, between 2010 and 2019, through the Information System for Notifiable Diseases. Providing an expanded view of the clinical and epidemiological factors that contribute to unfavorable outcomes in tuberculosis in the Brazilian population. Also, the findings recognized the use of the directly observed therapy (DOT) as an important approach to improve treatment outcomes, and a strategy to be encouraged and expanded to combat TB in Brazil. In addition, the stratified analysis by age group allows recognizing where to intervene at each age for promoting better outcomes and what are the risk and protection factors of each group for unfavorable outcomes.

Implications of all the available evidence

After the analysis of the cases reported between 2010 and 2019, we assessed the impact of public health measures carried out over the last decade. Furthermore, it was possible to identify the effectiveness and importance of using the DOT strategy, showing the association with favorable outcomes in the treatment of tuberculosis. In addition, we found that the population of young men with active tuberculosis in Brazil has shown the highest growth in the last 10 years, being a possible target population for public health measures.

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Table 1. Population characteristics by year.

Characteristics	2010 N=87171	2011 N=89735	2012 N=88229	2013 N=88339	2014 N=86967	2015 N=87105	2016 N=87820	2017 N=82303	2018 N=96292	2019 N=92353	X^2 trend p-value
Female. n. (%)	28867 (33·1)	29407 (32·8)	28734 (32·6)	28788 (32·6)	27824 (32·0)	27109 (31·1)	27202 (31·0)	27734 (30·0)	29195 (30·3)	27909 (30·2)	0·46
Age group. n. (%)											0·827
Child	1594 (1·82)	1641 (1·83)	1572 (1·78)	1618 (1·85)	1373 (1·57)	1324 (1·52)	1461 (1·68)	1558 (1·78)	1755 (2·01)	1770 (2·03)	
Young	14894 (17·08)	15454 (17·22)	15391 (17·4)	15195 (17·20)	14871 (17·06)	15442 (17·71)	15822 (18·15)	17127 (19·64)	18838 (21·61)	19555 (22·43)	
Adult	62576 (71·79)	64279 (71·63)	63196 (71·63)	63135 (71·47)	62522 (71·72)	61884 (70·99)	61841 (70·9)	64296 (73·76)	66190 (75·93)	62292 (71·45)	
Elderly	7766 (8·9)	8062 (8·98)	7752 (8·78)	8005 (9·06)	7818 (8·97)	8114 (9·3)	8309 (9·53)	8948 (10·3)	9099 (10·4)	8239 (9·45)	
Ethnicity. n. (%)											0·108
Asian	755 (0·87)	729 (0·81)	729 (0·83)	681 (0·77)	624 (0·72)	592 (0·68)	580 (0·66)	715 (0·77)	729 (0·76)	698 (0·76)	
Black	11681 (13·4)	12169 (13·6)	11985 (13·6)	11407 (12·9)	11345 (13·0)	11041 (12·7)	11182 (12·7)	11552 (12·5)	12364 (12·8)	11922 (12·9)	
Indigenous	889 (1·02)	1009 (1·12)	898 (1·02)	958 (1·08)	893 (1·03)	1017 (1·17)	989 (1·13)	930 (1·01)	951 (0·99)	930 (1·01)	
Pardo	35898 (41·2)	38310 (42·7)	38575 (43·7)	39433 (44·6)	39221 (45·1)	40155 (46·1)	41137 (46·8)	44548 (48·3)	47118 (48·9)	45354 (49·1)	
White	29960 (34·4)	30438 (33·9)	29616 (33·6)	28866 (32·7)	27792 (32·0)	27346 (31·4)	26887 (30·6)	27583 (29·9)	28387 (29·5)	26243 (28·4)	
Literate. n. (%)	38459 (44·1)	49055 (54·7)	48724 (55·2)	48702 (55·1)	47978 (55·2)	48241 (55·4)	48781 (55·5)	51194 (55·5)	54922 (57·0)	51851 (56·1)	0·16
HIV infection. n. (%)	9659 (11·1)	10080 (11·2)	10089 (11·4)	10174 (11·5)	10383 (11·9)	10097 (11·6)	9736 (11·1)	10119 (11·0)	9970 (10·4)	9124 (9·88)	**<0·001**
ART. n. (%)	23 (0·24)	21 (0·24)	32 (0·32)	128 (1·26)	953 (9·18)	2102 (20·81)	3292 (33·81)	3967 (39·2)	4020 (40·32)	3211 (35·19)	**<0·001**
Alcohol consumption. n.(%)	12851 (14·7)	13853 (15·4)	13953 (15·8)	14097 (16·0)	14176 (16·3)	15174 (17·4)	15568 (17·7)	16858 (18·3)	18227 (18·9)	17015 (18·4)	0·958
Illicit drug use. n. (%)	334 (0·38)	2098 (2·34)	2687 (3·05)	3269 (3·70)	5579 (6·42)	10342 (11·9)	11423 (13·0)	13467 (14·6)	15165 (15·7)	14522 (15·7)	**<0·001**
Smoking habits. n. (%)	106 (0·12)	240 (0·27)	1457 (1·65)	2096 (2·37)	5597 (6·44)	15826 (18·2)	18826 (21·4)	21328 (23·1)	23560 (24·5)	22490 (24·4)	**<0·001**
Diabetes. n. (%)	5101 (5·85)	5593 (6·23)	5727 (6·49)	5922 (6·70)	5707 (6·56)	6117 (7·02)	6385 (7·27)	6785 (7·35)	7356 (7·64)	7318 (7·92)	0·447
Smear positive. n. (%)	47715 (54·9)	48957 (56·5)	47961 (56·2)	47134 (53·4)	46739 (53·8)	45971 (53·9)	45501 (53·8)	45290 (51·1)	46153 (50·0)	42985 (48·8)	0·169
Culture positive. n. (%)	11387 (13·1)	12321 (13·7)	12968 (14·7)	13859 (15·7)	14972 (17·2)	18020 (20·7)	18358 (20·9)	20367 (22·1)	21267 (22·1)	15656 (17·0)	**0·03**
Abnormal X-ray . n. (%)	69168 (79·3)	71150 (79·3)	68990 (78·2)	68053 (77·0)	65748 (75·6)	63258 (72·6)	63371 (72·2)	64885 (70·3)	67911 (70·5)	64515 (69·9)	**0·01**
TB Status. n. (%)											0·399
New case	72151 (82·8)	74144 (82·6)	72552 (82·2)	72476 (82·0)	70951 (81·6)	70300 (80·7)	70631 (80·4)	73970 (80·1)	77091 (80·1)	73906 (80·0)	
Prior TB	14687 (16·8)	15330 (17·1)	15354 (17·4)	15550 (17·6)	15729 (18·1)	16518 (19·0)	16874 (19·2)	17996 (19·5)	18874 (19·6)	18004 (19·5)	
Treatment. n. (%)											**<0·001[a] 0·015[b]**
Received DOT	36870 (42·3)	40673 (45·3)	41717 (47·3)	40771 (46·2)	37291 (42·9)	29423 (33·8)	30736 (35·0)	32899 (35·6)	34594 (35·9)	22364 (24·2)	

No received DOT	38266 (43·9)	37247 (41·5)	34682 (39·3)	38073 (43·1)	35459 (40·8)	30986 (35·6)	32387 (36·9)	33580 (36·4)	33868 (35·2)	26953 (29·2)	
Type of TB. n. (%)											0·684
EPTB	11580 (13·3)	12058 (13·4)	11906 (13·5)	11893 (13·5)	11172 (12·8)	10747 (12·3)	11096 (12·6)	11477 (12·4)	12177 (12·6)	11804 (12·8)	
PTB	72567 (83·2)	74650 (83·2)	73181 (82·9)	73431 (83·1)	72871 (83·8)	73549 (84·4)	74023 (84·3)	78103 (84·6)	81120 (84·2)	77914 (84·4)	
PTB and EPTB	2996 (3·44)	3005 (3·35)	3123 (3·54)	2889 (3·27)	2854 (3·28)	2764 (3·17)	2665 (3·03)	2674 (2·90)	2958 (3·07)	2568 (2·78)	
Comorbidity. n. (%)											0·56
Cancer	805 (0·92)	802 (0·89)	877 (0·99)	758 (0·86)	744 (0·86)	755 (0·87)	787 (0·90)	770 (0·83)	851 (0·88)	770 (0·83)	
COPD	161 (0·18)	165 (0·18)	197 (0·22)	109 (0·12)	109 (0·13)	112 (0·13)	117 (0·13)	125 (0·14)	153 (0·16)	143 (0·15)	
Hypertension	7885 (9·05)	8301 (9·25)	8091 (9·17)	8576 (9·71)	8573 (9·86)	8796 (10·1)	9030 (10·3)	9706 (10·5)	9867 (10·2)	9269 (10·0)	
Renal disease	78 (0·09)	80 (0·09)	77 (0·09)	69 (0·08)	80 (0·09)	59 (0·07)	73 (0·08)	74 (0·08)	60 (0·06)	62 (0·07)	
Others	11850 (13·6)	12640 (14·1)	12529 (14·2)	11944 (13·5)	11710 (13·5)	12359 (14·2)	12543 (14·3)	13621 (14·8)	13844 (14·4)	14201 (15·4)	
No condition	66390 (76·2)	67745 (75·5)	66451 (75·3)	66878 (75·7)	65750 (75·6)	65017 (74·6)	65270 (74·3)	68007 (73·7)	71517 (74·3)	67904 (73·5)	
Outcome description. n. (%)											**<0·001**[a] 0·366[b]
Cure	59870 (68·7)	62367 (69·5)	59817 (67·8)	60694 (68·7)	59521 (68·4)	57977 (66·6)	59388 (67·6)	61493 (66·6)	60981 (63·3)	18516 (20·0)	
Death	6635 (7·61)	6686 (7·45)	6560 (7·44)	6702 (7·59)	6833 (7·86)	7019 (8·06)	6881 (7·84)	7152 (7·75)	7003 (7·27)	4917 (5·32)	
Failure	668 (0·77)	681 (0·76)	694 (0·79)	735 (0·83)	1070 (1·23)	1473 (1·69)	1480 (1·69)	1587 (1·72)	1683 (1·75)	1120 (1·21)	
Loss follow up	10643 (12·2)	10683 (11·9)	11017 (12·5)	11653 (13·2)	11395 (13·1)	10731 (12·3)	10991 (12·5)	11644 (12·6)	12021 (12·5)	4841 (5·24)	
Relapse	1860 (2·13)	1992 (2·22)	2116 (2·40)	2193 (2·48)	1755 (2·02)	1668 (1·91)	1872 (2·13)	2063 (2·24)	2075 (2·15)	1361 (1·47)	
Transferred out	5804 (6·66)	5954 (6·64)	5932 (6·72)	4708 (5·33)	4837 (5·56)	4905 (5·63)	4759 (5·42)	5194 (5·63)	6202 (6·44)	7138 (7·73)	
Outcome. n. (%)											**0·012**[a] 0·694[b]
Unfavorable	25610 (30·0)	25996 (29·4)	26319 (30·6)	25991 (30·0)	25890 (30·3)	25796 (30·8)	25983 (30·4)	27640 (31·0)	28984 (32·2)	19377 (51·1)	
Favorable	59870 (70·0)	62367 (70·6)	59817 (69·4)	60694 (70·0)	59521 (69·7)	57977 (69·2)	59388 (69·6)	61493 (69·0)	60981 (67·8)	18516 (48·9)	

Table note: Bold font indicates statistical significance. Data are shown as number and frequency (percentage). Data were compared between years using the Pearson's χ2trend test. Age Groups: Children (0-9·9 years); young (10-24·9 years); Adults (25-64·9 years); Elderly (≥65 years).

[a] Comparison between 2010 and 2010.

[b] Comparisons between 2010 and 2018

Abbreviations: DOT: directly observed treatment; COPD: chronic obstructive pulmonary disease; TB: Tuberculosis; PTB: Pulmonary Tuberculosis; EPTB: Extrapulmonary Tuberculosis.

Table 2. Population characteristics by age categories

Characteristics	Child N=15666	Young N=162589	Adult N=632211	Elderly N=82112	p-value
Female n. (%)	7434 (47·5)	56772 (34·9)	187995 (29·7)	29269 (35·6)	0·063
Ethnicity n. (%)					0·793
Asian	78 (0·50)	1252 (0·77)	4548 (0·72)	924 (1·13)	
Black	1412 (9·01)	20271 (12·5)	86369 (13·7)	8173 (9·95)	
Indigenous	1099 (7·02)	2101 (1·29)	4952 (0·78)	1181 (1·44)	
Pardo	7180 (45·8)	78417 (48·2)	288677 (45·7)	33797 (41·2)	
White	4566 (29·1)	48387 (29·8)	197042 (31·2)	32087 (39·1)	
Literate n. (%)	2199 (14·0)	111724 (68·7)	347495 (55·0)	26372 (32·1)	**<0·001**
HIV infection n. (%)	556 (3·55)	8976 (5·52)	87800 (13·9)	1804 (2·20)	**0·002**
ART n. (%)	108 (0·69)	2245 (1·38)	14933 (2·36)	413 (0·50)	0·624
Alcohol consumption n. (%)	0 (0·00)	12728 (7·83)	130850 (20·7)	7726 (9·41)	**<0·001**
Illicit drug use n. (%)	0 (0·00)	17962 (11·0)	60237 (9·53)	493 (0·60)	**0·002**
Smoking habits n. (%)	0 (0·00)	15320 (9·42)	87890 (13·9)	7988 (9·73)	**0·003**
Diabetes n. (%)	49 (0·31)	1563 (0·96)	46480 (7·35)	13742 (16·7)	**<0·001**
Smear positive n. (%)	1557 (10·7)	91707 (57·8)	333002 (54·0)	36669 (45·9)	**<0·001**
Culture positive n. (%)	656 (4·19)	30014 (18·5)	117133 (18·5)	10992 (13·4)	**0·008**
Abnormal X-ray n. (%)	11096 (70·8)	119658 (73·6)	469800 (74·3)	63793 (77·7)	0·739
TB Status n. (%)					0·09
New case	14378 (91·8)	140149 (86·2)	500527 (79·2)	69958 (85·2)	
Prior TB	1227 (7·83)	22057 (13·6)	129414 (20·5)	11672 (14·2)	
Supervised treatment n. (%)					0·958
Received DOT	5839 (37·3)	65867 (40·5)	243834 (38·6)	30481 (37·1)	
No received DOT	5492 (35·1)	61134 (37·6)	242838 (38·4)	30681 (37·4)	
Type of TB n. (%)					**0·004**
EPTB	4276 (27·3)	18174 (11·2)	82180 (13·0)	10712 (13·0)	
PTB	10700 (68·3)	140432 (86·4)	528018 (83·5)	69258 (84·3)	
PTB+EPTB	688 (4·39)	3904 (2·40)	21659 (3·43)	2083 (2·54)	
Comorbidity n. (%)					**<0·001**
Cancer	33 (0·21)	948 (0·58)	5059 (0·80)	1854 (2·26)	
COPD	6 (0·04)	25 (0·02)	492 (0·08)	868 (1·06)	
Hypertension	0 (0·00)	0 (0·00)	34245 (5·42)	53849 (65·6)	
Renal disease	1 (0·01)	80 (0·05)	295 (0·05)	336 (0·41)	
Others	2103 (13·4)	79727 (49·0)	41834 (6·62)	3485 (4·24)	
No condition	13523 (86·3)	81798 (50·3)	550279 (87·0)	21712 (26·4)	
Outcome description n. (%)					0·343
Cure	10842 (69·2)	107159 (65·9)	393360 (62·2)	47141 (57·4)	
Death	412 (2·63)	3542 (2·18)	46871 (7·41)	15256 (18·6)	
Failure	60 (0·38)	1652 (1·02)	8619 (1·36)	832 (1·01)	
Loss follow up	899 (5·74)	21985 (13·5)	78524 (12·4)	3932 (4·79)	
Relapse	591 (3·77)	1708 (1·05)	12801 (2·02)	3718 (4·53)	
Transferred out	1220 (7·79)	10143 (6·24)	39130 (6·19)	4558 (5·55)	
Outcome n. (%)					0·113
Unfavorable	3182 (22·7)	39030 (26·7)	185945 (32·1)	28296 (37·5)	

Favorable	10842 (77·3)	107159 (73·3)	393360 (67·9)	47141 (62·5)

Table note: Bold font indicates statistical significance. Data are shown as number and frequency (percentage). Data were compared between years using the Pearson's χ2trend test. Age Groups: Children (0-9·9 years); young (10-24·9 years); Adults (25-64·9 years); Elderly (≥65 years).
Abbreviations: DOT: directly observed treatment; COPD: chronic obstructive pulmonary disease; TB: Tuberculosis; PTB: Pulmonary Tuberculosis; EPTB: Extrapulmonary Tuberculosis.
Others comorbidities: It did not include hypertension, kidney disease, cancer and COPD.

Table 3. Population characteristics by categorical outcome.

Characteristics	All N=818210	Unfavorable N=257586	Favorable N=560624	p-Value	pδ-Value
Female, n. (%)	259110 (31·7)	72269 (28·1)	186841 (33·3)		1
Age group, n. (%)				0·241	0·5
Child	14024 (1·71)	3182 (1·23)	10842 (1·93)		
Young	146189 (17·87)	39030 (12·15)	107159 (19·11)		
Adult	559305 (68·35)	185945 (72·18)	373360 (66·6)		
Elderly	75437 (9·22)	28296 (10·9)	47141 (8·4)		
Ethnicity n. (%)				0·593	1
Asian	6223 (0·76)	1802 (0·70)	4421 (0·79)		
Black	106135 (13·0)	37494 (14·6)	68641 (12·2)		
Indigenous	8708 (1·06)	2149 (0·83)	6559 (1·17)		
Pardo	371627 (45·4)	120177 (46·7)	251450 (44·9)		
White	262253 (32·1)	74681 (29·0)	187572 (33·5)		
Literate, n. (%)	445662 (54·5)	125377 (48·7)	320285 (57·1)	0·294	0 (Δ = 0·14)
HIV infection, n. (%)	91882 (11·2)	49642 (19·3)	42240 (7·53)	**0·004**	0 (Δ = 1·38)
ART. n. (%)	15527 (16·9)	7650 (15·41)	7877 (18·64)	0·89	1
Alcohol consumption. n.(%)	131687 (16·0)	57421 (22·3)	74266 (13·2)	**0·065**	0 (Δ = 0·67)
Illicit drug use. n. (%)	68557 (8·37)	32511 (12·6)	36046 (6·42)	0·3	0 (Δ = 0·08)
Smoking habits. n. (%)	88922 (10·87)	34522 (13·4)	54396 (9·7)	0·449	1
Diabetes. n. (%)	56282 (6·88)	16557 (6·43)	39725 (7·09)	0·786	1
Smear positive. n. (%)	428296 (53·6)	123759 (49·3)	304537 (55·6)	0·453	1
Culture positive. n. (%)	148436 (18·1)	44187 (17·2)	104249 (18·6)	0·748	1
Abnormal X-ray . n. (%)	612756 (74·9)	194509 (75·5)	418247 (74·6)	1	1
TB Status. n. (%)				**0·014**	0 (Δ = 1·02)
New case	665236 (81·3)	181561 (70·5)	483675 (86·3)		
Prior TB	150310 (18·4)	74248 (28·8)	76062 (13·6)		
Treatment. n. (%)				**0·012**	0 (Δ = 0·96)
Received DOT	333100 (40·7)	73073 (28·4)	260027 (46·4)		
No received DOT	320530 (39·2)	108547 (42·1)	211983 (37·8)		
Type of TB				0·697	1
EPTB	105523 (12·9)	31243 (12·1)	74280 (13·2)		
PTB	686346 (83·9)	214434 (83·2)	471912 (84·2)		
PTB and EPTB	26234 (3·21)	11812 (4·59)	14422 (2·57)		
Comorbidity n. (%)				0.88	1
Cancer	7320 (0.89)	2565 (1.00)	4755 (0.85)		
COPD	1301 (0.16)	640 (0.25)	661 (0.12)		
Hypertension	80806 (9.88)	27707 (10.8)	53099 (9.47)		
Kidney disease	659 (0.08)	371 (0.14)	288 (0.05)		

Others	115928 (14.2)	33592 (13.0)	82336 (14.7)
No condition	612173 (74.8)	192703 (74.8)	419470 (74.8)

Table note: Bold font indicates statistical significance. Data are shown as number and frequency (percentage). Data were compared between years using the Pearson's χ2trend test. Age Groups: Children (0-9·9 years); young(10-24·9 years); Adults (25-64·9 years); Elderly(≥65 years).
Abbreviations: DOT: directly observed treatment; COPD: chronic obstructive pulmonary disease; TB: Tuberculosis; PTB: Pulmonary Tuberculosis; EPTB: Extrapulmonary Tuberculosis. Other comorbidities: did not include hypertension, kidney disease, cancer and COPD.

Figure Legends:

Figure 1. General population TB rates by sex (A) and age group (B) between 2010 and 2019. Mann-Kendal trend test was used to calculate changes in incidence among years. according to sex and/or age group. On A panel it is possible to observe that there was a small decrease in the incidence of women with tuberculosis (purple). In age stratification (B panel). only the incidence in children has not changed over the years. Age Groups: Children (0-9·9 years); young (10-24·9 years); Adults (25-64·9 years); Elderly (≥65 years).

Figure 2: Characteristics of each age group (A, B, C) and outcome category (D, E, F).
(A) Consumption habits. we observed that young people and adults have greater consumption habits of alcohol. cigarettes and illegal drugs than children and the elderly. (B) Comorbidities. While adults have a higher prevalence of HIV. The elderly has a higher prevalence of diabetes and hypertension. (C) Outcome description. The frequency of favorable outcome (cure) decreases according to age. being higher in children and lower in the elderly. (D) HIV status. Positive serology for HIV infection is correlated with an unfavorable treatment outcome in young. adults and elderly. (E) TB Status. Relapse cases of TB are correlated with an unfavorable treatment outcome in young and adults. (F) Observed Treatment. In all age groups. receive a DOT is correlated with a favorable treatment outcome. Age Groups: Children (0-9·9 years); young (10-24·9 years); Adults (25-64·9 years); Elderly(≥65 years).

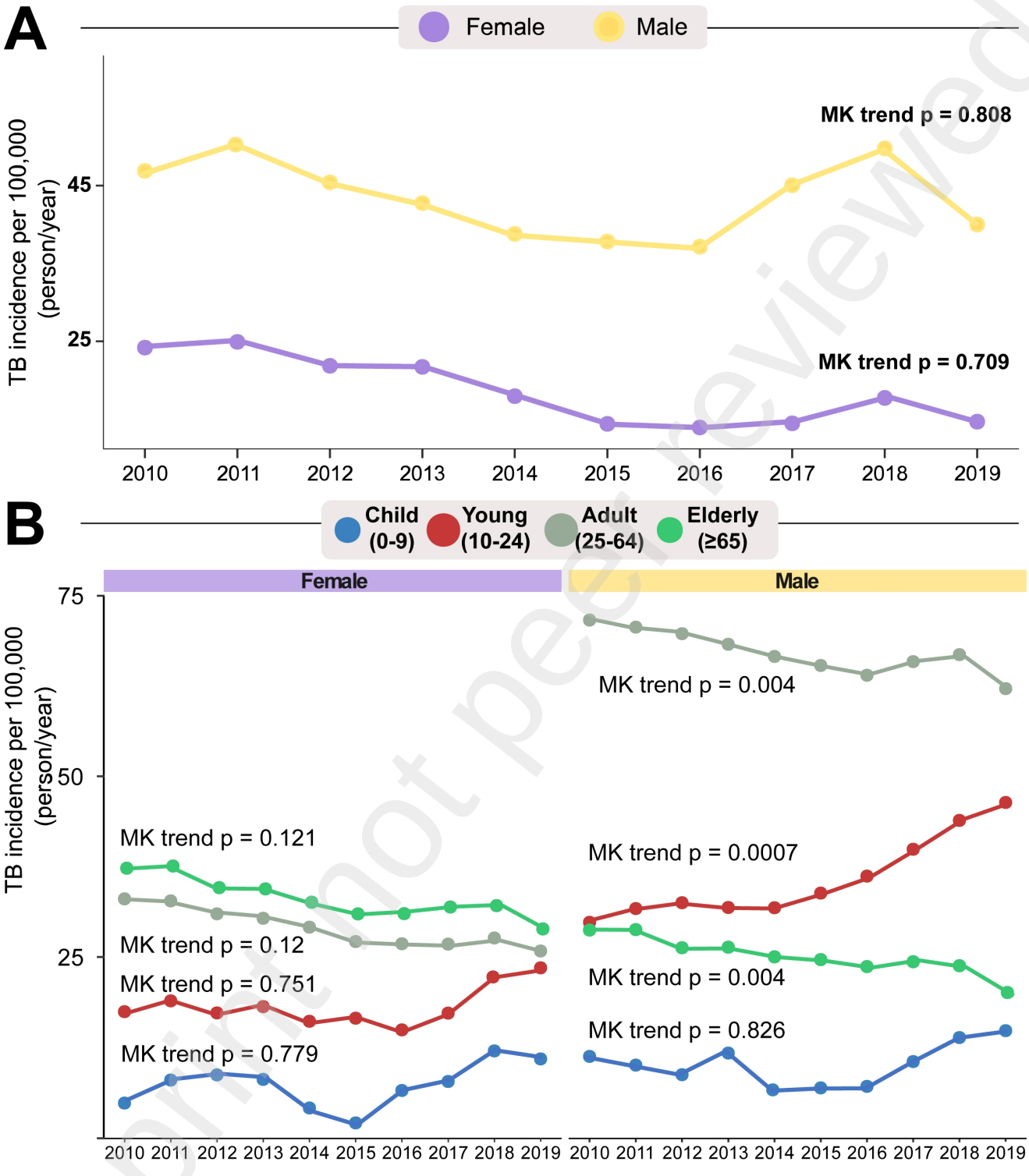
Figure 3: Backward stepwise logistic regression model test independent associations between all the relevant clinical and epidemiological parameters and treatment outcome in children (0-9 years). The unfavorable outcome was used as reference to test associations. Only parameters which remained with $p < 0{\cdot}05$ in in the adjusted model (95%CI. 95% confidence interval) were plotted. Adjustment was performed for each parameter: race (reference: indigenous); male (reference: female); illiterate(reference: literate); prior TB (reference: new case); no DOT (reference: Received DOT).Pulmonary TB (reference: Pulmonary and Extrapulmonary TB); Extrapulmonary TB (Reference: Pulmonary and Extrapulmonary TB); Pulmonary and Extrapulmonary TB (reference: Pulmonary TB); HIV infection (reference: without HIV infection); Alcohol Consumption (reference: no alcohol consumption); Diabetes (reference: no diabetes); Illicit drug use (reference: no illicit drug use); Smoking habit (reference: no smoking). Cancer (reference: no condition); COPD (reference: no condition); Kidney disease (reference: no condition); Hypertension (reference: no condition); Other comorbidities (reference: no condition); Abnormal chest x-ray (reference: normal chest x-ray). Abbreviations: TB: tuberculosis; DOT: directly observed treatment; COPD: chronic obstructive pulmonary disease.

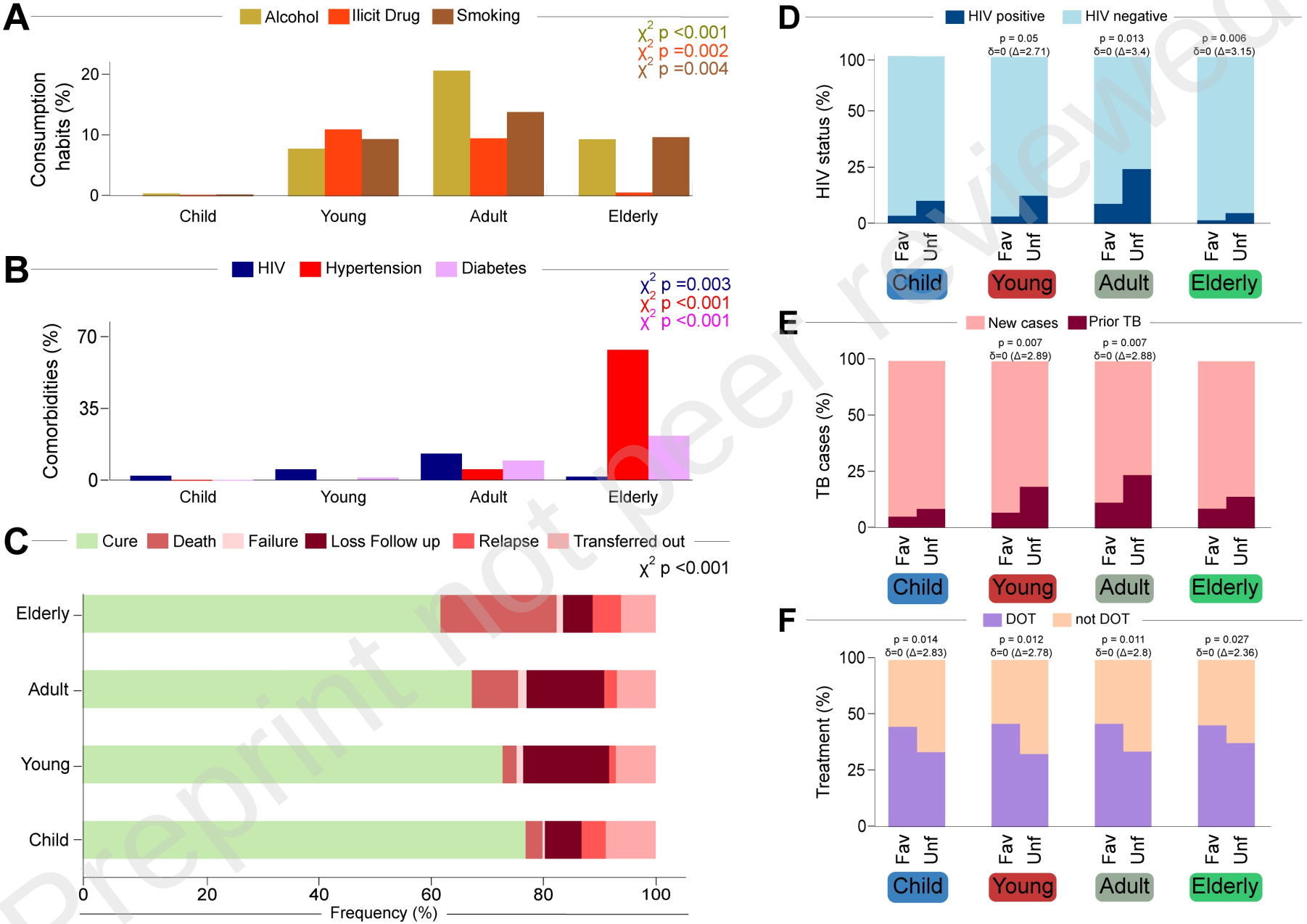
Figure 4: Backward stepwise logistic regression model test independent associations between all the relevant clinical and epidemiological parameters and treatment outcome in young group (10-24 years). The unfavorable outcome was used as reference to test associations. Only parameters which remained with $p < 0{\cdot}05$ in in the adjusted model (95%CI. 95% confidence interval) were plotted. Adjustment was performed for each parameter: race (reference: indigenous); male (reference: female); illiterate(reference: literate); prior TB (reference: new case); no DOT (reference: Received DOT).

Pulmonary TB (reference: Pulmonary and Extrapulmonary TB); Extrapulmonary TB (Reference: Pulmonary and Extrapulmonary TB); Pulmonary and Extrapulmonary TB (reference: Pulmonary TB); HIV infection (reference: without HIV infection); Alcohol Consumption (reference: no alcohol consumption); Diabetes (reference: no diabetes); Illicit drug use (reference: no illicit drug use); Smoking habit (reference: no smoking). Cancer (reference: no condition); COPD (reference: no condition); Kidney disease (reference: no condition); Hypertension (reference: no condition); Other comorbidities(reference: no condition); Abnormal chest x-ray (reference: normal chest x-ray).Abbreviations: TB: tuberculosis; DOT: directly observed treatment; COPD: chronic obstructive pulmonary disease; Other comorbidities: did not include HAS, kidney disease, cancer and COPD.

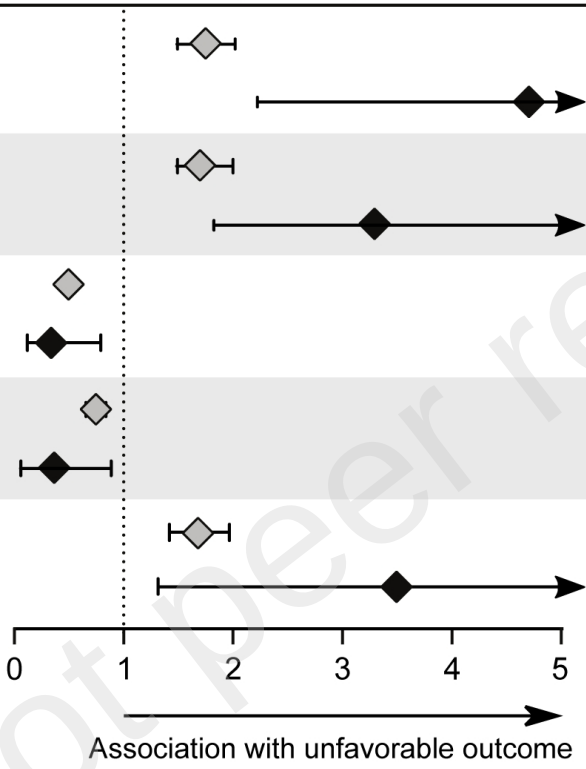
Figure 5: Backward stepwise logistic regression model test independent associations between all the relevant clinical and epidemiological parameters and treatment outcome in adult group (25-64). The unfavorable outcome was used as reference to test associations. Only parameters which remained with $p < 0{\cdot}05$ in in the adjusted model (95%CI. 95% confidence interval) were plotted. Adjustment was performed for each parameter: race (reference: indigenous); male (reference: female); illiterate(reference: literate); prior TB (reference: new case); no DOT (reference: DOT indication).Pulmonary TB (reference: Pulmonary and Extrapulmonary TB); Extrapulmonary TB (Reference: Pulmonary and Extrapulmonary TB); Pulmonary and Extrapulmonary TB (reference: Pulmonary TB); HIV infection (reference: without HIV infection); Alcohol Consumption (reference: no alcohol consumption); Diabetes (reference: no diabetes); Illicit drug use (reference: no illicit drug use); Smoking habit (reference: no smoking). Cancer (reference: no condition); COPD (reference: no condition); Kidney disease (reference: no condition); Hypertension (reference: no condition); Other comorbidities (reference: no condition); Abnormal chest x-ray (reference: normal chest x-ray). Abbreviations: TB: tuberculosis; DOT: directly observed treatment; COPD: chronic obstructive pulmonary disease.

Figure 6: Backward stepwise logistic regression model test independent associations between all the relevant clinical and epidemiological parameters and treatment outcome in elderly group (≥65 years). The unfavorable outcome was used as reference to test associations. Only parameters which remained with $p < 0{\cdot}05$ in in the adjusted model (95%CI. 95% confidence interval) were plotted. Adjustment was performed for each parameter: race (reference: indigenous); male (reference: female); illiterate(reference: literate); prior TB (reference: new case); no DOT (reference: DOT indication).Pulmonary TB (reference: Pulmonary and Extrapulmonary TB); Extrapulmonary TB (Reference: Pulmonary and Extrapulmonary TB); Pulmonary and Extrapulmonary TB (reference: Pulmonary TB); HIV infection (reference: without HIV infection); Alcohol Consumption (reference: no alcohol consumption); Diabetes (reference: no diabetes); Illicit drug use (reference: no illicit drug use); Smoking habit (reference: no smoking). Cancer (reference: no condition); COPD (reference: no condition); Kidney disease (reference: no condition); Hypertension (reference: no condition); Other comorbidities (reference: no condition); Abnormal chest x-ray (reference: normal chest x-ray). Abbreviations: TB: tuberculosis; DOT: directly observed treatment; COPD: chronic obstructive pulmonary disease; Other comorbidities: It did not include HAS. kidney disease. cancer and COPD.

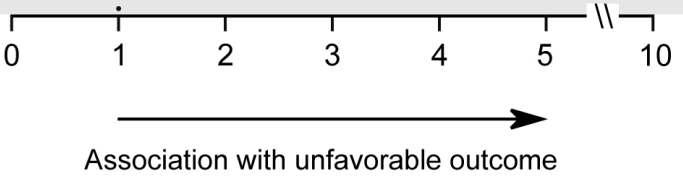




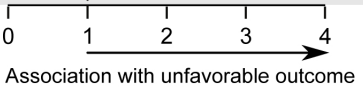
Characteristics	model	Odds ratio (95% CI)	p-value
Prior TB	unadjusted	1.81 (1.58-2.07)	<0.001
	adjusted	4.83 (2.17-10.76)	<0.001
No DOT	unadjusted	1.84 (1.67-2.03)	<0.001
	adjusted	3.38 (1.88-6.08)	<0.001
Pulmonary TB	unadjusted	0.58 (0.49-0.69)	<0.001
	adjusted	0.29 (0.11-0.77)	0.013
Extrapulmonary TB	unadjusted	0.71 (0.59-0.85)	<0.001
	adjusted	0.24 (0.07-0.80)	0.021
Pulmonary and Extrapulmonary TB	unadjusted	1.72 (1.44-2.06)	<0.001
	adjusted	3.45 (1.30-9.14)	0.013



Characteristics	model	Odds ratio (95% CI)	p-value
Race (White)	unadjusted	1.09 (0.97-1.22)	0.127
	adjusted	0.64 (0.47-0.88)	0.006
Male	unadjusted	1.26 (1.23-1.29)	<0.001
	adjusted	1.18 (1.10-1.27)	0.009
Iliterate	unadjusted	1.73 (1.65-1.81)	<0.001
	adjusted	1.49 (1.31-1.69)	<0.001
Prior TB	unadjusted	3.20 (3.11-3.30)	<0.001
	adjusted	3.17 (2.90-3.47)	<0.001
No DOT	unadjusted	1.92 (1.87-1.97)	<0.001
	adjusted	2.96 (2.76-3.17)	<0.001
HIV infection	unadjusted	4.42 (4.22-4.63)	<0.001
	adjusted	2.69 (2.35-3.08)	<0.001
Ilicit Drug Use	unadjusted	2.53 (2.44-2.63)	<0.001
	adjusted	1.99 (1.82-2.17)	<0.001
Smoking habits	unadjusted	2.01 (1.93-2.09)	<0.001
	adjusted	1.50 (1.36-1.65)	<0.001
Kidney disease	unadjusted	1.76 (1.21-2.77)	<0.001
	adjusted	9.89 (1.66-59.11)	0.012



Characteristics	model	Odds ratio (95% CI)	p-value
Race (White)	unadjusted	1.21 (1.13-1.30)	<0.001
	adjusted	0.64 (0.52-0.79)	<0.001
Race (Black)	unadjusted	1.70 (1.58-1.82)	<0.001
	adjusted	0.79 (0.64-0.97)	0.027
Race (Asian)	unadjusted	1.23 (1.12-1.35)	<0.001
	adjusted	0.62 (0.46-0.84)	0.002
Race (Pardo)	unadjusted	1.47 (1.38-1.58)	<0.001
	adjusted	0.69 (0.56-0.85)	0.001
Male	unadjusted	1.30 (1.28-1.31)	<0.001
	adjusted	1.08 (1.04-1.13)	<0.001
Iliterate	unadjusted	1.22 (1.20-1.24)	<0.001
	adjusted	1.18 (1.13-1.24)	<0.001
Prior TB	unadjusted	2.61 (2.58-2.64)	<0.001
	adjusted	2.35 (2.26-2.44)	<0.001
No DOT	unadjusted	2.69 (2.60-2.79)	<0.001
	adjusted	1.84 (1.82-1.87)	<0.001
Pulmonary TB	unadjusted	0.55 (0.53-0.57)	<0.001
	adjusted	0.87 (0.79-0.95)	0.002
Extrapulmonary TB	unadjusted	0.49 (0.48-0.51)	<0.001
	adjusted	0.80 (0.71-0.90)	<0.001
Pulmonary and Extrapulmonary TB	unadjusted	1.82 (1.77-1.87)	<0.001
	adjusted	1.17 (1.08-1.28)	<0.001
HIV infection	unadjusted	3.58 (3.52-3.63)	<0.001
	adjusted	2.42 (2.31-2.53)	<0.001
Alcohol consumption	unadjusted	2.00 (1.97-2.02)	<0.001
	adjusted	1.41 (1.36-1.47)	<0.001
Ilicit Drug Use	unadjusted	2.48 (2.43-2.52)	<0.001
	adjusted	1.94 (1.86-2.03)	<0.001
Smoking habits	unadjusted	1.55 (1.53-1.58)	<0.001
	adjusted	1.19 (1.14-1.24)	<0.001
Cancer	unadjusted	1.06 (0.99-1.12)	0.083
	adjusted	1.33 (1.09-1.64)	0.006
COPD	unadjusted	1.85 (1.54-2.22)	<0.001
	adjusted	1.78 (1.05-3.02)	0.032
Kidney disease	unadjusted	2.76 (2.17-3.52)	<0.001
	adjusted	3.11 (1.37-7.07)	0.007
Abnormal chest x-ray	unadjusted	1.09 (1.06-1.12)	<0.001
	adjusted	1.15 (1.05-1.25)	0.002



Characteristics	model	Odds ratio (95% CI)	p-value
Prior TB	unadjusted	1.75 (1.68-1.83)	<0.001
	adjusted	1.60 (1.38-1.85)	<0.001
No DOT	unadjusted	1.54 (1.49-1.60)	<0.001
	adjusted	1.80 (1.62-2.00)	<0.001
HIV infection	unadjusted	3.11 (2.82-3.44)	<0.001
	adjusted	2.69 (1.99-3.64)	<0.001
Alcohol consumption	unadjusted	1.57 (1.49-1.65)	<0.001
	adjusted	1.22 (1.04-1.44)	0.015
Ilicit Drugs Use	unadjusted	1.53 (1.27-1.86)	<0.001
	adjusted	2.01 (1.31-3.08)	<0.001
Smoking habits	unadjusted	1.54 (1.46-1.62)	<0.001
	adjusted	1.57 (1.38-1.79)	<0.001
Cancer	unadjusted	1.32 (1.20-1.46)	<0.001
	adjusted	1.69 (1.16-2.47)	0.007
COPD	unadjusted	1.86 (1.61-2.14)	<0.001
	adjusted	1.98 (1.28-3.05)	0.002
Others Comorbidities	unadjusted	1.69 (1.57-1.82)	<0.001
	adjusted	1.72 (1.34-2.19)	<0.001