

## Management Of Pediatric Pulmonary Tuberculosis Current Solutions And Challenges: Literature Review

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Article Info	Abstract
Article History: Received: 09 Desember 2024 Revised: 20 Desember 2024 Accepted: 22 Desember 2024	<b>Background:</b> Tuberculosis (TB) in children remains a significant global health concern, with many cases going undiagnosed. Mortality rates due to TB among children continue to rise, particularly in high-burden countries such as Ethiopia and South Africa.
Keywords: Pulmonary TB, Children, TB Screening, GeneXpert, Interventions	<b>Purpose:</b> This study aims to review various approaches and interventions that have been implemented to address the pediatric TB epidemic and assess their overall impact on child health.
Corresponding Author: Rikmal jaya Mandala Waluya University	<b>Methods:</b> This study utilized Boolean terms, and a systematic literature search was conducted across several databases, including ScienceDirect, PubMed, and Google Scholar.
Email: <a href="mailto:rikmaljaya60@gmail.com">rikmaljaya60@gmail.com</a>	<b>Results:</b> Diagnosis is often delayed due to non-specific symptoms and the difficulty of laboratory confirmation. While GeneXpert Ultra has improved detection accuracy, it has not fully addressed the diagnostic challenges.
	<b>Conclusion:</b> Findings indicate that screening and preventive treatment interventions are highly effective in improving child health outcomes. Although new diagnostic tools such as GeneXpert Ultra show great potential, significant challenges in the detection and management of pediatric TB remain. This review highlights the importance of a holistic approach to bridging the gaps in TB detection and treatment in children.

### Background

Tuberculosis (TB) in children continues to be a significant global health concern, with a substantial number of cases remaining undiagnosed. The World Health Organization (WHO) reported that in 2012, there were approximately 0.5 million new TB cases among children under the age of 15, accounting for 5.7% of the global TB burden in 2011. According to WHO data, the number of pediatric TB cases increased to 1.2 million in 2021, representing nearly 11% of all TB cases globally (Mokodompit et al., 2025). Although the proportion of pediatric TB cases may appear relatively small (5.7% in 2011 and 11% in 2021), the contribution of children to TB-related mortality rose sharply during the same period—from 4.6% to 14%. Studies have shown that over 96% of TB-related deaths in children occur among those who do not receive appropriate treatment (I. Putu Sudayasa et al., 2022).

Ethiopia is among the countries with a high TB burden, ranking seventh globally in 2021. WHO estimated that approximately 20,000 children in Ethiopia suffered from TB that

year, accounting for around 11.6% of all TB cases in the country (Andas et al., 2024). Since 2015, Ethiopia has adopted the use of GeneXpert MTB/RIF® as a primary diagnostic tool due to its higher sensitivity and specificity compared to conventional microscopy, thereby improving the accuracy of pediatric TB epidemiological data (Burusie et al., 2023).

To further enhance diagnostic accuracy, the GeneXpert Ultra test has been introduced, demonstrating greater effectiveness in detecting pulmonary TB (PTB) among children. However, challenges remain—particularly in obtaining bacteriological confirmation, which is often difficult in children with paucibacillary TB (Andas et al., 2022). Age-based routine screening interventions implemented in South Africa have shown promising outcomes, with screened children exhibiting improved treatment uptake and better health outcomes (Basile et al., 2022).

In this context, it is crucial to evaluate the effectiveness of various diagnostic and treatment strategies for pediatric TB. Existing research indicates that while interventions such as Bacillus Calmette–Guérin (BCG) vaccination and preventive TB therapy have proven effective, significant challenges remain in early detection and comprehensive management of pediatric TB (Wahyuni, S et al., 2022). These challenges must be addressed through a holistic and integrated approach. This literature aims to review the diverse strategies and interventions implemented in addressing the pediatric TB epidemic and their impact on overall child health outcomes (Howard-Jones & Marais, 2020).

## **Method**

Using Boolean terms, a systematic literature search was conducted across several databases, including ScienceDirect, PubMed, and Google Scholar. The selected articles were evaluated based on their relevance to the research questions, study methods, sample size, research design, findings, and the level of evidence applied in the studies.

## **Literature Search Strategy**

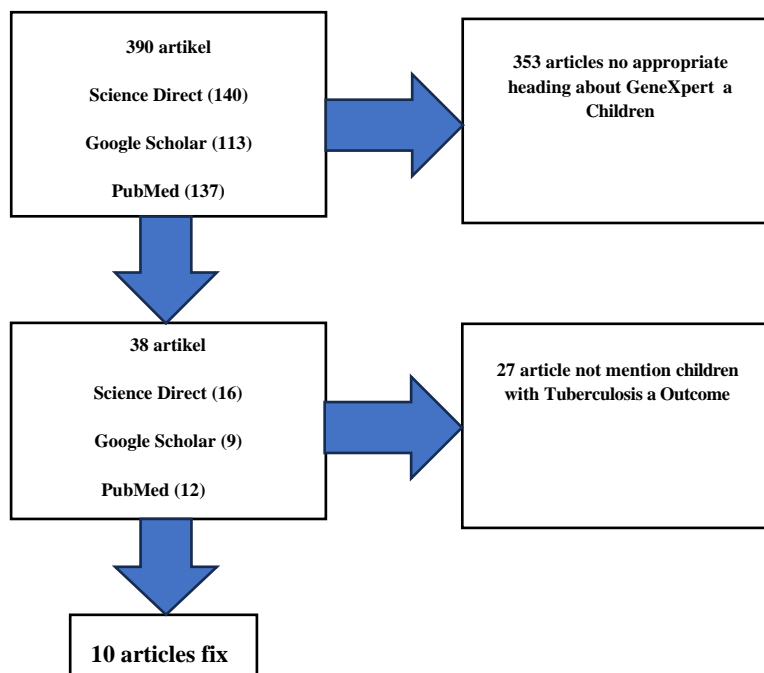
The authors conducted a systematic search for scientific articles using the PICO framework, as outlined below:

Patient : Children

Intervention : Intervention

Comparison : -

Outcome : Tuberculosis



Gambar 1. Literature Search

## Results

**Article 1** is titled *"Epidemiology of Childhood Tuberculosis and Predictors of Mortality Among Children Undergoing Tuberculosis Treatment in Central Ethiopia: An Extended Cox Model Survival Analysis."* According to this study, approximately 640 children aged 2 to 16 years with pulmonary tuberculosis were included. The data indicate that the majority of children contracted tuberculosis through household contact and community exposure. Among the 640 diagnosed children, 557 had documented household TB contact. A total of 45 children died, most of whom suffered from malnutrition. Children who were malnourished two months after initiating TB treatment had a significantly higher risk of mortality compared to those with normal nutritional status (Burusie et al., 2023).

**Article 2** concerns *"Management of Childhood Tuberculosis Infection in the Victorian Era: A Retrospective Clinical Audit of Factors Influencing Treatment Completion."* Among 402 participants with latent TB infection (TBI), 296 (74%) met the criteria for "complete" treatment. The most commonly used TB preventive therapy (TPT) regimen was six months of daily isoniazid (377 participants, 94%). Multivariate logistic regression analysis revealed that treatment completion was more likely among children and adolescents who underwent refugee health assessments (OR 2.31, 95% CI 1.34–4.00) or were concurrently treated for other medical conditions (OR 1.67, 95% CI 1.0–2.85), and less likely among those who experienced adverse effects (OR 0.32, 95% CI 0.11–0.94). Overall, TPT was well tolerated, with adverse effects reported in only 15 participants (3.7%) (Rebecca Helena Holmes, 2022).

**Article 3** is titled *"Paediatric Tuberculosis Diagnostics: Current Status and Future Directions."* The article highlights the persistent diagnostic challenges in pediatric TB. In 2020, an estimated 1.1 million children fell ill with TB, yet less than half were reported to

national TB programs. This diagnostic gap is primarily attributed to nonspecific symptoms, paucibacillary disease, and difficulties in obtaining quality specimens. However, progress has been made, including WHO-recommended rapid molecular diagnostics such as the Xpert MTB/RIF Ultra assay, which offers improved sensitivity (73%) compared to its predecessor. Stool is increasingly recognized as a child-friendly alternative specimen. WHO has also advocated for the use of clinical algorithms and host immune response biomarkers, including novel technologies like portable NAATs and host RNA-based testing, which show promising potential for the future (Basile et al., 2022).

**Article 4**, titled *"Childhood Tuberculosis: Screening, Diagnosis, and Management,"* emphasizes that pediatric TB remains a major public health issue in high-burden regions, primarily due to diagnostic difficulties and limited screening tools. While new diagnostic tools such as Xpert Ultra and urine LAM tests are promising, their implementation remains limited. The introduction of dispersible fixed-dose combination therapies has significantly improved treatment acceptability and adherence among children (Howard-Jones & Marais, 2020).

**Article 5**, titled *"Diagnostic Contribution of GeneXpert Ultra in Pediatric Pulmonary Tuberculosis,"* reports findings from 41 pediatric patients, of whom 63% (26/41) were diagnosed with pulmonary TB. Among these, 9 out of 26 cases (34%) were detected only by Ultra, with negative AFB and culture results. Ultra had a sensitivity of 50% (13/26) and specificity of 100% (15/15), with a positive predictive value (PPV) of 100% (13/13) and a negative predictive value (NPV) of 54% (15/28). Among the 28 patients with negative Ultra results, 13 (46%) were later diagnosed with TB, primarily by MoH-SS. When culture was used as the reference standard, the PPV and NPV were 67% and 100%, respectively (Battaglia et al., 2025).

**Article 6**, titled *"Effectiveness of Tuberculosis Screening Interventions in Children Based on Age,"* demonstrates that such interventions were most effective for the 0–14 age group. To evaluate the age-based effectiveness of intensive TB case-finding interventions, a six-step care cascade was used: screened, screen-positive, evaluated, diagnosed, treatment initiation, and favorable outcome (Brooks et al., 2022).

**Article 7**, titled *"Public Health Impact and Cost-Effectiveness of Screening for Active Tuberculosis Disease or Infection Among Children in South Africa,"* utilized a deterministic mathematical model to evaluate the effectiveness of age-based routine screening over a one-year period for children aged 0–5 years, with and without contact tracing and preventive therapy. Screening included symptom history, tuberculin skin testing, chest radiography, and confirmatory testing using GeneXpert Ultra. The study found that routine screening at age two, combined with contact tracing and preventive therapy, could prevent 11,900 TB cases (95% CI: 6,160–15,730), 1,360 deaths (95% CI: 260–3,800), and 40,000 DALYs (95% CI: 13,000–100,000) over one year. This combined strategy was cost-effective (incremental cost-effectiveness ratio of \$9,050 per DALY; 95% CI: 2,890–22,920), and remained cost-effective even with an annual infection risk of 1.6%. For risks between 0.8% and 1.6%, screening at age two was the dominant strategy (Brough et al., 2023).

**Article 8**, titled "*Current Treatment of Drug-Resistant Tuberculosis in Children*," reported that most children with RR/MDR-TB who receive appropriate treatment achieve high success rates (80–90%). However, undiagnosed and untreated children experience poor outcomes. Dodd et al. estimated that universal household screening could have prevented 2,350 child TB deaths in 2019. Moreover, if all child household contacts received levofloxacin-based TPT, an additional 5,620 TB cases and 1,240 deaths could have been prevented (Schaaf & Hughes, 2024).

**Article 9**, titled "*Long-Term Impact of Tuberculosis Disease on Early Childhood Health: A Prospective Birth Cohort Study*," prospectively followed children from birth to age five for TB, using diagnostic tools such as chest radiography and repeated Xpert MTB/RIF and liquid culture tests. The study also assessed the effects of TB diagnosis on wheezing episodes, lung function, and anthropometric measurements. Among 1,068 participants, 96 TB cases occurred (1,228 per 100,000 person-years [95% CI, 1,006–1,500]) over 7,815 child-years of follow-up. TB was associated with lower length-for-age (−0.40 [95% CI, −0.68 to −0.11]), weight-for-age (−0.30 [95% CI, −0.59 to −0.01]), and BMI-for-age z-scores (−0.54 [95% CI, −0.83 to −0.25]) at age five. Children with TB were also more likely to experience wheezing regardless of TB timing. Those diagnosed between 0 and 1 year had reduced time to reach peak tidal expiratory flow during total expiratory time (Martinez et al., 2023).

**Article 10**, titled "*Tuberculosis Transmission Risk Among Children in Hamburg, Germany*," found that of 3,154 confirmed TB cases, 79 (2.5%) were in children under 15 years, of whom 52 (58%) had pulmonary TB. Genotyping showed that 35 children (67%) belonged to secondary clusters, with adults as the source. Six immigrant children without known source cases were diagnosed with TB on average 48 weeks after arriving in Germany. Three German-born children were infected while visiting their parents' country of origin. Among 317 close contacts tested, only 21 (6.6%) were positive for LTBI. No secondary TB cases occurred during a mean follow-up of 551 weeks (Diel et al., 2023).

Table 1. Literature Review on Pediatric Tuberculosis

No	Author	Title	Objective	Method	Findings	Conclusion
1	Burusie et al., 2023	<i>Epidemiology of Tuberculosis in Children and Predictors of Death...</i>	To identify challenges in diagnosing and treating TB in children.	Literature review and clinical data analysis of pediatric TB patients.	Many children remain undiagnosed and untreated.	Better strategies are needed to improve early detection and treatment of pediatric TB.
2	Holmes, 2022	<i>Management of Tuberculosis Infection in Children in the Victorian Era...</i>	To assess factors influencing completion of preventive TB therapy in children with latent TB infection (LTBI).	Retrospective clinical audit using logistic regression on pediatric LTBI cases (2010–2016).	74% completed treatment; success was higher among children undergoing other treatments and lower in those with side effects.	Completion of TB preventive therapy is influenced by social, individual, and clinical factors. Shorter, child-friendly regimens are recommended.
3	Basile et al., 2022	<i>Diagnosis of Pediatric Tuberculosis: Now and the Future</i>	To review currently available diagnostic tools for childhood TB and future directions.	Literature review and WHO guideline analysis.	TB diagnosis in children remains low; however, tools like Xpert Ultra and stool specimens show promise.	More accurate, accessible, and child-friendly diagnostic tools are needed to enhance early detection and treatment.
4	Howard-	<i>Tuberculosis in</i>	To explore	Literature review	TB remains	The global burden

No	Author	Title	Objective	Method	Findings	Conclusion
	Jones & Marais, 2020	<i>Children: Screening, Diagnosis, and Management</i>	recent progress and challenges in screening, diagnosing, and managing pediatric TB.	and analysis of current evidence and policies.	difficult to diagnose and manage, especially in high-burden areas; new tests show promise but are not widely implemented.	of childhood TB is underestimated. Enhanced strategies for screening and care are urgently needed.
5	Battaglia et al., 2025	<i>The Contribution of GeneXpert Ultra Diagnostics to Pediatric Pulmonary Tuberculosis</i>	To evaluate the contribution of GeneXpert Ultra in diagnosing pediatric pulmonary TB in Brazil.	Prospective study of suspected pediatric TB cases (2020–2022).	GeneXpert Ultra detected 34% of cases with negative AFB and culture; sensitivity was 50%, specificity 100%.	GeneXpert Ultra significantly aids diagnosis of paucibacillary TB in children, but should be integrated with clinical evaluation.
6	Brooks et al., 2022	<i>Effectiveness of Tuberculosis Screening Interventions in Children Based on Age</i>	To evaluate age-specific effectiveness of active TB case-finding interventions.	Study conducted in 4 hospitals in Pakistan with verbal screening and clinical evaluation.	Out of 105,338 children screened, 1,417 were diagnosed; treatment success rate was 93.3%.	Active case-finding is effective for children aged 0–14, though evaluation gaps remain.
7	Brough et al., 2023	<i>Public Health and Cost-Effectiveness Impact of Screening for TB in Children in South Africa</i>	To evaluate the public health impact and cost-effectiveness of routine screening and contact tracing among children.	Deterministic mathematical modeling using epidemiological data.	Routine screening at age 2 plus contact tracing could prevent 11,900 TB cases and 1,360 deaths.	Routine screening is highly effective and cost-efficient in high-incidence areas.
8	Schaaf & Hughes, 2024	<i>Current Treatment of Drug-Resistant Tuberculosis in Children</i>	To describe characteristics of children with pulmonary TB at Dr. Moewardi Hospital.	Retrospective descriptive study based on medical records (ages 0–14).	Most patients were malnourished boys aged 1–5 with household TB contact.	Early detection is critical in managing pediatric TB, especially in young children with risk factors.
9	Schaaf & Hughes, 2024	<i>Long-Term Impact of Tuberculosis on Early Childhood Health</i>	To investigate long-term effects of TB on children's lung health.	Prospective cohort study from birth to age 5.	TB was associated with lower anthropometric z-scores and increased risk of wheezing.	Preventing TB in early life offers long-term benefits for child development.
10	Diel et al., 2023	<i>Risk of Tuberculosis Transmission in Children in Hamburg, Germany</i>	To analyze TB transmission risk among children in a low-incidence setting.	Whole genome sequencing (WGS) of Mtb and LTBI testing via QuantiFERON in close contacts.	Only 2.5% of TB cases were children; transmission from children was rare.	Young children with TB are unlikely to be transmission sources, supporting German guidelines.

## Discussion



The challenges of childhood tuberculosis (TB) are highly complex and require a comprehensive approach encompassing prevention, diagnosis, treatment, and long-term monitoring (Howard-Jones & Marais, 2020). One key aspect of this issue is the epidemiology of pediatric TB, in which household contact often serves as the primary source of infection. This underscores the need for improved education and preventive measures within families (Hadju et al., 2024). Moreover, the significant impact of malnutrition on mortality rates highlights the importance of integrating socio-economic considerations into TB treatment programs, making nutritional support a vital component of care (Burusie et al., 2023).

Diagnostic barriers present a major issue in managing pediatric TB, where non-specific symptoms and difficulties in sample collection contribute to underreporting and treatment delays (Purnamasari et al., 2024). While advancements in rapid molecular testing offer hope, limitations in accessibility and the need for trained health personnel emphasize the necessity for continued research to develop non-invasive and resource-appropriate diagnostic methods (Basile et al., 2022). The effectiveness of routine screening interventions, particularly for children aged 0–14 years, has been demonstrated; however, inconsistent implementation highlights the need for stronger public health policies and integration with existing child health programs (Brooks et al., 2022).

In the landscape of drug-resistant TB treatment in children, high success rates are observed when treatment is properly administered (Purnamasari et al., 2023). However, the risks faced by undiagnosed and untreated children underline the importance of proactive screening and preventive strategies. Universal household screening has emerged as a potentially life-saving intervention, deserving further support and investigation (Schaaf & Hughes, 2024). Additionally, the long-term consequences of TB on child health—including impaired growth and lung function—necessitate extended monitoring and tailored interventions to mitigate lasting impacts. These long-term effects may include structural changes in lung tissue and measurable limitations in ventilatory function (Martinez et al., 2023).

Finally, TB transmission dynamics in urban environments, particularly among immigrant populations, highlight the role of social determinants and the need for targeted interventions (Diel et al., 2023). Addressing factors such as poverty, overcrowding, and limited access to healthcare is essential to reduce TB transmission in vulnerable communities. In summary, effectively addressing pediatric TB requires a holistic strategy that includes robust prevention efforts, improved diagnostic tools, comprehensive treatment regimens, and ongoing monitoring—supported by strong public health policies and active community engagement (Howard-Jones & Marais, 2020).

## **Conclusion**

The management of tuberculosis (TB) in children demands a comprehensive and integrated approach due to the complexity of challenges involved. Education and preventive measures within households are crucial in reducing infection risk, particularly from close contacts. Additionally, malnutrition must be addressed, as it increases mortality rates among infected children. Barriers in TB diagnosis, caused by non-specific symptoms and difficulties

in sample collection, must be tackled by improving access to better diagnostic tools and providing medical personnel with appropriate training. Routine screening interventions for children have also proven highly effective, yet consistent implementation and strong public health policy support remain essential.

Furthermore, in the context of drug-resistant TB treatment, proactive screening and accurate therapy can enhance treatment success rates. The long-term impact of TB on children's growth and pulmonary health demonstrates the need for sustained monitoring and tailored interventions. By integrating all these aspects, we can significantly improve child health outcomes and reduce the burden of tuberculosis.

## Acknowledgement

We would like to express my sincere gratitude to all parties who contributed to the development of this paper. Special thanks go to the researchers and authors who provided valuable data and insights regarding pediatric tuberculosis. Their expertise, perspectives, and dedication were instrumental in deepening understanding of this issue.

We also appreciate the support of colleagues who offered constructive feedback and criticism, as well as my family for their continuous encouragement throughout the writing process. We hope this work will contribute positively and meaningfully to the efforts in addressing childhood tuberculosis in the future.

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