International Seminar and Workshop on Public Health Action
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Risk Factors for Tuberculosis Development in Patients with Comorbidities: A Systematic Review

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Article Info
Article History
Submitted: 14/08/2025
Revised: 12/09/2025
Accepted: 25/08/2025
Keywords:
TB with comorbidity ; age; Gender; malnutrition; TB-HIV; CKD

Abstract

Tuberculosis (TB) is an infectious disease caused by Mycobacterium tuberculosis. Comorbid conditions worsen TB outcomes, increasing mortality risk through immune system impairment and making treatment more challenging. his review aims to examine the various risk factors associated with TB in patients suffering from comorbid diseases. A systematic review was conducted, focusing on seven national and international articles selected using the PRISMA method. The databases utilized for the literature search included ProQuest, PubMed, and Google Scholar. The articles reviewed were published between 2020 and 2025 and met specific inclusion criteria. Studies show that male gender is the most dominant risk factor. Most TB respondents may experience nutritional intake deficits and weight loss. TB patients with HIV are mostly unmarried, have low education levels, and have a history of opportunistic infections, while patients with stage 3 to 5 CKD have a higher risk of TB. TB patients require integrated care to detect and manage TB alongside comorbidities. Additionally, TB sufferers should undergo regular screenings to monitor their health status and detect the emergence of comorbidities. This also serves as an intervention to prevent the transmission of pulmonary TB in the community, especially among close contacts.

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eISSN 3063-2439

Introduction

Tuberculosis (TB) is a contagious disease and the leading cause of death from a single chronic infectious agent, transmitted by the bacterium Mycobacterium tuberculosis, which primarily attacks the lungs and spreads when an infected person expels the bacteria into the air, for example through coughing (WHO, 2024). TB is a disease that can be both cured and prevented (WHO, 2025). However, comorbid conditions can worsen the health of someone who is already suffering from TB.

TB remains a major cause of mortality and morbidity among infectious diseases (Selvaraju et al., 2023). The World Health Organization (WHO) in 2023 reported 10.8 million people worldwide were infected with TB, including 6 million men, 3.6 million women, and 1.3 million children. India has the highest number of TB cases in the world, with an estimated TB incidence of 2.77 million cases in 2022. Indonesia ranks second globally, with 1,090,000 TB cases and 125,000 deaths annually (WHO, 2024). In 2024, approximately 885,000 TB cases were detected, with distribution showing 496,000 cases among men, 359,000 among women, and 135,000 in children aged 0–14 years. These statistics underscore the urgent need to strengthen prevention and treatment efforts across Indonesia (Ministry of Health of the Republic of Indonesia, 2025).

Several factors influence TB incidence in Indonesia, including sociodemographic factors (sex, age, education level, marital status, family income, type of occupation, BMI), environmental factors (exposure to sunlight in the home, presence of artificial ventilation, history of contact with TB patients, and household size), host-related factors (smoking habits), and comorbidities (HIV, diabetes, and asthma) (Handayani and Palino, 2025; Pralambang and Setiawan, 2021).

A person suffering from TB with comorbidities has a higher risk of death due to greater immune system weakness, and TB treatment can also become more complex and require special attention (Maharani, 2024). TB with comorbid HIV poses a significant burden, accounting for about 6.1% of new cases and being a leading cause of death among people with HIV (Wikipedia, 2025). Data from the CDC in 2023 also shows that 23.4% of TB patients in the U.S. have diabetes, making it the most common medical risk factor (CDC, 2025).

TB conditions with comorbidities require serious attention, as they have a negative impact on the patient's body. Although various studies have identified risk factors for tuberculosis (TB) in patients with comorbidities, most literature still focuses on single relationships such as TB-HIV or TB-diabetes, while studies on multi-comorbidities remain limited. The author is conducting a systematic review to summarize the scientific phenomenon regarding the risk factors for TB occurrence in patients with comorbidities. This aims to provide an overview of the condition of patients with TB and comorbidities.

Methods

This study uses a systematic review methodology. The databases used for literature search are Proquest, PubMed, Google Scholar, and various other online databases. The combinations of keywords used in the literature search are "comorbid pulmonary TB," "causal factors of pulmonary TB," and "TB with comorbidities." The author also utilized Boolean operators: ("Pulmonary Tuberculosis" OR "Lung Tuberculosis") AND ("Comorbidity" OR "HIV" OR "Diabetes Mellitus" OR "Asthma" OR "Chronic disease") AND ("Risk factor" OR "Determinant").

Article selection and quality assessment were conducted by the researchers according to the established criteria using a checklist. The inclusion criteria are that the articles must be quantitative studies published in either English or Indonesian between 2020 and 2025. Exclusion criteria include qualitative research articles, articles not accessible as full text, systematic reviews, literature reviews, and meta-analyses. Data extraction was performed using a standard Excel form that included study identity information, research design, population characteristics, type of TB, comorbid diseases, risk factors, outcomes, and effect sizes. Two researchers independently conducted the extraction, and any discrepancies were resolved through discussion until consensus was reached. The extracted data were then summarized in a study characteristics table for further analysis. Article selection was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 flow. At the identification stage, a total of 10,286 articles were obtained from various databases. Ultimately, 7 articles met the criteria and were analyzed further. The entire selection process is illustrated using a PRISMA diagram. The article selection following the PRISMA 2020 guidelines is presented in the following figure.

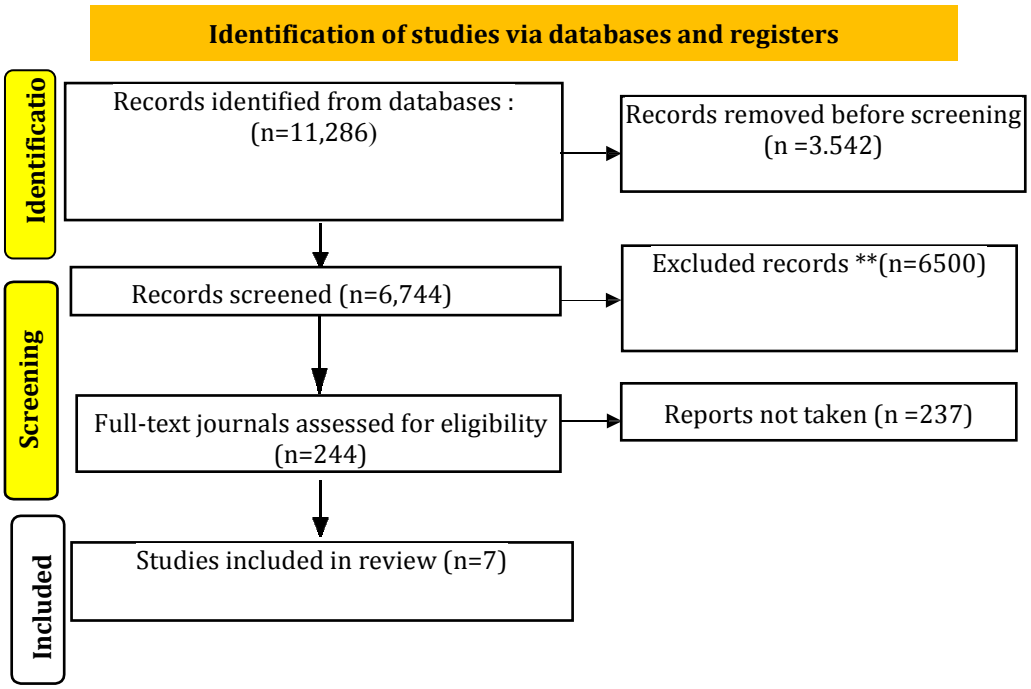

Figure 1. Systematic review flowchart: PRISMA

Results

The results of the systematic review process indicate that seven primary journals met the inclusion criteria and relevance requirements, with a primary focus on tuberculosis (TB) patients who have comorbid conditions. These journals were selected because they presented significant associations between the presence of comorbidities and an increased risk of TB occurrence, in terms of incidence, clinical severity, and treatment outcomes. The selected literature originated from reputable databases and underwent a rigorous selection process based on topic relevance, methodological rigor, data completeness, and publication within the last five years. To ensure transparency and traceability of the selection process, the search results are presented in a table summarizing the characteristics and key findings of each journal.

Table 1. Systematic review

Factor	Country	Research Title	Author & Year	Population & Sample	Research Design	Key Findings (aOR/CI/Prevalence)	Interpretation
Sociodemographics	Indonesia	Risk Factors of Pulmonary Tuberculosis in Type 2 Diabetes Mellitus in Yogyakarta	Nuraisyah et al., 2024	DM patients, 52 respondents (26 cases, 26 controls)	Case-control, regression logistics	DM women are more at risk of TB (aOR = 9.60; CI 0.14–55.96); protective old age (aOR = 0.24; CI 0.07–0.76)	Significant gender factors; women with DM are more susceptible to TB. Old age may be related to immunity & exposure patterns.
Comorbidities (NCDs)	Indonesia	Non-communicable comorbidities in pulmonary tuberculosis and healthcare utilization: analysis of 2021 Indonesian national health insurance data	Prasiska et al., 2024	BPJS 2021 data, 27,449 pulmonary TB patients	Cross-sectional, logistic regression	Comorbid prevalence of NCDs = 11.8% (COPD 4.71%, DM 4.2%, CVD 2.22%). Risk factors: age >60 years (aOR 5.16; CI 4.23–6.3), married (aOR 1.19; CI 1.05–1.34), not working (aOR 1.27; CI 1.08–1.49)	Comorbid NCDs increase TB susceptibility. There is a need for the integration of TB-NCD services, especially in the elderly.
Comorbidities (CKD)	English	The association between chronic kidney disease and tuberculosis : a comparative cohort	Ruzangi, Iwagami, Smeeth, Mangtani, and Nitsch, 2020	242,349 CKD + control patients, total 477,212 participants	Cohort Retrospective, Poisson Regression	TB incidence: CKD 14.63 vs non-CKD 9.89/100,000 PY. CKD increases the risk of TB (aRR 1.42; CI 1.01–1.85); stronger in ethnic	CKD increases the risk of TB even in low-burden countries. TB screening is

Factor	Country	Research Title	Author & Year	Population & Sample	Research Design	Key Findings (aOR/CI/Prevalence)	Interpretation
		study				minorities (aRR 2.83; CI 1.32–6.03)	important in CKD patients.
Comorbidities (HIV)	Indonesia	Overview of Opportunistic Tuberculosis Infections in People with HIV	Argista, Sitorus, and Najmah, 2024	74 people HIV positive for TB, total sampling	Description	The majority are men (86.5%), unmarried (68.9%), and have low education (83.8%). History of opportunistic TB infection in 41.9% of respondents	TB remains the main opportunistic infection in HIV. Social factors exacerbate the risk, early detection is important.
Comorbidities (malnutrition)	Indonesia	Early Detection of the Risk of Malnutrition in Children with Tuberculosis using STRONGKids	Riska Nur Suci Ayu and Rahmayati, 2023	Children aged 1–10 years with TB/suspected TB, n=20	Cross-sectional, STRONGKids screening	Risk of malnutrition: high 25%, medium 70%, low 5%	High malnutrition in TB children, shows the importance of nutrition screening from an early age.
Nutrition (Macronutrients)	Indonesia	Intake of Macromolecular Nutrition Status in Pulmonary Tuberculosis Subjects at Seputih Raman Health Center	Girinaha, Yekti, and Kusumo, 2022	30 pulmonary TB patients	Descriptive (24-hour food recall, Nutrisurvey)	60% of patients are underweight; Energy deficit 80%, carbohydrate deficit 80%, protein deficit 46.7%, fat deficit 53.3%	Macronutrient deficits are significant, especially carbohydrates. Nutrition education must emphasize balance, not just protein/fat.

Based on a synthesis of seven journals, it is known that sociodemographic factors, nutritional status, and comorbidities such as HIV, diabetes, and CKD play an important role in increasing vulnerability and worsening the course of TB. Differences in regional contexts show that HIV is more dominant in Africa, while diabetes and metabolic diseases dominate in Asia, and CKD/cancer is more prominent in developed countries. From a clinical perspective, these findings emphasize the importance of comorbidity screening (T2DM, HIV, CKD) from the beginning of TB diagnosis, integration of TB–NCD services, and targeted nutritional interventions especially in children and vulnerable groups. The implementation of this integrated approach not only has the potential to increase the success of therapy, but also prevent

recurrence and reduce mortality, thus becoming a key strategy in the prevention and management of TB comprehensively.

Discussion

Sociodemographic Risk Factors

The results of the journal review above show that sociodemographic factors play an important role in increasing susceptibility to TB. A study in Yogyakarta found that female type 2 diabetes mellitus patients had a higher risk of developing TB (aOR = 9.60) than men, while older age appeared to be protective (aOR = 0.24) (Nuraisyah et al., 2024). These results are different from the national population study in Indonesia which shows that old age (>60 years) is a strong predictor of the occurrence of TB–NCD comorbidities (aOR = 5.16) (Prasiska et al., 2024). These differences indicate that sociodemographic factors can affect TB risk through different pathways, both through biological and structural vulnerability. Biological susceptibility to TB is related to internal factors such as age, sex, immune status, and the presence of comorbidities, while structural vulnerability is more influenced by access to health services, education level, type of employment, and economic conditions. The theory of social determinants of health asserts that socio-economic factors have an important role in the distribution of infectious diseases, including TB. Recent evidence reinforces this, with a survey of TB prevalence in Vietnam showing that men have three times the risk of developing TB than women (OR = 3.0; CI 1.7–5.0), especially related to differences in behavior and environmental exposure (Nguyen et al., 2023). In line with these findings, the new study also reported that the prevalence of latent TB infection tends to be higher in adult men than in women, indicating a complex interaction between biological and social factors in increasing susceptibility to TB (Gaifer et al., 2025). Thus, the variation in research results in Indonesia is consistent with the global literature that emphasizes that the risk of TB is not only influenced by individual factors, but also very closely with the social conditions of the community.

Nutritional Risk Factors

Poor nutritional status appears consistently to be an important risk factor for TB. Research in Lampung shows that 60% of pulmonary TB patients are thin and 80% have energy deficits, especially carbohydrates (80%), proteins (46.7%), and fats (53.3%)(Girinaha et al., 2022). Similar results were obtained in children with TB, where 25% were at high risk of malnutrition and 70% were at moderate risk (Riska Nur Suci Ayu & Rahmayati, 2023). In the global context, the prevalence of undernutrition reaches 35.8% in TB patients, and is exacerbated by the presence of HIV (aOR = 6.18) and diabetes (aOR = 17.5) (Musuenge et al., 2020). This condition confirms that malnutrition is not only a consequence of TB, but a predisposing factor that worsens the course of the disease. Targeted nutrition interventions, including routine malnutrition screening and micronutrient supplementation, are urgently needed as part of TB management.

Biologically, deficiencies in energy and nutrients lower cellular immunity which is essential in fighting *Mycobacterium tuberculosis*, thus increasing the risk of latent infection progressing to active TB. A cohort review and prognosis study found that undernutrition increased the risk of active TB by about 2.23 times (HR 2.23; 95% CI 1.83-2.72) over a <10-year period compared to individuals with normal nutritional status (Franco et al., 2024). WHO in *Global Tuberculosis Report 2023* estimates that by 2022, around 2.2 million new TB cases worldwide could be directly attributed to undernourishment as a risk factor (WHO, 2025). In addition, studies in Ethiopia in patients with undernourished Rifampisin/MDR Resistant TB showed that they had a much higher chance of experiencing unsuccessful treatment outcomes (therapy failure, discontinuation, death) than those with normal or more nutritional status (Siraj et al., 2025). Therefore, screening of nutritional status from the beginning of TB diagnosis, the provision of nutritional support—whether through energy and protein supply, micronutrients, or feeding interventions—as well as health policies that prioritize vulnerable groups (children, low-income communities) are crucial to be included in national TB control programs.

HIV-Related Risks

TB is still the main opportunistic infection in people with HIV. A study in South Sumatra showed that 41.9% of HIV patients had TB, with the majority of respondents being poorly educated and unmarried (Argista et al., 2024). Globally, the burden of TB-HIV is highest in Africa, while in Asia the burden of HIV is relatively lower but other factors such as diabetes predominate. These differences show contextual variations: in countries with a high HIV burden, strengthening early detection and adherence to antiretroviral therapy (ART) is key, while in Asia there is a need to integrate TB programs with metabolic disease management.

CKD and the other NCD Comorbidities

Other chronic diseases also contribute to an increased risk of TB. A cohort study in the UK showed that CKD patients had a higher risk of developing TB (aRR = 1.42; CI 1.01–1.85), with a stronger risk in ethnic minority groups (aRR = 2.83) (Ruzangi et al., 2020). In Indonesia, national data confirms that the

prevalence of NCD comorbidities in TB patients reached 11.8%, with COPD (4.71%), DM (4.2%), and CVD (2.22%) as the dominant comorbidities (Prasiska et al., 2024). These differences in patterns reflect the different double burdens between regions: in Africa HIV is the main driver, in Asia diabetes and metabolic diseases dominate, while in developed countries CKD and cancer are more prominent.

Cross-study findings suggest that comorbidities amplify TB risk by different mechanisms according to regional contexts. HIV weakens cellular immunity thereby accelerating the progression of TB infection, predominant in Africa. Meanwhile, in Asia, diabetes worsens glucose control which impacts macrophage function, thereby increasing TB susceptibility. In developed countries, CKD and cancer play a role through immunosuppression due to chronic conditions and therapy. Therefore, TB prevention and control strategies should be tailored to the regional epidemiological profile.

These findings underscore the importance of more targeted public health interventions, namely TB screening integrated with HIV and NCD programs, nutritional support programs that emphasize not only protein but also energy and micronutrient balance; and strengthening health literacy and community-based interventions in low-educated and low-income groups. Cross-program integration will increase the effectiveness of TB prevention and control.

Various research results show that there is a link between TB and comorbid diseases, but there are a number of research limitations, namely the need for longitudinal studies to assess the long-term causal relationship between comorbidities and TB, the limitations of specific research for children who have higher nutritional susceptibility; and the lack of cross-country data comparisons that can explain contextual variations in more depth. Focusing on this area will strengthen the evidence base in designing more responsive TB policies.

Conclusion

This review confirms that tuberculosis is closely associated with a variety of comorbidities, including type 2 diabetes mellitus, chronic kidney disease, HIV, and poor nutritional status, with different variations in risk burden between regions. Clinically, comorbidities worsen the course of the disease, increase susceptibility, and slow recovery, especially in vulnerable groups such as children and patients with low immunity. Therefore, the urgent practical implications are the implementation of comorbidity screening (T2DM, CKD, HIV) in an integrated manner with TB services, as well as comprehensive nutritional support that emphasizes the balance of energy, protein, and micronutrients. From a policy perspective, integrated TB–NCD programs and population-based nutrition interventions are needed to reduce the double burden, especially in low-middle-income countries. However, the limited number of articles and the dominance of cross-sectional designs in this review signal the need for longitudinal and cross-cross-sectional comparative research to strengthen the scientific evidence and support more targeted policymaking.

Author Contributions

The authors have no conflicts of interest to declare.

Acknowledgments

The autors would like to thank the committee of the 5th international Seminar and Workshop on Public Health Action (ISWAOPHA 2025) for the opportunity and support in this publication process.

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References

Argista, Z. L., Sitorus, R. J., and Najmah. (2024). An Overview of Opportunistic Tuberculosis Infection in People With HIV in South Sumatra. *Domain Research: Journal of Multidisciplinary Research and Development*, *7*(1), 389–394. https://doi.org/10.38035/rrj.v7i1.1208

Binekada, I. M. C. (2024). *Influence characteristics inpatients to satisfaction services at Regional Hospital Konawe*. *1*(1), 12–16.

CDC. (2025). TB Surveillance Report. Retrieved July 9, 2025, from https://www.cdc.gov/tb-surveillance-report-2023/summary/risk-factors.html?utm_source=chatgpt.com

Girinaha, I. P. P., Yekti, R., and Kusumo, P. D. (2022). Intake of Macromolecular Nutrition Status in Pulmonary Tuberculosis Subjects at the Seputih Raman Health Center, Central Lampung. *Health Science Journal of Indonesia*, *13*(1). Retrieved from https://doi.org/10.22435/hsji.v13i1.6454

Handayani, L., and Palino, I. L. (2025). *Review article Analysis of Factors Influencing Open Defecation Behavior in Coastal Areas of Indonesia : A Review*. *2*(1), 140–151.

Ministry of Health of the Republic of Indonesia. (2025). The Indonesian Movement to End TB. Retrieved July 9, 2025, from https://kemkes.go.id/id/indonesias-movement-to-end-tb#:~:text=Berdasarkan Global TB Report 2024, around 14 deaths every hour.

Maharani, M. R. E. (2024). Comorbid Conditions in the TB Healing Process. Retrieved July 9, 2025, from https://kesmas-id.com/kondisi-komorbid-dalam-proses-penyembuhan-tb-yuk-cari-tahu/

Mandal, S., Rao, R., and Joshi, R. (2023). Estimating the Burden of Tuberculosis in India: A Modelling Study. *Indian Journal of Community Medicine*, *42*(1), 147–150. https://doi.org/10.4103/ijcm.IJCM

Mongan, R., and Fajar, F. (2017). Relationship Between Family Support and Medical Compliance in Patients With Pulmonary Tuberculosis in the Working Area of the Community Health Center of Abeli, Kendari. *Public Health of Indonesia*, *3*(1), 17–22. https://doi.org/10.36685/phi.v3i1.111

Musuenge, B. B., Poda, G. G., and Chen, P. C. (2020). Nutritional status of patients with tuberculosis and associated factors in the health centre region of burkina faso. *Nutrients*, *12*(9), 1–13. https://doi.org/10.3390/nu12092540

Nuraisyah, F., Juliana, N., Astaria, D., Khalisah, N., Fatih, D. M. F. Al, Dewi, S. K., ... Marwati, T. (2024). Risk Factors of Pulmonary Tuberculosis in Type 2 Diabetes Mellitus in Yogyakarta. *Journal of Epidemiology and Public Health*, *9*(2), 194–203. https://doi.org/10.26911/jepublichealth.2024.09.02.06

Pralambang, S. D., and Setiawan, S. (2021). Risk Factors for Tuberculosis in Indonesia. *Journal of Biostatistics, Population, and Health Informatics*, *2*(1). https://doi.org/10.7454/bikfokes.v2i1.1023

Prasiska, D. I., Chapagain, D. D., Osei, K. M., Rajaguru, V., Kang, S. J., Kim, T. H., ... Han, W. (2024). Non-communicable comorbidities in pulmonary tuberculosis and healthcare utilization: a cross-sectional study of 2021 Indonesian national health insurance data. *Archives of Public Health*, *82*(1), 1–10. https://doi.org/10.1186/s13690-024-01352-y

Riska Nur Suci Ayu, A., and Rahmayati, E. (2023). Early Detection of the Risk of Malnutrition in Children with Tuberculosis Using Screening Tools: STRONGKids. *Tambusai Health Journal*, *4*(4), 5846–5851. https://doi.org/10.31004/jkt.v4i4.21479

Ruzangi, J., Iwagami, M., Smeeth, L., Mangtani, P., and Nitsch, D. (2020). The association between chronic kidney disease and tuberculosis; A comparative cohort study in England. *BMC Nephrology*, *21*(1), 1–9. https://doi.org/10.1186/s12882-020-02065-4

Selvaraju, S., Velayutham, B., Rao, R., Rade, K., Thiruvengadam, K., Asthana, S., ... Bhargava, B. (2023). Prevalence and factors associated with tuberculosis infection in India. *Journal of Infection and Public Health*, *16*(12), 2058–2065. https://doi.org/10.1016/j.jiph.2023.10.009

Susilawaty, A., Basri, S., Haerana, B. T., Ane, R. La, Mappau, Z., and Ikhtiar, M. (2024). The Risk Factors Contributing to The Occurrence of Pulmonary Tuberculosis in The Small Island of South Sulawesi, Indonesia. *Public Health of Indonesia*, *10*(4), 104–116. https://doi.org/10.36685/PHI.V10I4.876

Ulva, S. M., and Hamsi, A. J. (2020). Risk factors for the incidence of pulmonary tuberculosis in the working area of the Lombakasih Health Center, Bombana Regency. *MIRACLE Journal Of Public Health*, *3*(2), 188–196. https://doi.org/10.36566/mjph/vol3.iss2/177

WHO. (2024). 2024 Global tuberculosis report. In *25 November 2024*. Retrieved from https://www.who.int/teams/global-tuberculosis-programme/tb-reports/global-tuberculosis-report-2024

WHO. (2025). Tuberculosis. Retrieved July 9, 2023, from https://www.who.int/news-room/fact-sheets/detail/tuberculosis

Wikipedia. (2025). Tuberculosis. Retrieved from https://en.wikipedia.org/wiki/Tuberculosis?utm