

## CHALLENGES TO TUBERCULOSIS TREATMENT ADHERENCE AMONG PEOPLE WHO USE ALCOHOL AND TOBACCO: A LITERATURE REVIEW

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**Highlights:** (1) Social, clinical, and behavioral factors influence adherence to tuberculosis treatment. (2) Limited access to directly observed therapy compromises continuity of tuberculosis treatment. (3) Psychosocial support is essential to improving treatment adherence in both populations.

PRE-PROOF

(as accepted)

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### ABSTRACT

**Objective:** To analyze the challenges to tuberculosis (TB) treatment adherence among people who use alcohol and tobacco. **Method:** An integrative literature review was conducted based on a guiding question formulated using the PVO framework to develop the search strategy. The descriptors “Tuberculosis,” “Alcoholics,” “Smokers,” “Treatment Adherence and Compliance,” “Medication Adherence,” and “Treatment Outcome,” as indexed in DeCS and MeSH, were used to search the PubMed, Scopus, Web of Science, and LILACS databases. Primary studies published between 2019 and 2024, available in full text and published in Portuguese, English, or Spanish, were included. **Results:** Among the 13 selected articles, factors associated with compromised TB treatment adherence, regardless of alcohol or tobacco use, included working age, male sex, Black race/skin color, low educational attainment, low income, TB/HIV coinfection, diabetes mellitus, illicit drug use, treatment re-entry following previous default, adverse drug reactions, homelessness, and the lack of provision of directly observed therapy. **Conclusion:** The findings indicate that socioeconomic, clinical, and behavioral conditions influence adherence to TB treatment, highlighting the need for strategies that address the specific characteristics of these populations, with the aim of interrupting the chain of transmission and controlling the disease.

**Keywords:** Tuberculosis; Alcoholics; Smokers; Medication Adherence; Treatment Outcome.

### INTRODUCTION

Tuberculosis (TB) is an airborne infectious disease caused by *Mycobacterium tuberculosis* and remains a major global public health problem.<sup>1</sup> In 2022, approximately 10.6 million people developed the disease worldwide, resulting in 1.3 million deaths, despite TB being preventable and treatable when diagnosed early and treatment adherence is ensured. Brazil ranks 16th among the 30 countries that collectively account for more than 80% of TB cases worldwide.<sup>2</sup> In the same year, the country reported 81,604 new cases and 5,845 deaths, corresponding to a mortality rate of 2.7 deaths per 100,000 inhabitants. This figure exceeds the target established by the World Health Organization (WHO) for 2035, which includes

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reducing TB incidence to fewer than 10 cases per 100,000 inhabitants and TB mortality by 95%.<sup>3</sup>

Treatment adherence is an essential component of disease control, as it directly affects treatment success, interruption of the chain of transmission, and prevention of unfavorable outcomes. Treatment adherence refers to patients' involvement in following therapeutic recommendations established in collaboration with healthcare professionals and depends on their active participation and integration of treatment into their daily routines.<sup>4</sup> However, several factors may compromise adherence, including the prolonged duration of treatment, adverse drug effects, difficulties in accessing healthcare services, and insufficient knowledge about the disease and its treatment.<sup>5</sup>

Given the importance of treatment adherence for therapeutic effectiveness, identifying factors that may compromise adherence is essential, particularly among populations at increased risk. In this regard, risk is defined as the likelihood that an individual will develop a disease, determined by a combination of biological, behavioral, social, and environmental factors that affect health.<sup>6</sup> For example, unfavorable socioeconomic conditions, when combined with alcohol use and tobacco smoking, increase susceptibility to TB and hinder treatment continuity, thereby compromising cure rates and increasing the risk of complications.<sup>7,8</sup>

In this context, people with a history of alcohol use disorder are considered a population at increased risk, as immunosuppression resulting from chronic alcohol consumption may impair the immune response to TB infection.<sup>9</sup> Excessive alcohol consumption is closely associated with challenges in TB control, increasing the likelihood of disease transmission, the risk of adverse drug reactions, and difficulties in treatment acceptance, ultimately contributing to higher mortality rates.<sup>10,11</sup>

Like alcohol, tobacco is a legal substance, which contributes to its widespread use among the population.<sup>12</sup> Exposure to tobacco smoke is a risk factor for latent TB infection and progression to active disease. Tobacco smoking is associated with a higher bacillary burden, an increased risk of disease reactivation, and a higher incidence of pulmonary cavitation.<sup>13,11</sup>

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Therefore, this study aimed to analyze the challenges to TB treatment adherence among people who use alcohol and tobacco.

### METHODS

This study is an integrative literature review, a research method that employs a comprehensive and systematic approach to searching for, appraising, and synthesizing available evidence on a specific topic.<sup>14</sup> Compared with other research methods, this approach is distinguished by its ability to incorporate experimental and quasi-experimental studies concurrently, thereby enabling a comprehensive understanding of the topic under investigation.<sup>15</sup> Furthermore, by bringing together and critically analyzing information from different sources, this approach seeks to summarize the current state of knowledge, identify gaps and inconsistencies in the literature, and highlight areas requiring further investigation. Thus, it contributes to the advancement of scientific knowledge across diverse fields.<sup>16</sup>

In this regard, the review method is structured into six distinct stages: (1) formulation of the research question; (2) selection of the databases; (3) definition of the inclusion and exclusion criteria; (4) database searching; (5) screening of the studies; and (6) appraisal and synthesis of the included studies.<sup>17</sup> Through these stages, the study sought to achieve a better understanding of the topic under investigation and provide a basis for the discussions presented herein.

Based on the foregoing, the following research question was formulated: **What are the main challenges faced by people who use alcohol and tobacco in adhering to TB treatment?** The question was developed using the PVO strategy (Table 1).<sup>18</sup>

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**Table 1.** PVO strategy used to formulate the research question for this integrative literature review, 2024.

| ACRONYM  | DEFINITION              | DESCRIPTION                          |
|----------|-------------------------|--------------------------------------|
| <b>P</b> | Problem to be addressed | Tuberculosis                         |
| <b>V</b> | Variables               | People who use alcohol and tobacco   |
| <b>O</b> | Outcome                 | Challenges in adherence to treatment |

**Source:** Prepared by the authors, 2024.

To formulate the search strategy, terms indexed in the Health Sciences Descriptors (DeCS) and the Medical Subject Headings (MeSH), along with their synonyms in Portuguese, English, and Spanish, were identified. These terms were combined using the Boolean operators AND and OR (Table 2).

The searches, conducted in April 2024, were performed in the PubMed, Scopus, and Web of Science databases through the journal portal of the Coordination for the Improvement of Higher Education Personnel (CAPES), using remote access via the Federated Academic Community (CAFe), with the search strategy in English. Subsequently, searches were conducted in Portuguese, English, and Spanish in the Latin American and Caribbean Literature on Health Sciences (LILACS), accessed through the Regional Portal of the Virtual Health Library (VHL). It should be noted that the searches were performed using the title, abstract, and subject descriptor/keyword fields (Table 2).

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**Table 2.** Search strategies according to the databases used, 2024.

| DATABASES                                               | SEARCH STRATEGY                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
|---------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>PubMed</b><br><b>Scopus</b><br><b>Web of Science</b> | (Tuberculosis OR "Infection, Mycobacterium tuberculosis" OR "Infections, Mycobacterium tuberculosis" OR "Koch Disease" OR "Koch's Disease" OR "Kochs Disease" OR "Mycobacterium tuberculosis Infection" OR "Mycobacterium tuberculosis Infections" OR Tuberculosis) AND (Alcoholics OR Alcoholic OR "Alcoholic, Skid Row" OR "Alcoholics, Skid Row" OR "Skid Row Alcoholic" OR "Skid Row Alcoholics" OR Smokers OR "Non-Tobacco Products Smoker" OR "Non-Tobacco Products Smokers" OR "Smoker" OR "Smoker, Non-Tobacco Products" OR "Smoker, Tobacco" OR "Smokers, Non Tobacco Products" OR "Smokers, Non-Tobacco Products" OR "Smokers, Tobacco" OR "Tobacco Smoker" OR "Tobacco Smokers" OR Vaper OR Vapers) AND ("Treatment Adherence and Compliance" OR "Adherence, Therapeutic" OR "Adherence, Treatment" OR "Therapeutic Adherence" OR "Therapeutic Adherence and Compliance" OR "Treatment Adherence" OR "Medication Adherence" OR "Adherence, Drug" OR "Adherence, Medication" OR "Compliance, Drug" OR "Compliance, Medication" OR "Drug Adherence" OR "Drug Compliance" OR "Medication Compliance" OR "Medication Non Adherence" OR "Medication Non Compliance" OR "Medication Nonadherence" OR "Medication Noncompliance" OR "Medication Persistence" OR "Non-Adherence, Medication" OR "Non-Compliance, Medication" OR "Nonadherence, Medication" OR "Noncompliance, Medication" OR "Persistence, Medication" OR "Treatment Outcome" OR "Clinical Effectiveness" OR "Clinical Efficacy" OR "Effectiveness, Clinical" OR "Effectiveness, Treatment" OR "Efficacy, Clinical" OR "Efficacy, Treatment" OR "Outcome, Patient-Relevant" OR "Outcome, Rehabilitation" OR "Outcome, Treatment" OR "Outcomes, Patient-Relevant" OR "Patient Relevant Outcome" OR "Patient-Relevant Outcome" OR "Patient-Relevant Outcomes" OR "Rehabilitation Outcome" OR "Treatment Effectiveness" OR "Treatment Efficacy") |
| <b>LILACS</b>                                           | (Tuberculose OR Tuberculosis OR "Infecção por Mycobacterium tuberculosis" OR "Pneumologia Sanitária" OR TB OR "Infection, Mycobacterium tuberculosis" OR "Infections, Mycobacterium tuberculosis" OR "Koch Disease" OR "Koch's Disease" OR "Kochs Disease" OR "Mycobacterium tuberculosis Infection" OR "Mycobacterium tuberculosis Infections" OR Tuberculosis OR "Infección por Mycobacterium tuberculosis") AND (Alcoólicos OR Alcoholics OR Alcohólicos OR Alcoolista OR Alcoolistas OR Alcoólatra OR Alcoólatras OR "Indigentes Alcoólicos" OR Alcoholic OR "Alcoholic, Skid Row" OR "Alcoholics, Skid Row" OR "Skid Row Alcoholic" OR "Skid Row Alcoholics" OR "Indigentes Alcohólicos" OR Fumantes OR Smokers OR Fumadores OR Fumante OR "Fumante de Tabaco" OR "Fumantes de Produtos sem Tabaco" OR "Fumantes de Tabaco" OR Tabagista OR Tabagistas OR Vapeador OR Vapeadores OR "Non-Tobacco Products Smoker" OR "Non-Tobacco Products Smokers" OR "Smoker" OR "Smoker, Non-Tobacco Products" OR "Smoker, Tobacco" OR "Smokers, Non Tobacco Products" OR "Smokers, Non-Tobacco Products" OR "Smokers, Tobacco" OR "Tobacco Smoker" OR "Tobacco Smokers" OR Vaper OR Vapers OR Fumador OR "Fumador de Tabaco" OR "Fumadores de Productos sin Tabaco" OR "Fumadores de Tabaco" OR Tabaquista OR Tabaquistas OR Vapeador OR Vapeadores) AND ("Cooperação e Adesão ao Tratamento" OR "Treatment Adherence and Compliance" OR "Cumplimiento y Adherencia al Tratamiento" OR "Aderência ao Tratamento" OR "Adesão ao Tratamento" OR "Adesão do Tratamento" OR "Adesão e Concordância com o Tratamento" OR "Adesão e Conformidade com o Tratamento" OR "Adesão e Cooperação com o Tratamento" OR "Adesão e Cumprimento do Tratamento" OR "Adesão e Cumprimento Terapêutico" OR "Adesão Terapêutica" OR "Adesão                                                                                                 |

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|--|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|  | <p>Terapêutica e Concordância" OR "Adesão Terapêutica e Cumprimento" OR "Concordância e Adesão ao Tratamento" OR "Conformidade e Adesão ao Tratamento" OR "Cooperação e Adesão Terapêutica" OR "Cumprimento e Adesão ao Tratamento" OR "Observância e Adesão ao Tratamento" OR "Submissão ao Tratamento" OR "Adherence, Therapeutic" OR "Adherence, Treatment" OR "Therapeutic Adherence" OR "Therapeutic Adherence and Compliance" OR "Treatment Adherence" OR "Adherencia al Tratamiento" OR "Adherencia Terapéutica" OR "Adherencia Terapéutica y Cumplimiento" OR "Adherencia y Cumplimiento del Tratamiento" OR "Adherencia y Cumplimiento Terapéutico" OR "Adhesión al Tratamiento" OR "Sometimiento al Tratamiento" OR "Adesão à Medicação" OR "Medication Adherence" OR "Cumplimiento de la Medicación" OR "Aderência à Medicação" OR "Aderência ao Medicamento" OR "Aderência ao Tratamento Medicamentoso" OR "Adesão ao Medicamento" OR "Adesão ao Tratamento Farmacológico" OR "Adesão ao Tratamento Medicamentoso" OR "Cumprimento do Tratamento Medicamentoso" OR "Duração do Tratamento Medicamentoso" OR "Falta de Aderência à Medicação" OR "Falta de Adesão à Medicação" OR "Falta de Adesão ao Medicamento" OR "Não Aderência à Medicação" OR "Não Aderência ao Medicamento" OR "Não Adesão à Medicação" OR "Não Adesão ao Medicamento" OR "Persistência da Medicação" OR "Submissão ao Medicamento" OR "Adherence, Drug" OR "Adherence, Medication" OR "Compliance, Drug" OR "Compliance, Medication" OR "Drug Adherence" OR "Drug Compliance" OR "Medication Compliance" OR "Medication Non Adherence" OR "Medication Non Compliance" OR "Medication Non-Adherence" OR "Medication Non-Compliance" OR "Medication Nonadherence" OR "Medication Noncompliance" OR "Medication Persistence" OR "Non-Adherence, Medication" OR "Non-Compliance, Medication" OR "Nonadherence, Medication" OR "Noncompliance, Medication" OR "Persistence, Medication" OR "Adherencia a los Medicamentos" OR "Adhesión a la Medicación" OR "Adhesión al Medicamento" OR "Adhesión al Tratamiento Farmacológico" OR "Cumplimiento de la Prescripción Medicamentosa" OR "Cumplimiento de Medicamentos" OR "No Adhesión al Tratamiento" OR "Sometimiento a la Prescripción de Medicamentos" OR "Resultado do Tratamento" OR "Treatment Outcome" OR "Resultado del Tratamiento" OR "Efetividade Clínica" OR "Efetividade de Tratamento" OR "Efetividade do Tratamento" OR "Eficácia Clínica" OR "Eficácia de Tratamento" OR "Eficácia do Tratamento" OR "Resultado da Reabilitação" OR "Resultado de Reabilitação" OR "Resultado de Tratamento" OR "Resultado Relevante ao Paciente" OR "Resultados da Promoção de Saúde" OR "Resultados de Intervenções em Saúde" OR "Resultados de Saúde" OR "Resultados Intermediários de Saúde" OR "Clinical Effectiveness" OR "Clinical Efficacy" OR "Effectiveness, Clinical" OR "Effectiveness, Treatment" OR "Efficacy, Clinical" OR "Efficacy, Treatment" OR "Outcome, Patient-Relevant" OR "Outcome, Rehabilitation" OR "Outcome, Treatment" OR "Outcomes, Patient-Relevant" OR "Patient Relevant Outcome" OR "Patient-Relevant Outcome" OR "Patient-Relevant Outcomes" OR "Rehabilitation Outcome" OR "Treatment Effectiveness" OR "Treatment Efficacy" OR "Efectividad Clínica" OR "Efectividad del Tratamiento" OR "Eficacia Clínica" OR "Eficacia del Tratamiento" OR "Rehabilitación Externa" OR "Resultado de la Rehabilitación" OR "Resultado Relevante al Paciente" OR "Resultado Relevante para el Paciente" OR "Resultados de Intervenciones en Salud" OR "Resultados de la Promoción de la Salud" OR "Resultados de Salud" OR "Resultados Intermedios de Salud")</p> |
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**Source:** Prepared by the authors, 2024.

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The inclusion criteria comprised primary studies available in full text, published between 2019 and 2024 in Portuguese, English, or Spanish. Review articles and publications belonging to the gray literature were excluded.

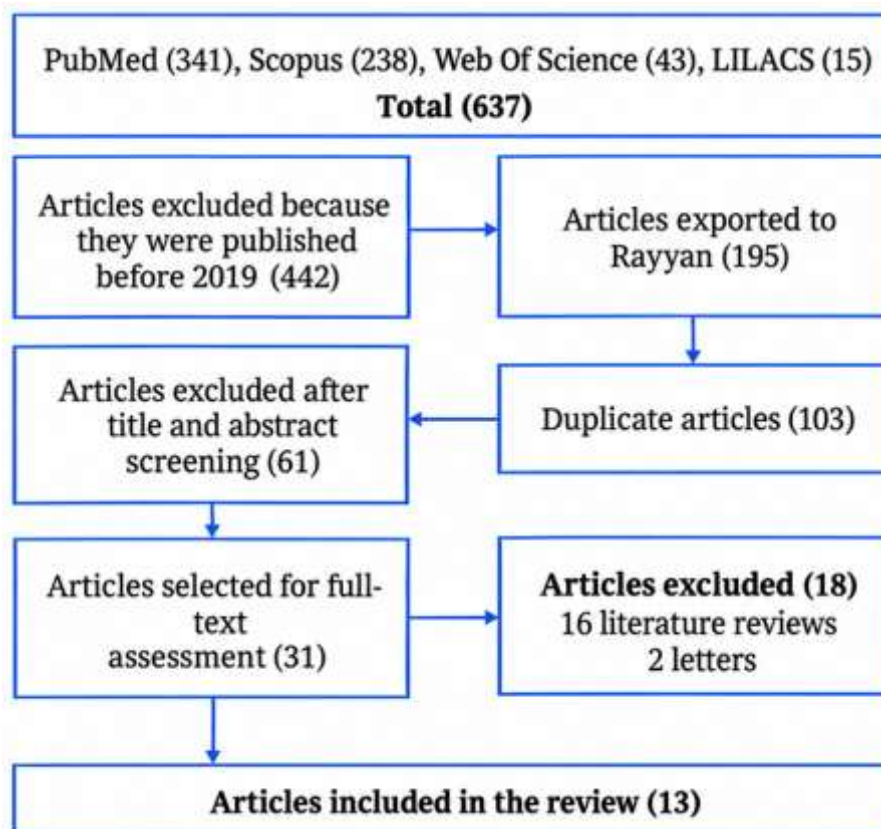
After the searches were conducted, the results were refined directly in the databases by applying the publication period filter. The remaining records were transferred to the Rayyan platform, developed by the Qatar Computing Research Institute (QCRI), where duplicate records were identified and removed. Subsequently, the remaining articles were independently assessed by two reviewers, who screened the titles and abstracts according to the eligibility criterion, namely, studies addressing challenges in adherence to TB treatment among people who use alcohol and tobacco. In cases of disagreement between the independent reviewers, a third reviewer was consulted to assist in resolving discrepancies. The selected articles were subsequently read in full.

### **RESULTS**

The database search yielded 637 articles. Of these, 442 were excluded at the database stage because they had been published before 2019. The remaining records were then exported to Rayyan, where 103 duplicate articles were identified and removed, and 61 were excluded because they addressed unrelated topics, such as human immunodeficiency virus (HIV), COVID-19, lung cancer, diabetes mellitus, rheumatoid arthritis, mucoepidermoid carcinoma, transplantation, hemoptysis, laryngitis, smoking cessation interventions, the reversed halo sign, and psoriasis. A total of 31 articles remained for full-text assessment. However, 16 of these were subsequently excluded because they were literature reviews, and two were letters to the editor, resulting in 13 articles included in this review (Figure 1).

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**Figure 1.** Flowchart of the articles selected for this integrative literature review, 2024.



**Source:** Prepared by the authors, 2024.

Most of the articles were published in English,<sup>19-29</sup> in 2021<sup>22-25</sup> and 2019,<sup>27-29,31</sup> with a cohort study design.<sup>19,20, 22,23,25,27,28</sup>

To present the findings of this review, a summary matrix was developed containing the following information: author(s), year of publication, study location, study design, objective, total number of participants, and main findings (Table 3).

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**Table 3.** Summary matrix of the articles selected for this integrative literature review, 2024.

| Authors/<br>Year                                               | Journal/<br>Country               | Objective                                                                                                                                               | Study Design               | Total Participants                                                                       | Main Findings                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                                 |
|----------------------------------------------------------------|-----------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------|------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                |                                   |                                                                                                                                                         |                            |                                                                                          | People who use alcohol                                                                                                                                                                                                                                                                                                                                                                                                                                | People who smoke                                                                                                                                                                                                                                                                                                                                                |
| Kaliner <i>et al.</i> (2023) <sup>19</sup>                     | Alcohol and Alcoholism/Israel     | To describe the demographic, clinical, and laboratory characteristics, as well as treatment outcomes, of patients with tuberculosis who use substances. | Retrospective Cohort Study | 150 patients with TB, divided into two groups: substance users (50) and non-users (100). | The study showed that patients with TB who used substances were predominantly male and young, were smokers, originated from the former Soviet Union, and were experiencing homelessness. They had no other chronic diseases, longer hospital stays, more prolonged treatment courses, higher rates of multidrug-resistant strains, a greater likelihood of treatment failure, and higher mortality compared with patients who did not use substances. |                                                                                                                                                                                                                                                                                                                                                                 |
| Nowiński; Wesolowski; Korzeniewska-Kosela (2023) <sup>20</sup> | Frontiers in Public Health/Poland | To investigate the impact of comorbidities on treatment outcomes and mortality rates among patients with TB in Poland.                                  | Retrospective Cohort Study | 19,217 patients with TB in Poland.                                                       | The study demonstrated that the presence of comorbidities, including alcohol use disorder, tobacco smoking, drug dependence, diabetes mellitus, HIV infection, immunosuppressive therapy, and cancer, increased the risk of loss to follow-up during TB treatment and was also associated with higher mortality rates.                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                 |
| Sharani <i>et al.</i> (2022) <sup>21</sup>                     | BMC Public Health/Malaysia        | To determine the factors associated with loss to follow-up among people who smoke and are undergoing TB treatment.                                      | Cross-Sectional Study      | 4,795 patients who smoked and had TB.                                                    | -                                                                                                                                                                                                                                                                                                                                                                                                                                                     | The main factors associated with loss to follow-up during TB treatment among people who smoke included being of working age (32–53 years), Malaysian nationality, residence in an urban area, low income, unemployment, low educational attainment, previous TB treatment, active case-finding, moderate lesions on chest radiography, and HIV-positive status. |

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|---------------------------------------------|-------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------|-------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---|
| Wekunda; Aduda; Guyah (2021) <sup>22</sup>  | Plos One/Kenya                                        | To identify and describe predictors of tuberculosis (TB) treatment interruption.                                                                                                           | Cohort Study                                                   | 291 patients with TB.   | Among the predictors of TB treatment interruption identified in the study were a tendency to neglect medication intake, forgetfulness, adverse drug effects, potential interactions between alcohol and TB treatment, overcrowded and poorly ventilated environments, and a greater likelihood of contact with people with TB.                                                          | - |
| Lima <i>et al.</i> (2021) <sup>23</sup>     | Heliyon/ Brazil                                       | To characterize loss to follow-up during TB treatment using individual and ecological determinants of health and to identify the predictive capacity of these risk factors.                | Cohort Study                                                   | 2,449 TB cases.         | The study revealed that being male, Black, aged 20–39 years, having 4–7 years of schooling, re-entry into treatment after previous default, alcohol, drug, or tobacco use, experiencing homelessness, living in municipalities with a high Human Development Index (HDI), and residing in areas with high income inequality were associated with loss to follow-up during TB treatment. |   |
| Plokhykh <i>et al.</i> (2021) <sup>24</sup> | Journal of Infection in Developing Countries/ Ukraine | To describe a cohort of patients with rifampicin-resistant tuberculosis (RR-TB) and high alcohol consumption treated under the Médecins Sans Frontières (MSF) Zhytomyr Project in Ukraine. | Uncontrolled longitudinal quasi-experimental descriptive study | 73 patients with RR-TB. | The study showed that patients who received the mental health intervention were classified as having hazardous or harmful alcohol consumption or alcohol dependence and had higher depression scores at baseline compared with the other groups. All patients experienced a reduction in depressive symptoms over the                                                                   | - |

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|                                           |                                |                                                                                                                     |                                 |                                                                                           | nine-month follow-up period, with culture conversion. |                                                                                                                                                                                                                                                  |
| Vargas <i>et al.</i> (2021) <sup>25</sup> | Rev. Assoc. Med. Bras./ Brazil | To assess the prevalence of tobacco smoking and its effects on treatment outcomes among patients with TB.           | Prospective Cohort Study        | 92 adult patients with pulmonary TB.                                                      | -                                                     | The study found that the prevalence of active smoking was 31.5%. Compared with non-active smokers, active smokers had a lower treatment success rate (62.1%) and a higher rate of loss to follow-up (31%).                                       |
| Khan <i>et al.</i> (2020) <sup>26</sup>   | BMC Public Health/ Malaysia    | To determine the prevalence of tobacco smoking and assess its effects on treatment outcomes among patients with TB. | Multicenter Retrospective Study | 9,337 patients with TB, divided into two groups: smokers (4,313) and non-smokers (5,024). | -                                                     | The study revealed a smoking prevalence of 46.2%. Most smokers completed their treatment, a finding like that observed among non-smokers. In addition, mortality, loss to follow-up, and treatment interruption rates were higher among smokers. |

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|---------------------------------------------------|------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------|---------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Espírito Santo <i>et al.</i> (2020) <sup>30</sup> | Revista de Enfermagem Referência /Brazil | To characterize the profile and psychoactive substance use patterns of patients undergoing TB treatment and to analyze the relationship between health-related variables, substance use, and treatment adherence from the perspective of Brief Intervention (BI). | Descriptive Correlational Epidemiological Study | 114 patients undergoing treatment for pulmonary and/or extrapulmonary TB. | Smokers who also consumed alcohol and those without chronic diseases had a greater need for BI. In addition, cannabis use was more prevalent among smokers. Regarding treatment adherence, a substantial proportion of patients reported tobacco use (40%), alcohol use (21.1%), cocaine use (13.7%), and cannabis use (10.5%).                    |
| Souza <i>et al.</i> (2019) <sup>31</sup>          | Rev. Gaúcha de Enf./Brazil               | To analyze factors associated with case outcomes and international border status among patients with TB and comorbidities.                                                                                                                                        | Exploratory Descriptive Epidemiological Study   | 227 TB cases with associated comorbidities.                               | The study showed that alcohol use disorder was the most frequent comorbidity among the cases analyzed and was associated with conditions of social deprivation and marginalization, as well as with increased susceptibility to TB and worsening of the clinical condition due to reduced immunity, malnutrition, and exposure to risk situations. |
| Gupta <i>et al.</i> (2019) <sup>27</sup>          | Indian Journal Of Community Health/India | To determine the effect of tobacco smoking on treatment outcomes among patients with TB at the end of six months of treatment.                                                                                                                                    | Prospective Cohort Study                        | 72 adult patients with TB.                                                | The study indicated that the prevalence of tobacco smoking was 37.5%, and the risk of unfavorable treatment outcomes was higher among smokers, users of smokeless tobacco, and individuals with a history of harmful alcohol use.                                                                                                                  |

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|-------------------------------------------|-----------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Thomas <i>et al.</i> (2019) <sup>28</sup> | Plos One/India                                                        | To assess the impact of tobacco smoking (never, former, and current smoking) and its combined effect with alcohol consumption on TB treatment outcomes in India. | Multicenter Prospective Cohort Study | 455 adult patients with pulmonary TB.                                                                                                                                                                                                    | The study demonstrated that the risk of treatment failure was higher among former smokers, the risk of TB recurrence was higher among current smokers, and the risk of death was higher among both groups. In addition, the combined effects of harmful alcohol use and tobacco smoking were associated with unfavorable treatment outcomes, particularly among former and current smokers. |
| Ma <i>et al.</i> (2019) <sup>29</sup>     | European Journal of Clinical Microbiology & Infectious Diseases/China | To investigate the combined effects of tobacco smoking and alcohol consumption on TB treatment outcomes.                                                         | Retrospective Study                  | 1,256 participants with TB, including: 76 current smokers and alcohol users, 325 former smokers and alcohol users, 366 current/former/never smokers and/or alcohol users, and 489 participants who had never smoked or consumed alcohol. | The study demonstrated that patients with TB who smoked and consumed alcohol were more likely to experience adverse drug reactions, had less improvement in pulmonary lesions, lower rates of culture conversion, and less favorable treatment outcomes compared with those without a history of tobacco smoking or alcohol consumption..                                                   |

**Source:** Prepared by the authors, 2024.

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Regarding the main findings reported across the studies, regardless of whether participants were people who used alcohol or tobacco, the factors identified as compromising adherence to TB treatment included working age,<sup>19,21,23</sup> male sex,<sup>19,23,25</sup> Black race/skin color,<sup>23</sup> low educational attainment,<sup>21,23</sup> low income,<sup>21,23</sup> TB/HIV coinfection,<sup>20,21,24</sup> diabetes mellitus,<sup>20,24</sup> illicit drug use,<sup>19,20,23,25,30</sup> re-entry into treatment after previous default,<sup>23</sup> adverse drug reactions,<sup>22,29</sup> homelessness,<sup>19,23</sup> and the lack of provision of directly observed therapy (DOT).<sup>21,22,31</sup>

### DISCUSSION

Regarding the sociodemographic characteristics identified in the studies, individuals who used alcohol and tobacco and experienced greater difficulties with treatment adherence were predominantly men of working age, with low educational attainment and low income.<sup>21-23,26,30</sup>

Loss to follow-up during TB treatment shows a clear disparity between sexes, with higher rates observed among men.<sup>26</sup> This discrepancy may be attributed to less consistent health-seeking behaviors and a higher prevalence of alcohol and tobacco use.<sup>22</sup> Conversely, the proportion of women who use alcohol and tobacco is poorly documented, possibly due to the social and cultural stigma associated with the use of these substances by women.<sup>22</sup> As such behavior often conflicts with socially established gender norms and expectations, many women may conceal or fail to report these habits, contributing to underreporting and hindering interpretation of the profile of TB cases.<sup>32</sup>

The age group most affected by loss to follow-up during TB treatment is 20–53 years,<sup>21-23</sup> corresponding to the economically productive population. Long working and study hours may limit access to healthcare services and adherence to treatment, increasing vulnerability to disease-related complications. Another barrier is the operating hours of healthcare services, which may overlap with work commitments, making access more difficult.<sup>33</sup> Furthermore, increasing age within this age group may adversely affect disease outcomes because of the higher prevalence of comorbidities, particularly when combined with alcohol and tobacco use, which may exacerbate disease progression and impair treatment effectiveness.<sup>23</sup>

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Low educational attainment is also a challenging factor for people who use alcohol and tobacco, as it may hinder their understanding of TB, the importance of treatment continuity, and the risks associated with treatment interruption, as well as their understanding of the interaction between these substances and the disease.<sup>21,30</sup> In addition, low educational attainment is associated with fewer employment opportunities, contributing to greater socioeconomic vulnerability.<sup>22</sup>

Patients with low income face challenges in accessing healthcare services because of indirect costs associated with treatment, such as transportation expenses, even when medications are government-subsidized, as is the case in Brazil.<sup>34</sup> Many patients work in informal or low-paying jobs, which puts them at risk of losing income when they need to take time away from work for medical appointments and treatment. This situation may lead some patients to discontinue treatment follow-up to support their families.<sup>21</sup>

Among the clinical conditions that affected treatment adherence in both populations, the most notable were diabetes mellitus, TB/HIV coinfection, illicit drug use, re-entry into treatment after previous default, adverse drug reactions, and homelessness.<sup>19-25,27-30</sup>

Regarding the presence of comorbidities such as diabetes mellitus and HIV infection in association with alcohol and tobacco use, studies indicate that these conditions are predictors of loss to follow-up during TB treatment, as they are associated with higher rates of treatment failure, disease recurrence, and mortality. This may be attributed to impaired immune function, a diminished response to TB treatment, drug-drug interactions, and adverse drug effects.<sup>20,21,24</sup>

Excessive alcohol consumption, as well as tobacco use, causes immunosuppression.<sup>27,30</sup> When combined with illicit drug use, the risk of unfavorable TB treatment outcomes increases considerably, as the use of these substances is associated with a reduced ability of alveolar macrophages to combat microorganisms<sup>19,26</sup> and a higher risk of liver injury, which may alter the pharmacokinetics of anti-TB drugs, resulting in reduced treatment effectiveness and favoring the emergence of antimicrobial-resistant strains.<sup>29</sup> Consequently, the need for hospitalization increases and treatment duration is prolonged.<sup>22,23</sup>

Re-entry into treatment after previous default is associated, according to the literature, with a higher likelihood of loss to follow-up during TB treatment due to the

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persistence or intensification of the factors that initially led the patient to discontinue treatment.<sup>23</sup> This may contribute to worsening signs and symptoms, particularly when associated with comorbidities such as alcohol use disorder and tobacco smoking.<sup>28</sup>

Patients experiencing homelessness are more likely to be lost to follow-up during TB treatment compared with the general population.<sup>35</sup> Excessive alcohol consumption may be used as a coping mechanism in response to adversities such as unstable housing conditions, limited access to healthcare, food insecurity, and insufficient financial resources.<sup>23</sup>

Additionally, low treatment adherence among people who smoke and are experiencing homelessness may be attributed to illicit drug use, unstable daily routines, and close contact with people with TB. These factors may contribute to reduced healthcare-seeking behavior, resulting in unfavorable treatment outcomes and challenges in disease management.<sup>21,36</sup>

Finally, regarding follow-up and treatment monitoring, the provision of directly observed therapy (DOT) was identified as a particularly relevant factor. Patients with TB who consume alcohol frequently fail to take their medications because they forget to do so while under the influence of alcohol.<sup>22</sup> Similarly, among patients who smoke, tobacco use may be prioritized over medication intake.<sup>21</sup>

In this regard, both populations were more likely to have poor treatment adherence when they were not receiving DOT, whether due to difficulties remembering to take their medication or attending follow-up appointments.<sup>21,22</sup> Additionally, the literature indicates that TB treatment outcomes are even less favorable in border areas because geographic factors hinder the implementation of DOT, particularly due to high population mobility.<sup>31</sup>

Thus, DOT emerges as an important tool for monitoring these populations, contributing to improved treatment adherence and reduced loss to follow-up.<sup>37</sup> In addition to facilitating supervision of medication intake, this approach promotes closer relationships between healthcare teams and patients, enabling the identification of factors that may compromise treatment continuity, such as alcohol and tobacco use.<sup>38</sup>

In light of the above, it is evident that the challenges faced by people who use alcohol and tobacco in adhering to TB treatment are multifaceted, extending beyond clinical aspects to encompass socioeconomic vulnerability.<sup>39</sup> Therefore, an integrated approach that includes

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social assistance and psychosocial support is needed to provide appropriate and effective care, achieve more favorable treatment outcomes, and ensure comprehensive healthcare.<sup>40</sup>

### **CONCLUSION**

The findings of this study indicated that, regardless of alcohol or tobacco use, factors that compromised adherence to TB treatment included male sex, being of economically productive age, Black race/skin color, low educational attainment, low income, TB/HIV coinfection, diabetes mellitus, illicit drug use, re-entry into treatment after previous default, adverse drug reactions, homelessness, and the lack of provision of directly observed therapy (DOT).

Considering these findings, it is essential to consider interventions that address the specific needs of these populations, including the promotion of support groups within Primary Health Care (PHC), which can provide support for alcohol and tobacco cessation. Health education campaigns emphasizing the importance of treatment continuity are also needed, as is improved access through the provision of directly observed therapy (DOT), an intervention associated with improved treatment adherence and reduced loss to follow-up.

As a limitation of this study, it is important to highlight the limited number of databases searched, as well as the lack of an assessment of the methodological quality of the studies included in this review. Furthermore, future studies are needed to elucidate the challenges faced by people who use alcohol and tobacco in adhering to TB treatment from their own perspectives, to inform targeted interventions for these populations and, consequently, achieve more favorable health outcomes.

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