

## Abandonment of tuberculosis treatment: an integrative review

## Abandono do tratamento da tuberculose: uma revisão integrativa

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**RESUMO | INTRODUÇÃO:** O abandono do tratamento da tuberculose (TB) auxilia no ciclo de propagação e contágio da doença, aumento dos custos, resistência medicamentosa e da morbimortalidade. Desta forma, este estudo buscou descrever os fatores de risco para o paciente de TB abandonar o tratamento, segundo a literatura nacional e internacional. **METODOLOGIA:** Trata-se de uma revisão integrativa da literatura, realizada nas bases de dados da Literatura Latino-Americana e do Caribe em Ciências da Saúde (LILACS) e Literatura Internacional em Ciências da Saúde (MEDLINE), a partir dos artigos científicos completos, publicados no período entre 2007 a 2017, em open access, nos idiomas português, inglês e espanhol, bem como aqueles que abordassem nos resultados os fatores de risco para o abandono ao tratamento da TB. **RESULTADOS:** Foram encontrados 145 artigos científicos, dos quais 125 foram excluídos por não atenderem os critérios previamente estabelecidos, totalizando 20 artigos científicos para serem lidos e analisados na íntegra. Verificou-se que os aspectos sociodemográficos (uso de drogas, idade, sexo masculino, baixa escolaridade e renda, área rural, acessibilidade e estigma da doença), clínicos (coinfecção TB/HIV, abandono prévio, forma clínica extrapulmonar, comorbidades) e do tratamento (fase inicial da terapia, efeitos adversos, melhora sintomática) contribuem para o abandono do tratamento. **CONCLUSÃO:** Esta revisão aponta a necessidade de identificar precocemente os pacientes de TB vulneráveis ao desfecho, para então, utilizar as estratégias disponíveis, a exemplo do tratamento diretamente observado, visando garantir a adesão e, consequentemente, a cura.

**DESCRITORES:** Tuberculose; Pacientes Desistentes do Tratamento; Fatores de Risco; Adesão à Medicação.

**ABSTRACT | INTRODUCTION:** The abandonment of tuberculosis (TB) treatment assists in the spread and infection of the disease, increasing costs, drug resistance and morbidity and mortality. In this way, this study sought to describe the risk factors for TB patient to abandon the treatment, according to the national and international literature. **METHODOLOGY:** It is an integrative literature review, held in the databases of the Latin American literature and Caribbean Health Sciences (LILACS) and International Health Sciences Literature (MEDLINE), from scientific articles, published in the period from 2007 to 2017, in open access, in the languages Portuguese, English and Spanish, as well as those who approached the results to the risk factors for the abandonment to the treatment of TB. **RESULTS:** 145 scientific papers were found, of which 125 were excluded because they did not meet the previously established criteria, totaling 20 scientific articles to be read and analyzed in their entirety. The socio-demographic aspects (drug use, age, male sex, low schooling and income, rural area, accessibility and stigma of disease), clinical (TB / HIV co-infection, previous abandonment, extra pulmonary clinical form, comorbidities) and treatment (initial phase of therapy, adverse effects, symptomatic improvement) contribute to treatment withdrawal. **CONCLUSION:** This review points out the need to identify early TB patients vulnerable to closure, for then, use the strategies available, directly observed treatment, aiming to ensure adherence and, consequently, the cure.

**DESCRIPTORS:** Tuberculosis. Patient Dropouts. Risk Factors. Medication Adherence.

## Introduction

Tuberculosis (TB) is a worldwide disease and a serious public health problem, with approximately 10,4 million new TB cases reported in 2015, causing 1,8 million deaths worldwide, especially in underdeveloped countries, overcoming HIV and malaria together<sup>1</sup>.

Social vulnerabilities, TB/HIV co-infection and drug resistance further aggravate this scenario, increasing the incidence coefficient and the probability of unfavorable outcomes<sup>2</sup>, such as the abandonment of TB treatment, assists in the spread and infection of the disease, increasing costs, drug resistance and morbidity and mortality<sup>3</sup>.

In Brazil, it is estimated that by 2035, 7.092 TB deaths would be avoided due to the progressive decrease in treatment abandonment<sup>2</sup>. However, what was observed in the year 2015 is that the disease remains with unfavorable outcomes, with a low cure rate (74,2%) and high for abandonment (11%), which are below the goals recommended by the World Health Organization (WHO), of at least 85% and up to 5%, respectively<sup>2</sup>.

In addition, the country is part of a group of 30 countries responsible for 80% of the burden of TB in the world<sup>1</sup>, registering in 2015, 69 thousand new cases of the disease with an incidence rate stipulated in 34,2 cases/100 thousand inhabitants, showing that the country still has not been able to reach the goals set by the WHO as a policy until 2035 (less than 10 cases of TB/100 thousand inhabitants)<sup>2</sup>.

Therefore, in order to guarantee adherence to treatment and control of the disease, the WHO has developed the Directly Observed Treatment Short-Course (DOTS) strategy, one of the pillars being Directly Observed Treatment (DOT)<sup>4</sup>. However, the difficulty of access and organization of the health services, as well as the lack of co-responsibility of the professionals for early detection of the cases, directly influence the delay of diagnosis and initiation of the treatment, contributing to nonadherence.

In this way, identifying the profile of TB patients vulnerable to abandonment and the factors that can trigger such an outcome becomes an essential tool for the establishment of actions and strategies involving

the management, organization of health services and professionals, aiming at adherence and disease control. Therefore, this study sought to describe the risk factors for TB patient to abandon the treatment, according to the national and international literature.

## Methodology

It is an integrative literature review, conducted in July 2017, based on the guiding question: what are the risk factors for the TB patient to abandon treatment?

The survey was held in the databases of the Latin American literature and Caribbean Health Sciences (LILACS) and International Health Sciences Literature (MEDLINE), according to the descriptors indexed in the Medical Subject Headings (MESH): "Tuberculosis", "Risk Factors", "Patient Dropouts" and "Medication Adherence".

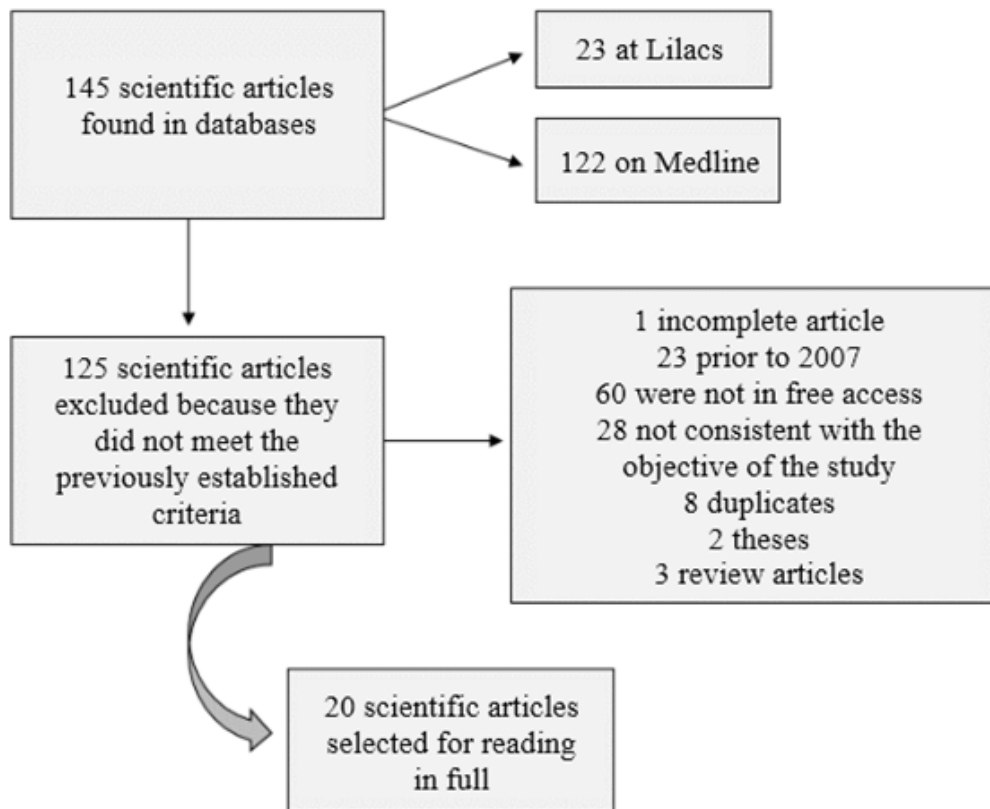
For the bibliographic search, we used the combination of descriptors through the booleans AND and OR. Thus, the expressions used were (Tuberculosis) AND ("Risk Factors") AND ("Medication Adherence"), as well as (Tuberculosis) AND ("Risk Factors") AND ("Patient Dropouts").

The inclusion criteria for this study were complete scientific articles, published in the period from 2007 to 2017, in open access, in the languages Portuguese, English and Spanish, as well as those who approached the results to the risk factors for the abandonment to the treatment of TB. Duplicate articles, theses, dissertations, monographs, editorials, review articles, letters and manuals were excluded.

## Results

From the data base search, 145 scientific papers were found, of which 23 were available in Lilacs and 122 in Medline. Of these, 125 were excluded because they did not meet the previously established criteria, of which 1 was not a complete article, 23 were prior to the previously selected period, 60 were not available for free access, 28 did not present relevant results for the purpose of this review, since the focus of the study was antiretroviral treatment or therapy, epidemiology, diagnosis, multiresistance, latent tuberculosis infection, death, immigrants, spatial distribution and technological support. In addition, 8 were duplicates, 2 were theses and 3 review articles. Therefore, 20 scientific papers<sup>3,5-23</sup> were selected to be read and analyzed in full (Figure 1).

Figure 1. Stages of the article selection process for the integrative review of the literature of this study



Most articles were in English (60%), published in 2013 (25%) and produced in the international scene (60%). In Brazil, studies were carried out in the states of Maranhão<sup>3</sup>, Rio de Janeiro<sup>5</sup>, Rio Grande do Sul<sup>6</sup>, Paraná<sup>7</sup>, Pernambuco<sup>8</sup> and Minas Gerais<sup>9</sup>. Besides that, multicentric studies were conducted in distinct Brazilian municipalities (Manaus and Fortaleza<sup>10</sup>), and in border countries (Brazil, Colombia, Peru and Venezuela<sup>11</sup>). Regarding the type of study, were done predominantly case-control studies in 8 scientific articles (Table 1).

**Table 1.** Distribution of the articles of this review by year of publication, country, language and type of study carried out

Year of Publication	Country	Language	Type of study
2016	Korea	English	Case-control <sup>12</sup>
2016	Ethiopia	English	Cross-sectional <sup>13</sup>
2016	Peru	Spanish	Retrospective case-control <sup>14</sup>
2015	Argentina	English	Cross-sectional <sup>15</sup>
2015	South Africa	English	Cross-sectional <sup>16</sup>
2015	Ethiopia	English	Case-control <sup>17</sup>
2014	Brazil	Portuguese	Cross-sectional analytical <sup>3</sup>
2013	Brazil	Portuguese	Cross-sectional <sup>11</sup>
2013	South Africa	English	Cross-sectional <sup>18</sup>
2013	United States	English	Case series <sup>19</sup>
2013	United States	English	Case-control <sup>20</sup>
2013	Republic of Moldova	English	Retrospective Cohort <sup>21</sup>
2012	Brazil	Portuguese	Case-control <sup>10</sup>
2012	Brazil	Portuguese	Cohort <sup>5</sup>
2012	Nigeria	English	Retrospective Cohort <sup>22</sup>
2011	Brazil	Portuguese	Case-control <sup>6</sup>
2011	Kenya	English	Case-control <sup>23</sup>
2010	Brazil	Portuguese	Cross-sectional <sup>7</sup>
2007	Brazil	English	Cohort <sup>8</sup>
2007	Brazil	Portuguese	Case-control <sup>9</sup>

With regard to the risk factors for abandonment, sociodemographic, clinical and treatment aspects were identified.

As for sociodemographic, most of the TB patients used licit and/or illicit drugs (55%), were young adults (5%), men (30%), low schooling (30%), low income (25%), living in rural areas (15%), with no understanding of the disease (15%), with difficulties in accessing health services, illiterate, without fixed housing and with stigma on the disease (10%) (Table 2).

In addition, in terms of clinical aspects, the majority of those who discontinued treatment were co-infected with TB/HIV (35%), with a history of previous abandonment or reentry after abandonment (25%), extrapulmonary clinical form (15%), positive sputum cultures after 2 months of treatment and presence of comorbidities (10%) (Table 2).

And for treatment-related factors, the first 3 months of therapy (30%), adverse drug effects (20%), improvement of clinical signs and symptoms, hospital treatment and drug treatment regimen (10%) contributed to the abandonment (Table 2).

**Table 2.** Identification of the risk factors that influenced the abandonment of tuberculosis treatment, according to the literature review in LILACS and MEDLINE, from 2007 to 2017

Risk factors		Number of articles
<b>SOCIODEMOGRAPHIC FACTORS</b>	Use of licit and/or illicit drugs	11
	Age	10
	Male	6
	Low education level	6
	Low income or economy class	5
	Residence in rural area	3
	Lack of TB information	3
	Access to health services	2
	Illiteracy	2
	Lack of fixed housing or homeless	2
	Stigma of disease	2
	Others*	10
<b>CLINICAL FACTORS</b>	TB/ HIV Coinfection	7
	History of previous abandonment or re-entry after abandonment	5
	Extrapulmonary TB	3
	Positive cultures after 2 months of therapy	2
	Comorbidities	2
	Others*	7
<b>TREATMENT FACTORS</b>	Initial treatment phase	6
	Adverse drug effects	4
	Improvement of clinical symptoms	2
	Hospital treatment	2
	Treatment regimen	2
	Others*	7

\* Other - risk factors for treatment abandonment that were cited only once. Sociodemographic (non-white ethnicity, mental illness, unemployment, inadequate food, not living with family members, living alone, lack of basic sanitation, head of household does not have health insurance, no license to perform examinations, incarcerated); clinical (Multidrug-resistant TB, pre-treatment, medical reasons, cavitory disease, HIV-positive partner, extensive lung injury, negative smear at the start of treatment, no follow-up smear microscopy in the second, fourth and sixth month) and treatment (low psychological evaluation, use of herbal medicines, treatment by a non-pulmonologist, organization of health services, double therapy, lack of contact person).

## Discussion

### Socio-demographic predictors for the abandonment

The use of licit and/or illicit drugs was the most mentioned. Alcoholism is cited in several literatures as a classic factor for the negative outcomes of TB treatment<sup>6,8,23</sup>, in which its abuse implies forgetting medication intake and potentiating hepatotoxic effects<sup>23</sup>. In addition, the association of one or more

drugs with tobacco greatly increases the health risks<sup>18</sup> and, consequently, the treatment of the disease.

The age-related outcome reflects the proportion of young adults affected by TB who are normally alcoholic, do not feed adequately, do not accept the disease, have a relationship of conflicts with the professional<sup>3,6,7</sup>, as well as the presence of comorbidities<sup>13</sup>.

On the other hand, this factor deserves a watchful eye since it is a productive and working class that, when getting sick, lose their employment relationship or even die early<sup>3</sup>, which may reflect on the socioeconomic development of the place or country in which they reside<sup>13</sup>.

Besides that, age is associated with males, cited in several studies<sup>7,10,15,16,18,23</sup>, in which the demands of work and family responsibility make it difficult for patients to go to the health clinic and may lead to the interruption of medication or follow-up<sup>8,22</sup>.

Some authors have brought the combination between low schooling and low income as contributing factors for low adherence and frequent abandonment of treatment<sup>5,14</sup>. Thus, low socio-demographic level related to poverty, such as education and income, shows the social content of the disease<sup>6,7</sup>.

A study carried out in Recife shows that illiteracy generates weaknesses in terms of access to information, transportation costs to the health place and business day lost on the job<sup>8</sup>. Given this, health professionals should take special care during treatment with patients with low educational level or illiterates through link building, supervision and incentive to adherence<sup>7</sup>.

Still as far as to the low socioeconomic level, TB patients who abandon treatment do so by choosing priorities in the face of the few resources to meet their demands and meet basic needs, such as food and transportation<sup>23</sup>, economic restrictions as well as being in a favorable environment that does not bring positive health results<sup>18</sup>.

According to a study carried out in Belo Horizonte, unemployment is associated with the outcome due to the fact that the individual worries about their subsistence and postpones the demand for health care, unlike the employees who abandon treatment for fear of losing it<sup>9</sup>, which highlights the vulnerabilities to which TB patients are exposed.

Regarding the place of residence in rural areas, TB patients may have less knowledge regarding the treatment of the disease, which adds to the distance of their residences from the health center<sup>10,13</sup>, to the lack of orientation regarding the decentralization of assistance and implementation of the DOT<sup>9</sup>.

Thus, in order to reverse this scenario, the expansion of the Family Health Strategy coupled with the increase in DOT coverage, transfer of TB cases to the urban area<sup>10,22</sup>, provision of transportation vouchers for consultation may influence the reduction in treatment abandonment.

Factors associated with living conditions reveal that health is influenced by social inequality in the place of residence<sup>15</sup>. According to Bamrah and collaborators (2013), in a study carried out in the United States, cases of abandonment among TB patients who do not have fixed housing or who are homeless, suggest a local transmission with high bacillary load due to unhealthy conditions which are submitted, which facilitates the risk and transmission of the disease among this highly mobile population<sup>19</sup>.

The lack of information about TB suggests the need for health professionals to have a pre-treatment health education, explanations about the disease, your treatment, side effects, and the importance of completing the treatment<sup>23</sup>, as the greater knowledge on TB increases the empowerment of patients and motivates them to adhere to treatment, making them co-responsible for the treatment of their illness<sup>9,12</sup>.

On the other hand, cultural and regional factors are associated with non-knowledge of the disease, such as attributing similarity to HIV/aids, which contributes to TB stigma<sup>23</sup>. Because of this, some TB patients prefer to perform the treatment in a place far from their home<sup>9</sup>, contributing to the outcome of the abandonment.

Mental illness contributes to abandonment because, faced with a chronic condition, such as TB, it needs special care against the answers of people in the social and family group, from the daily difficulties in patient care to the lack of knowledge of the disease<sup>3</sup>.

### **The abandonment of treatment associated with clinical factors**

TB/HIV co-infection was responsible for 11% of all TB cases in the world in 2015<sup>1</sup>, which corroborates the findings of this review that brings it as the most cited among the clinical risk factors. A study conducted by Muture and collaborators (2011) in Kenya, shows that 54,9% of the patients were co-



infected with TB/HIV, which made them have higher transportation costs because they had to attend separate clinics for the treatment of both diseases<sup>23</sup>.

Concomitant to this, the increase in the side effects and loading of drugs for dual treatment<sup>18,22</sup>, impacts the daily life of these patients who have demands associated with work and family<sup>18</sup>, forming a double challenge that can contribute to the unfavorable prognosis and outcome of the disease<sup>6,17</sup>.

Thus, the planning of actions with TB/HIV coinfecting patients, health education and surveillance actions may help in monitoring and treatment<sup>8</sup>, in addition to avoiding the mortality of these cases<sup>5</sup>.

The history of previous abandonment or reentry after abandonment is important to detect the risk of a new episode of abandonment<sup>12</sup>. A multicenter study conducted in countries bordering Brazil states, that such individuals are 3 times more likely to not complete treatment<sup>11</sup>, which suggests the importance of completing primary treatment with adequate follow-up and support<sup>8</sup>.

Due to a tendency to treat the extrapulmonary clinical form for more than 12 months<sup>20</sup>, the diagnosis is invasive, there is a low probability of bacillus culture and clinical evaluation is uncertain<sup>12</sup>, the abandonment related to these extrapulmonary cases, suggests a delay in diagnosis and treatment, which makes it possible for the disease to become more severe and, thus, cure is more difficult to achieve<sup>8,13</sup>.

Treatment abandonment is associated with an increase in drug resistance rates<sup>16</sup>, not only because the treatment needs to be longer, but also because of the side effects of more toxic drugs and, in some cases, the lack of clinical improvement<sup>21</sup>, which increases the risk of transmission between people living and working close to these TB patients<sup>18</sup>.

The smears of monthly control are used to follow up the cases and to reduce the outcome of the abandonment by up to 12 times<sup>11</sup>, as a result, it allows the monitoring of the case by the health professional.

In this sense, positive sputum cultures after 2 months of treatment<sup>20</sup> are questioned on how the follow-up of

these cases it is done, considering that antituberculosis medications cause negative responses if continuous treatment is performed<sup>17</sup>.

### **The treatment as a risk factor for abandonment**

The initial phase of the treatment corresponds to the event of a rapid symptomatic improvement<sup>12</sup> because the drugs rapidly reduce the bacillary charge<sup>23</sup>. In this sense, TB patients abandon treatment because they feel they are cured by the improvement of signs and symptoms<sup>3,6,22</sup>, together with a lack of information about this event<sup>23</sup>.

In view of this, health professionals should promote guidance regarding this initial phase of treatment through health education, and supervise the cases with potential risk of abandonment through the support of the multiprofessional team<sup>22</sup>.

According to Orofino and collaborators (2012), in a study carried out in Rio de Janeiro, the number of drugs used, in some cases, is a consequence of the abandonment, since some TB patients are in retreatment because they have abandoned other times<sup>5</sup>, which contributes to increase the probability of cases related to drug resistance.

In addition, this fact may be due to side effects, a factor cited in some studies<sup>9,12,20,23</sup>, which suggests a reevaluation of new drugs that are more effective and less toxic<sup>20</sup>.

Supervision of medication intake and monitoring of cases until cure is one of the proposals of the DOT<sup>4</sup>. Because of this, studies show that this targets stipulated by the WHO, assists in the adherence and success of the treatment<sup>13,17,20</sup>. However, in a study in South Africa, even TB patients were followed up with DOT, the dropout rate was high (30%), which suggests that other factors are associated with the outcome<sup>16</sup>, such as the fragility of the link and reception between professional-user-family.

Thus, knowing the risk factors helps in a positive and constructive way in the disease control programs and in the development of strategies for TB patients with a higher risk of abandonment<sup>19</sup>.

## Conclusions

This study allowed to identify sociodemographic, clinical and treatment factors that, associated or not, contribute to an unfavorable outcome, such as treatment abandonment.

In this sense, there has been a lack of national studies that address the issue, which reveals a gap in scientific production in underdeveloped places that bring TB as a real epidemic. Faced with this, knowing the risk factors for abandonment at the national level becomes a challenge for the control of the disease in the country.

This review points out the need to identify early TB patients vulnerable to the outcome, for then, use the strategies available, such as DOT, aiming to ensure adherence and, consequently, the cure.

## Acknowledgements

We are grateful to the Center for Study and Research in Collective Health (CEPESCO) of the Federal University of Rondônia (UNIR) and the National Scientific and Technological Development Council (CNPq) for the financing of a scientific initiation grant (PIBIC 2016-2017).

## Author contributions

MRL Ferreira worked on the design, analysis and interpretation of results, article writing and critical review. RO Bonfim, TC Siqueira and NH Orfão contributed to the writing of the article. All authors approved the final written version to be published.

## Competing interests

No financial, legal or political competing interests with third parties (government, commercial, private foundation, etc.) were disclosed for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc.).

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