Review

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Integrating narrative and bibliometric approaches to examine factors and impacts of tuberculosis treatment non-compliance

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ABSTRACT

Background: Tuberculosis (TB) treatment non-compliance remains a significant global public health issue, undermining disease control efforts and leading to adverse clinical and epidemiological outcomes. While considerable research has explored this issue, gaps remain in understanding the multifactorial influences on non-compliance, particularly its key factors and impacts, as well as the interconnections that exacerbate these challenges. This study integrates narrative and bibliometric approaches to critically synthesize and visualize factors contributing to TB treatment non-compliance and its impacts. By addressing research gaps, this study aims to provide a comprehensive framework for understanding the multifactorial challenges and proposing evidence-informed strategies to address clinical and epidemiological issues.

Methods: A systematic search of Scopus, EBSCO (Medline), ScienceDirect, and PubMed databases identified empirical studies published up to December 2024. Thematic synthesis categorized factors into overarching themes, while bibliometric analysis using VOSviewer software visualized factors and their interconnections.

Results: The review identified key factors such as poor tuberculosis knowledge, stigma, side effects, and economic constraints, interacting with demographic, psychological, and systemic barriers. Network visualization highlighted the interconnections among these factors, illustrating how they compound to exacerbate non-compliance. Clinical and epidemiological impacts include MDR/XDR-TB, prolonged treatment, and community transmission.

Conclusions: TB treatment non-compliance arises from a complex interplay of individual, socio-economic, and healthcare-related factors. This review emphasizes the importance of integrated narrative and bibliometric approaches to develop context-specific strategies for improving adherence, reducing the global TB burden, and guiding future research and policy.

Key words: Tuberculosis, Treatment non-compliance, Multidrug-resistant tuberculosis, Adherence

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Introduction

Tuberculosis (TB) remains one of the leading causes of mortality worldwide, exacerbated by treatment non-compliance, which undermines global efforts to control the disease [1]. Despite advancements in treatment protocols, adherence challenges persist, particularly in regions with limited resources [2–4]. Non-compliance not only prolongs the infectious period but also increases the likelihood of treatment failure, relapse, multidrug-resistant TB (MDR-TB), and extensively drug-resistant TB (XDR-TB) [5].

Existing literature highlights numerous factors influencing treatment adherence, including socio-demographic, behavioral, and systemic barriers [6]. A previous study emphasize the multifaceted nature of medication adherence among elderly TB patients, identifying individual, interpersonal, and organizational factors as critical for understanding adherence behaviors [7]. Similarly, other research provides an overview of risk factors associated with treatment lost to follow-up in developing countries, highlighting socio-economic determinants such as poverty, low education levels, and systemic healthcare challenges [8]. In addition, a systematic review with meta-analysis study, further elucidate predictive factors for treatment success, including younger age, non-drinking status, and early sputum smear conversion, underscoring the importance of timely intervention and patient support [9].

However, while these studies offer valuable insights, they highlight gaps in understanding region-specific adherence patterns, which refer to variations in treatment adherence shaped by local socio-economic conditions, cultural practices, and healthcare system structures. For example, economic barriers and limited accessibility to healthcare facilities are prevalent in low-income settings [2,10,11], whereas social vulnerabilities such as homelessness and drug abuse are more common in high-income contexts [12].

Given the multifactorial nature of TB treatment non-compliance, a narrative review integrated with bibliometric analysis is particularly well-suited for addressing this research problem [13]. By integrating diverse evidence, narrative reviews provide a holistic understanding of complex factors, while bibliometric analysis offers a data-driven perspective to visualize relationships and highlight interconnections. This study aims to synthesize existing evidence to identify key factors and analyze their impacts, highlighting research gaps and proposing evidence-informed strategies to reduce non-compliance and improve TB treatment outcomes.

Methods

Study design

This study employed a comprehensive narrative-bibliometric review design to critically synthesize evidence on key factors contributing to TB treatment non-compliance and its impacts [14]. Thematic synthesis was utilized to systematically analyze qualitative data from selected studies, focusing on identifying, organizing, and interpreting factors contributing to non-compliance and their clinical and epidemiological implications. Bibliometric analysis, conducted using VOSviewer software, visualized key factors and their interconnections, providing a quantitative perspective to enhance qualitative findings.

The integration of thematic synthesis and bibliometric analysis enabled a comprehensive understanding of TB treatment non-compliance. While thematic synthesis categorized qualitative insights into overarching themes, bibliometric analysis uncovered relationships and trends across the data. This dual-method approach addressed gaps in existing research, which often focus exclusively on either qualitative or quantitative dimensions, and provided actionable insights for clinical practice and policy development.

Data sources and search strategy

This study conducted a comprehensive search of relevant peer-reviewed literature using four major electronic databases: Scopus, EBSCO (Medline), ScienceDirect, and PubMed. These databases were selected for their extensive coverage of peer-reviewed literature in healthcare and biomedical sciences. The search aimed to retrieve studies that focused on non-compliance with TB treatment, exploring the key factors and impacts of this phenomenon. The search included articles

published up to December 2024, ensuring the inclusion of the most recent and relevant studies.

The SPIDER framework guided the review process to ensure a systematic approach [15]. The study sample focused on patients diagnosed with TB who exhibit non-compliance with treatment. The phenomenon of interest included key factors influencing non-compliance and impacts both clinically (e.g., drug resistance, health complications) and epidemiologically (e.g., disease spread, increased burden on healthcare systems). A combination of keywords and Boolean operators was used to ensure inclusivity and precision in the search. The search string used was: ("Tuberculosis" OR "TB") AND ("Non-compliance" OR "Non-adherence" OR "Treatment default") AND ("Factors" OR "Impacts").

The search process across the databases yielded 2,406 articles. After removing 42 duplicates and excluding 78 articles that were not properly recorded in the system, 2,286 articles remained. Titles and abstracts were screened, resulting in 170 articles relevant to factors contributing to non-compliance and its impacts. A full-text review narrowed this selection to 97 articles, which specifically analyzed factors and impacts of TB treatment non-compliance. Among these, 79 articles discussed factors, 9 articles focused on impacts, and 9 articles addressed both aspects (Figure 1).

The studies included diverse methodologies, such as cohort, case-control, cross-sectional, and qualitative studies, spanning multiple countries and regions. Participant demographics varied widely, with sample sizes ranging from small qualitative studies (e.g., 17 participants) to large-scale cohort studies (e.g., 46,818 participants; see Appendix 1 for details) [16–112].

Inclusion and exclusion criteria

The inclusion and exclusion criteria ensured that only relevant and high-quality studies were selected for this review. Studies were included if they focused on TB patients exhibiting non-compliance or non-adherence to treatment regimens. Eligible studies addressed factors influencing non-compliance and clinical or epidemiological impacts. Studies employing qualitative (e.g., interviews, focus group discussions), quantitative (e.g., surveys, statistical analysis), or mixed-methods designs were included. Only peer-reviewed articles published in English were considered.

Exclusion criteria were applied to exclude studies focusing solely on populations adhering to TB treatment, non-empirical studies (e.g., commentaries, editorials), and grey literature. Articles with incomplete data or insufficient details for thematic or bibliometric analysis were also excluded. These criteria ensured that the studies included aligned with the research objectives, provided empirical data, and contributed to a comprehensive understanding of TB treatment non-compliance.

Data extraction

Data extraction was conducted systematically to ensure the inclusion of all relevant information necessary for the thematic and bibliometric analyses. A standardized data extraction form was developed, capturing key details from each study, including the author(s), year of publication, study location, sample size, study design, key findings, and factors related to TB treatment non-compliance and their clinical or epidemiological impacts. Two independent reviewers performed the data extraction to enhance accuracy and minimize bias. Any discrepancies between the reviewers were resolved through discussion or consultation with a third reviewer. Extracted data were then organized into a structured database to facilitate thematic synthesis and bibliometric analysis.

Thematic synthesis

Thematic synthesis was conducted to systematically analyze the factors contributing to TB treatment non-compliance and its associated impacts [113]. The process followed three main steps: identifying factors, grouping them into sub-themes, and consolidating them into overarching themes. This structured approach ensured a systematic categorization of the data extracted from the included studies. In the first step, factors and impacts were identified from the included studies and documented systematically.

In the second step, the identified factors and impacts were grouped into sub-themes based on shared characteristics or commonalities. This grouping process facilitated the organization of data into manageable and

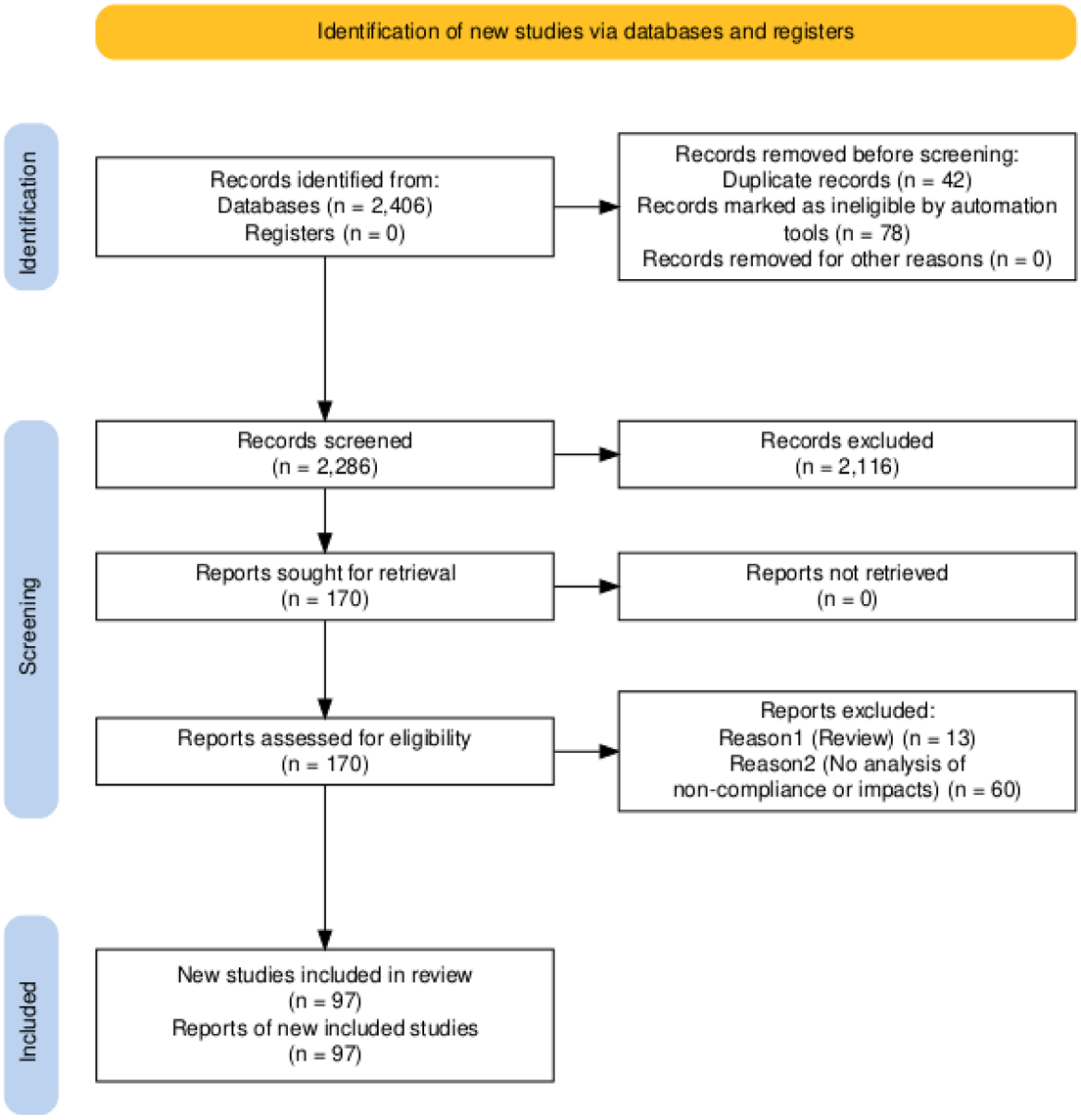

Figure 1. Flowchart of study identification, screening, and inclusion.

meaningful categories for further analysis, ensuring that all relevant aspects were captured comprehensively. In the final step, sub-themes were consolidated into overarching themes that reflect the multifactorial nature of TB treatment non-compliance and its impacts.

Bibliometric analysis

Bibliometric analysis was conducted to complement the thematic synthesis by providing a quantitative evaluation of the key factors, patterns, interconnections, and impacts associated with TB treatment non-compliance [114]. The process began by identifying variables related to factors and impacts of non-compliance, as determined during the thematic synthesis. These variables were then input into the metadata of the included articles as keywords for analysis.

The bibliometric analysis employed heatmap analysis and network visualization to examine co-occurrence patterns and relationships among the variables systematically. Data analysis was conducted using VOSviewer software, which facilitated the visualization of co-occurrence networks and intensity maps.

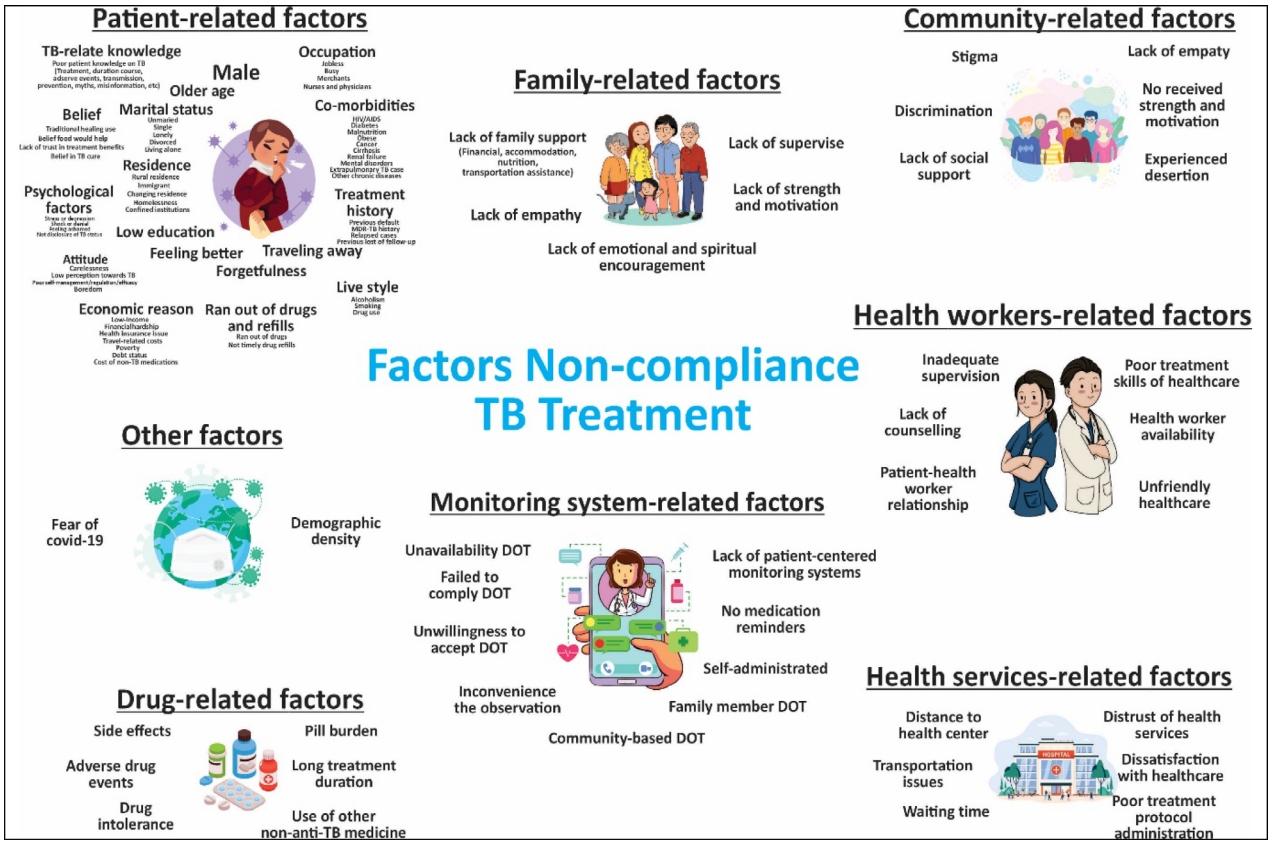

Figure 2. Thematic synthesis analyzes factors of non-compliance TB treatment.

These visualizations provided insights into the relationships and interconnections among the variables, illustrating their multifactorial nature in the context of TB treatment non-compliance.

Results and Discussion

Factors non-compliance TB treatment

The study identifies various factors contributing to non-compliance in TB treatment. Thematic analysis is categorized into patient-related, family and community-related, healthcare worker-related, health system-related factors, monitoring system, drug-related, and other factors (Figure 2).

Patient-related factors

Patient-related factors include demographics such as gender, marital status, and age play a pivotal role, with males [20,58,74,75,80,88,91,96,107], unmarried or divorced individuals [34,38,53,54,56,60], and older adults [25,36,37,39,42,43,48,58,64,66,71,74,80,91,96] more frequently exhibiting non-compliance. Residence status further contributes, as patients from rural areas [23,24,37,58,81–83], immigrants [54,56,60,99], nomads [24,95,100], or those homelessness [33,49,96] or living in confined institutions [54] face unique barriers. Educational attainment is another critical factor, with illiteracy or low education levels associated with poor adherence due to limited understanding of TB treatment protocols [23,24,28,35,42,56,58,63,80,86,90, 94–96,106,107,109]. Occupational constraints, including unemployment [25,47,65,66,69,78,89,100,107], overworking [34,51,57,60,73,91,111], or occupations with limited flexibility (e.g., merchants, healthcare workers) [43,67], also exacerbate non-compliance.

Economic factors, such as low-income levels [23,31,33,39,41,53,85,86,88,97,102], financial hardship [38,52,56,60,84,100,101,106,112], lack of health insurance [39,56,97,99], or travel-related costs

[51,57,62,75,108], significantly hinder treatment adherence. Poverty, food shortages [73,101], debt [34], and the costs of non-TB-related medications [62] further compound this challenge. Lifestyle factors, including alcoholism [19,22,26,31,33,44,49,62,65, 66,70,75,80,88,89,95,96,102,107,108,111], smoking [25,26,29,31,40,42,44,53,58,70,75,89,96,104,107], and drug use [33,49,54,65,96,106–108], are consistently linked to non-compliance, as they can interfere with both physical health and the ability to adhere to medication schedules.

Patients with a history of treatment abandonment [29,33,48,49,54,66,80,83,88,95], MDR-TB [59,82], relapsed cases [70], or previous lost to follow-up [108] are at a higher risk of non-compliance. Co-morbidities, such as HIV/AIDS [22,28,31,33,37,44,49,51,53, 54,64,74,80,83,88,96,110], diabetes [39,80,96], obesity [107], or malnutrition [48,64], cancer [110], renal failure [39], mental disorders [80], extrapulmonary TB case [37] and other chronic diseases [23,52,65,80,82,106,111], create additional barriers by increasing the complexity of treatment regimens. Poor TB-related knowledge, including misconceptions about the disease, its treatment, and prevention [17,19,22,26,27,29,34,42,47,51,53,62,66,69, 70,72,78,79,84–90,94,100,102,105,107, 108,111,112], as well as reliance on traditional [17,44, 72,73,82,88,95,101,102], perception that food provisions would help finish treatment [95], belief in TB cure [47], or lack of trust in treatment efficacy [40], further diminish adherence.

Psychological factors such as depression, stress, hopelessness [27,31,45,51,85], shock or denial about illness [55,87], feelings of shame [87,95], and fear of disclosure [29,90] amplify non-compliance. Negative attitudes such as lack of awareness or carelessness about his illness [40,43,54,62,67,91,103,108], boredom [51], low perception towards TB severity [17,67,69,70,82,87], often accompanied by low self-management [17,18,92], increase non-compliance. Symptom-related factors, such as feeling better or being cured prematurely, often lead patients to discontinue treatment prematurely [25,27, 42,60,63,70,72,79,84,85,89,91,95,100]. Forgetfulness [25,31,42,43,51,63,86,110,111], traveling away from home [18,31,42,43,51,86,111], and running out of drugs [27,31,51,75] or not timely refills [19,31], also contribute to treatment discontinuation.

Family-related factors

Family-related factors significantly influence TB treatment adherence, with the lack of family support being a critical barrier to compliance. Patients who do not receive financial assistance, help with accommodation or nutrition, or support for transportation often struggle to access consistent care. Moreover, the absence of supervision, emotional encouragement, and motivation from family members can diminish patients' commitment to their treatment regimens. A lack of empathy, emotional and spiritual encouragement within the family environment further exacerbates feelings of isolation and hopelessness, which are common among TB patients. Addressing this issue requires engaging families as active participants in the treatment process by providing education and fostering supportive environments to enhance adherence and improve patient outcomes [17,18,21,24,35,51,72, 78,94,97,98,103,109].

Community-related factors

Community-related factors play a pivotal role in influencing TB treatment adherence, with stigma [26,40,42,53,56,66,73,78,84,85,87,88,97,101,103, 104,108] and discrimination [17,101] being significant barriers. Patients often face negative attitudes and social exclusion, which can discourage them from seeking or continuing treatment. The lack of social support, empathy, and compassion from friends further compounds this challenge, leaving patients feeling isolated and unsupported [84,85,98]. Experiences of desertion, neglect, and emotional disengagement from social networks undermine the strength and motivation needed to adhere to treatment regimens [98]. Addressing these community-level barriers requires comprehensive strategies that include stigma-reduction programs, community education, and the promotion of empathetic, inclusive social environments to foster better adherence and treatment outcomes.

Health workers-related factors

Health worker-related factors significantly impact TB treatment adherence, with inadequate engagement and support from healthcare providers serving as key barriers. The lack of regular visits, telemonitoring, supervision, or surveillance by health workers often results in reduced patient compliance [20,34,36,41, 42,56,60,63,66,79,97,112]. Insufficient information, advice, or counseling about TB therapy further limits patients' understanding and commitment to their treatment regimens [19,21,35,40,43,62,95,97,100]. Poor communication [51,57,78,85,86,94,98,101,111] and an unfriendly or dismissive [25,57,89,95] from healthcare workers weaken the patient-provider relationship, discouraging patients from seeking help or adhering to their care plans. Additionally, the unavailability or lack of responsibility and support from health workers [17,19,38,96,101,103], combined with inadequate treatment skills [17], compromises the quality of care patients receive. Addressing these issues requires training healthcare providers to improve communication, foster patient-centered relationships, and enhance their technical and interpersonal skills to build trust and support adherence.

Health services-related factors

Health service-related factors significantly influence TB treatment adherence, particularly in areas with limited healthcare access. Long distances to health centers [24,25,42,47,53,62,69,70,73,85,89], extended travel times, and inadequate transportation options pose substantial barriers for patients, especially in geographically remote areas [26,41,88,97]. Poor infrastructure and inaccessibility to healthcare services further exacerbate these challenges, often discouraging patients from seeking or continuing treatment [32,97,103,105]. Extended waiting times at healthcare facilities [44,88,102,104] and dissatisfaction with the quality of care [84] also contribute to non-compliance. Factors such as distrust of health [87,103] and poor administration of treatment protocols [97] undermine patient confidence and adherence. Addressing these issues requires strengthening healthcare infrastructure, improving transportation support, optimizing service delivery, and enhancing the quality and reliability of healthcare to foster better adherence outcomes.

Monitoring system-related factors

Monitoring system-related factors play a crucial role in TB treatment adherence. The absence or unavailability of Directly Observed Treatment (DOT) programs significantly reduces compliance [17,96,101], as patients may lack the necessary supervision and support. Failed compliance [57,80,83] with or unwillingness to accept DOT [55,67,82], often due to the inconvenience of observation methods [40,57], further exacerbates non-adherence. Alternative monitoring approaches, such as community-based [26,74] or family-member-led DOT [107], can provide more accessible and flexible support, though they may not always be effectively implemented. Additionally, self-administration of medication without proper oversight increases the risk of missed doses [112]. The lack of medication dose reminders [98] and patient-centered monitoring systems [97] highlights the need for tailored solutions that prioritize convenience, accessibility, and engagement to enhance adherence and treatment success.

Drug-related factors

Drug-related factors significantly contribute to non-compliance with TB treatment, as the challenges associated with medication often deter patients from completing their regimens. Side effects [17,25,27,42,43,47,51–53,60,62,63,78,79,81,82, 84–87,91,97,101,102] and adverse drug events [23,56,66,71,94], such as nausea, vomiting, or fatigue, are among the most common barriers, leading to discomfort and reduced motivation to adhere. Drug intolerance further complicates adherence [103,106], particularly for patients with co-morbidities requiring concurrent use of non-anti-TB medications [22,107]. The prolonged duration of TB treatment [51,85] and the associated pill burden [32] amplify the difficulty, making it harder for patients to remain consistent. Addressing these barriers requires comprehensive

strategies, including effective management of side effects, patient education, and support systems to mitigate the psychological and physical burden of TB therapy.

Other factors

Additional factors, such as fear of COVID-19 during the pandemic [25] and high demographic density [41], have also influenced TB treatment adherence. The fear of contracting COVID-19 in healthcare settings led many patients to delay or avoid seeking care, disrupting treatment continuity. High population density, particularly in urban areas, creates challenges in maintaining effective treatment monitoring and infection control, further discouraging adherence. These factors underscore the need for adaptive healthcare strategies, such as telemedicine, community-based interventions, and infection prevention measures, to ensure uninterrupted TB treatment during public health crises and in densely populated regions.

Key factors, patterns, and interconnections in TB treatment non-compliance

The heatmap and network visualization analyses together provide a comprehensive understanding of the factors contributing to TB treatment non-compliance (Figures 3 and 4). The heatmap highlights the prominence and intensity of individual factors using a color-coded scale, where poor tuberculosis knowledge emerges as the most critical determinant, represented by its central position and intense red color. Surrounding this central factor are stigma, side effects, alcoholism, low education, and HIV/AIDS, which appear in red and yellow hues, reflecting their significant influence on non-compliance. Moderately impactful factors, such as older age, financial hardship, low income, forgetfulness, and lack of family support, are shown in yellow and green, illustrating the combined effects of economic, psychological, and logistical barriers on treatment adherence. Less prominent factors, such as inadequate supervision, transportation issues, and unfriendly healthcare, are highlighted in blue and green yet remain relevant, particularly in resource-limited settings.

The network visualization builds on this by revealing the interconnections and clustering of these factors into distinct thematic groups. Behavioral and demographic factors, such as alcoholism, older age, and male gender, interact with economic and structural barriers, including financial hardship, distance to health centers, and health insurance problems, illustrating how demographic vulnerabilities are compounded by systemic challenges. Treatment-related factors, such as side effects, feeling better prematurely, and lack of counseling, interact with psychosocial factors like stigma, stress or depression, and low perception of TB severity, forming a web of interconnected barriers. The analysis highlights that these factors are interconnected rather than isolated, but interact dynamically. Certain factors, such as alcoholism and financial hardship, serve as bridges between multiple clusters. Together, these analyses underscore the multifactorial and interconnected nature of TB treatment non-compliance. The heatmap provides insights into the severity and individual prominence of factors, while the network visualization emphasizes their relationships and thematic clustering.

TB treatment non-compliance arises from a multifaceted interplay of individual, social, and systemic factors. Poor tuberculosis knowledge and low education levels/low health literacy are significant contributors to treatment non-compliance, hindering patients' ability to understand the disease, follow complex treatment regimens, and recognize the consequences of non-adherence. This issue is further compounded by healthcare providers' inadequate knowledge, which limits their ability to effectively educate and support patients [115]. Previous research underscores that low health literacy impairs patients' capacity to navigate treatment protocols and manage associated challenges, leading to poor adherence and suboptimal outcomes [116]. Targeted health literacy programs are essential to overcome these barriers.

The stigma surrounding TB is another significant barrier, leading to fear of discrimination, concealment of illness, and reduced self-worth, which are often compounded by depressive symptoms [117]. Addressing stigma through educational interventions, mental health support, and community engagement is crucial to improving adherence. Adverse drug reactions, such

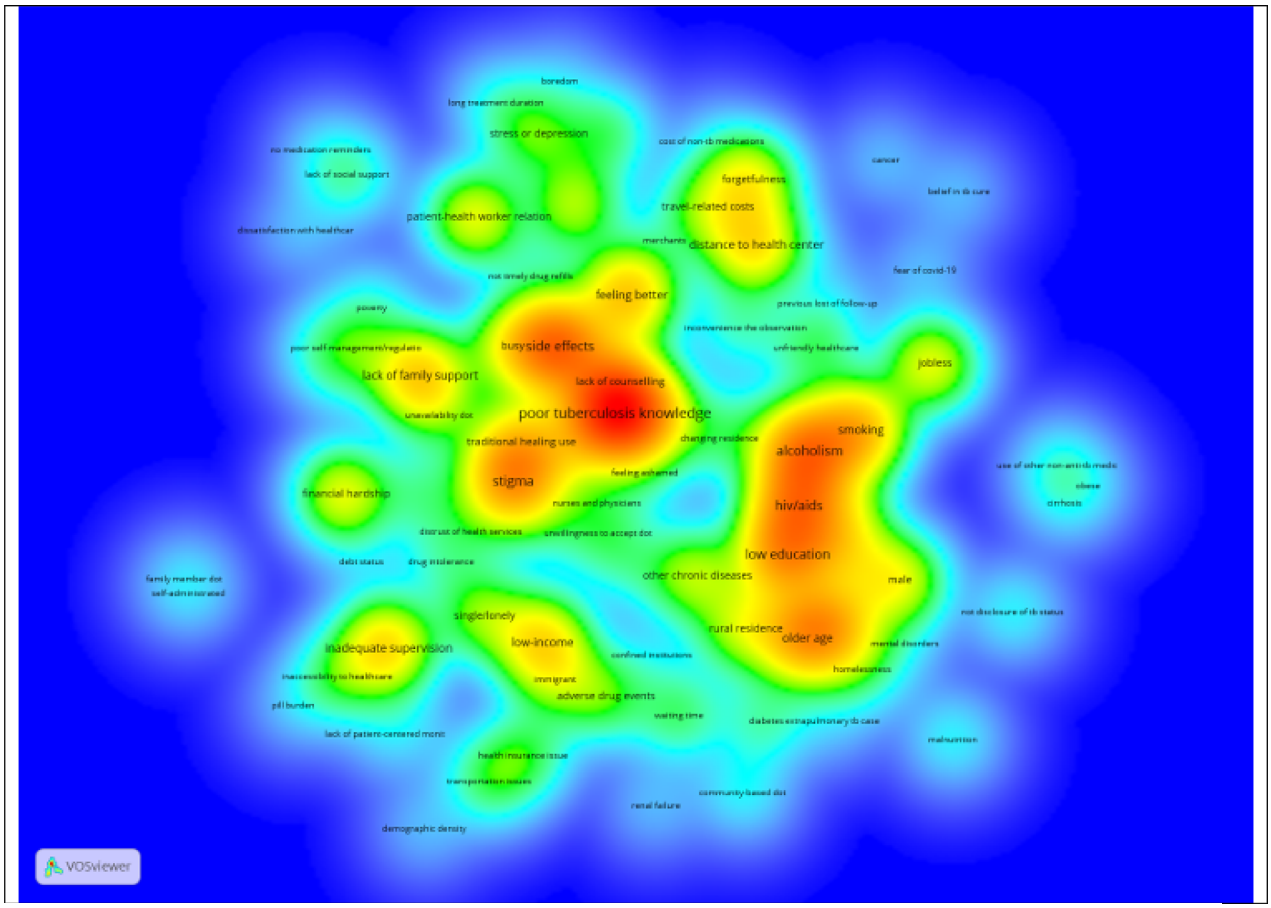

Figure 3. Heatmap analysis of key factors influencing TB treatment non-compliance.

as nausea, vomiting, and fatigue, are common deterrents to treatment continuation, particularly when patients perceive medications as harmful [118]. Similarly, alcoholism significantly impacts adherence by impairing immune function, mental health, and social stability, with studies showing a twofold increase in non-compliance among alcohol users [119].

Co-morbidities, particularly TB-HIV co-infection, complicate adherence due to the burden of managing multiple medications and the stigma associated with both diseases [120]. Older patients face additional challenges, including cognitive decline, social isolation, and co-morbidities, which require tailored interventions like medication reminders and family involvement [121]. Financial hardship and low income also hinder access to healthcare services, transportation, and supplementary medications, exacerbating non-compliance [122]. Addressing economic constraints through financial assistance and community-based healthcare services can significantly improve adherence.

Forgetfulness, often influenced by stress, anxiety, or cognitive decline, is another prevalent factor, particularly among older adults [123]. Interventions such as mobile phone reminders are important to enhance adherence rates [124]. Social support, especially from family members, is critical for adherence, and the absence of such support is strongly associated with treatment discontinuation. Family education and involvement in the treatment process are effective strategies to address this issue [125].

Systemic factors, such as inadequate supervision and unfriendly healthcare environments, further undermine adherence. Lack of follow-up and dismissive

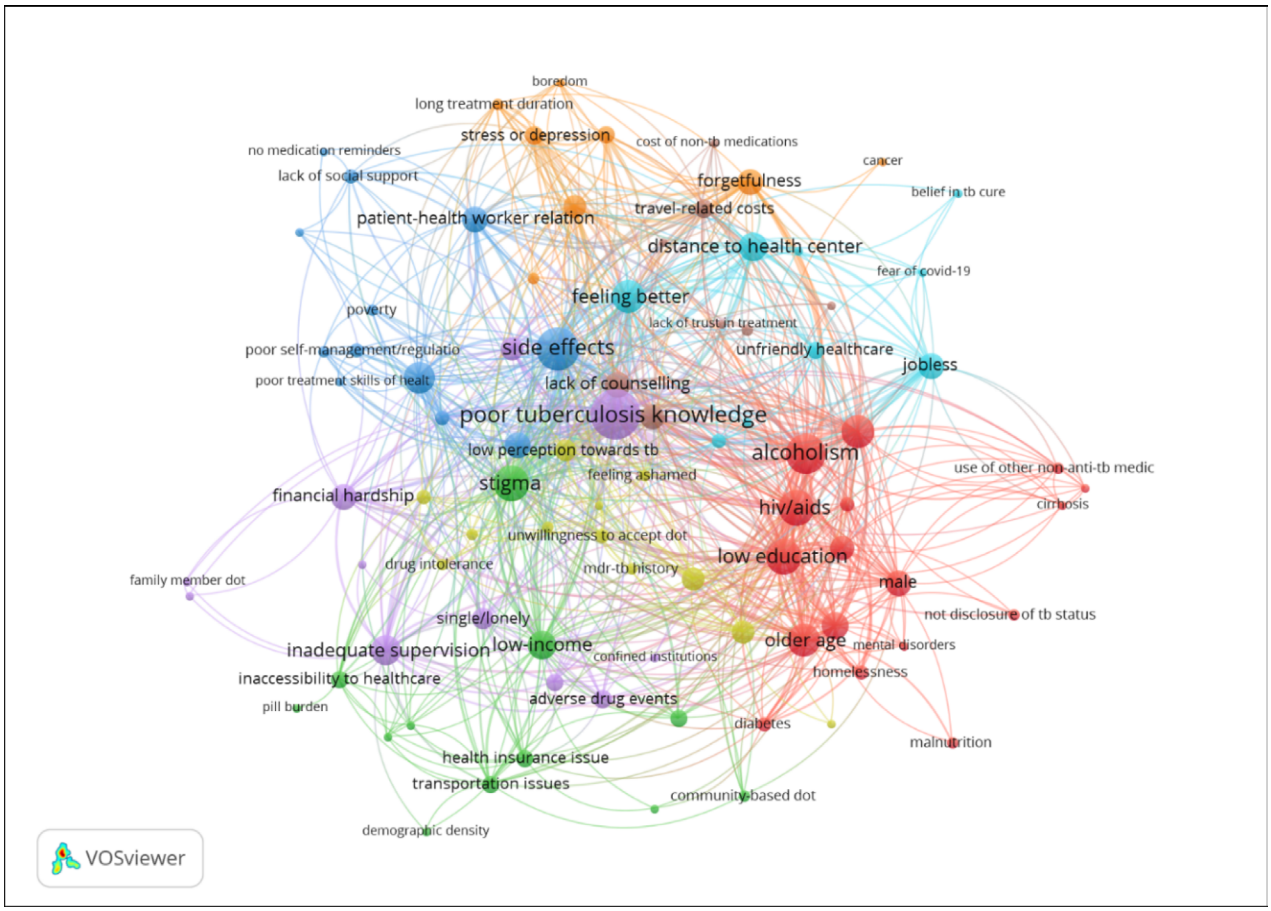

Figure 4. Network visualization analysis: patterns and interconnections of TB treatment non-compliance.

attitudes from healthcare providers discourage patients from completing treatment [11]. Effective supervision strategies, such as the video directly observed therapy during tuberculosis treatment, and patient-centered care approaches can foster trust and accountability [126]. Additionally, logistical barriers, such as long distances to healthcare facilities and unreliable transportation, discourage access to treatment [6]. Solutions like mobile clinics, transportation subsidies, and decentralized treatment centers are necessary to overcome these challenges.

Key factors and patterns of TB treatment non-compliance across income levels

The analysis of factors contributing to TB treatment non-compliance reveals variations across country income levels (Table 1). In low-income countries, such as Ethiopia [18,29,40,43,44,47,62,81,86,90,101, 109–111], Kenya [72,88,102], and Uganda [19,48,55,59, 64,74], economic challenges like low income, poverty, and distance to healthcare centers dominate, compounded by poor tuberculosis knowledge, stigma, and unfriendly healthcare environments. These issues are exacerbated by cultural practices, such as reliance on traditional healing and limited healthcare access. Lower-middle-income countries, including Indonesia [21,58,79,84,100,105], India [31,51,75,91,97,98], and Nigeria [32,37,53,89], experience a combination of economic and psychosocial barriers, with financial hardship, side effects, and premature discontinuation due to feeling better being prominent. Psychosocial factors, such as stigma and poor patient-healthcare worker relationships, further hinder adherence, especially in urbanizing regions where transportation issues and busy schedules are common.

In upper-middle-income countries, such as Brazil [22,28,41,80,96,106], China [17,23,34,36,52,56,60 ,63,66,69,71,94,99,112], and South Africa [83,95],

Table 1. Key factors and patterns of non-compliance TB treatment across income-level countries.

Classification	Key Factors	Country
Low-Income Countries	Low income and poverty	e.g., Ethiopia, Kenya, Uganda
	Distance to healthcare centers	e.g., Ethiopia, Uganda
	Poor tuberculosis knowledge	e.g., Ethiopia, Uganda
	Stigma and lack of counselling	e.g., Ethiopia, Uganda
	Alcoholism and smoking	e.g., Ethiopia, Kenya
	Unfriendly healthcare environments and inadequate supervision	e.g., Ethiopia, Uganda
Lower-Middle-Income Countries	Financial hardship	e.g., Indonesia, India, Nigeria
	Side effects of medication	e.g., Indonesia, India
	Feeling better prematurely, leading to discontinuation	e.g., Indonesia, India
	Stigma and poor patient-health worker relationships	e.g., Nigeria, Indonesia, India
	Lack of social or family support	e.g., Indonesia, India, Nigeria
Upper-Middle-Income Countries	Alcoholism and drug use	e.g., Brazil, South Africa
	Low education and financial hardship	e.g., Brazil, China
	Adverse drug events and side effects	e.g., China, South Africa
	HIV/AIDS and other chronic diseases	e.g., Brazil, South Africa
	Stigma and distrust of healthcare systems	e.g., South Africa, China
High-Income Countries	Homelessness and low income; Alcoholism and drug use; HIV/AIDS and chronic diseases; Poor tuberculosis knowledge; Stigma and Previous defaults	e.g., USA, Spain

the interplay of alcoholism, drug use, chronic diseases (e.g., HIV/AIDS), and adverse drug events contributes to non-compliance. Systemic issues, including healthcare inefficiencies and inadequate patient support systems, are also prevalent. Meanwhile, in high-income countries, including the United States [33,107], Canada [107], and Spain [20,49,54], social vulnerabilities, such as homelessness, low income, and substance abuse, are primary barriers. These factors coexist with challenges in addressing healthcare accessibility for marginalized populations, along with stigma and poor tuberculosis knowledge among certain groups. Despite these variations, several factors are universal across all income levels, including poor tuberculosis knowledge, side effects of medication, and stigma, which consistently undermine treatment adherence.

Impact of non-compliance TB treatment

The heatmap and network visualization analyses together provide a comprehensive understanding of the clinical and epidemiological impacts of TB treatment non-compliance (Figures 5 and 6). The heatmap highlights the severity of individual outcomes, with MDR/XDR-TB emerging as the most critical consequence, represented by its central position and intense red color [16,33,39,47,50,61,71,77,93]. This outcome underscores the significant challenges posed by non-adherence, as MDR/XDR-TB requires longer and more complex treatment regimens involving second-line medications [33]. The visualization also emphasizes other distinct impacts, including unsuccessful treatment outcomes [16,33,46,65,83], low cure rates [30,36,68,74], high mortality [36,39,50,65,74,83], and increased hospital admissions [39], which further strain healthcare systems by necessitating prolonged or intensive care for advanced or drug-resistant cases.

The network visualization complements this perspective by revealing the interconnections between these outcomes, clustering them into two main categories: clinical consequences and a single epidemiological impact. Clinical consequences such as MDR/XDR-TB are intricately linked to longer treatment durations, unsuccessful treatment outcomes, and high

Figure 5. Heatmap analysis of the impact of non-compliance TB treatment.

mortality rates, creating a cascading effect that compounds the burden on individual patients and healthcare systems. In contrast, TB reinfection appears as a distinct epidemiological outcome [35,76], representing the continued transmission of TB within communities. Although less interconnected with other outcomes, its intensity highlights the far-reaching public health implications of non-compliance, perpetuating disease cycles and undermining TB control efforts globally.

By integrating these analyses, the findings illustrate the dual burden of TB treatment non-compliance: severe clinical impacts that affect individual recovery and healthcare capacity and epidemiological consequences that sustain community-level transmission. This dual perspective underscores the urgency of addressing treatment non-compliance through targeted interventions, including improving patient adherence, reducing barriers to treatment, and enhancing public health strategies to control disease transmission.

Non-compliance allows drug-resistant bacteria to proliferate, complicating treatment and increasing the risk of treatment failure. Studies have shown that patients who default on treatment have twice the risk of developing MDR-TB, particularly those with a history of prior treatment failure or co-morbidities such as HIV/AIDS. This cycle of resistance leads to prolonged and more complex treatment regimens, higher mortality rates, and significant healthcare costs [127,128].

Non-compliance also results in increased hospital admissions and financial strain on healthcare systems, further exacerbating the burden on public health resources.

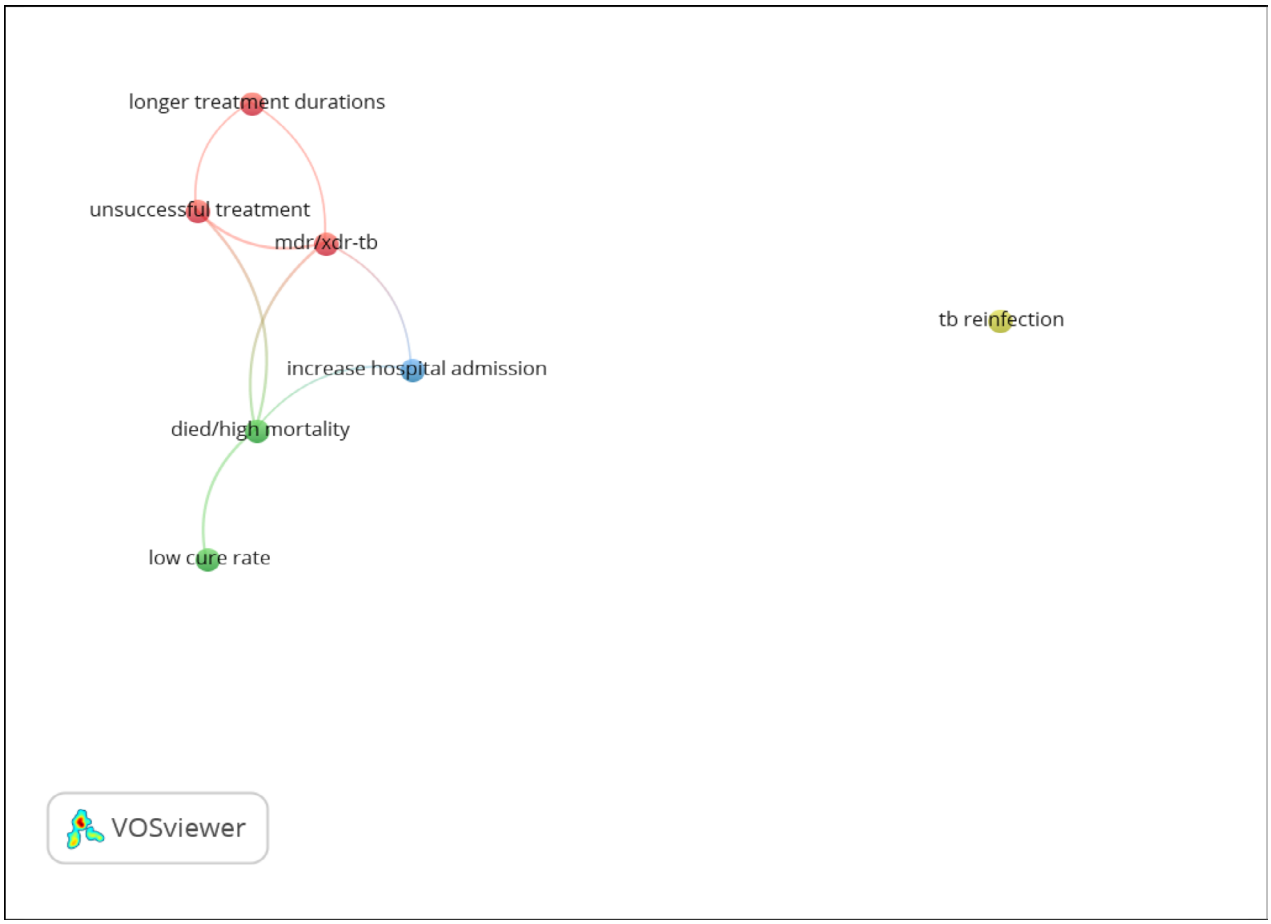

Figure 6. Network visualization analysis: patterns and interconnection of the impact of non-compliance TB treatment.

For example, patients with MDR-TB or XDR-TB often require prolonged hospitalization, diverting resources from preventive measures and increasing the economic impact of TB management [129]. Furthermore, non-compliance heightens the risk of TB reinfection, perpetuating community transmission and undermining TB control efforts. Patients who fail to adhere to treatment are more susceptible to reinfection, particularly in high-burden settings with limited access to healthcare [130].

Study limitations

Many studies lacked comprehensive regional representation, with data disproportionately originating from low- and middle-income countries. High-income countries were underrepresented, particularly regarding the role of social vulnerabilities such as homelessness and substance abuse in TB non-compliance. This regional imbalance limits the generalizability of findings to diverse socio-economic contexts and healthcare systems. Potential biases in the reviewed studies are also evident. Most studies were cross-sectional, providing a snapshot of non-compliance factors but failing to capture changes in adherence behaviors over time. Additionally, studies often relied on self-reported data, which can introduce recall bias and social desirability bias, particularly for sensitive factors like stigma, substance use, or financial hardship.

Conclusion

This narrative-bibliometric review provides critical insights into the multifactorial influences driving TB treatment non-compliance and its clinical and epidemiological impacts. The findings highlight the

interplay of key factors, including poor tuberculosis knowledge, stigma, medication side effects, economic barriers, and logistical challenges, which interact with psychological, demographic, and systemic barriers. These multifaceted challenges lead to significant clinical consequences such as MDR/XDR-TB, prolonged treatment durations, unsuccessful treatment outcomes, and increased mortality, as well as epidemiological repercussions, including TB reinfection and sustained transmission within communities.

From a clinical perspective, tailored, patient-centered approaches are essential. Health professionals should prioritize education, address medication-related concerns, and foster trustful relationships to reduce stigma and improve adherence. Optimizing counseling and monitoring systems, such as DOT, is crucial to ensure consistent patient follow-up and adherence monitoring.

On a policy level, the review underscores the need to strengthen healthcare systems by addressing systemic barriers, such as limited access to healthcare facilities, inadequate transportation, and poor supervision. Policies should focus on alleviating financial burdens, particularly in low- and middle-income countries, by subsidizing treatment costs and integrating TB care into broader health services. Public health campaigns are equally vital to reduce stigma and raise awareness about TB, targeting psychosocial barriers to adherence.

From a research perspective, this study emphasizes the importance of longitudinal and intervention-based research to evaluate the effectiveness of strategies aimed at improving TB treatment adherence. Bibliometric analysis identified gaps in the current literature, underscoring the need for context-specific studies that explore socio-cultural dimensions and innovative solutions, such as digital adherence technologies, to enhance monitoring and support.

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Appendix 1. Characteristics of studies (n=97).

No	Author	Title	Year	Location	Study Design	Population	Sample Size	Variables Related to Treatment Non-Adherence	Or Impact Non-Adherence
1.	Caminero et all	Evaluation of a directly observed six-month fully intermittent treatment regimen for tuberculosis in patients suspected of poor compliance	1996	Spain	Cohort study	Homeless, intravenous drug abusers, chronic alcoholics, HIV-infected patients, and those who had previously abandoned treatment	102	• Homelessness • Chronic alcoholism • Drug abuse • HIV • Previous treatment abandonment	
2.	Pablos-Méndez et all	Nonadherence in Tuberculosis Treatment: Predictors and Consequences in New York City	1997	New York City, USA	Retrospective cohort study	184 TB patients newly diagnosed in April 1991	184	• Homelessness • Drug use • Alcoholism • HIV infection • Income level (low) • Previous treatment history	• Longer to convert to negative culture/ Required longer treatment durations • More likely to acquire drug resistance • Had a lower likelihood of completing treatment
3.	Kaona, et all	An assessment of factors contributing to treatment adherence and knowledge of TB transmission among patients on TB treatment	2004	Ndola, Zambia	Cross-sectional	TB patients	400	• Patients beginning to feel better • Lack of knowledge on the benefits of completing a course • Running out of drugs at home • Side effects of TB medication • Loss of hope to live	
4.	Khan, et all	Tuberculosis patient adherence to direct observation: results of a social study in Pakistan	2005	Rawalpindi, Pakistan	Mixed methods (survey, interviews, FGDs)	TB patients from a randomized controlled trial on DOTS treatment (health worker, family member, self-administered)	497 (32 in-depth interview patients)	• Failed to comply DOT • Inconvenience of the method of observation • Time and travel costs • Patient's occupational reasons (busy) • Patient-provider interaction • Health worker attitudes	

5.	Gelmanova, et all	Barriers to successful tuberculosis treatment in Tomsk, Russian Federation: non-adherence, default, and the acquisition of multidrug resistance	2007	Tomsk, Siberia, Russia	Retrospective cohort study	Newly diagnosed adult TB patients	237	• Substance abuse • Alcoholism • Co-morbidities • Unemployed	Poor treatment outcomes (Failed, Default, Died)
6.	Xu et all	Adherence to anti-tuberculosis treatment among pulmonary tuberculosis patients: a qualitative and quantitative study	2009	Jiangsu Province, China	Mixed-method (Quantitative & Qualitative)	Sputum-smear positive TB patients across 13 counties	670	• Illiteracy • Marital status (divorced/widowed) • Lack of health insurance • Migration status • Adverse drug reactions • Financial burden • Social stigma • Lack of visits/observed by health workers	
7.	Widjanarko, et all	Factors that influence treatment adherence of tuberculosis patients living in Java, Indonesia	2009	Central Java, Indonesia	Qualitative descriptive study	TB patients from public and private hospitals in Java	63 (31 adherent and 32 nonadherent patients)	• Feeling better • Financial burden/lack of money • Lack of social support • Dissatisfaction with healthcare staff • Poor patient knowledge on TB • Feeling worse • Side effects • Stigma	
8.	Caylà, et all	Tuberculosis treatment adherence and fatality in Spain	2009	Spain	Prospective cohort study	Patients diagnosed with TB from 61 collaborators in 53 hospitals	1490 patients	• Immigrant status • Living alone • Confined institutions • Previous TB treatment • Drug use • Difficulty in understanding treatment • HIV-infection	

(*Continued*)

No	Author	Title	Year	Location	Study Design	Population	Sample Size	Variables Related to Treatment Non-Adherence	Or Impact Non-Adherence
9.	Bagchi et all	Determinants of Poor Adherence to Anti-Tuberculosis Treatment in Mumbai, India	2010	Mumbai, India	Cross-sectional study	Pulmonary TB patients receiving DOTS therapy at government centers	538	• Gender (male) • Smoking during treatment • Alcohol consumption • Travel-related costs • Shortage of drugs	
10.	Ai et all	Factors associated with low cure rate of tuberculosis in remote poor areas of Shaanxi Province, China: a case control study	2010	Shaanxi Province, China	Case-control study	New smear-positive TB cases in 30 counties with low cure rates	659		Low cure rate
11.	Muture et all	Factors associated with default from treatment among tuberculosis patients in Nairobi province, Kenya: A case-control study	2011	Nairobi, Kenya	Case-control study	TB patients in Nairobi, 30 high-volume treatment centers	945 (defaulters) + 1033 (controls)	• Inadequate TB knowledge • Herbal medication use • Low income • Alcohol abuse • Previous default • HIV co-infection • Male gender • Stigma • Transportation issues • Waiting time for services at facility	
12.	Mittal and Gupta	Noncompliance to DOTS: How it can be Decreased	2011	Agra, India	Cross-sectional study	TB patients receiving DOTS treatment in Agra	900	• Old Age • Sex (male) • Occupation (Busy, Lack of time) • Side effects of medication • Improvement in symptoms • Lack of awareness	
13.	Ayisi et all	Care seeking and attitudes towards treatment compliance by newly enrolled tuberculosis patients in the district treatment programme in rural western Kenya: a qualitative study	2011	Rural Western Kenya	Qualitative study	Newly enrolled pulmonary TB patients in rural western Kenya	31	• Delay in seeking care (due to misinterpretation of symptoms, lack of funds) • Self-treatment with herbal remedies • Lack of knowledge on the duration of treatment • Cessation of treatment when symptoms subside • Lack of family support	

14.	Zhou et all	Adherence to Tuberculosis Treatment among Migrant Pulmonary Tuberculosis Patients in Shandong, China: A Quantitative Survey Study	2012	Shandong, China	Cross-sectional study	Smear-positive pulmonary TB migrant patients	314	• Marital status (divorced or bereft of spouse) • TB-related health education • Weak treatment supervision • Over working hours • Debt status (Economi)
15.	Garrido, et al	Factors Associated with Tuberculosis Treatment Default in an Endemic Area of the Brazilian Amazon: A Case-Control Study	2012	Amazonas State, Brazil	Case-control study	TB patients	11,312 (1,584 cases and 9,728 Controls)	• Sex (male) • Previous default • HIV positivity • Diabetes • Mental disorders • Other comorbidities • Alcoholism • Low education level • Older age • DOT failure
16.	Finlay, et all	Patient- and provider-level risk factors associated with default from tuberculosis treatment, South Africa, 2002: a case-control study	2012	South Africa	Case-control study	TB patients from 8 provinces, both new and re-treatment cases	1164 (232 cases, 932 controls)	• Poor healthcare worker attitude • Changing residence during TB treatment • Lack of formal education • Feeling ashamed to have TB • Not receiving adequate counseling about their treatment • Alcohol use • Traditional healers • Felt better • History of previous TB treatment default • Perception that food provisions would help finish treatment
17.	Slama et all	Factors associated with treatment default by tuberculosis patients in Fez, Morocco	2013	Fez, Morocco	Case-control study	Tuberculosis patients (defaulters and non-defaulters) from TB control units in Fez	320	• Relapsed cases • Smoking • Alcohol use • Distance to health center • Lack of sufficient explanation about the disease • Perception of being cured

(*Continued*)

No	Author	Title	Year	Location	Study Design	Population	Sample Size	Variables Related to Treatment Non-Adherence	Or Impact Non-Adherence
18.	Chirwa et all	Levels of Tuberculosis Treatment Adherence among Sputum Smear Positive Pulmonary Tuberculosis Patients Attending Care at Zomba Central Hospital, Southern Malawi	2013	Zomba, Malawi	Descriptive study	Smear-positive pulmonary TB patients at Zomba Central Hospital	524		Less likely to be cured TB
19.	Adane et all	Non-Adherence to Anti-Tuberculosis Treatment and Determinant Factors among Patients with Tuberculosis in Northwest Ethiopia	2013	Northwest Ethiopia	Cross-sectional survey	TB patients receiving treatment at health facilities in North Gondar	280	• Forgetfulness • Continuation phase of chemotherapy • HIV co-infection	
20.	Kiros et all	Adherence to anti-tuberculosis treatment in Tigray, Northern Ethiopia	2014	Mekelle Zone, Tigray Region, Ethiopia	Cross-sectional study	TB patients from public health facilities in Mekelle Zone	278	• Drug side effects • Knowledge about TB prevention • Employment (No) • Belief in TB cure • Distance to health facility	Potential for MDR-TB development due to intermittent treatment interruptions.
21.	Ibrahim et all	Factors associated with interruption of treatment among Pulmonary Tuberculosis patients in Plateau State, Nigeria	2014	Plateau State, Nigeria	Cross-sectional study	Pulmonary TB patients in Plateau State	378	• Distance from treatment site • Lack of knowledge of treatment duration • Cigarette smoking • Alcohol use • Feeling well • Employment status (Unemployed) • Unfriendly attitudes of health workers	

22.	Rondags et all	Factors Influencing Non-Adherence to Tuberculosis Treatment in Jepara, Central Java, Indonesia	2014	Jepara, Central Java, Indonesia	Qualitative study	TB patients from community health centers and private medical facilities	17	• Knowledge about TB • Changing treatment facilities • Feeling healthy • Financial issues • Job-related issues (Jobless) • Lack of sufficient information and inconsistent support from healthcare providers	
23.	Alobu et all	Risk factors of treatment default and death among tuberculosis patients in a resource-limited setting	2014	Ebonyi State, Nigeria	Retrospective cohort study	Adult TB patients treated in two large health facilities in Ebonyi State	1,668	• Older age • Extrapulmonary TB case • Residence (rural) • HIV co-infection	
24.	Méda, et all	Medication-adherence predictors among patients with tuberculosis or human immunodeficiency virus infection in Burkina Faso	2014	Burkina Faso	Cross-sectional study	TB and HIV patients from two main regions in Burkina Faso	1043 (309 TB, 553 TB with HIV, 181 coinfected)	• Alcohol use • Drug use • Ever been lost to follow-up • Unawareness of disease transmission • Knowledge about TB transmission • Attitude (Low) • Stigma • Financial access to care	
25.	Ershova et all	Evaluation of adherence to national treatment guidelines among tuberculosis patients in three provinces of South Africa	2014	South Africa	Cohort study	TB patients in Gauteng, KwaZulu-Natal, and Mpumalanga provinces	741	• Incomplete DOT (only intensive phase) • Previous treatment default • Rural settings • HIV status	Poor outcome (defaulted, failure, died)
26.	Tang et all	Non-adherence to anti-tuberculosis treatment among internal migrants with pulmonary tuberculosis in Shenzhen, China: A cross-sectional study	2015	Shenzhen, China	Cross-sectional study	Internal migrant TB patients in Shenzhen	794	• Unemployed • Lack of knowledge about TB treatment • Long travel time to nearest healthcare center • Perceived importance of medication adherence	

(*Continued*)

No	Author	Title	Year	Location	Study Design	Population	Sample Size	Variables Related to Treatment Non-Adherence	Or Impact Non-Adherence
27.	Lei et all	Are tuberculosis patients adherent to prescribed treatments in China? Results of a prospective cohort study	2016	Chongqing, China	Prospective cohort study	Newly confirmed TB patients from 3 counties in Chongqing	481	• Treatment supervision (Self-administrated and family member) • Lack of home visit by health care • Financial burden • TB-related education	
28.	Fagundez et all	Treatment Adherence of Tuberculosis Patients Attending Two Reference Units in Equatorial Guinea	2016	Bata and Malabo, Equatorial Guinea	Cross-sectional study	TB patients attending TB reference units in Equatorial Guinea	98	• Low educational level • Lack of family support • Lack of medical advice	TB Re-infection
29.	Horter et all	Where there is hope: a qualitative study examining patients' adherence to multi-drug resistant tuberculosis treatment in Karakalpakstan, Uzbekistan	2016	Karakalpakstan, Uzbekistan	Qualitative study	MDR-TB patients undergoing treatment	52	• Loss of Hope (Doubt, disbelief shock, denial) • Quality of knowledge (Inadequate information and Understanding, Myths and misinformation) • Loss of autonomy (especially in married women) • Distrust of health services • Stigma • Shame • Negative perceptions of side effects	
30.	Ali and Prins	Patient non-adherence to tuberculosis treatment in Sudan: socio-demographic factors influencing non-adherence to tuberculosis therapy in Khartoum State	2016	Khartoum State, Sudan	Case-control study	TB patients receiving treatment in Khartoum state treatment centers	315	• Educational level • Rural residence • Patient movement (changing address) • Lack of family support • Distance from treatment center	

31.	Cadosch et all	The Role of Adherence and Retreatment in De Novo Emergence of MDR-TB	2016	Zurich, Switzerland	Computational modeling study	TB patients undergoing treatment with standard regimens	Simulated 10,000 patients	Unsuccesfull treatment
32.	Cremers et all	Tuberculosis patients' pre-hospital delay and non-compliance with a longstanding DOT programme: a mixed methods study in urban Zambia	2016	Lusaka, Zambia	Mixed methods study	TB patients attending Kanyama clinic in Lusaka, Zambia	300	• Time constraints • Long distance to clinic • Alternative health care seeking (traditional, faith healing) • Stigma • Poverty and food shortages
33.	Moro, et all	Factors Associated With Noncompletion of Latent Tuberculosis Infection Treatment: Experience From the PREVENT TB Trial in the United States and Canada	2016	United States, Canada	Post-hoc exploratory analysis of a randomized, open-label trial	Adults enrolled in the PREVENT TB trial at North American sites	6232	• Sex (male) • Low education level • Obese • Alcohol consumption • Drug use • Cirrhosis • Smoking • Concomitant medication • Unemployed • Missing early clinic visits
34.	Viegas et all	Association of outcomes with comprehension, adherence and behavioral characteristics of tuberculosis patients using fixed-dose combination therapy in Contagem, Minas Gerais, Brazil	2017	Contagem, Minas Gerais, Brazil	Prospective cohort study	TB patients receiving fixed-dose combination therapy in Contagem	83	• Alcohol consumption • HIV/AIDS status • Comprehension about TB • Use of other non-anti-TB medicine

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No	Author	Title	Year	Location	Study Design	Population	Sample Size	Variables Related to Treatment Non-Adherence	Or Impact Non-Adherence
35.	Mulogo et all	Determinants of treatment completion among rural smear positive pulmonary tuberculosis patients: a cross-sectional survey conducted in south-western Uganda	2017	Rwampara, Southwestern Uganda	Cross-sectional study	Smear-positive pulmonary TB patients in Rwampara Health Sub-District	128	• Pre-treatment counselling • Counselling at follow-up • Timely drug refills • Alcohol consumption • Health worker availability	
36.	Hassard et all	Patient attitudes towards community-based tuberculosis DOT and adherence to treatment in an urban setting; Kampala, Uganda	2017	Kampala, Uganda	Cross-sectional study	Patients in the continuation phase of pulmonary TB treatment	201	• No need for a treatment observer • Rejecting TB	
37.	Ayele et all	Self-reported adherence and associated factors to isoniazid preventive therapy for latent tuberculosis among people living with HIV/AIDS at health centers in Gondar town, North West Ethiopia	2017	Gondar, Ethiopia	Prospective cross-sectional study	People living with HIV/AIDS on Isoniazid preventive therapy (IPT) at health centers in Gondar	154	• Older Age • Occupation (Merchants) • Lack of explanation of therapy • Carelessness • Forgetfulness • Being away from home • Side effects	
38.	Ali and Prins	Disease and treatment-related factors associated with tuberculosis treatment default in Khartoum State, Sudan: a case-control study	2017	Khartoum State, Sudan	Case-control	TB patients	315 (105 cases, 210 controls)	• Rural residence • Not being on a DOTS programme • Side effects of TB medication • Previous history of TB (relapse, MDR-TB, treatment failure) • Poor response to treatment • Seeking traditional remedies • Have chronic diseases	

39.	Wanyonyi, et all	Factors associated with interruption of tuberculosis treatment among patients in Nandi County, Kenya 2015	2017	Nandi County, Kenya	Cross-sectional	TB patients who were initiated on treatment	252	• Less of income • Alcohol consumption • Waiting time at treatment center ≥ 1 hour • Use of herbal medication • Side effects • Inadequate knowledge of TB transmission
40.	Boru, et all	Factors contributing to non-adherence with treatment among TB patients in Sodo Woreda, Gurage Zone, Southern Ethiopia: A qualitative study	2017	Sodo Woreda, Gurage Zone, Southern Ethiopia	Qualitative study (in-depth interviews)	TB patients with interrupted or poor adherence to treatment	22	• Lack of money • Food insecurity • Poor communication between health care providers and patients • Beliefs in traditional healing system • Unavailability of the DOTS service innearby health facilities • Side effects • Stigma • Discrimination
41.	Woimo, et all	The prevalence and factors associated with anti-tuberculosis treatment non-adherence among pulmonary tuberculosis patients in public health care facilities in South Ethiopia: a cross-sectional study	2017	South Ethiopia	Cross-sectional survey (quantitative & qualitative methods)	Pulmonary TB patients from 17 health centers and one hospital	261 patients	• Alcohol consumption • Medication side effect • Poor knowledge of TB and treatment • Distance to treatment center (>10 km) • Lack of health information at every visit • Cost of non-TB related medications • Cost of transportation • Lack of awareness about importance of treatment completion

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No	Author	Title	Year	Location	Study Design	Population	Sample Size	Variables Related to Treatment Non-Adherence	Or Impact Non-Adherence
42.	Negandhi, et all	Rapid assessment of facilitators and barriers related to the acceptance, challenges and community perception of daily regimen for treating tuberculosis in India	2017	Maharashtra, Bihar, Sikkim, India	Rapid assessment (qualitative in-depth interviews)	Health system personnel (medical officers, district TB officers, DOTS providers)	62	• Accessibility • Transportation issues • Out-of-pocket expenses • loss of wages • Lack of trained service providers • Poor treatment protocol administration • Inadequate supervision • Side effects of medication • Patient-centered care needs • Family support • Stigma	
43.	Janmeja et all	Factors predicting treatment success in multi-drug resistant tuberculosis patients treated under programmatic conditions	2018	Chandigarh, India	Retrospective study	MDR-TB patients treated with Cat-IV regimen from Chandigarh and surrounding districts	256		Multi-drug resistant tuberculosis (MDR-TB)
44.	Mekonnen and Azagew	Non-adherence to anti-tuberculosis treatment, reasons and associated factors among TB patients attending at Gondar town health centers, Northwest Ethiopia	2018	Gondar, Ethiopia	Cross-sectional study	TB patients attending health centers in Gondar	314	• Co-morbidity • Knowledge about TB and anti-TB therapy • Patient-provider relationship; • Alcohol intake • Forgetting • Being busy with other work • Being out of home/town	
45.	Gong et all	Treatment adherence among sputum smear-positive pulmonary tuberculosis patients in Xinjiang, China: a prospective study	2018	Xinjiang, China	Prospective study	Sputum smear-positive pulmonary TB patients diagnosed between 2014 and 2015	8289	• Old Age • Actual management supervise medication	• Low cure rate • Mortality

46.	Azizi et all	Determinants of adherence to tuberculosis treatment in Iranian patients: Application of health belief model	2018	Saveh, Iran	Cohort study	TB patients from Saveh Tuberculosis Control Center	297	• Perceived threat • Perceived Benefits • Perceived Barriers • Perceived Self-efficacy
47.	Ruru et all	Factors associated with non-adherence during tuberculosis treatment among patients treated with DOTS strategy in Jayapura, Papua Province, Indonesia	2018	Jayapura, Papua Province, Indonesia	Case-control study	TB patients treated at public health centers in Jayapura	264	• Difficulty accessing healthcare • Lack of TB knowledge
48.	Maciel et all	Social determinants of pulmonary tuberculosis treatment non-adherence in Rio de Janeiro, Brazil	2018	Rio de Janeiro, Brazil	Ecological study	Districts of Rio de Janeiro	160 neighborhoods	• Economic conditions • Infrastructure • Demographic density • Lack of quality of TB surveillance and control
49.	Gebreweld, et all	Factors influencing adherence to tuberculosis treatment in Asmara, Eritrea: a qualitative study	2018	Asmara, Eritrea	Qualitative study (in-depth interviews, focus group discussions, key informant interviews)	TB patients from three health facilities	39 participants (12 in-depth interviews, 3 key informant interviews, 3 focus groups)	• Lack of knowledge about TB • Long treatment duration • Felt cured • Loss of income • Stigma • Lack of social support • Drug side effects • Poor communication with healthcare providers • Distances to health facilities • Stress and feelings of hopelessness

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No	Author	Title	Year	Location	Study Design	Population	Sample Size	Variables Related to Treatment Non-Adherence	Or Impact Non-Adherence
50.	Kawatsu, et all	A combination of quantitative and qualitative methods in investigating risk factors for lost to follow-up for tuberculosis treatment in Japan – Are physicians and nurses at a particular risk?	2018	Japan	Mixed methods (quantitative and qualitative)	Pulmonary TB patients aged 15–64 from national TB surveillance data and focus groups with public health nurses	5,760 (from surveillance), 13 (FGD participants)	• Occupation (nurses and physicians) • Difficult to make medication taking a routine • Low risk perception towards TB • Unwillingness to accept DOTS	
51.	Wang et all	Drug Non-Adherence and Reasons Among Multidrug-Resistant Tuberculosis Patients In Guizhou, China: A Cross-Sectional Study	2019	Guizhou, China	Cross-sectional study	MDR-TB patients treated at a hospital in Guizhou	202	• Side effect • Financial hardship • Co-morbidities	
52.	Fang et all	Factors Influencing Completion of Treatment Among Pulmonary Tuberculosis Patients	2019	Anhui, People's Republic of China	Cross-sectional study	Pulmonary TB patients from six counties (districts) in Anhui	262	• Forgetting • Side effects • Symptomatic improvement • Education background • Lower tracked by the rural medical staff	
53.	Tola et all	Intermittent treatment interruption and its effect on multidrug resistant tuberculosis treatment outcome in Ethiopia	2019	Ethiopia	Retrospective cohort study	MDR-TB patients treated in Ethiopia from 2009–2019	407		• Unsuccessful treatment outcome • MDR-TB resistance

54.	AlSahafi et all	High non-compliance rate with anti-tuberculosis treatment: a need to shift facility-based directly observed therapy short course (DOTS) to community mobile outreach team supervision in Saudi Arabia	2019	Jeddah, Saudi Arabia	Comparative cross-sectional study	TB patients undergoing DOTS treatment at PHCC in Jeddah	200	• Old Age • Educational status • Smoking • Lack of healthcare team supervision • Distance to health facility • Understanding of TB and treatment • Do not feel better with TB symptoms • Initial rapid improvement perceived as cure) • Forget to take medicine • Afraid of the treatment side effects • Social stigma • Travelling outside	
55.	Okethwangu et all	Multidrug-resistant tuberculosis outbreak associated with poor treatment adherence and delayed treatment: Arua District, Uganda, 2013–2017	2019	Arua District, Uganda	Outbreak investigation study	MDR-TB patients diagnosed at Arua Regional Referral Hospital	33		Multi-drug resistant tuberculosis (MDR-TB)
56.	Fekadu et all	Adherence to Anti-Tuberculosis Treatment Among Pediatric Patients at Nekemte Specialized Hospital, Western Ethiopia	2020	Nekemte, Ethiopia	Cross-sectional study	Pediatric TB patients (≤15 years) receiving treatment	202	• Residence (rural) • Side effects	
57.	Izudi et all	Treatment success and mortality among adults with tuberculosis in rural eastern Uganda: a retrospective cohort study	2020	Rural Eastern Uganda	Retrospective cohort study	Adults with bacteriologically confirmed pulmonary TB in rural Uganda	987	• HIV infection • Age >50 • Male sex • Community-based DOTS	• Low treatment success rate • Mortality rate

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No	Author	Title	Year	Location	Study Design	Population	Sample Size	Variables Related to Treatment Non-Adherence	Or Impact Non-Adherence
58.	Du et all	Determinants of Medication Adherence for Pulmonary Tuberculosis Patients During Continuation Phase in Dalian, Northeast China	2020	Dalian, Northeast China	Cross-sectional, multi-center survey	Pulmonary TB outpatients in Dalian, China	564	• Age older • Employment status (unemploy) • Tuberculosis knowledge • Alcohol consumption • History of TB treatment • Adverse drug reactions • Stigma • Medication supervision	
59.	Ajema et all	Factors associated with non-adherence to anti-tuberculosis treatment among tuberculosis patients in Gamo Gofa zone, southern Ethiopia: cross-sectional study	2020	Gamo Gofa Zone, Southern Ethiopia	Cross-sectional study	TB patients on treatment in selected health facilities in Gamo Gofa Zone	289	• Failure to disclose TB status to family • Lack of information about adverse events • Past TB treatment history • Smoking	
60.	Chen et all	The effects of family, society, and national policy support on treatment adherence among newly diagnosed tuberculosis patients	2020	Dalian, Liaoning, China	Cross-sectional study	Newly diagnosed TB patients at Dalian Tuberculosis Hospital	481	• Lack of family support (supervise treatment, spiritual encouragement) • Doctor-patient relationship TB-related knowledge • Lower educational • Suffered adverse drug reactions	
61.	Zhang, et all	Factors Influencing Medication Nonadherence to Pulmonary Tuberculosis Treatment in Tibet, China: A Qualitative Study from the Patient Perspective	2020	Tibet, China	Qualitative study (in-depth semistructured interviews)	TB patients	17	• Lack of knowledge about TB treatment • Poor self-management • Poor self-regulation • Misperception of health • Medication side effects • Lack of DOT • Effect of traditional Tibetan medicine • Poor treatment skills of healthcare staff • Lack of family support • Discrimination	

62.	Xing et all	Adherence to Multidrug Resistant Tuberculosis Treatment and Case Management in Chongqing, China – A Mixed Method Research Study	2021	Chongqing, China	Mixed-method (Quantitative & Qualitative)	MDR-TB patients diagnosed with WHO-defined MDR-TB	132	• Side effects • Busy at work schedule • Symptom improvement • Financial difficulties • Migrant status • Marital status (unmarried) • Lack supervised by health care
63.	Gashu et all	Adherence to TB treatment remains low during continuation phase among adult patients in Northwest Ethiopia	2021	Northwest Ethiopia	Cross-sectional study	Adult TB patients in the continuation phase	307	• Educational level • Provider-patient relationship • Patient knowledge on TB treatment • Family wealth index • Forgetfulness • Traveling away from home • Feeling sick • Fear of side effects
64.	Gebremariam et all	Determinants of adherence to anti-TB treatment and associated factors among adult TB patients in Gondar city administration, Northwest Ethiopia: based on health belief model perspective	2021	Gondar, Ethiopia	Cross-sectional study	Adult TB patients in Gondar city health facilities	265	• Lack of treatment supporter • Difficulties in taking drugs regularly • Perceived benefit • Perceived self-efficacy • Travel time
65.	Iweama et all	Nonadherence to tuberculosis treatment and associated factors among patients using directly observed treatment short-course in north-west Nigeria: A cross-sectional study	2021	Kano and Kaduna, Nigeria	Cross-sectional study	TB patients using DOTS in public health facilities in Kano and Kaduna States	390	• Low monthly income • Marital status (widowed) • Distance to DOTS center / health facility • TB/HIV co-infection • TB stigmatization • Tobacco smoking • Knowledge of TB • Side effects

(*Continued*)

No	Author	Title	Year	Location	Study Design	Population	Sample Size	Variables Related to Treatment Non-Adherence	Or Impact Non-Adherence
66.	Kizito et all	Risk factors for mortality among patients diagnosed with multi-drug resistant tuberculosis in Uganda: a case-control study	2021	Uganda	Case-control study	MDR-TB patients diagnosed and treated in 2016	198		• Multidrug-resistant tuberculosis (MDR-TB) • Mortality
67.	Workie et all	Treatment Interruption Among Drug-Susceptible Pulmonary Tuberculosis Patients in Southern Ethiopia	2021	Southern Ethiopia	Case-control study	Pulmonary TB patients in South Ari district, Southern Ethiopia	255	• Alcohol consumption • Smoking habits • Use of traditional medicine • HIV co-infection • Waiting time at the health facility	
68.	Zhang et all	Treatment outcomes of patients with multidrug and extensively drug-resistant tuberculosis in Zhejiang, China	2021	Zhejiang, China	Cohort study	M/XDR-TB patients treated at nine referral hospitals in Zhejiang	262	• Age > 60 years • Adverse drug effects	Extensively drug-resistant tuberculosis (M/XDR-TB)
69.	Karat et all	"You have to change your whole life": A qualitative study of the dynamics of treatment adherence among adults with tuberculosis in the United Kingdom	2021	United Kingdom	Qualitative study	Adults with tuberculosis undergoing treatment, and their caregivers	22	• Personal (knowledge of TB, Beliefs, mental health) • Social (family support, stigma) • Structural (housing, employment) • Health system (relationship with healthcare providers) • Treatment-related (side effects, treatment routine)	

70.	Nirmal et all	"If not for this support, I would have left the treatment!": Qualitative study exploring the role of social support on medication adherence among pulmonary tuberculosis patients in Western India	2021	Western India	Qualitative study	Pulmonary tuberculosis patients in Bhiwandi, Maharashtra	37	• Lack of empathy and Compassion from the family • Lack of empathy and Compassion from afriends • Neglect (Experienced desertion, lack of care, and emotional support from family) • Neglect (Experienced desertion, lack of care, and emotional support from a friends) • Lack of Strength and Motivation (No received strength and motivation from family) • Lack of Strength and Motivation (No received strength and motivation from a friends) • Lack of tangible aid (Experienced financial, accommodation, nutrition, and transportation assistance) • Insufficient provider interaction and lack of detailed guidance from healthcare workers • No medication doses reminders (Constant daily reminders for medication doses were reported)
71.	Adisa et all	Knowledge about tuberculosis, treatment adherence and outcome among ambulatory patients with drug-sensitive tuberculosis in two directly-observed treatment centres in Southwest Nigeria	2021	Southwest Nigeria	Mixed-methods (cross-sectional survey and retrospective review)	ambulatory DS-TB patients	140	• Inaccessibility to healthcare facility • Pill burden

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No	Author	Title	Year	Location	Study Design	Population	Sample Size	Variables Related to Treatment Non-Adherence	Or Impact Non-Adherence
72.	Batte et all	Prevalence and factors associated with non-adherence to multi-drug resistant tuberculosis (MDR-TB) treatment at Mulago National Referral Hospital, Kampala, Uganda	2021	Kampala, Uganda	Cohort study	MDR-TB patients treated at Mulago National Referral Hospital	227	• Previous DR-TB treatment	
73.	Subbaraman et all	Understanding Nonadherence to Tuberculosis Medications in India Using Urine Drug Metabolite Testing: A Cohort Study	2021	Chennai, Vellore, Mumbai, India	Cohort study with urine metabolite testing	Adult drug-susceptible TB patients, including people with HIV	650	• Low wage • Alcohol use • Smoking • Long time to collect medication refills • HIV status • Traveling from home • Forgetting • Feeling depressed • Running out of pills	
74.	Asriwati, et all	Risk factors analysis of non-compliance of Tuberculosis (TB) patients taking medicine in Puskesmas Polonia, Medan, 2021	2021	Medan, Indonesia	Case-control study	TB patients in Polonia Health Center Medan	136 (68 cases, 68 controls)	• Role of health workers (give motivation; supervision) • Side effects • Feeling healthy • Knowledge	
75.	Huddart et all	Adherence trajectory as an on-treatment risk indicator among drug-resistant TB patients in the Philippines	2022	Philippines	Retrospective analysis	Drug-resistant TB patients receiving treatment between 2013 and 2016	596		Drug-resistant TB (DR TB) and extremely drug-resistant (XDR) TB

76.	Grigoryan et all	Factors Influencing Treatment Adherence Among Drug-Sensitive Tuberculosis (DS-TB) Patients in Armenia: A Qualitative Study	2022	Yerevan, Armenia	Qualitative study	Former DS-TB patients, family members, TB healthcare providers	16 (patients) + 2 (family) + 3 (physicians)	• Awareness of TB • Trust in healthcare providers • Social support (providers, family, and friends) • Stigma • Tolerance of medications • Accessibility and affordability of treatment services
77.	Kebede et all	Nonadherence Predictors to Tuberculosis Medications among TB Patients in Gambella Region of Ethiopia	2022	Gambella, Ethiopia	Case-control study	TB patients treated at public health facilities in Gambella	296	• Perceived stigma • Lack of counselling • Smoking • Undermining severity of TB • Lack of trust in treatment benefits • Privacy (lack of confidentiality and protection)
78.	Zhu et all	Factors Associated with Non-Adherence for Prescribed Treatment in 201 Patients with Multidrug-Resistant and Rifampicin-Resistant Tuberculosis in Anhui Province, China	2022	Anhui Province, China	Cross-sectional survey	MDR/RR-TB patients attending treatment centers in Anhui	201	• Adverse events • Suburban areas • Low education level • Low monthly income • Other chronic diseases
79.	de Aguiar et all	Factors associated with non-completion of latent tuberculosis infection treatment in Rio de Janeiro, Brazil: A non-matched case control study	2022	Rio de Janeiro, Brazil	Case-control study	Contacts of active TB patients treated at University Hospital	518	• Drug use • Drug intolerance • Co-morbidities

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No	Author	Title	Year	Location	Study Design	Population	Sample Size	Variables Related to Treatment Non-Adherence	Or Impact Non-Adherence
80.	Nursasi et all	Impact of Instrumental Support from Family on Medication Adherence among Tuberculosis Patients in Bogor City, West Java, Indonesia	2022	Bogor City, West Java, Indonesia	Cross-sectional study	TB patients in 12 primary health centers in Bogor	106	• Family support (financial, transportation, medication reminders)	
81.	Suliman et all	Risk factors for early TB treatment interruption among newly diagnosed patients in Malaysia	2022	Selangor, Malaysia	Prospective multicenter cohort study	Pulmonary TB smear-positive patients in Selangor, Malaysia	439	• Current smoker • Stigma • Waiting time at treatment center	
82.	Motappa, et all	Appraisal on patient compliance and factors influencing the daily regimen of anti-tubercular drugs in Mangalore city: A cross-sectional study	2022	Mangalore, India	Cross-sectional	TB patients	200	• HIV status • Poor patient-provider relationship • Ran out of drugs at home • Side effects of TB medication • Support of family during treatment duration • Lack of money for transportation • Treatment satisfaction at the health center • Boredom • Knowledge about TB treatment • Feeling of depression • Forgetting • Being busy with other work • Being out of home/town • Side effects of TB medication • Treatment course is long	

83.	Gonçalves et all	Factors affecting successful antituberculosis treatment: a single-center experience	2023	Presidente Prudente, São Paulo, Brazil	Retrospective cross-sectional study	TB patients treated at a reference service from 2010–2016	348	• Less education • HIV/AIDS status	
84.	Laza et all	Latent tuberculosis infection treatment completion in Biscay: differences between regimens and monitoring approaches	2023	Biscay, Spain	Retrospective cohort study	Contacts of smear-positive TB patients from five hospitals in Biscay	3,066	• Sex (male) • Lack of nurse telemonitoring	
85.	Lolong et all	Non-adherence to anti-tuberculosis treatment, reasons and associated factors among pulmonary tuberculosis patients in the communities in Indonesia	2023	Indonesia	Cross-sectional study	Pulmonary TB patients across 33 provinces in Indonesia	2,045	• Gender (male) • Old age • Smoking • Low education level • Region (rural residence)	
86.	Lee et all	The incidence of tuberculosis recurrence: Impacts of treatment duration and adherence to standard anti-tuberculous therapy	2023	Taiwan	Cohort study	Patients with pulmonary tuberculosis from Taiwan's National Health Insurance Database	33,298		Increased TB recurrence
87.	Anye et all	Depression, anxiety and medication adherence among tuberculosis patients attending treatment centres in Fako Division, Cameroon: cross-sectional study	2023	Fako Division, Cameroon	Cross-sectional study	TB patients attending treatment centers in Fako Division	375	• Depression	

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No	Author	Title	Year	Location	Study Design	Population	Sample Size	Variables Related to Treatment Non-Adherence	Or Impact Non-Adherence
88.	Anley all	Prognostication of treatment non-compliance among patients with multidrug-resistant tuberculosis in the course of their follow-up: a logistic regression–based machine learning algorithm	2023	Northwest Ethiopia	Retrospective follow-up study	517 MDR-TB patients enrolled in two referral hospitals	517	• Educational status • Treatment supporter	
89.	Amkongo, et all	Factors associated with the unsuccessful TB treatment outcomes in the northern regions of Namibia: a mixed methods study	2023	Kunene and Oshana regions, Namibia	Mixed methods (quantitative & qualitative)	TB patients from health records and healthcare workers involved in DOTS	4,477 records (from ETR.net), 13 key informants	• Type of DOT (community-based DOTS) • Alcoholism • Smoking • Geographical access (transport, nomadism) • Stigma • Lack of proper TB understanding	
90.	Lin and Xiang	Factors Associated with Non-Adherence to Treatment Among Migrants with MDR-TB in Wuhan, China: A Cross-Sectional Study	2024	Wuhan, China	Cross-sectional study	Migrants with MDR-TB vs. local residents	292	• Migration status • Medical insurance • Out-of-pocket expenses	
91.	Tirore et all	Non-adherence to anti-tuberculosis treatment and associated factors among TB patients in public health facilities of Hossana town, Southern Ethiopia, 2022	2024	Hossana, Ethiopia	Cross-sectional study	TB patients from four public health facilities in Hossana	233	• Low formal educational • Poor TB knowledge • Not disclosure of TB status to family	

92.	Lee et all	Predictors, mortality, and health outcomes of intensive phase non-adherence to a regimen in patients with drug-susceptible tuberculosis: a nationwide linkage database	2024	South Korea	Nationwide cohort study	Drug-susceptible pulmonary TB patients starting WHO-recommended regimens	46,818	• Old Age • Comorbidities (Diabetes, History of renal failure etc) • Income level (Low income) • Health insurance	• Progression to MDR/XDR TB; • Poor health outcomes (new hospital admission for pneumonia, admission to an intensive care unit (ICU), and use of mechanical ventilation; • Risk of mortality
93.	Hassani et all	Relationship of family caregivers' associated factors with medication adherence among elderly with tuberculosis in Iran	2024	Tehran, Iran	Descriptive-analytical study	Elderly patients with TB and their family caregivers from Masih Daneshvari Hospital	305	• Marital status (single, widowed or lonely) • Caregiving responsibility • Financial hardship	
94.	Omar et all	Assessment of Non-Adherence to Anti-TB Drugs and Associated Factors Among Patients Attending TB Treatment Centers During COVID-19 Pandemic in Mogadishu, Somalia: A Cross-Sectional Study	2024	Mogadishu, Somalia	Cross-sectional study	TB patients attending three TB centers in Mogadishu	255	• Forgetting medication • Feeling well • Side effects • Fear of covid-19 (during pandemic) • Age • Unemployment • Smoking • Proximity to health facility • Healthcare provider attitudes	
95.	Almeida et all	Factors associated with unsuccessful tuberculosis treatment in Manaus, Amazonas, from 2011 to 2021	2024	Manaus, Amazonas, Brazil	Ecological study	All new TB cases in Manaus from 2011 to 2021	25,754	• Male • Old Age • HIV+ • Diabetes • Use of alcohol • tobacco or other drugs • No DOT • Low education level • Homeless	

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No	Author	Title	Year	Location	Study Design	Population	Sample Size	Variables Related to Treatment Non-Adherence	Or Impact Non-Adherence
96.	Engoru et all	Malnutrition and unsuccessful tuberculosis treatment among people with multi-drug resistant tuberculosis in Uganda: A retrospective analysis	2024	Uganda	Retrospective analysis	Persons with MDR-TB at Mubende Regional Referral Hospital	98	• Older age • Malnutrition • Previous TB treatment	Multi-drug resistant tuberculosis (MDR-TB)
97.	Opito et all	Treatment success rate and associated factors among drug susceptible tuberculosis individuals in St. Kizito Hospital, Matany, Napak district, Karamoja region. A retrospective study	2024	Karamoja, Uganda	Retrospective cohort study	Drug-susceptible TB patients treated at St. Kizito Hospital	1234	• Older Age • Undernutrition;HIV status	