

## Treatment loss to follow-up for tuberculosis in childhood and adolescence: analysis of associated factors

Perda de seguimento do tratamento da tuberculose na infância e adolescência: análise dos fatores associados

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### ABSTRACT

**Objective:** to analyze factors associated with treatment loss to follow-up for tuberculosis among children and adolescents. **Methods:** retrospective, analytical study including all new tuberculosis cases aged 0–19 years. Data were obtained from the Notifiable Diseases Information System. Multiple linear regression was used to estimate associations between sociodemographic, clinical-epidemiological, and therapeutic variables and loss to follow-up. **Results:** the proportion of loss to follow-up was 8.0%. Factors associated with loss to follow-up were not undergoing chest radiography ( $p < 0.001$ ), not undergoing HIV testing ( $p = 0.002$ ), and not receiving directly observed treatment ( $p < 0.001$ ). **Conclusion:** findings support comprehensive strategies to reduce loss to follow-up in pediatric and adolescent tuberculosis, including expanded access to diagnostic and follow-up services and stronger bonds between health professionals and families. **Contributions to practice:** increase uptake of HIV testing and chest radiography, and intensify directly observed treatment implementation, including the use of digital technologies.

**Descriptors:** Tuberculosis; Child; Adolescent; Patient Dropouts; Risk Factors.

### RESUMO

**Objetivo:** analisar os fatores associados à perda de seguimento do tratamento da tuberculose na infância e adolescência. **Métodos:** estudo retrospectivo e analítico. A população foi constituída por todos os casos novos de tuberculose, de 0 a 19 anos de idade. Os dados foram coletados do Sistema Informação de Agravos de Notificação. Foi realizada uma regressão linear múltipla para estimar a associação entre as variáveis sociodemográficas, clínico-epidemiológicas e terapêuticas com a perda de seguimento do tratamento. **Resultados:** a proporção da perda de seguimento do tratamento foi de 8,0%. Os fatores associados foram a não realização de raio X ( $p < 0,001$ ), do teste de HIV ( $p = 0,002$ ) e do tratamento diretamente observado ( $p < 0,001$ ). **Conclusão:** os achados indicam a necessidade para adoção de estratégias abrangentes para reduzir a perda de seguimento do tratamento de tuberculose em crianças e adolescentes, como ampliar a oferta de serviços de diagnóstico e acompanhamento de tuberculose, além de fortalecer o vínculo dos profissionais de saúde com os familiares dessa população. **Contribuições para a prática:** recomenda-se a ampliação da realização dos testes de HIV e radiografia de tórax. É essencial a intensificação do tratamento diretamente observado, inclusive com uso de tecnologias digitais.

**Descritores:** Tuberculose; Criança; Adolescente; Pacientes Desistentes do Tratamento; Fatores de Risco.

## Introduction

Tuberculosis remains a major public health issue in Brazil. Recent data show rising incidence nationally, with projections of continued increase through 2030, jeopardizing Brazil's commitment to the tuberculosis-related sustainable development goals<sup>(1)</sup>. In 2018, 9.4% of reported tuberculosis cases in Brazil occurred in individuals < 19 years. The cure rate was 76.8%, and the treatment abandonment rate was 10.4%<sup>(2)</sup>. Tuberculosis mortality rates per 100,000 population in 2020 were 0.16, 0.05, and 0.22 in the 0–4, 5–9, and 10–19-year age groups, respectively<sup>(3)</sup>.

Epidemiologic analyses of tuberculosis in children and adolescents remain limited. In addition, tuberculosis is often underreported in the pediatric and adolescent population, which may lead to underestimation of morbidity and mortality in this group. Such undercounting can misguide public resource allocation and hinder the implementation of targeted interventions aimed at disease control and treatment success<sup>(4)</sup>.

Tuberculosis is historically linked to social inequality, reflecting socioeconomic conditions and unequal access to health services. Its magnitude and impact make it a priority disease for prevention and control strategies, particularly in vulnerable populations where early detection and appropriate treatment are critical to reducing morbidity and mortality among children and adolescents<sup>(5)</sup>.

Treatment loss to follow-up during childhood and adolescence poses a substantial barrier to tuberculosis control. Adherence may be undermined by multiple factors, including limited access to health services, poor understanding of the need for continuous therapy, adverse drug effects, and socioeconomic barriers<sup>(6)</sup>. Children rely on caregiver support and commitment to follow the therapeutic regimen. Adolescents — who are gaining autonomy — may show greater resistance to sustained treatment<sup>(5,7)</sup>.

Few studies have examined factors influencing

tuberculosis treatment loss to follow-up in children and adolescents, and to our knowledge none have addressed this problem in the state of Mato Grosso. Understanding the determinants of treatment interruption is essential to inform targeted actions. Among these, priority actions include enhancing patient follow-up, training health professionals, and reducing barriers to access and adherence. Such measures can strengthen tuberculosis control among children and adolescents. In this context, this study aimed to analyze factors associated with treatment loss to follow-up for tuberculosis among children and adolescents.

## Methods

### Study design and period

This was a retrospective, analytical study of new tuberculosis cases among children and adolescents residing in the state of Mato Grosso, Brazil. Data were extracted from the Brazilian Notifiable Diseases Information System (SINAN) on February 24, 2024, and analyses covered the period from January 1, 2007, to December 31, 2022. Reporting followed the Strengthening the Reporting of Observational Studies in Epidemiology guidelines.

### Setting

Mato Grosso is located in Brazil's Central-West region, south of the Amazon Forest. With an area of 903,202.5 km<sup>2</sup>, it encompasses three major continental biomes — Amazon, Pantanal, and Cerrado. The state has 141 cities and an estimated population of 3,658,649; children (0–9 years) and adolescents (10–19 years) represent 15.4% and 14.6% of this population, respectively, with a predominance of self-identified mixed-race (*pardo*) individuals<sup>(8)</sup>.

## Study population

The study included all new tuberculosis cases aged 0–19 years notified to SINAN between 2007 and 2022 in Mato Grosso. This time series corresponds to the entire period with available data in SINAN. The age range was selected to define children and adolescents<sup>(9)</sup>. A new tuberculosis case was defined as an individual who had never used anti-tuberculosis medication or had used it for fewer than 30 days<sup>(10)</sup>. Exclusions were cases classified as relapse, return after loss to follow-up, transfer, change in diagnosis, drug-resistant tuberculosis, regimen change, or treatment failure, as these do not characterize treatment discontinuation.

## Data sources and collection

Data were obtained from SINAN via the Department of Informatics of the Unified Health System<sup>(11)</sup>. The following filters were applied for download: Data source “SINAN — Notifiable Diseases Information System” > Mode “Data” > File type “TUBE — Tuberculosis” > Years “2007–2022.” The dataset was organized in Microsoft Excel and double-checked to identify potential inconsistencies.

## Data analysis

The dependent variable was loss to follow-up, defined as cases closed as “abandonment” or “primary abandonment.” Abandonment was defined as interrupting medication for  $\geq 30$  consecutive days; primary abandonment as  $< 30$  days of medication with interruption for  $> 30$  days or no treatment initiation<sup>(10)</sup>.

Independent variables were grouped into two domains: i) sociodemographic factors — age, sex, and race/skin color; and ii) clinical-epidemiologic and therapeutic factors — including tuberculosis clinical form; whether diagnostic sputum smear microscopy,

sputum culture, histopathology, and chest radiography were performed; HIV testing; receipt of directly observed treatment; time from diagnosis to treatment initiation; and the numbers of reported and examined contacts.

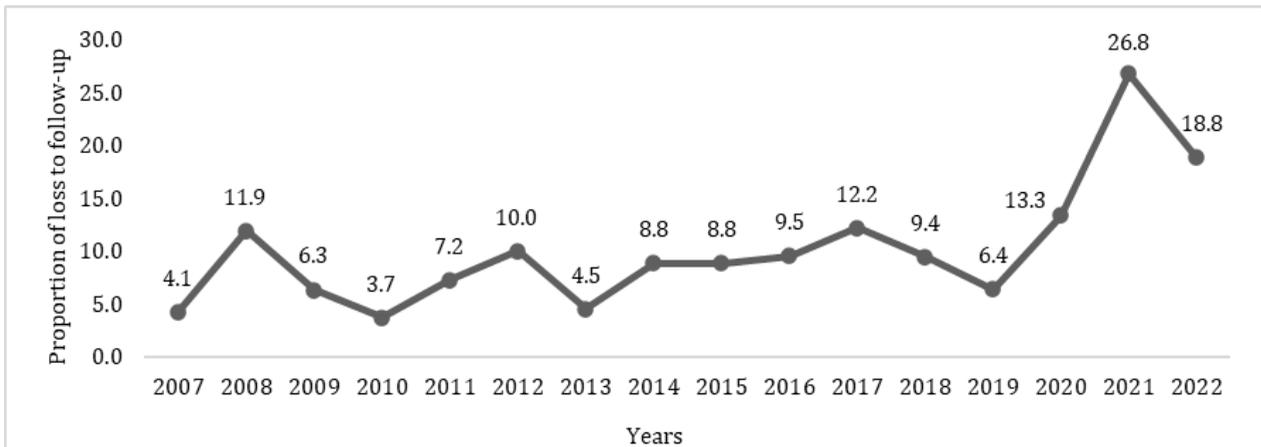
Differences in proportions between groups with and without treatment discontinuation were assessed using Pearson’s Chi-square ( $\chi^2$ ) test or Fisher’s exact test, with a two-sided significance level of 5%. Crude and adjusted odds ratio (OR) with 95% confidence intervals (CI) were estimated to identify factors associated with the outcome. Variables with  $p < 0.20$  in univariable analysis and  $\geq 50\%$  data completeness were considered for multivariable modeling. Statistical significance in the final model was set at  $p < 0.05$  (Wald test). Collinearity was assessed using the variance inflation factor. Analyses were performed in R.

## Ethical aspects

This study is part of the parent project “Sociodemographic, environmental, and clinical-epidemiologic aspects of treatment abandonment in socially determined diseases in the state of Mato Grosso,” approved by the Human Research Ethics Committee at Universidade Federal de Rondonópolis (Certificate of Submission for Ethical Appraisal: 76904224.0.0000.0126; approval No. 6,679,133/2024).

## Results

From 2007 to 2022, 22,845 tuberculosis cases were reported in Mato Grosso; of these, 1,892 involved individuals  $\leq 19$  years. After applying exclusion criteria, 1,697 cases remained for analysis. The overall proportion of treatment loss to follow-up among children and adolescents was 8.0% ( $n = 142$ ). The lowest annual proportion occurred in 2010 (3.7%), whereas the highest was observed in 2021 (26.8%) (Figure 1).



**Figure 1** – Proportion of treatment loss to follow-up for tuberculosis among children and adolescents (2007-2022). Mato Grosso, MT, Brazil, 2024

Among individuals with loss to follow-up, most were male (n = 76; 53.5%) and self-identified as pardo (n = 76; 53.5%). Clinico-epidemiologic characteristics in this group included a predominance of pulmonary tuberculosis (n = 127; 89.4%), with 88 (62.0%) undergoing sputum smear microscopy and 102 (71.8%) undergoing chest radiography. Conversely, most did not undergo sputum culture (n = 132; 93.0%), histopathology (n = 122; 85.9%), HIV testing (n = 72; 50.7%), or

directly observed treatment (n = 50; 35.9%). Half initiated treatment on the same day as diagnosis (n = 71; 50.0%). Regarding contact investigation, 67 (47.2%) reported and 45 (31.7%) had 1-3 contacts examined.

There was a statistically higher proportion of treatment discontinuation according to age, race/skin color, sputum smear microscopy, chest radiography, HIV testing, directly observed treatment, and the numbers of reported and examined contacts (Table 1).

**Table 1** – Loss to follow-up during tuberculosis treatment among children and adolescents, by sociodemographic, clinical-epidemiologic, and therapeutic characteristics (2007-2022). Mato Grosso, MT, Brazil, 2024

Variables	Yes	No	Total	p-value*
	n (%)	n (%)	n (%)	
Age (years)				< 0.001
0-12	41 (28.9)	745 (47.9)	786 (46.3)	
13-19	101 (71.1)	810 (52.1)	911 (53.7)	
Sex				0.782
Female	66 (46.5)	704 (45.3)	770 (45.4)	
Male	76 (53.5)	851 (54.7)	927 (54.6)	
Race/skin color				< 0.001
White	21 (14.8)	253 (16.3)	274 (16.1)	
Black	21 (14.8)	109 (7.0)	130 (7.7)	
Yellow	1 (0.7)	14 (0.9)	15 (0.9)	
Brown	76 (53.5)	568 (36.5)	644 (37.9)	
Indigenous	20 (14.1)	588 (37.8)	608 (35.8)	
Missing/not reported	3 (2.1)	23 (1.5)	26 (1.6)	
Tuberculosis clinical form				1.000
Pulmonary	127 (89.4)	1,387 (89.2)	1,514 (89.2)	
Other forms	15 (10.6)	164 (10.5)	179 (10.5)	
Missing/not reported	0 (0)	4 (0.3)	4 (0.3)	
Sputum smear microscopy				0.012
Performed	88 (62.0)	765 (49.2)	853 (50.3)	
Not performed	54 (38.0)	786 (50.5)	840 (49.4)	
Missing/not reported	0 (0)	4 (0.3)	4 (0.3)	

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Variables	Yes	No	Total	p-value*
	n (%)	n (%)	n (%)	
Sputum culture				0.463
Performed	10 (7.0)	155 (10.0)	165 (9.7)	
Not performed	132 (93.0)	1,397 (89.8)	1,529 (90.1)	
Missing/not reported	0 (0)	3 (0.2)	3 (0.2)	
Histopathology				0.753
Performed	16 (11.3)	189 (12.2)	205 (12.1)	
Not performed	122 (85.9)	1,333 (85.7)	1,455 (85.7)	
Missing/not reported	4 (2.8)	33 (2.1)	37 (2.2)	
Chest radiography				< 0.001
Performed	102 (71.8)	1,315 (84.6)	1,417 (83.5)	
Not performed	38 (26.8)	198 (12.7)	236 (13.9)	
Missing/not reported	2 (1.4)	42 (2.7)	44 (2.6)	
HIV testing				0.002
Performed	70 (49.3)	1,002 (64.4)	1,072 (63.2)	
Not performed	72 (50.7)	550 (35.4)	622 (36.6)	
Missing/not reported	0 (0)	3 (0.2)	3 (0.2)	
Directly observed treatment				< 0.001
Yes	50 (35.2)	915 (58.8)	965 (56.9)	
No	51 (35.9)	379 (24.4)	430 (25.3)	
Missing/not reported	41 (28.9)	261 (16.8)	302 (17.8)	
Time from diagnosis to treatment start (days)				0.967
Same day	71 (50.0)	784 (50.4)	855 (50.4)	
1-7	38 (26.8)	445 (28.6)	483 (28.5)	
8-14	9 (6.3)	89 (5.7)	98 (5.8)	
15-21	3 (2.1)	38 (2.4)	41 (2.4)	
≥ 22	18 (12.7)	167 (10.7)	185 (10.9)	
Missing/not reported	3 (2.1)	32 (2.1)	35 (2.0)	
Number of reported contacts				0.028
None	13 (9.2)	177 (11.4)	190 (11.2)	
1-3	67 (47.2)	541 (34.8)	608 (35.8)	
≥ 4	59 (41.5)	806 (52.0)	868 (51.2)	
Missing/not reported	3 (2.1)	28 (1.8)	31 (1.8)	
Number of examined contacts				0.006
None	26 (18.3)	199 (12.8)	225 (13.3)	
1-3	45 (31.7)	508 (32.7)	553 (32.6)	
≥ 4	39 (27.5)	614 (39.5)	653 (38.5)	
Missing/not reported	32 (22.5)	234 (15.0)	266 (15.6)	

\*Pearson's Chi-square test or Fisher's exact test, as appropriate; HIV: Human Immunodeficiency Virus

Table 2 presents the multivariable regression results. In the final model, tuberculosis treatment discontinuation among children and adolescents was associated with not undergoing chest radiography (odds

ratio [OR] = 2.26; 95% confidence interval [CI] 1.30-3.93), not undergoing HIV testing (OR = 1.78; 95% CI 1.11-2.84), and not receiving directly observed treatment (OR = 2.47; 95% CI 1.55-3.93).

**Table 2** – Multivariable regression of tuberculosis treatment loss to follow-up among children and adolescents by sociodemographic, clinical-epidemiologic, and therapeutic characteristics (2007-2022). Mato Grosso, MT, Brasil, 2024

Variable	Crude OR (95% CI)	Adjusted OR (95% CI)
Chest radiography		
Performed	1	1
Not performed	2.54 (1.51-4.28)*	2.26 (1.30-3.93)*
HIV test		
Performed	1	1
Not performed	1.90 (1.22-2.97)*	1.78 (1.11-2.84)*
Directly observed treatment		
Yes	1	1
No	2.50 (1.60-3.90)*	2.47 (1.55-3.93)*
Number of reported contacts		
1-3	1	1
≥ 4	0.59 (0.37-0.93)	0.61 (0.38-1.00)
None	0.60 (0.26-1.37)	0.68 (0.29-1.60)

\*p < 0.05. OR: Odds ratio; CI: Confidence interval; HIV: Human Immunodeficiency Virus

## Discussion

The World Health Organization (WHO) recommends a loss-to-follow-up rate below 5% to ensure adequate tuberculosis control<sup>(12)</sup>. In this study, the proportion of treatment discontinuation among children and adolescents was 8.0%, exceeding that benchmark. Similar findings have been reported in patients aged 0–18 years, with a 7.0% treatment abandonment rate<sup>(7)</sup>. Among adolescents with tuberculosis, treatment success has also fallen short of WHO targets, with 17% experiencing unfavorable outcomes<sup>(13)</sup>. By contrast, only 3.0% of patients < 15 years who initiated directly observed therapy discontinued treatment<sup>(14)</sup>.

The treatment of tuberculosis requires sustained adherence to a prolonged, multidrug regimen. Health services should tailor age-appropriate interventions that address the specific needs of children and adolescents. Adolescent-centered strategies can improve outcomes in this group<sup>(6)</sup>. Monitoring and adherence-support tools — such as mobile text reminders, digital pillboxes, and video-observed therapy — are

promising options, particularly given the digital context in which many young people live<sup>(15)</sup>.

This study also documented higher loss to follow-up proportions from 2020 to 2022, likely reflecting the impact of the COVID-19 pandemic. Globally, increases in treatment failure and mortality during this period were observed<sup>(16)</sup>. The reallocation of human and material resources to meet COVID-19 demands disrupted tuberculosis case follow-up. During the pandemic, programs reported fewer monthly follow-up smears, reduced use of directly observed therapy, constrained drug supply, difficulties tracing defaulters, and weakened patient–provider bonds. Patients faced additional challenges, including financial constraints, mobility restrictions due to social distancing, and fear of infection — all of which may have impeded progress toward tuberculosis control targets<sup>(17)</sup>.

Evidence on factors associated with treatment abandonment in pediatric and adolescent tuberculosis remains limited. Because minors depend on parents or guardians, treatment success is closely linked to family engagement. Caregiver-focused education and counseling are therefore essential to promote adherence. Notably, a key barrier to pediatric tuberculosis treatment is caregivers' limited awareness of the disease and its risks<sup>(6,18)</sup>.

HIV test non-performance was associated with treatment discontinuation among children and adolescents with tuberculosis. Testing is offered free of charge in Family Health Strategy units and Counseling and Testing Centers. Prior studies across different age groups have likewise reported associations between not undergoing HIV testing and unfavorable treatment outcomes<sup>(19-20)</sup>. In addition, failure to perform chest radiography was associated with treatment interruption, consistent with findings from a city in the Amazon region<sup>(21)</sup>.

HIV testing and chest radiography are recommended follow-up examinations during tuberculosis treatment in children and adolescents<sup>(2)</sup>. Non-performance of these tests indicates gaps in patient follow-up and deficiencies in care. Beyond limiting diagnos-

tic accuracy and treatment monitoring, the lack or unavailability of HIV testing and chest radiography may indirectly contribute to abandonment by undermining the continuity and perceived integrity of care, thereby reducing motivation to adhere to treatment<sup>(22)</sup>.

directly observed treatment entails supervised ingestion of medications, preferably on all weekdays, conducted by health professionals or trained personnel under their guidance. Directly observed treatment applies to all tuberculosis patients and offers opportunities to strengthen bonds between the health team, patients, and families, as well as to identify early factors that compromise adherence<sup>(11)</sup>. In this context, the Family Health Strategy has functioned as a facilitator of directly observed treatment, with positive impacts on disease control and higher probabilities of favorable outcomes<sup>(23)</sup>.

In the present cohort, a higher proportion of loss to follow-up occurred among those who did not receive directly observed treatment. In Brazil, evidence suggests that unsupervised treatment is a significant risk factor for abandonment<sup>(24)</sup>. Conversely, directly observed treatment delivered by trained health professionals is associated with better therapeutic outcomes. Skilled providers and patient-centered care models can improve adherence and increase the likelihood of treatment success<sup>(25)</sup>.

Barriers to directly observed treatment adherence are linked primarily to limited understanding of its importance and to unfavorable socioeconomic conditions that impede access to health services. On the provider side, workload and structural constraints may hinder systematic implementation of directly observed treatment-supporting actions<sup>(26)</sup>. Building shared responsibility between health services and users is a key strategy to improve tuberculosis outcomes. Full decentralization of care to primary health care, supported by matrix-based collaboration that involves specialists and surveillance teams, could strengthen decentralized management of patients with tuberculosis<sup>(27-28)</sup>.

Although professional supervision via directly

observed treatment is essential, major challenges to follow-up frequently arise from family and psychosocial contexts — such as poverty, food insecurity, undernutrition, and difficulties organizing caregivers' routines. These factors weaken adherence even when professional support is available, indicating that discontinuation cannot be attributed solely to the health team<sup>(29)</sup>. Intersectoral strategies that support families are therefore needed to mitigate social barriers and facilitate treatment completion.

Underreporting of contacts can impair epidemiologic surveillance, adherence, and the interruption of tuberculosis transmission. Contact tracing is associated with higher treatment success and a > 60% reduction in the odds of loss to follow-up. By engaging household and social contacts, contact tracing also increases social support for the index case — potentially strengthening ties between health services and families and contributing to treatment success<sup>(30)</sup>.

## Study limitations

This study has limitations inherent to the use of secondary data from the national notifiable diseases system. The analyses are subject to incomplete records, underreporting, and potential data-entry errors. Additional constraints include reliance on the information available in SINAN and the lack of more recent data for 2023 and 2024. Analyses with updated datasets are needed to provide more consistent, contextually accurate assessments. These issues may affect the precision of our estimates and the understanding of determinants of treatment adherence in tuberculosis. Despite these constraints, the study offers valuable insights into factors influencing therapeutic success among children and adolescents in Mato Grosso.

## Contributions to practice

Findings highlight the need to strengthen diagnostic and follow-up routines for tuberculosis within primary and secondary care, ensuring broader co-

verage of key examinations such as HIV testing and chest radiography. Sensitization and training of health professionals should emphasize the systematic use of these tests to prevent diagnostic delays and support treatment success. The results also underscore the importance of directly observed treatment, coupled with strategies that leverage digital tools — e.g., messaging applications, telemonitoring, video-observed therapy, automated defaulter alerts, and electronic scheduling for medication dispensing. More effective contact surveillance policies are likewise needed to ensure adequate tracing and follow-up, interrupt transmission chains, and reduce treatment discontinuation. Finally, the findings reinforce the need for public policies tailored to the specific needs of children and adolescents and for improvements in the quality of information systems, which are essential for planning and evaluating tuberculosis control actions.

## Conclusion

Loss to follow-up among children and adolescents with tuberculosis was associated with health service-related factors, including not undergoing chest radiography, not undergoing HIV testing, and not receiving directly observed treatment. These results point to the need to expand access to diagnostic and follow-up services for individuals aged 0–19 years and to strengthen the bond between health teams and parents/guardians of pediatric and adolescent patients, thereby supporting therapeutic success.

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## Authors' contributions

Data analysis and interpretation, manuscript drafting, and final approval: Melo LFL. Data analy-

sis and interpretation, final approval: Peixoto TS, Olinda RA. Critical revision for important intellectual content and final approval: Oliveira JCS, Silva JPN. Conception and design; data analysis and interpretation; critical revision for important intellectual content; final approval of the version to be published; agreement to be accountable for all aspects of the work related to accuracy: Goulart LS.

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