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**境外学者发表的结核病英文文章摘要**

**（108篇）**

**PubMed Publication date: 2025/6/23 --- 2025/6/29**

**(tuberculosis[Title/Abstract]) AND (English[Language])**

**1. Nat Biomed Eng. 2025 Jun 27. doi: 10.1038/s41551-025-01441-5. Online ahead of**

**print.**

Self-powered rapid antigen-specific T-cell response assay for Mycobacterium

tuberculosis infections.

Ning B(1)(2), Chandra S(3)(4), Pan Y(3)(4), Sharan R(5), Ha N(6), Singh S(3)(4),

Portillo Varela A(7), Li L(3)(4), Wu Q(8), Kay A(7), Maphalala GP(9), Adu-Gyamfi

C(10), Carrero Longlax S(7), Mandalakas AM(7), Mehra S(5), Lyon CJ(3)(4),

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Interferon-gamma release assays (IGRAs) that evaluate an individual's T-cell

activation response to Mycobacterium tuberculosis (M.tb)-specific peptides serve

an important role in diagnosing tuberculosis (TB). However, there are

substantial challenges to the use of IGRAs in resource-limited settings.

Further, IGRA diagnostic performance can also be compromised in anergic

individuals. Here we describe a microfluidic chip-based antigen-specific T-cell

response assay (ASTRA) that automates the detection of M.tb-specific T-cell

activation responses to facilitate screening for latent M.tb infection and TB.

We observe that ASTRA demonstrates high specificity for M.tb infection in

independent patient cohorts. Compared with IGRA, ASTRA shows greater diagnostic

sensitivity in individuals with HIV-1 co-infections (93.8% versus 67%),

comparable diagnostic sensitivity in HIV-negative individuals (92.8%) and faster

detection (4 h versus 24-48 h). We also find that a self-powered ASTRA chip that

analysed microsample (~25 μl) whole-blood samples produced comparable results.

ASTRA holds the potential to facilitate efforts to control the global TB

epidemic and serve as a versatile platform for analysing T-cell responses across

various infectious diseases and immunotherapeutic interventions.

© 2025. The Author(s).

DOI: 10.1038/s41551-025-01441-5

PMID: 40579486

**2. JACC Case Rep. 2025 Jun 25;30(16):103956. doi: 10.1016/j.jaccas.2025.103956.**

Severe Calcific Constrictive Pericarditis From Remotely Treated Tuberculosis.

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**BACKGROUND:** Constrictive pericarditis from tuberculosis is a rare but serious

consequence of a tuberculosis infection, especially in nonendemic areas.

**CASE SUMMARY:** A 40-year-old man with a history of tuberculosis as a child that

was treated with antituberculosis medications presented with heart failure. He

was found to have severe calcific constrictive pericarditis from his remote

tuberculosis infection, leading to biventricular failure and volume overload.

The patient was optimized with guideline-directed medical therapy and

intravenous diuresis, and he successfully underwent pericardiectomy with marked

improvement in symptoms and quality of life.

**DISCUSSION:** We present a rare case of severe calcific constrictive pericarditis

that manifested clinically decades after the initial tuberculosis infection.

Multimodality imaging, which includes echocardiography, cardiac computed

tomography, and cardiac magnetic resonance, is valuable for diagnosing and

guiding treatment for constrictive pericarditis.

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PMID: 40579091

**3. PLOS Glob Public Health. 2025 Jun 27;5(6):e0004873. doi:**

**10.1371/journal.pgph.0004873. eCollection 2025.**

Association of clinical laboratory parameters with latent tuberculosis infection

among healthcare workers of primary health centers-A cross-sectional

observational study.

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Tan HY(7), Balakrishnan P(8), Murugesan A(9), Rajeshkumar M(2), Frederick A(1),

Senthil Kumar M(1), PriyaRaj P(1), Prabhakaran J(1), Sangeetha P(1), Arunpathy

P(1), Charu R(1), Muruganandam N(10), Sakate DM(11), Jayakumar D(2), Dhandapani

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Healthcare workers (HCWs) are at high risk of tuberculosis (TB) infection due to

their continued occupational exposure to patients with active TB disease. The

prevalence of latent TB infections (LTBI) among the HCWs of primary healthcare

centers (PHCs) has seldom been investigated. PHCs provide effective and

preventive medical care largely for the rural population. Comparatively, the

HCWs of PHCs are likely to have an increased risk of occupational exposure and

reactivation of LTBI. A cross-sectional study (March-April 2024) was carried out

to assess the prevalence of LTBI among the HCWs of 64 PHCs across Thiruvallur

district, India. Blood samples (n = 392) were analyzed using a commercial

QuantiFERON-TB Gold Plus assay. A comprehensive hematological, biochemical, and

immunological workup was performed, including cell count, blood glucose

determination, liver/renal function tests, and serum ferritin concentration

estimation, which were subsequently correlated with LTBI status using

multivariate logistic regression analysis. The study revealed an LTBI prevalence

of 25.3% (n = 99) among HCWs of PHCs. The red cell distribution width (RDW) was

significantly associated (p = 0.002) with LTBI positivity among the different

parameters analyzed. Factors such as individuals' age (p = 0.029), underlying

comorbid conditions (30.3%; p = 0.035), and longer employment duration (28%;

p = 0.034) were significantly associated with IGRA positivity. Further, IGRA

positivity was significantly associated with decreased RDW standard deviation

(RDW-SD). This phenomenon was observed especially among females, the obese, and

participants with the 'O' blood group. Although the exact prevalence of LTBI in

the general population is not known, it is estimated to range from 20-48%. The

study reported the prevalence of LTBI among HCWs of PHCs (25.3%) and factors

associated with IGRA positivity including age, underlying comorbid conditions,

and years of employment. Our findings will aid in developing and establishing an

appropriate framework for TB screening and clinical testing guidance for HCWs.

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**4. PLoS One. 2025 Jun 27;20(6):e0326428. doi: 10.1371/journal.pone.0326428.**

**eCollection 2025.**

Needs assessment and preparedness of the primary health care network for

scaling-up preventive tuberculosis treatment in 5 Brazilian capitals.

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This study aims to conduct a needs and preparedness assessment of public primary

care units to scale up tuberculosis infection diagnosis and tuberculosis

preventive treatment in 5 Brazilian capitals. This observational operational

study was carried out across five Brazilian high tuberculosis-burden cities.

Clinics with at least one monthly new tuberculosis case were included. Data on

Purified Protein Derivative (PPD) storage, tuberculin skin testing (TST) and

interferon-gamma release assay (IGRA) availability, personnel qualified for

performing TST, radiological facilities and tuberculosis preventive treatment

drug availability, were gathered between August 2023 and January 2024. Out of

285 clinics included, 78% (CI95%: 73%-82%) did not offer TST on-site, with only

28% (CI95%: 22%3%) having staff qualified to perform TST, and 35% (CI95%:

29%-40%) lacking dedicated refrigerators for PPD storage. Most (97%, CI95%:

94%-99%) clinics did not collect IGRA testing, with an average distance of 6.7

km (CI95%: 5%-7%) to IGRA labs and a turnaround time of 11.7 days (CI95%: 9%13%)

for results. Most (87%, CI95%: 83%-91%) do not offer on-site radiological

testing. The primary care network was unprepared to scaling up tuberculosis

infection testing. Key issues include unavailability of TST mainly because of

insufficient qualified personnel. Without accelerated qualification of staff for

TST, scaling up tuberculosis preventive treatment will be impossible.

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DOI: 10.1371/journal.pone.0326428

PMID: 40577400 [Indexed for MEDLINE]

**5. Ann Afr Med. 2025 Jun 27. doi: 10.4103/aam.aam\_105\_25. Online ahead of print.**

Tracheoesophageal Fistula as a Rare Cause of Persistent Pulmonary Tuberculosis

Symptoms.

[Article in English, French; Abstract available in French from the publisher]

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Tracheoesophageal fistula (TEF) is a rare yet severe complication of

tuberculosis (TB), often leading to persistent symptoms, recurrent infections,

and treatment failure. Its early recognition and appropriate management are

crucial to improving patient outcomes. We report the case of a 24-year-old woman

with pulmonary TB who presented with persistent fever, copious expectoration,

and progressive weight loss despite receiving anti-tubercular therapy (ATT) for

3 months. She developed a right pneumothorax, requiring Malecot catheter

insertion, and was referred to our institute due to poor treatment response.

Differential diagnoses, including drug-resistant TB and malabsorption, were

ruled out. Clinical suspicion of TEF arose due to worsening cough on swallowing.

Bronchoscopy confirmed a TEF, five tracheal rings above the carina, measuring

7-8 mm in diameter. A computed tomography scan delineated its extent, and

bronchoalveolar lavage analysis confirmed Mycobacterium TB. The patient was

managed with nasogastric feeding, intravenous antibiotics, and ATT continuation.

Her condition improved significantly within 10 days. TEF is a rare but serious

complication of pulmonary TB that can significantly impact treatment success.

Early recognition, nutritional support, and ATT continuation are crucial for

improved outcomes and preventing complications this case underscores the

importance of considering TEF in patients with persistent symptoms despite

standard TB treatment.

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PMID: 40576416

**6. mBio. 2025 Jun 27:e0097125. doi: 10.1128/mbio.00971-25. Online ahead of print.**

A split ALFA tag-nanobody system for protein localization and proximity

proteomics in mycobacteria.

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Tuberculosis remains a globally significant infection, and new insights into the

biology of Mycobacterium tuberculosis are badly needed. Discovery of protein

localization and protein complex composition are powerful approaches to

determine protein function but have not been widely applied in mycobacteria, in

part due to technical barriers. Here we develop a multifunctional system that

utilizes the ALFA tag and functional protein fusions to an anti-ALFA nanobody

(NBALFA) to target proteins in fast- and slow-growing mycobacteria. Insertion of

the ALFA epitope tag on the target protein, coupled with conditional expression

of the NBALFA fused to a fluorescent protein, faithfully recapitulates cytosolic

and membrane protein localization by fluorescent microscopy in living cells.

Targeted NBALFA can relocalize an ALFA-tagged protein to inclusion bodies or the

cytoplasmic membrane, demonstrating enforced protein localization. Finally, the

conditional expression of the NBALFA fused to TurboID for proximity proteomics

allowed the identification of known partner proteins of the RNA polymerase

complex and the PKS13 mycolic acid biosynthesis protein. We conclude that the

split ALFA tag-nanobody system is a flexible platform for discovering protein

biology in mycobacteria.

IMPORTANCE: This study establishes a new platform for discovery proteomics in

mycobacteria using a new nanobody-based approach. The findings will be of

interest for all bacteriologists as the approach will be applicable to a variety

of microbial systems.

DOI: 10.1128/mbio.00971-25

PMID: 40576343

**7. World J Virol. 2025 Jun 25;14(2):102668. doi: 10.5501/wjv.v14.i2.102668.**

Bibliometric analysis of research on spinal tuberculosis in last 5 years.

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**BACKGROUND:** Spinal tuberculosis (TB), also known as Pott's spine, remains a

significant global health issue, particularly in regions with a high TB burden.

The disease presents complex challenges in diagnosis, management, and treatment,

prompting a growing interest in research over recent years. The advancements in

imaging, diagnostics, and treatment strategies have driven an increased focus on

publishing clinical outcomes, review articles, and case series related to spinal

TB (STB).

**AIM:** To perform a bibliometric analysis of STB research published over the last

5 years (2019-2023) to identify trends in publication volume, contributions by

country, and the nature of the research being conducted.

**METHODS:** A comprehensive bibliometric analysis was conducted using the PubMed

database, focusing on research articles published between 2019 and 2023.

Keywords such as "spine tuberculosis," "spinal TB," "TB spine," and "Pott's

spine" were utilized to capture relevant publications. Articles were analyzed

based on the type of research (e.g., case reports, review articles, cohort

studies, randomized controlled trials [RCTs]), number of citations, and country

of origin based on the corresponding author's details. Further subgroup analysis

was performed according to the TB burden in various countries to assess research

trends in high-burden regions.

**RESULTS:** A total of 528 articles met the inclusion criteria for this

bibliometric analysis. The majority of articles were published between 2020 and

2023 (440/528; 83.3%), while the lowest number was published in 2019 (88/528;

16.7%). India led the global contributions with 25.8% of the total publications,

followed by China (19.9%) and the United States (10.4%). Combined, African

countries contributed 6.8% of the research on STB. Regarding the type of

articles, case reports and case series dominated the literature (353/528;

66.9%), followed by review articles (120/528; 22.7%) and cohort studies (45/528;

8.5%). Only 1.9% (10/528) of the studies were RCTs. Countries such as the United

States, Germany, the United Kingdom, and Japan have pioneered the use of

artificial intelligence (AI) in the diagnostic processes for STB, while India,

China, South Africa, and other countries have been pivotal in conducting

clinical trials and improving clinical management strategies.

**CONCLUSION:** This bibliometric analysis revealed a significant increase in STB

research over the last 5 years, with India and China being the leading

contributors. However, most publications are case reports or case series, with a

limited number of RCTs. The results highlighted the need for more high-quality

research, especially in terms of RCTs and innovations in diagnostic

technologies. Additionally, the application of AI to STB diagnostics shows

promise in developed countries, while high-burden countries are focusing on

clinical trials and management strategies.

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**8. Respirol Case Rep. 2025 Jun 25;13(6):e70257. doi: 10.1002/rcr2.70257.**

**eCollection 2025 Jun.**

Melioidosis Presenting as Chronic Pneumonia With Soft Tissue Abscess in a

Diabetic Patient Initially Treated for Tuberculosis: A Case Report From Vietnam.

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A 46-year-old diabetic Vietnamese engineer presented with a 2-month fever and

left foot swelling. Chest imaging showed bilateral nodules with right apical

cavitation, prompting empirical anti-tuberculosis therapy. Despite positive

Xpert MTB/RIF and 1 month of treatment, his condition worsened. Bronchoscopy

culture isolated Burkholderia pseudomallei. Treatment with ceftazidime and

trimethoprim-sulfamethoxazole led to complete recovery. Negative MGIT culture

excluded tuberculosis co-infection. This case highlights the diagnostic

challenge when melioidosis mimics tuberculosis in endemic regions, particularly

in diabetic patients. Positive molecular tuberculosis tests may reflect the

previous infection, emphasising the need for culture confirmation and clinical

correlation.

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Australia, Ltd on behalf of The Asian Pacific Society of Respirology.

DOI: 10.1002/rcr2.70257

PMCID: PMC12197865

PMID: 40575398

**9. BMC Glob Public Health. 2025 Jun 27;3(1):56. doi: 10.1186/s44263-025-00153-x.**

Modelling the effect of a nutritional shock on tuberculosis in India.

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**BACKGROUND:** Environmental or social changes and shocks that reduce access to

adequate nutrition have potential consequences for tuberculosis (TB), as

undernutrition is a major driver of TB incidence and poor TB treatment outcomes.

**METHODS:** We developed a transmission model of TB in India with an explicit body

mass index (BMI) strata linked to disease progression and treatment outcomes,

calibrated to country-specific TB estimates. We projected nutritional shock

scenarios affecting supply chains, similar to those experienced at the beginning

of the war in Ukraine, using the LandSyMM food system model, compared to a

continuation of previous food system trends. Within each scenario, increases in

food, fertiliser, and energy prices were linked to changes in the population BMI

distribution by food availability and prices. We estimated the impact on TB

incidence and mortality in India between 2022 and 2035 of these nutritional

shock scenarios compared to maintenance of prior trends.

**RESULTS:** The worst-case scenario, involving sustained increases in food,

fertiliser, and energy prices, predicted that shocks increasing undernutrition

could result in a 5.0% (95% uncertainty interval = 4.4, 5.9) and 4.9% (4.2, 5.9)

increase in TB incidence and mortality respectively in India in 2035 compared to

continuation of previous food system trends. In this scenario, an additional 1.1

million (0.9, 1.3) TB episodes and 177.5 thousand (144.7, 224.3) TB deaths were

predicted to occur between 2022 and 2035.

**CONCLUSIONS:** Shocks affecting the population-level BMI distribution could lead

to changes in the burden of TB disease. Our findings suggest that the impact of

crises on TB disease may be underestimated if the impacts of external shocks on

nutrition are not explicitly considered.

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**10. Immunol Res. 2025 Jun 26;73(1):99. doi: 10.1007/s12026-025-09657-y.**

Immunomodulatory activity of 4-(Benzyloxy)phenol facilitates intracellular

mycobacterial clearance through p53 mediated IL-35 signaling dependent

JAK1/STAT3 pathway in human macrophages.

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Mycobacterium tuberculosis (M. tuberculosis), the causative agent of

tuberculosis (TB), modulates host immune responses by regulating various

cytokines. Precise regulation of these cytokines renders the host pathogen-free,

whereas their dysregulation increases the susceptibility to infection. Hence,

induction of host protective cytokines using immunomodulators to promote M.

tuberculosis clearance has a rewarding impact in the context of TB treatment.

This study explored the immunomodulatory activity of 4-(Benzyloxy)phenol (4-BOP)

in mycobacteria infected differentiated THP-1 cells through IL-35 (an

anti-inflammatory cytokine) production. Initially, we observed an increased mRNA

and protein level expression of IL-35 and its cognate receptor upon 4-BOP

treatment in mycobacteria-infected dTHP-1 cells. IL-35 receptor activation

further led to phosphorylation of JAK1/STAT3, culminating in increased

phagosome-lysosome fusion through elevation of intracellular Ca2+ level.

Blocking IL-35 receptors using siRNA-mediated approach against IL-12Rβ2 and

gp130 or the JAK1/STAT3 associated signaling with specific inhibitors like

Baricitinib and Stattic promoted the intracellular mycobacterial survival by

compromising Ca2+-phagosome-lysosome fusion pathway. Further, we identified a

direct regulatory role of p53 (known to be activated by 4-BOP) on IL-35

production, and inhibition of p53 using PFT-α surprisingly abrogated the IL-35

mediated signaling axis. Collectively, our results demonstrated a host defensive

role of 4-BOP-induced Il-35 signaling in mycobacteria-infected dTHP-1 cells

through the JAK1/STAT3 mediated Ca2+-phagosome-lysosome fusion pathway. These

results suggest that 4-BOP may serve as a potent HDT candidate for regulating

inflammation and enhancing host defense in TB infection.

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**11. Eur Respir J. 2025 Jun 26:2402521. doi: 10.1183/13993003.02521-2024. Online**

**ahead of print.**

The relationship between a known diagnosis of tuberculosis and symptom

reporting: implications for case detection strategies.

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PMID: 40571321

**12. Lancet Respir Med. 2025 Jun 23:S2213-2600(25)00195-X. doi:**

**10.1016/S2213-2600(25)00195-X. Online ahead of print.**

Integrated care for tuberculosis and lung health.

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PMID: 40570874

**13. Lancet Microbe. 2025 Jun 23:101055. doi: 10.1016/j.lanmic.2024.101055. Online**

**ahead of print.**

Centrifuge-free stool processing methods for Xpert MTB/RIF Ultra tuberculosis

diagnosis in children in Uganda and Zambia: an observational, prospective,

diagnostic accuracy study.

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M, Mugisha IT, Akankwasa G, Nyehangane D, Mulenga V, Shankalala P, Hambulo C,

Kapotwe V, Ngambi M, Kanyama M, Chrwa U, Chifunda K, Undundu G, Zulu S, Nawakwi

G, Siasulingana T, Himwaze DA, Chilonga J, Chimbini M, Chilanga M, Chola D,

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**BACKGROUND:** WHO recommends Xpert MTB/RIF Ultra (Ultra) for stool testing for

tuberculosis diagnosis in children. Stool processing requires removal of debris

and PCR inhibitors, frequently by using centrifugation, which can be an

implementation barrier for low-income and middle-income countries (LMICs). We

evaluated the diagnostic accuracy of Ultra on stool using three centrifuge-free

processing methods, the simple one-step (SOS), stool processing kit (SPK), and

the optimised sucrose flotation (OSF) methods against a microbiological

reference standard (MRS).

**METHODS:** In this observational, prospective, multicountry, diagnostic accuracy

study, we collected two respiratory samples and two stool samples in children

younger than 15 years with presumptive tuberculosis in one hospital in Uganda

and two hospitals in Zambia for Ultra testing and culture (on respiratory

samples only). We defined positive MRS as positive culture or Ultra on

respiratory sample and negative MRS as two negative respiratory samples by

either culture or Ultra. We assessed the perception of the laboratory operators

of test ease-of-use using a self-administered questionnaire at all sites. This

study is registered with ClinicalTrials.gov (NCT04203628) and the Pan African

Clinical Trial Registry (PACTR202006814433059).

**FINDINGS:** Of the 216 children enrolled between Jan 13, 2020, and Dec 31, 2021,

215 were included in the study and of these 104 (48·4%) were female and 211

(51·6%) were male, the median age was 1·8 years (IQR 1·1-4·8), 68 (31·6%) were HIV positive, and 38 (17·7%) were MRS positive. For one or both stool samples, depending on availability, the sensitivity of stool Ultra against MRS was 69·7% (95% CI 51·3-84·4) for SOS, 69·7% (51·3-84·4) for SPK, and 73·5% (55·6-87·1) for OSF (McNemar test p>0·6 for all), with a specificity above 96% for all methods. The SOS stool method was considered the easiest by six of seven operators because it required least manipulation and no additional reagents.

**INTERPRETATION:** Centrifuge-free stool processing methods could improve access to

microbiological diagnosis of tuberculosis in LMICs. These results contributed to

the WHO endorsement of the SOS and OSF methods.

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**ahead of print.**

Tuberculosis in Morocco: Disease duration, weight loss and malnutrition.

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**BACKGROUND:** Tuberculosis remains a serious challenge in public health worldwide.

Changes in patients' delays in diagnosis and illness can complicate the disease.

Understanding the factors affecting the delays is crucial to the development of

effective prevention and treatment strategies.

OBJECTIVES: The aim of our study is to analyze and identify the association

between the duration of illness, weight status and changes in dietary habits of

TB patients as well as addressing the importance of dietary habits in improving

tuberculosis outcomes.

**METHODS:** A cross-sectional study was carried out on a sample of 480 tuberculosis

patients.

**RESULTS:** The results revealed that the mean (SD) duration of the disease was

5.98 months (6.8), while the mean (SD) diagnostic duration was 3.35 months

(6.01). Significant difference was observed in diagnostic duration between TB

types (p = 0.018). Mean weight loss during the disease (SD) was 7.34 kg (5.21)

with a significant difference between age groups (p < 0.001) and between TB

types (p < 0.001). During the disease, patients lost an average of 1.72 kg/m2 of

their BMI (p < 0.001). Around 84 % of patients have changed their eating habits.

Weight loss and changes in dietary habits were significantly associated with

increased disease duration.

**CONCLUSIONS:** Changes in eating habits, marked by weight loss and reduction in

patients' food intake significantly prolonged the disease's duration. Healthcare

professionals are called to be aware of the impact of eating habits on the

progression and duration of tuberculosis, and to encourage their patients to

adopt healthy eating practices.

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**15. PLOS Glob Public Health. 2025 Jun 26;5(6):e0004016. doi:**

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Evaluating the health impact, health-system costs and cost-effectiveness of

using TrueNat on stool samples compared to usual care for the diagnosis of

paediatric tuberculosis in primary care settings: A modelling analysis.

Mafirakureva N(1), Daniel OK(2), Olayinka OJ(2), Ochei KC(3), Klinkenberg E(4),

Ihesie A(3), Nongo D(3), Eneogu RA(3), Mwansasu A(5), Elom EU(6), Aderonke

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The World Health Organisation (WHO) recommends rapid molecular diagnostics to

improve bacteriological confirmation of tuberculosis in children. TrueNat MTB,

MTB Plus and MTB-RIF Dx assays (Molbio Diagnostics, India), recommended by WHO,

hold potential as point-of-care tests in resource-limited settings. Using stool

samples with these assays could enhance testing access, improve linkage to care,

reduce costs, and increase cost-effectiveness over traditional methods. However,

evidence on their costs and cost-effectiveness is limited and needed for

informed policy decisions on adoption and scale up. We used a decision-tree

analytic modelling approach, time-and-motion study, and routine data to estimate

the potential impact of implementing stool-based TrueNat testing for the

diagnosis of pulmonary tuberculosis in children within Nigerian primary

healthcare settings on healthcare outcomes, resource use, health system costs,

and cost-effectiveness relative to the standard of care (SoC). The cost per test

was $13.06 (standard deviation; $0.77) for TrueNat and $16.25 (standard

deviation; $1.34) for Xpert. For every 100 children with presumptive

tuberculosis, the stool-based TrueNat testing intervention was projected to

increase case detection rate by 2 (95% uncertainty interval [UI 0-6]) cases and

bacteriological confirmation by 21% (95% UI 11-32). Diagnoses at primary health

centres (PHC) would increase by 22% (95% UI 11-32), averting 1 (95% UI 0-2)

deaths and 15 (95% UI -4-41) discounted DALYs. Although resource use and health

system costs increased by $2,682 (95% UI 1,039-4,731) per 100 children, the

incremental cost-effectiveness ratio of $183 per DALY averted suggests

cost-effectiveness at thresholds of 0.5 × GDP per capita. Implementing

stool-based TrueNat testing has potential to increase access and reduce direct

health system costs associated with the diagnosis of pulmonary tuberculosis in

children in routine health care settings. Such an approach is likely to

represent a good value for money compared to SoC.

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original author and source are credited.

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**16. PLoS One. 2025 Jun 26;20(6):e0326784. doi: 10.1371/journal.pone.0326784.**

**eCollection 2025.**

Approaches and results of intersectoral actions for tuberculosis control in the

world: A scoping review.

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**BACKGROUND:** Tuberculosis is a neglected disease with a wide global scope that

overcomes public health challenges, also constituting an obstacle to social

development. In the effort to control the disease, Tuberculosis Control Programs

around the world have aligned their actions with the World Health Organization

End TB Strategy, which emphasizes intersectorality as a fundamental component

for effective disease control.

**OBJECTIVE:** To map the approaches and results of intersectoral tuberculosis

control actions at the global scenario.

**METHODOLOGY:** This scoping review followed the PRISMA (Preferred Reporting Items

for Systematic Reviews and Meta-Analyses) guidelines and the Joanna Briggs

Institute manual, ensuring methodological rigor and transparency. The review

protocol was registered in the Open Science Framework. Searches were carried out

in indexed databases and in the gray literature. Data collection took place by

two independent reviewers, with results stored and organized in spreadsheets.

**RESULTS:** Three hundred and ninety-six (396) studies were identified, of which 60

were analyzed in full, resulting in the inclusion of 11 studies for the final

review. It was evidenced that intersectoral articulation is fundamental in

tuberculosis control, involving sectors such as health, education, social

assistance and justice, to ensure adequate health care and social support,

particularly for vulnerable populations. Community education and awareness

played a central role in treatment adherence and reducing stigma, while resource

mobilization was needed to maintain health services, especially in contexts of

scarcity.

**CONCLUSION:** The integration of intersectoral services, involvement of

non-governmental organizations and active community participation are essential

elements for effective tuberculosis control. The findings reinforce the

importance of addressing the social determinants of health to achieve the

objectives of the End TB strategy, promoting an environment conducive to the

prevention, early detection and effective treatment of the disease.

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**17. PLOS Glob Public Health. 2025 Jun 26;5(6):e0004065. doi:**

**10.1371/journal.pgph.0004065. eCollection 2025.**

The feasibility of respondent-driven sampling with people who use drugs in rural

Western Cape, South Africa: A qualitative study.

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The Western Cape is South Africa's epicentre for tuberculosis (TB) and smoked

drug use such as methamphetamine and methaqualone (Mandrax). Despite this, there

are limited studies on people who smoke drugs (PWSD) with TB disease in South

Africa, partly due to recruitment challenges. Respondent-driven sampling (RDS)

is a network-based sampling method used to recruit such key populations. The aim

of this qualitative study is to explore the appropriateness and feasibility of

RDS as a method for recruiting PWSD for a planned study on TB transmission in

this setting. We conducted ten focus group discussions (n = 84) with men and

women from Worcester, a rural town in the Western Cape, who self-reported

current methamphetamine and/or methaqualone use. Participants were recruited

through an existing TB study or community-based outreach. Discussion topics

included use of illicit drugs within social networks, feasibility of using RDS

methods for recruiting PWSD, and logistical recommendations for the use of RDS

and planned study participation. Data were analyzed using thematic analysis.

Results indicate drug use by participants across large social networks which is

favorable for RDS methods. The key themes were: 1) drug-use social network

characteristics including demographic and geographic differences; 2)

perspectives of PWSD on RDS methods; 3) potential challenges to proposed RDS

recruitment and participation in a larger research study for PWSD, and 4)

participant recommendations to enhance the uptake of RDS and study participation

by PWSD. RDS seems to be a feasible method to recruit PWSD and improve the

possibility of reaching a diverse sample of PWSD, with clear recommendations

from participants regarding how to recruit participants for larger research

studies. The current study indicates that conducting formative, qualitative

research can assist researchers with RDS study design and planning for

additional study activities. Trial Registration: ClinicalTrials.gov

NCT041515602.

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**eCollection 2025.**

Serratia sp. traits distinguish the lung microbiome of patients with

tuberculosis and non-tuberculous mycobacterial lung diseases.

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**BACKGROUND:** Pathogenic mycobacteria, such as Mycobacterium tuberculosis complex

(Mtbc), and non-tuberculous mycobacteria (NTMs) can cause severe chronic

pulmonary infections. However, not all infected patients develop active disease,

and it remains unclear whether key lung microbiome taxa play a role in the

pathogenesis of tuberculosis (TB) and NTM lung diseases (LD). Here, we aim to

further define the lung microbiome composition in TB, and NTM-LD prior to the

initiation of therapy.

**STUDY DESIGN:** We employed 16S rRNA amplicon sequencing to characterize the

baseline microbiome in bronchoalveolar lavage fluid (BALF) from patients

diagnosed with TB (n = 23), NTM-LD (n = 19), or non-infectious inflammatory

disease (n = 4). We applied depletion of human cells, removal of extracellular

DNA, implementation of a decontamination strategy, and exploratory

whole-metagenome sequencing (WMS) of selected specimens.

**RESULTS:** Genera Serratia and unclassified Yersiniaceae dominated the lung

microbiome of most patients with a mean relative abundance of >15% and >70%,

respectively. However, at the sub-genus level, as determined by amplicon

sequence variants (ASVs), TB-patients exhibited increased community diversity,

and distinct signatures of ASV\_7, ASV\_21 abundances which resulted in a

significant association with disease state. Exploratory WMS, and ASV similarity

analyses suggested the presence of Serratia liquefaciens, Serratia grimesii,

Serratia myotis and/or Serratia quinivorans in TB and NTM-LD patients.

**CONCLUSIONS:** The lung microbiome of TB-patients harbored a distinct, and

heterogenous structure, with specific occurrences of certain Serratia traits.

Some of these traits may play a role in understanding the microbial interactions

in the lung microbiome of patients infected with Mtbc.

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**print.**

Mycobacterium tuberculosis TtfA is a Highly Stable Membrane-Anchored DNA-Binding

Protein.

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Mycobacterium tuberculosis (Mtb), the causative agent of tuberculosis (TB), is a

deadly intracellular pathogen, with a persistent infectivity and high morbidity

rate. Mtb has successfully evaded drugs and modern antibiotics, while also

developing resistance and adaptability. To obtain newer avenues for therapeutics

against Mtb, we proposed to identify and characterize membrane proteins of Mtb.

To this end, we report the successful characterization of the locus rv0383c,

which codes for a 284-residue membrane-anchored protein. We show that the

protein product, named TtfA, possesses an N-terminal transmembrane helix, a low

complexity region, an α + β central region, and a C-terminally highly

unstructured region. Our studies reveal that the extramembranous domain

possesses non-specific DNA-binding ability. Additionally, TtfA folds into a

highly stable structure that resists thermal unfolding. TtfA is selectively

sensitive to the surrounding pH. The promising outcomes we obtain with TtfA as

one of the next-generation antibiotic targets against Mtb can pave the way for

characterizing other membrane proteins toward finding long-term cures for this

endemic disease.

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**Epub 2025 Jun 27.**

Effect of exposure to ambient particulate matter on risk of developing pulmonary

tuberculosis: A systematic review and meta-analysis.

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Tuberculosis (TB) is a major global health challenge, particularly in polluted

areas. The relationship between ambient particulate matter and TB risk remains

unclear, making this systematic review and meta-analysis (SRMA) vital for

assessing this link. This SRMA aimed to estimate the association between

exposure to ambient particulate matter (PM10 and PM2.5) and the risk of

pulmonary tuberculosis (PTB) infection. A literature search was conducted in

PubMed, Web of Science, and Cochrane (English-language studies) on January 29,

2024. The review followed PRISMA Guidelines (2020) for comprehensive literature

searches, data extraction, and quality assessment of included studies. A

random-effects model was used for meta-analysis to estimate pooled effect sizes

and assess heterogeneity. Study quality and publication bias were also

evaluated. Of the 507 articles identified, 25 met the inclusion criteria.

Long-term PM2.5 exposure was linked to a 26% increase in PTB risk (RR =1.26, 95%

CI: 1.07-1.48), while short-term exposure raised the risk by 10% (RR =1.10, 95%

CI: 0.98-1.25). Long-term PM10 exposure increased PTB risk by 7% (RR =1.07, 95%

CI: 1.02-1.12), with short-term exposure showing a similar increase (RR =1.07,

95% CI: 0.95-1.17). Subgroup analysis revealed PTB risk increased by 15% in

males and 29% in females for PM2.5, and by 10% in males and 7% in females for

PM10. A 10 µg/m³ increase in Particulate matter is associated with a higher risk

of pulmonary tuberculosis, highlighting the need for targeted public health

measures to reduce particulate exposure, especially in high-risk urban and

industrial areas.

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Bridging the gap: Early detection of pulmonary tuberculosis among PLHIV in

Western Rajasthan, India.

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**BACKGROUND:** Tuberculosis (TB) remains a leading cause of mortality among people

living with HIV (PLHIV), with delayed diagnosis contributing significantly to

poor outcomes. Early detection through systematic screening and diagnostic tools

is essential to reduce morbidity and mortality in this high-risk population.

This study aimed to evaluate the utility of the World Health Organization (WHO)

four-symptom screen (fever, cough, weight loss, and night sweats), using Xpert

MTB/RIF (Cepheid, Sunnyvale, California) as the gold standard for early

detection of pulmonary TB in HIV-positive patients.

**METHODS:** A total of 249 HIV-positive patients attending a tertiary care centre

in Western India were screened using the WHO four-symptom tool. All patients,

regardless of symptoms, underwent testing with Xpert MTB/RIF. Sensitivity,

specificity, and predictive values were calculated for the symptom screen and

individual symptoms. Univariate and multivariate analysis was performed to

determine significance (P < 0.05).

**RESULTS:** The WHO four-symptom screen identified 40.2% of participants (n = 100)

as screen-positive. Xpert MTB/RIF confirmed pulmonary TB in 5.6% (n = 14) of the

total population. The combined sensitivity and specificity of the WHO symptom

screen were 85.7% and 62.6%, respectively, with a high negative predictive value

of 98.7%. Fever and cough were the most significant predictors (P < 0.05) in

multivariate analysis.

**CONCLUSION:** The study highlights the importance of systematic TB screening among

PLHIV using the WHO symptom tool in conjunction with molecular diagnostics. This

approach facilitates early diagnosis and treatment, contributing to better

health outcomes and aligns with global TB elimination strategies.

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Treatment outcomes of bedaquiline-based longer oral antitubercular regimens in

Indian children above five years of age.

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**BACKGROUND AND OBJECTIVE:** This study evaluates the treatment outcomes and

adverse drug reactions (ADRs) of longer oral bedaquiline (BDQ)-based (without

delamanid) antitubercular therapy (ATT) regimens in children aged 5-18 years.

**METHODS:** A retrospective study was conducted between June 2021 and February

2024. We included 105 children diagnosed with drug-resistant tuberculosis

(DR-TB) and treated with longer oral BDQ-based regimens. Duration of treatment

was based on clinico-radiological resolution and multiple ADRs. Data on

demographics, clinical features, resistance patterns, treatment regimens,

outcomes, and adverse effects were analyzed.

**RESULTS:** Mean age was 11.29 ± 3.20 years, with a male-to-female ratio of 0.42:1.

Prior ATT exposure was reported in 61 (58.1%), with previous treatment failure

in 34 (55.7% of those with prior exposure) patients. BDQ was administered for a

median duration of 6 months, with 14 (13.33%) requiring extension. BMLCC

(bedaquiline-moxifloxacin-linezolid-cycloserine-clofazimine) regimen was

received by 61 (58.1%), and BLCC ± additional drugs

(bedaquiline-linezolid-clofazimine-cycloserine) regimen was received by 30

(28.6%) patients. Treatment completion was achieved in 75 (71.43%) patients with

a mean duration of 22.50 ± 7.50 months, of which 35 (46.67%) required treatment

for 18 months, 32 (42.67%) required treatment for more than 18 months, and 8

(10.67%) patients required treatment stoppage before 18 months in view of

multiple ADRs. Fifty-one (48.6%) patients had ADRs, including QTc prolongation

in 25 (23.8%), psychosis 11 (10.5%), and vomiting 7 (6.7%).

**CONCLUSION:** BDQ-based regimens are effective in treating pediatric DR-TB, with

high treatment completion rates. However, the duration of treatment is 18 months

or longer in most patients based on clinico-radiological resolution. ADRs,

particularly QTcF prolongation, warrant close monitoring and follow-up.

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Sensitivity and specificity of Gene Xpert Ultra in extrapulmonary tuberculosis

(EPTB).

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**INTRODUCTION:** Gene Xpert sensitivity is low in paucibacillary conditions like

extrapulmonary tuberculosis (EPTB); to overcome that, Gene Xpert Ultra was

introduced. This study aims to assess Gene Xpert Ultra's diagnostic accuracy in

EPTB.

**METHODS:** This prospective observational study was conducted at Apollo Hospital,

Greams Road, Chennai, Tamil Nadu, India, from May 2022 to April 2023. A total of

200 patients, 39 (19.5%) abdominal, 61 (30.5%) musculoskeletal, one (0.5%) bone

marrow, 50 (25%) lymph nodes, 11 (5.5%) CNS, two (1%) upper airway, one (0.5%)

cardiovascular, and 35 (17.5%) pleural cases were enrolled. Samples were

analyzed for Gene Xpert Ultra, MGIT culture, cytology, and histopathology

wherever feasible with tuberculosis. Tissue sampling was performed rather than

bodily fluid in all cases except in CNS and abscess, where CSF and pus were

analyzed, respectively. Gene Xpert Ultra was then compared with MGIT culture and

Composite reference standard (CRS).

**RESULTS:** The pooled sensitivity and specificity of Gene Xpert Ultra were 96.18%

and 18.84% against MGIT and 94.30% and 100% against CRS. The lowest sensitivity

(90%) was in CSF, and the highest (100%) was in pleura against CRS.

**CONCLUSION:** Gene Xpert Ultra has high sensitivity and specificity in tissue

samples in various system involvements. This study recommends employing Gene

Xpert Ultra in EPTB and further encourages tissue sample testing.

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**24. Respirol Case Rep. 2025 Jun 25;13(6):e70248. doi: 10.1002/rcr2.70248.**

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Coexistence of Tuberculosis and Lophomoniasis in a Patient With Alzheimer's

Disease.

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The coexistence of lophomoniasis and tuberculosis (TB), both airborne diseases,

is relatively uncommon. Co-infections like these can complicate treatment

strategies due to overlapping symptoms and potential drug interactions. We

report a rare case of comorbidity involving two pulmonary diseases,

lophomoniasis and TB, in an 82-year-old woman with Alzheimer's disease (AD) from

northern Iran. Her primary symptoms included weakness, lethargy, dyspnea, sputum

production, night sweats, and significant weight loss. Both TB and lophomoniasis

can compromise the immune system, potentially worsening the progression or

severity of AD by increasing susceptibility to infections or enhancing

neuroinflammation. Following the prescription of appropriate drug regimens for

both diseases, the patient was discharged from the hospital in stable condition.

Overall, it is crucial to consider lophomoniasis in the differential diagnosis

of patients with pulmonary tuberculosis, especially in endemic areas where both

infections are prevalent, to ensure timely diagnosis and effective management.

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U.S. Tuberculosis Cases Are on the Rise.

Roush K.

Risk of infection, however, remains low.

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**26. Eur Respir Rev. 2025 Jun 25;34(176):240289. doi: 10.1183/16000617.0289-2024.**

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(18)F-fluorodeoxyglucose PET/CT scans for thoracic tuberculosis: current

evidence and future perspectives.

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The advent of positron emission tomography (PET) combined with computed

tomography (CT) in the field of inflammatory/infectious diseases heralds an era

of personalised disease management using these noninvasive technologies. This

nuclear medicine technique can be a useful tool in tuberculosis (TB) for

assessing the extent of extrapulmonary disease, evaluating treatment response

and identifying patients at higher risk of disease relapse. The fusion of

functional imaging provided by PET with the anatomical and morphological details

captured by CT has enabled clinicians to better understand the dynamics of the

pathophysiology and natural course of Mycobacterium tuberculosis infection.

Using its whole-body field of view, host responses are most commonly visualised

using 18F-fluorodeoxyglucose, which reflects the glycolytic activity of cells.

The strict indications for PET/CT in TB are matched by the caution required in

interpreting its qualitative, quantitative and volumetric imaging patterns. In

this narrative review, we aim to summarise evidence supporting the use of this

molecular imaging modality in thoracic presentations of TB, particularly

pulmonary and lymph node involvement, together with concepts to aid in the

reporting and interpretation of the tests. We will also explore future

indications for PET/CT in TB and discuss challenges to its routine use.

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**27. J Infect Dis. 2025 Jun 26:jiaf341. doi: 10.1093/infdis/jiaf341. Online ahead of print.**

Risk of cancer after tuberculosis disease among people with HIV in Denmark: a

nationwide population-based cohort study.

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**BACKGROUND:** The long-term cancer risk following TB disease in people with HIV

remains unclear. We aimed to assess cancer risk following TB in a nationwide

cohort of people with HIV in Denmark.

**METHODS:** We conducted a population-based cohort study including all individuals

enrolled in the Danish HIV Cohort Study from 1995-2020. TB and cancer diagnoses

were identified through nationwide registries. Incidence rates (IRs) and

adjusted incidence rate ratios (aIRRs) were calculated using Poisson regression,

adjusting for time-varying CD4 count, age, sex, and Charlson Comorbidity Index

(CCI). Additionally, we calculated aIRRs stratified by age-group, sex, CCI and

CD4-count.

**RESULTS:** Among 6,135 people with HIV (median age: 37.1 years, 74.1% male), 319

had a TB diagnosis. During 62,878 person-years of follow-up (PYFU), 451 cancers

were observed, including 55 lung cancers. The overall cancer IR among people

with HIV without previous TB disease was 18.6 per 1,000 PYFU (95%confidence

interval: 16.9-20.4), and 19.0 per 1,000 PYFU (95%CI: 10.4-25.6) among people

with HIV following TB (aIRR: 1.1, 95%CI: 0.7-1.8). For lung cancer, the aIRR

after TB was 1.7 (95%CI: 0.5-5.5). In stratified analyses, aIRRs were slightly

higher among women (1.3, 95%CI: 0.6-2.9) and those aged ≥50 years (1.4, 95%CI:

0.8-2.4).

**CONCLUSION:** In this nationwide cohort of more than 6,000 people with HIV

followed for up to 25 years, we observed no increased risk of cancer following

TB disease. These findings do not support changes to continued standardized

cancer surveillance in people with HIV and TB.

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**28. Comput Biol Med. 2025 Jun 24;195:110554. doi: 10.1016/j.compbiomed.2025.110554. Online ahead of print.**

Streamlining tuberculosis detection with foundation model-based weakly

supervised transformer.

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Tuberculosis (TB) remains a major global health challenge, particularly in low-

and middle-income countries. Traditional microscopy-based diagnostics are

labor-intensive and error-prone, while automated deep learning models often

require detailed expert annotations and intensive preprocessing, limiting their

scalability. To address these challenges, we propose a weakly supervised

approach for detecting Mycobacterium tuberculosis (MTB) in microscopy images,

leveraging UNI, a foundation model pretrained on millions of pathology images.

Our method encodes microscopy images as sequences of patch-level embeddings

using UNI and applies a Transformer encoder to classify each image using only

image-level labels, without requiring detailed annotations. This framework

minimizes preprocessing, reduces annotation costs, and enhances scalability. Our

model was trained and tested on large, diverse datasets, achieving high PR-AUC

scores (0.943-0.974), demonstrating strong performance and robustness. This

success highlights the potential of our approach, which introduces two key

innovations not previously explored for automated TB detection: leveraging

cross-domain transfer learning by applying UNI for MTB detection and using a

weakly supervised approach that relies only on image-level labels, significantly

reducing the annotation burden compared to traditional fully supervised methods.

Our results underscore the feasibility of foundation models in TB diagnostics

and broader medical imaging applications. This scalable, weakly supervised

approach demonstrates promising experimental results, highlighting its potential

to significantly reduce annotation requirements and streamline TB detection

workflows, particularly relevant to resource-limited settings.

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development and hepatotoxicity of rifamycins Derivatives.

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**INTRODUCTION:** Rifamycins are a class of antibiotics crucial for the treatment of

tuberculosis (TB). Although the development of rifamycin derivatives has

revolutionized TB therapy, they are associated with hepatotoxicity, which limits

their clinical use.

**AREAS COVERED:** This review summarizes the development, clinical applications,

and hepatotoxicity of rifamycin derivatives. We highlight the mechanisms of

rifamycin drug-induced liver injury (DILI) and discuss strategies to improve the

safety profiles of rifamycin derivatives. Relevant literature was reviewed by

searching PubMed and Scifinder for articles published up to January 2025.

**EXPERT OPINION:** The hepatotoxicity of rifamycin derivatives remains a challenge

in clinical practice. Further research is needed to clarify the detailed

mechanisms of rifamycin-induced liver injury. Mechanism-based strategies are

also expected to prevent the toxicity of rifamycin derivatives.

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**30. mBio. 2025 Jun 25:e0148425. doi: 10.1128/mbio.01484-25. Online ahead of print.**

Vitamin C potentiates the killing of Mycobacterium tuberculosis by bedaquiline

through metabolic disruption.

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Tuberculosis (TB), a disease caused by the bacterium Mycobacterium tuberculosis

(Mtb), continues to pose a major global health threat, exacerbated by the

emergence of drug-resistant strains and the lengthy treatment regimens required

for effective management. Bedaquiline (BDQ), a key component in novel regimens

for multidrug-resistant (MDR) TB, has demonstrated significant efficacy but is

threatened by rising resistance. Our study investigates the potential of vitamin

C to enhance BDQ's activity and prevent resistance. We found that combining BDQ

with vitamin C sterilized drug-susceptible and MDR Mtb cultures in vitro within

21 days, achieving a 6-log reduction in colony-forming units. This combination

also enhanced Mtb killing in infected human macrophages and peripheral blood

mononuclear cells. Transcriptomic analysis revealed that the BDQ/vitamin C

combination induces widespread metabolic disruption in Mtb, characterized by

upregulation of stress response and metal ion homeostasis genes and

downregulation of energy metabolism and cell wall biosynthesis genes.

Mechanistic studies implicated reactive oxygen species and disrupted copper

homeostasis as contributing factors to the sterilization effect. These findings

highlight the potential of using vitamin C as an adjunct therapy with BDQ,

offering a promising strategy to enhance drug efficacy and mitigate emerging

drug resistance during MDR-TB treatment.

**IMPORTANCE:** Tuberculosis (TB) remains a major global health problem, especially

as drug-resistant forms become more common and harder to treat. Bedaquiline is

one of the most important new drugs for treating these resistant infections, but

resistance to bedaquiline is also starting to appear. This study found that the

combination of vitamin C and bedaquiline sterilizes Mycobacterium tuberculosis

cultures in vitro while potentiating bedaquiline activity in infected human

macrophage cells. The combination appears to overwhelm the bacteria by creating

stress and disrupting essential functions, like energy production and metal

balance. These results suggest that vitamin C, a safe and inexpensive

supplement, could be used alongside existing drugs to make treatment faster and

more effective while also helping to prevent resistance.

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**31. Cochrane Database Syst Rev. 2025 Jun 25;6(6):CD015806. doi:**

**10.1002/14651858.CD015806.pub2.**

Low-complexity manual nucleic acid amplification tests for pulmonary

tuberculosis in children.

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Update of

 doi: 10.1002/14651858.CD015806.

**BACKGROUND:** Accurate and prompt diagnosis of tuberculosis in children is

challenging due to non-specific clinical presentation and the low bacillary load

of samples. Low-complexity manual nucleic acid amplification tests (LC-mNAATs)

such as loop-mediated isothermal amplification (TB-LAMP) are World Health

Organization (WHO)-recommended rapid molecular diagnostic tests. Even in

resource-limited settings, they have good diagnostic accuracy in adults.

**OBJECTIVES:** To determine the diagnostic accuracy of LC-mNAATs for the detection

of pulmonary tuberculosis in children (< 10 years) with presumptive pulmonary

tuberculosis. Secondary objectives 1. To compare the diagnostic accuracy of

LC-mNAATs and Xpert MTB/RIF Ultra for the detection of pulmonary tuberculosis in

children with presumptive pulmonary tuberculosis. 2. To compare the diagnostic

accuracy of LC-mNAATs and smear microscopy for detecting pulmonary tuberculosis

in children when TB-LAMP is considered as a replacement test for smear

microscopy. 3. To determine the diagnostic accuracy of LC-mNAATs for the

detection of pulmonary tuberculosis if used as an add-on test amongst sputum

smear-negative children. 4. To investigate potential sources of heterogeneity in

the diagnostic accuracy of LC-mNAATs due to factors such as smear status, age,

HIV status, setting, and tuberculosis burden.

**SEARCH METHODS:** We searched CENTRAL, MEDLINE, Embase, Science Citation Index,

Biosis Previews, Global Index Medicus, SCOPUS, WHO ICTRP, and ClinicalTrials.gov

on 2 October 2023 for published articles and trials in progress without language

or time limits. We screened the reference lists of included articles, conference

abstracts, tuberculosis reviews, and guidelines. We searched ProQuest

Dissertations & Theses A&I for dissertations. We approached the Stop TB

Partnership, FIND, and other experts on tuberculosis for ongoing and unpublished

studies. A WHO public call was made between 30 November 2023 and 15 February

2024 for ongoing and unpublished studies from manufacturers and researchers.

**SELECTION CRITERIA:** We included cross-sectional and cohort studies that

evaluated LC-mNAATs in children (< 10 years) against microbiological or

composite reference standards. Our index test was TB-LAMP, and comparator index

tests were Xpert MTB/RIF Ultra and smear microscopy. The microbiological

reference standard included automated liquid culture, solid culture, or a

combination of both methods. We considered only design-locked, marketed

technologies.

**DATA COLLECTION AND ANALYSIS:** Four review authors, in pairs, independently

screened titles and abstracts and assessed the full texts of potentially

eligible articles. A fifth review author resolved any disagreements. We tailored

and applied the QUADAS-2 and QUADAS-C tools to assess the risk of bias and

applicability. Six review authors, in three pairs, extracted data and performed

methodological quality assessment. A seventh review author resolved any

disagreements. We contacted the primary study authors for missing data. We

assessed the certainty of evidence using the GRADEpro GDT online tool.

**MAIN RESULTS:** We included four eligible studies (303 participants). Three

studies took place in low- and middle-income countries, with two studies from

countries with a high tuberculosis burden. All four studies assessed different

respiratory and non-respiratory specimen types and evaluated TB-LAMP against the

microbiological reference standard. We judged one study to have an unclear risk

of bias in two domains of QUADAS-2. The risk of bias was low for most of the

studies. One study recruited inpatients from tertiary hospitals, causing high

applicability concerns. Three studies (67 children, including eight with

pulmonary tuberculosis) evaluated respiratory samples (sputum, broncho-alveolar

lavage, and tracheal aspirate). The sensitivities were between 60% and 100%, and

the specificities were between 95% and 100% (very low-certainty (sensitivity)

and low-certainty (specificity) evidence). Three studies (176 participants,

including 14 children with pulmonary tuberculosis) used gastric aspirate; the

sensitivity was not estimable in two studies, and was 64% in the third study.

The specificities were between 93% and 100%. The sensitivity was 100% (95%

confidence interval (CI) 29 to 100), and the specificity was 96% (95% CI 88 to

100) in gastric lavage from one study. One study (144 participants, 12 children

with pulmonary tuberculosis) assessed diagnostic accuracy using nasopharyngeal

aspirate. The sensitivity was 58% (95% CI 28 to 85), and the specificity was 94%

(95% CI 88 to 97). The same study (seven children with pulmonary tuberculosis)

also evaluated stool specimens, and the sensitivity and specificity were 100%

(95% CI 59 to 100) and 92% (95% CI 86 to 96), respectively. We did not perform a

meta-analysis due to limited data. Interpretation of the results Respiratory

samples For every 1000 children tested, if 100 had tuberculosis according to

culture, 60 to 100 with tuberculosis would be identified as positive by the

TB-LAMP. Of the 900 children without tuberculosis, 855 to 900 would be

identified as negative by the test. Gastric aspirate For every 1000 children

tested, if 100 had tuberculosis according to culture, 64 with tuberculosis would

be identified as positive by the TB-LAMP. Of the 900 children without

tuberculosis, 837 to 900 would be identified as negative by the test. Gastric

lavage For every 1000 children tested, if 100 had tuberculosis according to

culture, 135 would be TB-LAMP positive, of which 100 would have tuberculosis

(true positives), and 35 would not have tuberculosis (false positives); 865

would be TB-LAMP negative, of which 864 would not have tuberculosis (true

negatives), and one would have tuberculosis (false negatives). Nasopharyngeal

aspirate For every 1000 children tested, if 100 had tuberculosis according to

culture, 112 would be TB-LAMP positives, of which 58 would have tuberculosis

(true positives), and 54 would not have tuberculosis (false positives); 888

would test negative, of which 846 would not have tuberculosis (true negatives),

and 42 would have tuberculosis (false negatives). Stool For every 1000 children

tested, if 100 had tuberculosis according to culture, 171 would be TB-LAMP

positive, of which 99 would have tuberculosis (true positives), and 72 would not

have tuberculosis (false positives); 829 would test negative, of which 828 would

not have tuberculosis (true negatives) and one child would have tuberculosis

(false negative).

**AUTHORS' CONCLUSIONS:** Evidence on the diagnostic accuracy of LC-mNAATs for the

detection of pulmonary tuberculosis in children is limited due to few and small

studies. Adequately powered studies evaluating LC-mNAATs in children are needed.

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**32. PLoS One. 2025 Jun 24;20(6):e0326033. doi: 10.1371/journal.pone.0326033.**

**eCollection 2025.**

Health-Related Quality of Life measured with EQ-5D-5L among tuberculosis

patients in Addis Ababa, Ethiopia: Institutional-based cross-sectional study.

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**BACKGROUND:** Tuberculosis (TB) substantially compromises health-related quality

of life (HRQoL), yet limited studies have assessed its impact on Ethiopian

patients using the EQ-5D instrument. This study evaluates HRQoL, estimates

health state utility values, and identifies associated factors among TB patients

in Ethiopia.

**METHODS:** A cross-sectional study was conducted across 20 public health centers

in Addis Ababa, Ethiopia, involving 672 TB patients selected via proportional

allocation. HRQoL was measured using the EuroQol five-dimension five-level

(EQ-5D-5L) tool. Predictors of utility scores were analyzed using the

Kruskal-Wallis test and Tobit censored regression models.

**RESULTS:** Anxiety/depression was the most frequently affected dimension (55.4% of

participants). The mean EQ-5D-5L utility score was 0.91 (SD ± 0.14), and the

mean EQ-VAS score was 80.6 (SD ± 15.6). Older age (55-64 years: β = -0.067,

p < 0.001; ≥ 65 years: β = -0.383, p < 0.001) and unemployment (β = -0.119,

p < 0.001) were associated with significantly lower HRQoL. Conversely, higher

income (β = 0.056, p < 0.001), absence of comorbidities (β = 0.059, p < 0.001),

and mid-treatment duration (4-5 months: β = 0.029, p = 0.011) correlated with

better HRQoL.

**CONCLUSION:** The findings underscore the influence of socio-demographic and

clinical factors on HRQoL among TB patients in Ethiopia, calling for targeted

interventions and policy reforms to enhance treatment outcomes and patient

support.

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**33. PLOS Glob Public Health. 2025 Jun 24;5(6):e0004742. doi:**

**10.1371/journal.pgph.0004742. eCollection 2025.**

Provider perspectives on empirical antibiotic treatment for tuberculosis-like

symptoms in South Africa's private general practice sector: A qualitative study

in two cities.

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While tuberculosis (TB) in South Africa is commonly treated in the public

sector, some clients first seek care in the private sector. Research has

demonstrated that private general practitioners (GPs) perform less well than do

public sector care providers in TB testing and drug-dispensing practices. We

aimed to describe GPs' decision-making practices related to empiric antibiotic

treatment when presented with symptoms that may be related to TB, to inform

potential interventions. Within a larger study on private sector TB management,

we qualitatively interviewed 30 purposively selected GPs, who varied by gender,

age, practice community, and how they managed TB and HIV in the parent study.

Data were analysed through coding and constant comparison. GPs acknowledged the

common use of broad-spectrum antibiotics for respiratory symptoms, driven by

experience treating presumed bacterial infections and by a desire to rule out

other causes before referring clients for potentially inconvenient TB tests in

the private or public sector. Management decisions were susceptible to perceived

or expressed pressure from clients, who may expect on-the-spot treatment.

Additionally, GPs indicated using antibiotics to mitigate financial strain on

economically vulnerable clients. Empirical antibiotic treatment for

presentations that may be related to TB in the private sector, which can delay

TB diagnosis, could be explained by the absence of accessible and affordable TB

and general bacteriologic tests at the point of care, leading GPs to, among

others, seek to 'rule out' possible bacterial infection. Potential interventions

include increasing the salience of inappropriate antibiotic use, heightening

GPs' suspicion index for TB, and linking GPs directly to public sector TB tests

for clients.

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**34. PLoS One. 2025 Jun 24;20(6):e0326342. doi: 10.1371/journal.pone.0326342.**

**eCollection 2025.**

Feasibility and acceptability of GeneXpert MTB/XDR implementation among

healthcare workers in three low-middle income African countries.

Keller S(1), Naidoo K(2)(3), Zekarias M(4), Israel-Isah S(5), Shaka M(4), Gule

G(2)(3), Naidoo A(2)(3), Bathnna M(5), Dlamini-Miti JN(6), Yae K(4), Okpokoro

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Baltimore, Maryland, United States of America.

**BACKGROUND:** Xpert MTB/XDR (Xpert-XDR) testing can significantly shorten time to

initiating appropriate drug-resistant tuberculosis (DR-TB) treatment, but its

introduction may impact laboratory workflow, especially in laboratories not

currently performing drug susceptibility testing. This study evaluated the

feasibility and acceptability of implementing the Xpert-XDR for rapid triage and

selection of all-oral regimens for DR-TB.

**METHOD:** This was a multi-country, multi-site qualitative study conducted between

July and November 2023, as part of the larger TriAD (Triage test for All oral DR

TB drugs) study implemented in South Africa, Ethiopia, and Nigeria. We conducted

semi-structured in-depth interviews with clinicians, nurses and laboratory staff

at each study site until thematic saturation was achieved. Additionally, we

interviewed policy makers (n = 9) and people with TB (PWTB) (n = 11), to provide

additional insight on the implementation of this new diagnostic assay.

**RESULTS:** Healthcare workers (n = 61) found the new workflow feasible and

acceptable. It was the increased speed in which PWTB would receive a correct

diagnosis and appropriate treatment that provided the biggest benefit to moving

to Xpert-XDR for healthcare workers and PWTB. Laboratory staff mentioned that

Xpert-XDR had expedited and simplified the laboratory workflows.

Role-appropriate and ongoing training is a key factor in effective

implementation as described by policy makers and healthcare workers alike.

Barriers impacting the ability to perform Xpert-XDR included unstable power

supply, internet, and temperature control. Additionally, the Xpert MTB/Rif Ultra

test has higher sensitivity for the detection of TB than the Xpert-XDR test,

leading to discordant test results.

**CONCLUSION:** This study showed that implementation of Xpert-XDR in health

facilities is both feasible and acceptable by all types of healthcare workers.

Some barriers with Xpert-XDR are not exclusive to this particular diagnostic

tool but are important to address when policy makers are deciding which tools to

implement.

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**35. PLOS Digit Health. 2025 Jun 24;4(6):e0000898. doi: 10.1371/journal.pdig.0000898. eCollection 2025 Jun.**

An evaluation of telehealth services at New York City tuberculosis clinics

throughout the COVID-19 pandemic.

Gao GE(1), Easton AV(1), Salerno MM(1), Angulo M(1), Buchanan C(2), Ingram

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In March 2020, three New York City (NYC) Department of Health and Mental Hygiene

Tuberculosis (TB) clinics suspended most in-person services due to the COVID-19

pandemic and rapidly implemented telehealth to provide remote TB care. We

conducted a prospective cohort study of patients with TB or latent TB infection

(LTBI), who received treatment from TB clinics between April 2020 and December

2022, to compare telehealth and in-clinic services. To evaluate the success and

breadth of the telehealth program, we compared patients who utilized telehealth

with those who did not, analyzing differences in demographic characteristics and

key outcomes, including utilization of telehealth, appointment completion, and

treatment completion. "Telehealth patients" completed at least one scheduled

telehealth visit during the study period. We conducted bivariate analyses

comparing telehealth versus in-clinic patients. 56% (497/885) of patients with

TB and 45% (954/2127) of patients with LTBI had a telehealth visit. Among

patients with TB, no disparities in proportions of telehealth and in-clinic

patients were observed for age (p = 0.31) or primary language spoken (p = 0.37).

Among patients with LTBI, younger patients were more likely to use telehealth

(p < 0.001). Using mixed-effects logistic regression models, the AOR of

completing a telehealth visit was lower compared to in-clinic for patients with

TB (0.77, CI:0.65-0.91). However, excluding April to June 2020, the AORs of

completing a telehealth visit were comparable to an in-clinic visit for patients

with TB (0.94, CI:0.77-1.14) and for patients with LTBI (0.96, CI:0.82-1.13).

Among 641 patients with drug-susceptible TB, 95% (333/352) of telehealth

patients completed treatment within one year compared to 88% (254/289) of

in-clinic patients (p = 0.002). This result is limited to the descriptive

summary of this study population. During the COVID-19 pandemic, NYC Health

Department provided telehealth to many patients with TB and LTBI of diverse

demographics, and telehealth services were mostly comparable to in-clinic

services.

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**36. PLOS Glob Public Health. 2025 Jun 24;5(6):e0004719. doi:**

**10.1371/journal.pgph.0004719. eCollection 2025.**

Broadening the vaccine metaphor: The adequate balanced food (ABF) vaccine

against tuberculosis (Acid-fast bacilli/AFB) and more.

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(2)Department of Medicine, McGill University, Montreal, Canada.

Nutrition is essential to survival, health, and protection from disease across

the lifespan. In the 1970s, an adequate diet was described as the most effective

vaccine available for respiratory, diarrheal, and other common infections, as

nutritional supplementation reduced these in the setting of undernutrition.

Recently, the RATIONS (Reducing Activation of Tuberculosis through Improvement

Of Nutritional Status) trial showed the efficacy of nutritional supplementation

in reducing TB incidence in households by up to 50%, and an editorial used the

metaphor of food as a vaccine for tuberculosis. This essay provides a historical

overview of nutrition and TB prevention, with reports of reduced TB incidence

from nutritional supplementation in World War II prisoner-of-war camps. This

essay discusses additional evidence supporting McKeown's proposition that the

historical decline of TB in countries like the UK was related to improvements in

nutrition. Undernutrition is the leading risk for tuberculosis incidence

globally, the underlying cause of 45% of 4.9 million deaths in children under

five years annually. Undernutrition in early life is a risk factor for many

non-communicable diseases, and its effect on cognition and growth perpetuates

both undernutrition and poverty intergenerationally. The essay broadens the

vaccine metaphor to describe adequate balanced food (ABF) as a vaccine for TB

and many public health problems, with a unique product profile. It concludes

with a reminder that nutrition acts by optimizing immune function - the most

powerful system/vaccine we have for TB prevention; draws attention to emerging

threats to food security like climate change and conflicts, and proposes that

the answer to the prevention of TB may lie in better population health rather

than only a war on the bacillus.

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**37. J Cutan Med Surg. 2025 Jun 24:12034754251351851. doi: 10.1177/12034754251351851. Online ahead of print.**

Characteristics, Management, and Outcomes of Latent Tuberculosis Reactivation

Following the Use of Biologics for Psoriasis: A Systematic Review.

Seeburruth D(1), McGuinty J(1), Sood S(1), Lapa T(2), Akuffo-Addo E(2), Piguet

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DOI: 10.1177/12034754251351851

PMID: 40552546

**38. J Law Med Ethics. 2025 Jun 24:1-3. doi: 10.1017/jme.2025.10128. Online ahead of print.**

"Everything is Tuberculosis" - Except the Law?

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In "Everything is Tuberculosis," author John Green assesses the intricacies of

the communicable condition, TB, as a source of significant morbidity and

mortality globally over centuries. Despite available vaccines, treatments, and

protocols, tens of millions are infected and over a million persons will die

from TB in 2025 alone. In searching for answers to mitigate this global scourge,

however, Green looks past a key factor - specifically the role of law - as a

primary tool for prevention and control.

DOI: 10.1017/jme.2025.10128

PMID: 40552457

**39. Health Sci Rep. 2025 Jun 23;8(6):e70953. doi: 10.1002/hsr2.70953. eCollection**

**2025 Jun.**

Prevalence, Risk Factors and Residential Variation Among HIV/TB Coinfected

Mortality in Fenote Selam Hospital, Amhara Region: A Retrospective Study.

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**BACKGROUND AND AIM:** HIV-TB co-infection is a worldwide health concern that

arises when an individual has both HIV and tuberculosis (TB) infections.

Ethiopia is one of the top 30 nations in the world with the highest rates of TB

and HIV. The goal of this study was to determine the variables that influence

adult HIV/TB coinfected patients' mortality as well as the nutritional

differences in mortality by level of residency.

**METHOD:** In this study, 417 patients that met our criteria were included in this

study. We employed a multilevel logistic regression model.

**RESULT:** 12.9% of HIV/TB coinfected patients died during the research period. It

was discovered that important predictors of HIV/TB coinfected mortality included

functional status, age of patients, WHO clinical stages, nutritional status, CD4

levels, regimen, and BMI. In our study, patients who fell into the bedridden

functional status group, those who were in the fourth WHO clinical stage (stage

IV), those who were older, those whose therapies were second-line regimens, and

those with low CD4 cell counts were greater at risk of passing away.

**CONCLUSION:** This study showed that, individuals with HIV/TB co-infection were

more likely to die and that this risk varied depending on the patient's place of

residency (rural areas were more at risk).

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**40. ERJ Open Res. 2025 Jun 23;11(3):00839-2024. doi: 10.1183/23120541.00839-2024.**

**eCollection 2025 May.**

Lack of weight gain and increased mortality during and after treatment among

adults with drug-resistant tuberculosis: a retrospective cohort study in

Georgia, 2009-2020.

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(4)Swiss Tropical and Public Health Institute, Allschwil, Switzerland.

**BACKGROUND:** While low body mass index (BMI) is associated with poor tuberculosis

(TB) treatment outcomes, the impact of weight gain during TB treatment is

unclear. To address this knowledge gap, we assessed whether a lack of weight

gain is associated with all-cause mortality during and after TB treatment.

**METHODS:** We conducted a retrospective cohort study among adults with newly

diagnosed multidrug or extensively drug-resistant (MDR/XDR) pulmonary TB in

Georgia between 2009-2020. The exposure was a change in BMI during the first

3-6 months of TB treatment. All-cause mortality during and after TB treatment

was assessed using the National Death Registry. We used competing-risk Cox

proportional hazard models to estimate adjusted hazard ratios (aHRs) between BMI

change and all-cause mortality.

**RESULTS:** Among 720 adult participants, 21% had low BMI (<18.5 kg·m-2) at

treatment initiation and 9% died either during (n=16) or after treatment (n=50).

During the first 3-6 months of TB treatment, 17% lost weight and 14% had no

weight change. Among 479 adults with normal baseline BMI (≥18.5-<25 kg·m-2),

weight loss was associated with an increased risk of death during TB treatment

(aHR 5.25, 95% CI 1.31-21.10). Among 149 adults with a low baseline BMI, no

change in BMI was associated with increased post-TB treatment mortality (aHR

4.99, 95% CI 1.25-19.94).

**CONCLUSIONS:** Weight loss during TB treatment (among those with normal baseline

BMI) or no weight gain (among those with low baseline BMI) was associated with

increased rates of all-cause mortality. Our findings suggest that scaling up

weight management interventions among those with M/XDR TB may be beneficial.

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PMCID: PMC12183741

PMID: 40551793

**41. ERJ Open Res. 2025 Jun 23;11(3):00818-2024. doi: 10.1183/23120541.00818-2024.**

**eCollection 2025 May.**

Latent tuberculosis infection screening of adult close contacts: a cost-utility

analysis.

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**BACKGROUND:** The 2016 National Institute for Health and Care Excellence

guidelines recommended the tuberculin skin test (TST), at a 5-mm induration size

cut-off, for the diagnosis of latent tuberculosis infection (LTBI) among adult

close contacts of active tuberculosis (TB) cases. This study analysed a

well-characterised cohort of adult close contacts in London and assessed the

cost-effectiveness of LTBI screening strategies with combinations of TST and

interferon-γ release assays (IGRAs) in a decision-analytic model.

**METHODS:** Close contacts of pulmonary TB cases who were tested with TST and IGRA

between January 2008 and December 2010 were retrospectively reviewed. Using an

NHS perspective and lifetime horizon, a decision-analytic Markov model was used

to compare costs and quality-adjusted life-years (QALYs) associated with five

screening strategies followed by LTBI treatment: 1) TST alone; 2) QuantiFERON-TB

Gold In-Tube (QFT) alone; 3) T-SPOT.TB (T-SPOT) alone; 4) TST positive followed

by QFT; 5) TST positive followed by T-SPOT.

**RESULTS:** This study included 381 asymptomatic close contacts aged 18 to 65 years

(mean±sd 35.2±11.3). 75.3% had received BCG vaccination. Among the five

strategies, for a willingness-to-pay threshold of GBP 25 000 and using

incremental net monetary benefit (INMB) with TST as comparator, the IGRA-alone

strategies were the most cost-effective, marginally QFT over T-SPOT (QFT: GBP

214; T-SPOT: GBP 199).

**CONCLUSION:** Single-step IGRA, particularly QuantiFERON, is preferable for LTBI

screening of adult close contacts of pulmonary TB cases.

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PMCID: PMC12183743

PMID: 40551790

**42. Community Health Equity Res Policy. 2025 Jun 23:2752535X251355731. doi:**

**10.1177/2752535X251355731. Online ahead of print.**

A Community Rights and Gender Assessment of Tuberculosis Diagnosis, Treatment

and Care in Lebanon.

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TB remains a significant global health challenge despite being preventable and

curable. The Global Plan to End TB 2023-2030 is underpinned by a rights-based,

public health and people-centred approach to ending TB. Lebanon is a low TB

endemic country, where for the first time a community, rights, and gender (CRG)

assessment of the national TB response was conducted in 2024. Despite the

universal availability and cost-free access to TB care in Lebanon, systemic

barriers continue to hinder patient accessibility. Low disease awareness,

transportation costs, financial challenges, and pervasive stigma frequently

compel individuals to conceal their TB diagnosis, thereby undermining contact

tracing and treatment adherence. Beyond medical treatment, TB patients receive

minimal psychosocial or financial support, disproportionately affecting key

vulnerable groups who are already marginalized in Lebanese society. Insufficient

community engagement and chronic funding shortages further weaken the Lebanese

TB response. While Lebanon upholds advanced medical protocols, its outdated TB

laws fail to protect crucial patient rights, including privacy, confidentiality,

and informed consent. Gender disparities also persist, with a lack of

gender-specific data to inform policies, and inadequate sensitization among

healthcare personnel (e.g., transgender women, women with HIV, women who use

drugs). There is a pressing need for accountability mechanisms for TB program

implementers and labor protections to prevent workplace discrimination against

TB patients. Strengthening the National TB Program and addressing the structural

deficiencies in Lebanon through targeted interventions, legal reforms, and a

gender-inclusive, rights-based approach is essential to ensuring available,

accessible, acceptable and quality TB services in Lebanon.

DOI: 10.1177/2752535X251355731

PMID: 40551385

**43. Trop Med Int Health. 2025 Jun 23. doi: 10.1111/tmi.14140. Online ahead of print.**

Effect of glycemic control on tuberculosis treatment outcomes among patients

with tuberculosis and diabetes mellitus: A systematic review and meta-analysis.

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**INTRODUCTION:** Tuberculosis (TB) and diabetes mellitus comorbidity can lead to

poor TB treatment outcomes, particularly with uncontrolled blood glucose levels.

Understanding the impact of glycemic control on TB treatment outcomes is

essential.

**OBJECTIVE:** To synthesise evidence on the association between glycemic control

and TB treatment outcomes in patients with TB and diabetes mellitus.

**METHODOLOGY:** A systematic review was conducted using Medline, Embase, Scopus,

Web of Science, Cumulative Index to Nursing and Allied Health Literature

(CINAHL) and Google Scholar for all types of studies published between 1975 and

May 2024, including adult TB patients of >18 years of age, with or without

diabetes mellitus for whom blood glucose testing along with TB treatment outcome

comparison with glucose levels (low/high) was reported were considered for

inclusion. A random-effects model was used for meta-analysis, heterogeneity was

assessed using I-squared statistics, subgroup and sensitivity analysis was

performed followed by publication bias assessment.

**RESULTS:** Of 576 identified studies, 12 met the inclusion criteria, analysing

2320 cases (1572 with uncontrolled high blood glucose [≥7% HbA1c] and 748 with

controlled low blood glucose [<7% HbA1c]). Low certainty evidence shows that

patients with uncontrolled high glucose had a 1.91 times higher risk of TB

treatment failure (risk ratios [RR] = 1.91, 95% confidence interval [CI]

1.81-3.07, p = 0.008), and a 2.97 times higher risk of sputum positivity at

3 months (RR = 2.97, 95% CI 1.10-8.07, p = 0.03). Subgroup and sensitivity

analyses showed significant improvement in pooled effects, lowering of

heterogeneity and narrower CIs. For overall pooled effect, substantial

heterogeneity was observed; therefore, the interpretation and generalisation of

results should be done with caution.

**CONCLUSION:** A low certainty evidence shows that uncontrolled high blood glycemic

level significantly impacts TB treatment outcomes, increasing treatment failure

and sputum positivity among TB patients with diabetes mellitus.

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Wiley & Sons Ltd.

DOI: 10.1111/tmi.14140

PMID: 40551384

**44. Commun Biol. 2025 Jun 23;8(1):950. doi: 10.1038/s42003-025-08337-9.**

Human alveolar macrophage response to Mycobacterium tuberculosis: immune

characteristics underlying large inter-individual variability.

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X(6), Lin S(6), Williams AM(3), Wewers MD(7), Curry HM(8), Zhang H(9), Cai H(9),

Kunsevi-Kilola C(10), Tshivhula H(10), Walzl G(10), Restrepo BI(11)(12),

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Mycobacterium tuberculosis (M.tb) infection infects human alveolar macrophages

(HAMs). In freshly isolated HAMs from 28 healthy adults, we observe large

inter-individual differences in bacterial uptake and growth, with tenfold

variation in M.tb load by 72 h. While M.tb infection triggers expression changes

of numerous host mRNAs, we examined which genes are most variably expressed (VE

genes) between donors, as potential biomarkers of individual tuberculosis (TB)

risk. The HAM RNA transcriptome following infection revealed thousands of

differentially expressed (DE) genes and differential secretion of 25/27

proteins. Yet only 324 DE genes represent VE genes detected exclusively among DE

genes in infected cells. Of 36 DE genes detected at all time points (2, 24, and

72 h), 14 are VE genes, indicating early emergence of the VE gene profile. 9/27

DE proteins following infection were encoded by VE genes. Systems analysis of VE

RNAs identified a top-scoring network anchored by IL1B, involved in TB immune

response. Independent M.tb-HAM transcriptome results from a TB-endemic region

show significant overlap in DE genes, including VE genes identified in the main

study. Thus, we identify a VE gene network activated upon M.tb-HAM infection

with high inter-person variability, guiding studies on determining individual

risk of M.tb infection and/or disease.

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DOI: 10.1038/s42003-025-08337-9

PMCID: PMC12185700

PMID: 40550843 [Indexed for MEDLINE]

**45. Acta Paediatr. 2025 Jun 23. doi: 10.1111/apa.70182. Online ahead of print.**

The Paediatric BCG Vaccine Century: From Historical Success to Future

Innovations.

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**AIM:** The tuberculosis (TB) vaccine, Bacille-Calmette-Guérin (BCG), protects

infants against severe forms of primary TB. Yet, it does not protect against

pulmonary reactivation TB in adults.

**METHODS:** A literature review was conducted between 1st January and 28th February

2025 using PubMed, Google Scholar and reports of the World Health Organization.

**RESULTS:** Protection against TB includes innate and acquired cellular immunity

and infants are more susceptible due to immature immunity. Immunopathology of

infant TB is characterised by formation of small granulomas in the lung often

followed by dissemination to other organs. Infection in adults is frequently

contained until immunity is weakened and TB disease develops. Novel vaccines are

being developed mostly for adolescents and adults, but two live attenuated

vaccines are currently assessed in infants in Phase III clinical trials.

Globally, TB remains a major health threat and countries of the global south

bear the major TB burden. Today, Sweden, similar to other high-income countries,

has a low incidence. General vaccination has therefore been terminated and

targeted BCG vaccination is offered to infants at higher risk.

**CONCLUSION:** Together with short-treatment and rapid diagnosis, novel vaccines

profoundly contribute to the fight against TB in all age groups.

© 2025 The Author(s). Acta Paediatrica published by John Wiley & Sons Ltd on

behalf of Foundation Acta Paediatrica.

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PMID: 40548838

**46. Microbiol Spectr. 2025 Jun 23:e0060225. doi: 10.1128/spectrum.00602-25. Online ahead of print.**

Use of a convolutional neural network for direct detection of acid-fast bacilli

from clinical specimens.

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Mycobacteria, including Mycobacterium tuberculosis (MTB) and non-tuberculosis

mycobacteria (NTM), are important causes of infectious disease and cause

significant mortality and morbidity globally. Fast detection is extremely

important to reduce transmission and mortality associated with these infectious

agents. Manual smear microscopy is a cost-effective tool for diagnosing and

monitoring of these organisms; however, it is labor-intensive and requires

highly-trained personnel. We present the development of an artificial

intelligence computer vision process using a deep convolutional neural network

to detect acid-fast bacilli (AFB) from Kinyoun acid-fast stained slides. We

collected 231 clinical specimens between August 2023 and June 2024. Following

acid-fast staining, whole slide images (WSI) were digitized, and AFB organisms

were manually annotated. A machine learning computer vision model was trained

using 11,411 annotated organisms across 109 WSI. Model predictions were

correlated with final culture-confirmed results. The final model estimated AFB

density per 1000 x microscope field of view (FOV). Using a density threshold of

≥10-2 AFB/1000xFOV (corresponding to 1 + per Clinical and Laboratory Standards

Institute (CLSI) guideline M48) to predict positive culture results, the model

correctly classified 68% of validation slides, with a sensitivity of 79% and

specificity of 63%. Manual AO compared to final culture read showed sensitivity

of 76% and specificity of 96%. Although performance of our model was not

sufficient to be clinically implemented in our laboratory, our study provides a

framework for AI-based AFB detection and a publicly available data set to

support future advancements in automated detection of AFB.IMPORTANCEWe present

the development of an artificial intelligence model to detect acid-fast bacilli

(AFB) directly from stained clinical smears. While the model's current

performance requires further improvement to be clinically useful in our lab, we

detail our approach and share our expertly annotated data set to support future

advancements in this area. By building on our work, researchers can develop

better algorithms to improve the diagnosis of AFB, reducing the burden on

laboratory staff and improving diagnostic speed and accuracy of these medically

important organisms.

DOI: 10.1128/spectrum.00602-25

PMID: 40548735

**47. Infect Immun. 2025 Jun 23:e0017725. doi: 10.1128/iai.00177-25. Online ahead of print.**

Characterizing PET CT patterns and bacterial dissemination features of

tuberculosis relapse in the macaque model.

Maiello P(#)(1)(2), Diedrich C(#)(2)(3), Rutledge T(2)(3), Rodgers M(1)(2),

Kracinovsky K(1)(2), Borish HJ(1)(2), White A(1)(2), Hopkins F(4), Chao MC(4),

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Tuberculosis (TB) relapse after appropriate drug treatment is poorly understood

but critical to developing shorter treatment regimens. Using a cynomolgus

macaque model of human TB, macaques with active TB disease were treated with a

short course of isoniazid and rifampin and subsequently infected with SIV.

Serial clinical, microbiologic, immunologic, and position emission and computed

tomography (PET CT) assessments were performed to identify risk factors of

relapse. Of the 12 animals, eight developed radiologically defined relapse,

including four that had clinical and/or microbiologic signs. Greater gross

pathology and bacterial burden were observed in relapse animals. PET CT

characteristics before, during, and at the end of the treatment were similar

among relapse and non-relapse animals. We show that complete sterilization or

very low Mtb burden is protective against SIV-induced TB relapse but cannot be

predicted by PET CT. Using barcoded M. tuberculosis, we found that Mtb

dissemination during relapse originated from both lung and thoracic lymph nodes,

underscoring the importance of lymph nodes as a reservoir. By matching barcoded

Mtb and serial PET CT, we also demonstrate that not every site of persistent Mtb

growth after drug treatment is capable of dissemination and relapse,

underscoring the complex nature of drug treatment and relapse.

DOI: 10.1128/iai.00177-25

PMID: 40548727

**48. J Infect Dis. 2025 Jun 17:jiaf326. doi: 10.1093/infdis/jiaf326. Online ahead of print.**

Molecular epidemiology of Mycobacterium tuberculosis across three distinct

geographic sites in South Africa.

Ryckman TS(1)(2), Hopkins L(3), Tang L(4), Biche P(2)(3), Mohlamonyane M(5),

Morolo M(6), Nonyane BAS(2)(7), Ahmed K(6)(8)(9), Martinson N(2)(5)(10),

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**BACKGROUND:** Whole genome sequence (WGS) data can generate insights about

Mycobacterium tuberculosis (Mtb) transmission. We used WGS and linked

epidemiology data from a recent randomized trial to characterize Mtb relatedness

across three geographically distinct South African sites.

**METHODS:** We sequenced culture isolates from participants with culture-positive

TB in the Kharituwe study, which evaluated household contact investigation

strategies in one urban and two rural sites. We adapted a previous bioinformatic

pipeline to clean, extract, and filter Mtb reads, perform reference alignment,

calculate single nucleotide polymorphism (SNP) distances between isolates, and

group isolates into clusters linked by recent transmission, based on three

SNP-based cutoffs. Sequence data were linked to individual data on demographics

and risk factors. We analyzed clustering across and within study sites and used

log binomial regression to assess characteristics associated with clustering.

**RESULTS:** At a cutoff of 12 SNPs, 213 out of 714 sequenced isolates passing

quality control filters were clustered. While only 3 out of 45 pairs included

participants from different sites, the majority of clusters with ≥4 participants

included representation from at least 2 sites. Expanding to a 20-SNP cutoff

revealed a large cluster containing 10% of isolates, with urban/rural

representation mirroring that of all the isolates (61% urban, 39% rural).

Participants from the urban site, TB household contacts, and participants

reporting a history of incarceration were more likely to be in a cluster.

**CONCLUSIONS:** Observed clustering and strain diversity across sites indicate the

presence of multiple ongoing and geographically dispersed outbreaks in this

setting.

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**49. J Infect Dis. 2025 Jun 17:jiaf320. doi: 10.1093/infdis/jiaf320. Online ahead of print.**

Risk factors associated with TB infection among household contacts of

microbiologically confirmed pulmonary TB patients in three high TB burden

countries.

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Ngobeni M(1), Mudzengi D(1)(7), Minja LT(5), Chirwa T(2), Lönnroth K(8), Dreyer

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**BACKGROUND:** Although tuberculosis (TB) preventive therapy (TPT) guidelines

support testing for TB infection (TBI) in household contacts (HHCs), this adds

operational complexity and cost and has often been abandoned. To understand

utility of testing, we determined prevalence and risk factors for TBI and TPT

eligibility among HHCs.

**METHODS:** In a cross-sectional study conducted from July 2021-September 2022 in

Lesotho, South Africa, and Tanzania, we enrolled people with

microbiologically-confirmed pulmonary TB (PWTB) and their HHCs. HHCs were

screened and tested for TB and TBI using Xpert Ultra and

QuantiFERON-TB-Gold-Plus, respectively. Generalised linear modelling was used to

determine factors associated with TBI, using robust standard errors. TPT

eligibility was determined using World Health Organisation criteria.

**RESULTS:** We enrolled 342 PWTB and 964 HHCs: 61.9% (597/964) were female with a

median age of 18 years (interquartile range: 8-39). Overall, TB prevalence was

3.4% (25/739, 95% Confidence Interval (CI): 2.2-4.9), while TBI prevalence was

48.7% (348/714, 95%CI: 45.0-52.5). Having TBI increased with age per year

(adjusted Odds Ratio (aOR) 1.02, 95%CI: 1.01-1.03), being from Lesotho (aOR

1.82, 95%CI: 1.04-3.20), previous TB history (aOR 2.25, 95%CI: 1.05-4.79), and

being HIV negative (aOR 2.30, 95%CI: 1.31-4.04). Overall, 62.2% (518/833, 95%CI:

58.8-65.5) were eligible for TPT.

**CONCLUSION:** Almost half of TB exposed HHCs aged ≥5 years had TBI. Approximately

two thirds of HHCs were eligible for TPT, implying that providing TPT without

prior testing for TBI may be warranted in this population. Further work on

cost-effectiveness is warranted when new tests become available.

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**50. IJID Reg. 2025 May 16;15:100673. doi: 10.1016/j.ijregi.2025.100673. eCollection 2025 Jun.**

Estimating childhood tuberculosis incidence and under-reporting in Gedeo Zone,

Ethiopia: a Bayesian hidden Markov model.

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University, Dilla, Ethiopia.

**OBJECTIVES:** To estimate the incidence and under-reported cases of childhood

tuberculosis (TB) in rural Ethiopia.

**METHODS:** We used a Bayesian hidden Markov model with Spatio-temporal random

effects to analyze TB notification data from rural areas between 2018 and 2023.

Spatial dependence and HIV infection were included as covariates for estimating

TB incidence, while the availability of diagnostic services informed the case

detection process. Sensitivity analysis were conducted to assess the robustness

of the results with alternative prior distributions.

**RESULTS:** Childhood TB incidence in the Gedeo Zone increased from 141 cases per

100,000 population (95% uncertainty interval: 96-193) in 2018 to 157 cases (95%

uncertainty interval: 114-207) in 2023. Estimated case detection rates ranged

from 56 cases per 100,000 in 2018 to 62 in 2023, indicating substantial

under-reporting. Spatial lags of TB notifications predicted incidence in

adjacent areas. Sensitivity analysis confirmed result robustness.

**CONCLUSIONS:** The gap between estimated TB incidence and reported cases

highlights the urgent need to strengthen TB surveillance in the study area.

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PMID: 40575492

**51. J Clin Tuberc Other Mycobact Dis. 2025 Jun 7;40:100537. doi:**

**10.1016/j.jctube.2025.100537. eCollection 2025 Aug.**

First insights into the genetic composition of M. tuberculosis population

circulating in Kosovo.

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Miftari A(3), Shkodra X(3), Jakupi X(3), Kacaniku Z(3), Kozińska M(4), Zabost

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Tuberculosis incidence in Kosovo is among one of the highest in Europe at

33/100,000 citizens. While World Health Organization encourages epidemiological

monitoring of tuberculosis transmission, studies regarding M. tuberculosis

population structure in the Balkan region are limited. Here, we used

spoligotyping and whole genome sequencing to describe the variation of M.

tuberculosis strains circulating in Kosovo. We used samples isolated from

patients in the period 2021/2022. We found that the vast majority of isolated

strains belonged to spoligotype based Euro-American lineage, five strains

belonged to East-Asian lineage, and one was M. caprae. We described the general

characteristics of the M. tuberculosis population in our study and identified

chains of transmission based on whole genome sequencing data of selected

samples. Our data will be a reference point for subsequent studies of M.

tuberculosis population in Kosovo.

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PMCID: PMC12197985

PMID: 40575015

**52. Pharmaceutics. 2025 May 27;17(6):705. doi: 10.3390/pharmaceutics17060705.**

Assessment of Innovative Dry Powders for Inhalation of a Synergistic Combination

Against Mycobacterium tuberculosis in Infected Macrophages and Mice.

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**Background/Objectives:** In vitro, vancomycin (VAN) and tetrahydrolipstatin (THL)

together have been shown to synergistically inhibit Mycobacterium tuberculosis

(Mtb), the world's most infectious killer. The poor oral bioavailability of VAN

and THL and predominant tropism of Mtb infection to the lungs and alveolar

macrophages make pulmonary administration highly attractive. This study aimed to

develop and assess the efficacy of dry powders for inhalation of VAN

microparticles embedded with THL. **Methods:** The dry powders produced by

spray-drying, with or without hydrogenated castor oil (HCO), were characterized

for their physicochemical properties among others by HPLC-DAD. The

fast-screening impactor was used to determine powder aerodynamic properties, and

VAN and THL releases were established from the paddle over disk method.

Biological activities were assessed in a new M. bovis-infected macrophage model

and in Mtb-infected mice. **Results and Discussion:** The addition of 25% HCO

enables co-deposition (fine particle dose) at the desired weight ratio and

co-releasing of VAN and THL in aqueous media. Microparticles with 0% to 50% HCO

drastically reduced cytoplasmic Mycobacterium bovis survival (99.9% to 62.5%,

respectively), with higher efficacy at low HCO concentration. Consequently,

VAN/THL with or without 25% HCO was evaluated in Mtb-infected mice. Although no

decrease in Mtb lung burden was observed after two weeks of administration, the

endotracheal administration of VAN 500 mg/kg and THL 50 mg/kg with 25% HCO

administrated three times during five days concomitantly with daily oral

rifampicin (10 mg/kg) demonstrated 2-fold bacterial burden reduction compared to

the group treated with RIF alone. **Conclusions:** HCO was crucial for obtaining a

fine particle dose at the synergistic weight ratio (VAN/THL 10:1) and for

releasing both drugs in aqueous media. With oral administration of the

first-line rifampicin, the dry powder VAN/THL/25% HCO was able to exert a

potential anti-tubercular effect in vivo in Mtb-infected mice after five days.

DOI: 10.3390/pharmaceutics17060705

PMID: 40574018

**53. Pharmaceutics. 2025 May 22;17(6):680. doi: 10.3390/pharmaceutics17060680.**

Formulation of Topical Drug Delivery Systems Containing a Fixed-Dose

Isoniazid-Rifampicin Combination Using the Self-Emulsification Mechanism.

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**Background:** Tuberculosis remains a significant global health issue, and the rise

of drug-resistant strains is becoming increasingly concerning. Currently,

treatment options are limited to systemic regimens; however, developing topical

drug delivery systems could offer advantages for treating cutaneous tuberculosis

(CTB) when applied directly to the lesions. We developed topical emulsions using

the self-emulsification mechanism that combine fixed doses of isoniazid (INH)

and rifampicin (RIF) using a quality-by-design approach. **Methods:** Preformulation

studies pertaining to drug solubility in various solvents, the construction of

pseudoternary diagrams to identify self-emulsification regions for each tested

excipient combination, and the preparation of checkpoint formulations were

conducted and visually examined. Formulations displaying no physical

instabilities were subsequently exposed to characterization experiments,

including droplet size determination, zeta potential, size distribution,

viscosity, pH, self-emulsification, cloud point, robustness to dilution, and

thermodynamic stability assessment. Three selected formulations were

consequently subjected to membrane release experiments, followed by skin

diffusion studies, and INH and RIF stability in these emulsions was determined,

because these drugs have a known interaction. **Conclusions:** While incorporating

essential oils in a topical formulation improved RIF solubility, it also

resulted in several instabilities. RIF exhibited greater susceptibility to

degradation under higher temperatures and lower pH conditions. However, drug

release from all formulations tested was confirmed. Notably, olive oil

microemulsions demonstrated the most favorable characteristics for dermal drug

delivery; nonetheless, drug diffusion into and through the skin (which was not

desired) could not be quantified. Despite these challenges, the findings

indicate that topical drug delivery systems using the self-emulsification

process can facilitate the direct treatment of CTB.

DOI: 10.3390/pharmaceutics17060680

PMID: 40573994

**54. Vaccines (Basel). 2025 Jun 3;13(6):606. doi: 10.3390/vaccines13060606.**

Recombinant Mycobacterium bovis BCG-Based HIV Vaccine: Failures and Promising

Approaches for a Successful Vaccine Strategy.

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During 2022, AIDS claimed a life every minute and about 9.2 million HIV-infected

people were not on treatment. In addition, a person living with HIV is estimated

to be 20-30 times more susceptible to developing active tuberculosis. Every

year, 130,000 infants are newly infected, with vertical transmission being the

main cause of pediatric HIV infection. Thus, the development of an effective,

safe, and accessible vaccine for neonates and/or adults is an urgent need to

prevent or control HIV infection or progression to AIDS. An effective HIV

vaccine should induce long-lasting mucosal immunity, broadly neutralizing

antibodies, innate immunity, and robust stimulation of CD4+ and CD8+ T-cell

responses. Recombinant BCG is a promising live-attenuated bacterial vaccine

vector because of its capacity to stimulate T-cell immunity. As a slow-growing

microorganism, it provides prolonged low-level antigenic exposure upon infecting

macrophages and APCs, potentially stimulating both effector and memory T-cell

responses. BCG is considered safe and is currently administered to 80% of

infants in countries where it is part of the national immunization program.

Additionally, BCG offers several benefits as a live vaccine vehicle since it is

cost-effective, easy to mass-produce, and heat stable. It is also well-suited

for newborns, as maternal antibodies do not interfere with its efficacy.

Furthermore, BCG has a strong safety profile, having been administered to over

three billion people as a TB vaccine. In this review, we provide an extensive

summary of the literature relating to immunogenicity studies in animal models

performed since 2011. Moreover, we provide a comprehensive analysis of the key

factors influencing the design of recombinant BCG as a live vaccine vehicle: (i)

expression vectors; (ii) selection of HIV immunogen; (iii) promoters to regulate

gene expression; (iv) BCG strain and BCG codon optimization; (v) genetic plasmid

stability; (vi) influence of preexisting immunity, route, and dose immunization;

and (vii) safety profile.

DOI: 10.3390/vaccines13060606

PMID: 40573937

**55. Vaccines (Basel). 2025 May 28;13(6):578. doi: 10.3390/vaccines13060578.**

The Impact of Bacillus Calmette-Guérin Vaccination and Mycobacterium bovis

Infection on Diagnostic Antibody Tests for Mycobacterial Infections.

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**BACKGROUND:** Bovine tuberculosis (bTB) is an infectious disease which causes

significant damage to the farming industry and remains a disease of global

significance. Although control strategies have focused on a test and cull

approach primarily based around specific cell-mediated immune responses,

serological assays are increasingly being used as a supplementary test alongside

skin testing and interferon-gamma release (IGRA) assays. The UK is moving

towards the use of the Bacillus Calmette-Guérin (BCG) vaccination of cattle as

an additional targeted control tool against bTB. However, there are concerns

over its potential impact on the outcomes of bTB diagnostic tests and other

non-TB assays, such as serological tests for Mycobacterium avium subsp.

paratuberculosis (MAP).

**METHODS:** We investigated the performance of commercially available serology

tests designed to detect bTB and MAP using serum samples from BCG-vaccinated

animals which were subsequently infected with Mycobacterium bovis (M. bovis).

**RESULTS:** BCG vaccination per se did not significantly impact the specificity of

serological diagnostic tests for bTB or Johne's disease. However, increased

numbers of false-positive responses in bTB serology tests were seen in

BCG-vaccinated animals 3 weeks following a tuberculin skin test, where up to 23%

and 54% of animals gave a positive result in IDEXX and Enferplex tests,

respectively. Furthermore, M. bovis infection gave rise to false-positive test

results for Johne's disease, irrespective of the animals' prior BCG vaccination

status.

**CONCLUSIONS:** Caution should be taken when assessing results from serology tests

for bTB if tuberculin skin testing has occurred shortly before collection of

blood from BCG-vaccinated cattle. Furthermore, these results highlight the

potential for misdiagnosis of MAP infection when using serology tests in

bTB-infected cattle.

DOI: 10.3390/vaccines13060578

PMID: 40573909

**56. Pharmaceuticals (Basel). 2025 Jun 13;18(6):891. doi: 10.3390/ph18060891.**

M. avium Complex Pulmonary Infections: Therapeutic Obstacles and Progress in

Drug Development.

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Worldwide, several million people are infected with mycobacteria such as

Mycobacterium tuberculosis (M. tb) or non-tuberculous mycobacteria (NTM). In

2023, 10.8 million cases and 1.25 million deaths due to M. tb were recorded. In

Europe and North America, the emergence of NTM is tending to outstrip that of M.

tb. Among pulmonary NTM, Mycobacterium avium complex (MAC) is the most common,

accounting for 80% of NTM infections. First-line treatment requires the

combination of at least three antibiotics over a long period and with different

mechanisms of action to limit cross-resistance. The challenge is to discover

more effective new anti-MAC molecules to reduce the duration of treatment and to

overcome resistant strains. The aim of this review is to present an overview of

the challenges posed by MAC infection such as side effects, reinfections and

resistance mechanisms. The latest therapeutic options such as the optimized

combination therapy, drug repurposing and the development of new formulations,

as well as new anti-MAC compounds currently in (pre)clinical trials will also be

discussed.

DOI: 10.3390/ph18060891

PMID: 40573286

**57. Pharmaceuticals (Basel). 2025 May 26;18(6):797. doi: 10.3390/ph18060797.**

Design, Synthesis, and In Vitro Evaluation of

4-(Arylchalcogenyl)methyl)-1H-1,2,3-triazol-1-yl-menadione: Exploring Their

Potential Against Tuberculosis.

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**Background/Objectives:** In this study, a novel series of

4-(arylchalcogenyl)methyl)-1H-1,2,3-Triazol-1-yl-menadione derivatives were

synthesized to explore their potential as new antituberculosis (anti-TB) agents.

Selenium-containing compounds are known for their significant antimycobacterial

activity, which motivated their inclusion in the design. **Methods:** The target

compounds were synthesized via a copper(I)-catalyzed azide-alkyne cycloaddition

(CuAAC) reaction, affording yields ranging from 34% to 93%. All compounds were

evaluated in vitro for anti-TB activity against Mycobacterium tuberculosis H37Rv

(ATCC 27294), as well as a drug-resistant strain (T113/09). **Results:** Several

selenium-containing derivatives exhibited promising activity. Compounds 9b and

9g were equipotent to the first-line anti-TB drug, and one compound surpassed

its activity. Notably, compounds 9a, 9b, 9g, and 9h also showed efficacy against

the INH- and RIF-resistant Mtb strain T113/09. **Conclusions**: The efficacy of

selenium-containing triazole-menadione hybrids against both sensitive and

resistant Mtb strains highlight their potential as candidates for addressing

antimicrobial resistance in TB treatment. Further investigations are required to

understand their mechanisms of action and assess their in vivo therapeutic

potential..

DOI: 10.3390/ph18060797

PMID: 40573194

**58. Medicina (Kaunas). 2025 Jun 17;61(6):1096. doi: 10.3390/medicina61061096.**

Adenosine Deaminase and Systemic Immune Inflammatory Index-A Biomarker Duet

Signature of Pulmonary Tuberculosis Severity.

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**Background and Objectives:** The role of adenosine deaminase (ADA) in pulmonary

tuberculosis (PTB) remains insufficiently defined in advanced forms of disease.

Likewise, the systemic immune inflammatory index (SII) has not been validated in

severe PTB. This 6-year prospective observational study aims to evaluate

biomarker signatures of serum ADA and SII. **Materials and Methods**: According to

the PTB case definition, 232 adult patients were divided into group 1, with a

positive bacteriologic exam (n = 168), and group 2, without bacteriological

confirmation (n = 64). ADA serum levels were compared by age, gender,

nutritional status, morphologic and bacteriological pattern of PTB lesions,

survival status, along with serum levels of other inflammatory biomarkers. All

patients with comorbidities, interfering with the level of ADA, were excluded to

avoid bias. **Results:** A total cohort of 208 PTB adults, aged 54.37 ± 14.365

years, included 156 males. The overall mortality was 11.53%. Death occurred

after a mean interval of 1.63 ± 3.228 months after PTB diagnosis. ADA serum mean

levels were 32.94 ± 9.146 IU/L, significantly higher in G1 (p = 0.002), in

patients with delayed diagnosis of PTB (p = 0.000), with lung cavitation (p =

0.003), and death as a poor outcome (p ˂ 0.02). SII had a mean value of 1752.226

± 2704.150, significantly increased in bacteriologically confirmed PTB cases (p

= 0.018), delayed diagnosis (p = 0.002), cavitary advanced pulmonary

tuberculosis (APT) (p = 0.002), and deceased (p = 0.003). Both an ADA cut-off

elevated risk value of over 30 IU/L and SII of over 902 were fulfilled by 73

patients, with 2.10 higher risk of advanced PTB (p = 0.006) and 4.49 higher risk

of mortality (p = 0.000). **Conclusions**: Serum ADA and SII are recommended as

predictors of advanced and severe pulmonary TB. These findings indicate that ADA

and SII, when elevated together, delineate a high-risk PTB phenotype with

greater disease severity and early mortality. The combination offers a

pragmatic, biomarker-based approach to risk stratification in PTB.

DOI: 10.3390/medicina61061096

PMCID: PMC12194894

PMID: 40572784 [Indexed for MEDLINE]

**59. Medicina (Kaunas). 2025 Jun 9;61(6):1060. doi: 10.3390/medicina61061060.**

Resistance Rates of Mycobacterium tuberculosis Complex Strains: A Retrospective

Study in Türkiye.

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**Background and Objectives:** Tuberculosis (TB) is one of the most common

infectious diseases in developing countries. The resistance of the causative

agent, Mycobacterium tuberculosis, to two or more first-line anti-TB drugs

results in multidrug-resistant (MDR) TB, posing a serious challenge to the

control of TB worldwide. This study was designed to determine the changes in

drug resistance over time in TB strains isolated from patients in all

departments of Uludağ University Hospital in western Türkiye. Materials and

**Methods:** We retrospectively analyzed 104,598 clinical samples sent to our

laboratory for the investigation of the presence of TB between 1996 and 2023.

BACTEC 460 TB, BACTEC MGIT 960 culture systems and Löwenstein-Jensen medium were

used for the culture of these samples. The susceptibility of M. tuberculosis

complex strains grown in culture to isoniazid (INH) (0.1 μg/mL), rifampicin

(RIF) (1.0 μg/mL), ethambutol (ETB) (5.0 μg/mL) and streptomycin (SM) (1.0

μg/mL) antibiotics was studied according to the manufacturer's recommendation.

**Results:** Out of 104,598 patient samples, 2752 (2.6%) were culture-positive, and

the susceptibility test results of 1869 of these were analyzed. Of the isolates,

358 (19.2%) were found to be resistant to at least one first-line drug, i.e.,

INH, RIF, ETB, or SM. In addition, 2.9% were resistant to two or more first-line

drugs. **Conclusions**: Drug susceptibility testing is essential to ensure the

optimal treatment and control of drug-resistant TB strains. This study

highlights the value of ongoing efforts to control tuberculosis drug resistance

in the fight against this disease.

DOI: 10.3390/medicina61061060

PMCID: PMC12195593

PMID: 40572748 [Indexed for MEDLINE]

**60. Microorganisms. 2025 Jun 4;13(6):1306. doi: 10.3390/microorganisms13061306.**

Whole-Genome Sequence Analysis to Assess Mutations in Efflux Pumps in

Mycobacterium tuberculosis: The Influence in Drug Resistance.

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Efflux pumps are proteins related to the transport of molecules in bacteria, and

some of them have been recently reported to be involved in drug resistance (DR)

in Mycobacterium tuberculosis. In addition, the association with type 2 diabetes

mellitus (T2DM) has been considered a factor favoring the development of drug

resistance. Therefore, the aim of this study was to characterize, by analysis of

M. tuberculosis genomes, the variants in efflux pump genes and to determine the

level of association with T2DM and DR. Nearly 400 Mtb genomes from individuals

with and without T2DM and with and without DR were recovered. Of the 164 efflux

pump genes analyzed, 10 lack any variant, while 154 genes presented from 3 to 19

variants. The variant S217P in mmpL13a (Rv1145) was the most abundant, found in

98 (25%) isolates. A significant association was observed between 19 variants

and DR, and between 20 variants and T2DM (p ≤ 0.005). Although preliminary, the

results show a tendency for certain variants to appear in tuberculosis isolates

from individuals with DR and T2DM, demonstrating the possible influence of the

host in the evolution of tuberculosis. Further studies are necessary to confirm

the participation of these variants in the efflux pump function in tuberculosis.

DOI: 10.3390/microorganisms13061306

PMCID: PMC12195134

PMID: 40572193

**61. Microorganisms. 2025 May 30;13(6):1283. doi: 10.3390/microorganisms13061283.**

Central Nervous System Infections Caused by Bacillus Calmette-Guerin: Case

Report and Narrative Literature Review.

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Bacillus Calmette-Guerin (BCG) central nervous system (CNS) infections are one

of the rarest complications following BCG exposure. A 77-year-old male, with

bladder cancer previously treated with BCG instillation, presented with fever,

confusion, and brain magnetic resonance imaging (MRI) consistent with

encephalitis one month after the last BCG instillation. Cerebrospinal fluid

(CSF) showed marked hypoglycorrhachia, hyperproteinorrachia, and lymphocytic

pleocytosis. Despite CSF culture negativity, the presentation was considered

suggestive of BCG-related encephalitis, and the empirical standard

antitubercular treatment (rifampin, isoniazid and ethambutol), plus

dexamethasone, was initiated. Following initial improvement, gait ataxia and

hemiplegia were observed at the 4-month follow-up. MRI revealed an excluded

enlarged left lateral ventricle with signs of ventriculitis, requiring surgical

drainage. CSF collected during neurosurgery resulted positive on PCR for M.

tuberculosis complex. Adjunctive linezolid was initiated, replaced by

levofloxacin due to adverse events after 2 weeks. The patient was discharged

following a normal CSF analysis. Oral antitubercular therapy was prescribed for

14 months and there were no signs of relapse at the 24-month follow-up.

Previously, 16 cases of CNS BCGitis have been reported, without any cases of

clinical relapse during antitubercular treatment. Furthermore, our study reports

the use of linezolid as a 4th antitubercular drug for CNS BCGitis.

DOI: 10.3390/microorganisms13061283

PMCID: PMC12195324

PMID: 40572171

**62. Tuberculosis (Edinb). 2025 Jun 19;154:102665. doi: 10.1016/j.tube.2025.102665.**

**Online ahead of print.**

CRISPRi-mediated repression of efflux pumps reveals Rv1258c as a key contributor

to pyrazinamide resistance in Mycobacterium tuberculosis.

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DOI: 10.1016/j.tube.2025.102665

PMID: 40570617

**63. J Infect Dis. 2025 Jun 17:jiaf277. doi: 10.1093/infdis/jiaf277. Online ahead of print.**

Sex Differences in Vaccine-Induced Immunity and Protection Against Mycobacterium

tuberculosis.

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Tuberculosis (TB) remains a leading global cause of death, with approximately

1.3 million fatalities annually. While males are more susceptible to TB, the

underlying immune differences and their impact on vaccine efficacy are not fully

understood. In this study, we vaccinated male and female C57BL/6 mice with BCG

and 2 recombinant derivatives, VPM1002 and BCGΔBCG1419c, and assessed their

protection against Mycobacterium tuberculosis (Mtb) HN878. While all 3 vaccines

showed comparable efficacy in females, BCG did not protect males from

Mtb-induced death. Instead, recombinant vaccines provided improved protection in

males. Vaccination of males with BCGΔBCG1419c, but not BCG, enhanced CD8 T-cell

and B-cell recall responses in vaccine-draining lymph nodes, and reduced lung

inflammation after Mtb challenge. These findings underscore the impact of sex

differences on vaccine efficacy and suggest that future research should consider

sex as a biological variable to optimize TB vaccination strategies.

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**64. medRxiv [Preprint]. 2025 Apr 16:2025.04.15.25325605. doi:**

**10.1101/2025.04.15.25325605.**

Community variability in TB-related stigma in South Africa: an ecologic analysis

from the MISSED TB Outcomes Study.

Kipp AM, Olivier D, Skonje N, Majiza L, Free E, Preacher KJ, Daftary A,

Ngcelwane N, Medina-Marino A.

**BACKGROUND:** Tuberculosis (TB) stigma is a critical barrier to timely diagnosis

and treatment. Although stigma originates within communities, few studies have

quantified community-level TB stigma or its variability across geographic

contexts. This study describes methods for capturing community-level TB stigma

and examines stigma variability across 93 urban, peri-urban, and rural

communities in Buffalo City Metropolitan Health District, South Africa.

**METHODS:** As part of the MISSED TB Outcomes Study, heads of household (HoHs) were

surveyed in a geographically clustered random sample of households across

demarcated study communities. Validated scales were used to measure perceived

community-level TB stigma, HIV stigma, and TB/HIV knowledge. Demographic data,

including self-reported household TB and HIV history, were also captured.

Community-level data, including TB and HIV stigma, were generated by aggregating

individual responses within each study community. Associations between TB stigma

and other community-level variables were analyzed using robust linear

regression.

**RESULTS:** Surveys were completed by 3,869 households across 93 communities.

Median community TB stigma scores varied significantly by community location,

with rural communities reporting the lowest stigma and peri-urban communities

the highest. TB stigma was positively associated with HIV stigma across all

community types, with the strongest associations in urban and rural communities.

No associations were observed between TB stigma and TB prevalence, TB knowledge,

or household demographics after adjusting for community location.

**CONCLUSIONS:** TB stigma varied meaningfully across communities and was influenced

by urbanicity and HIV stigma. These findings suggest that stigma-reduction

interventions must be tailored to local contexts and consider community-level

determinants beyond individual knowledge or TB burden. The identified

variability in TB stigma will inform future multilevel analyses of the TB care

cascade in South Africa.

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PMCID: PMC12191136

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**65. iScience. 2025 May 27;28(6):112760. doi: 10.1016/j.isci.2025.112760. eCollection 2025 Jun 20.**

Inflammation and dyslipidaemia in combined diabetes and tuberculosis; a cohort

study.

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Diabetes mellitus (DM) increases tuberculosis (TB) susceptibility and worsens

outcomes. Since inflammation and lipid metabolism are implicated in both

diseases, we examined if combined TB and DM (TB-DM) increases inflammation or

dyslipidaemia. In plasma from individuals with DM (n = 96), TB (n = 93), and

TB-DM (n = 91), we measured 92 inflammatory proteins and 250 primarily

lipid-related metabolites, repeating measurements after two months of TB

treatment. Inflammation was primarily driven by TB, but higher in TB-DM. In

TB-DM, the proteins osteoprotegerin (OPG), signaling lymphocytic activation

molecule (SLAMF1), adenosine deaminase (ADA), interleukin-10 receptor subunit

beta (IL-10RB), and tumor necrosis factor receptor superfamily member 9 (TNFSR9)

were differentially abundant, and IL-17A/C predicted treatment failure. Disease

severity correlated with inflammation and dyslipidaemia. Inflammation decreased

with TB treatment, both in TB and TB-DM. Dyslipidaemia was primarily driven by

DM, but more pro-atherogenic in TB-DM, with elevated VLDL and apolipoprotein B

(ApoB). Despite TB treatment, pro-atherogenicity persisted. Stronger

inflammation and dyslipidaemia may account for worse disease outcomes in TB-DM

and warrant further action to prevent cardiovascular events.

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**66. Open Forum Infect Dis. 2025 Jun 4;12(6):ofaf303. doi: 10.1093/ofid/ofaf303.**

**eCollection 2025 Jun.**

Mental Health, Substance Use, and Tuberculosis Preventive Therapy in People With

HIV: A Prospective Cohort Study.

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Internal Medicine, Yale School of Medicine, New Haven, Connecticut, USA.

**BACKGROUND:** Because of the association of mental health and substance use

disorders with higher HIV mortality and decreased retention in care, we

investigated their frequency and impact on tuberculosis preventive therapy (TPT)

adherence and completion among people with HIV (PWHIV) initiating TPT.

**METHODS:** We conducted a prospective, longitudinal cohort study with a nested

mixed methods study in 2 Johannesburg, South Africa, facilities. Participants

were PWHIV on antiretroviral therapy initiating TPT between August and December

2023. We measured TPT adherence and completion with electronic medication boxes.

We used validated tools to measure symptoms of anxiety, depression, alcohol use,

and other substance use at enrollment and 12 weeks. We constructed multivariable

regression models to determine associations of these variables with TPT

adherence and completion, adjusting for age, sex, and time on antiretroviral

therapy. We interviewed participants about mental health and experiences with

TPT and analyzed responses using deductive content analysis.

**RESULTS:** Among 224 PWHIV, 111 (50%) completed TPT. Eighty-one (36%) screened

positive for depression symptoms and 63 (28%) for anxiety symptoms. Seventy-six

(34%) reported unhealthy alcohol use and 60 (27%) tobacco use. Using

multivariable models adjusting for confounders, only depression symptoms were

significantly and negatively associated with adherence (9% fewer doses; 95%

confidence interval, .4-16; P = .032) and completion (odds ratio, 0.48; 95%

confidence interval, .26-.90; P = .021). Participant narratives highlighted the

negative influence of mental health on adherence and the need for social and

psychological support services.

**CONCLUSIONS:** Symptoms of depression, anxiety, unhealthy alcohol use, and tobacco

use were common among PWHIV initiating TPT. Depression symptoms were strongly

and independently associated with TPT nonadherence and noncompletion.

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Infectious Diseases Society of America.

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**67. Pan Afr Med J. 2025 Feb 24;50:59. doi: 10.11604/pamj.2025.50.59.31398.**

**eCollection 2025.**

Barriers to GeneXpert utilization for tuberculosis detection at a regional

referral hospital in Malawi: a qualitative study.

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**INTRODUCTION:** GeneXpert is the recommended diagnostic test for HIV-associated

tuberculosis (TB). However, GeneXpert utilization is suboptimal in many

countries. We explored the utilization of GeneXpert in an urban, regional

referral hospital in northern Malawi using qualitative methods.

**METHODS:** in this cross-sectional qualitative study, a purposive sample of eight

key informants from the TB clinic and laboratory was selected from outpatient

and inpatient wards. An interview guide was used to conduct in-depth interviews

to explore barriers to GeneXpert utilization. Interview data were analyzed using

thematic analysis.

**RESULTS:** barriers to GeneXpert utilization appeared in three main themes:

healthcare providers, institutions and operational-related factors. Healthcare

provider factors included inadequate knowledge and training on differences in

eligibility criteria for testing and GeneXpert algorithms by clinicians and

laboratory technicians and poor interdepartmental communication. Institutional

factors included staff shortages, heavy workloads and financial constraints.

Operational factors included technical factors, e.g. power interruptions,

GeneXpert module failures and poor sample quality and the restrictiveness of the

algorithm.

**CONCLUSION:** the study identified multiple factors that lead to GeneXpert

underutilization. GeneXpert-specific training is required to address many of the

provider-related barriers to utilization. This study highlighted the importance

of assessing context-specific barriers to inform interventions to improve

GeneXpert utilization.

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PMID: 40567442 [Indexed for MEDLINE]

**68. Genes (Basel). 2025 Jun 18;16(6):716. doi: 10.3390/genes16060716.**

Bioinformatics-Driven Identification of Ferroptosis-Related Gene Signatures

Distinguishing Active and Latent Tuberculosis.

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**BACKGROUND:** Tuberculosis (TB) remains a major global public health challenge,

and diagnosing it can be difficult due to issues such as distinguishing active

TB from latent TB infection (LTBI), as well as the sample collection process,

which is often time-consuming and lacks sensitivity and specificity. Ferroptosis

is emerging as an important factor in TB pathogenesis; however, its underlying

molecular mechanisms are not fully understood. Thus, there is a critical need to

establish ferroptosis-related diagnostic biomarkers for tuberculosis (TB).

**METHODS:** This study aimed to identify and validate potential ferroptosis-related

genes in TB infection while enhancing clinical diagnostic accuracy through

bioinformatics-driven gene identification. The microarray expression profile

dataset GSE28623 from the Gene Expression Omnibus (GEO) database was used to

identify ferroptosis-related differentially expressed genes (FR-DEGs) associated

with TB. Subsequently, these genes were used for immune cell infiltration, Gene

Set Enrichment Analysis (GSEA), functional enrichment and correlation analyses.

Hub genes were identified using Weighted Gene Co-expression Network Analysis

(WGCNA) and validated in independent datasets GSE37250, GSE39940, GSE19437, and

GSE31348.

**RESULTS:** A total of 21 FR-DEGs were identified. Among them, four hub genes

(ACSL1, PARP9, TLR4, and ATG3) were identified as diagnostic biomarkers. These

biomarkers were enriched in immune-response related pathways and were validated.

Immune cell infiltration, GSEA, functional enrichment and correlation analyses

revealed that multiple immune cell types could be activated by FR-DEGs.

Throughout anti-TB therapy, the expression of the four hub gene signatures

significantly decreased in patients cured of TB.

**CONCLUSIONS:** In conclusion, ferroptosis plays a key role in TB pathogenesis.

These four hub gene signatures are linked with TB treatment effectiveness and

show promise as biomarkers for differentiating TB from LTBI.

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PMCID: PMC12192361

PMID: 40565608 [Indexed for MEDLINE]

**69. Genes (Basel). 2025 Jun 18;16(6):715. doi: 10.3390/genes16060715.**

Identification of Gene Expression Biomarkers Predictive of Latent Tuberculosis

Infection Using Machine Learning Approaches.

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Latent tuberculosis infection (LTBi) affects nearly a quarter of the global

population, yet current diagnostic methods are limited by low sensitivity and

specificity. This study applied an integrative bioinformatics framework,

incorporating machine learning techniques, to identify robust gene expression

biomarkers associated with LTBi. We analyzed four publicly available

transcriptomic datasets from peripheral blood mononuclear cells (PBMCs),

representing latent, active, and healthy states. Differentially expressed genes

(DEGs) were identified, followed by gene ontology (GO) enrichment, functional

clustering, and miRNA interaction analysis. Semantic similarity, unsupervised

clustering, and pathway enrichment were applied to refine the gene list. Key

biomarkers were prioritized using receiver operating characteristic (ROC) curve

analysis, with CCL2 and CXCL10 emerging as top candidates (AUC > 0.85). This

multi-step approach demonstrates the potential of combining transcriptomic

profiling with established machine learning and bioinformatics tools to uncover

candidate biomarkers for improved LTBi detection, and it also provides a

foundation for future experimental validation.

DOI: 10.3390/genes16060715

PMCID: PMC12192713

PMID: 40565607 [Indexed for MEDLINE]

**70. Bioengineering (Basel). 2025 Jun 9;12(6):630. doi:**

**10.3390/bioengineering12060630.**

Active and Inactive Tuberculosis Classification Using Convolutional Neural

Networks with MLP-Mixer.

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Early detection of tuberculosis plays a critical role in effective treatment

management. Like active tuberculosis, early identification of inactive forms

such as latent or healed tuberculosis is essential to prevent future

reactivation. In this study, we developed a deep-learning-based binary

classification model to distinguish between active and inactive tuberculosis

cases. Our model architecture incorporated an EfficientNet backbone with an

MLP-Mixer classification head and was fine-tuned on a dataset annotated by

Cheonan Soonchunhyang Hospital. To enhance predictive performance, we applied

transfer learning using weights pre-trained on the JFT-300M dataset via the

Noisy Student training method. Unlike conventional models, our approach achieved

competitive results, with an accuracy of 96.3%, a sensitivity of 95.9%, and a

specificity of 96.6% on the test set. These promising outcomes suggest that our

model could serve as a valuable asset to support clinical decision-making and

streamline early screening workflows for latent tuberculosis.

DOI: 10.3390/bioengineering12060630

PMCID: PMC12189041

PMID: 40564446

**71. Vet Sci. 2025 May 29;12(6):527. doi: 10.3390/vetsci12060527.**

Identification of Non-Tuberculous Mycobacteria in Iberian Lynx (Lynx pardinus)

and Their Impact on Its Health.

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The Iberian lynx (Lynx pardinus) population has been increasing in recent years

thanks to the collaboration of several associations within the framework of the

Life Lynxconnect project, which promotes captive breeding for the subsequent

release of specimens into the environment. It is therefore important to know

their population status, the diseases to which these animals are exposed, and

how they affect their repopulation. In this sense, this study aims to study how

the presence of mycobacteria affects the lynx population in Extremadura

(southwest of Spain). To this end, blood samples, tracheal swabs, and

tracheobronchial washings from live-captured lynxes, as well as mediastinal and

mesenteric lymph nodes from roadkill animals, were collected. The association

between the presence of mycobacteria and various factors-including body

condition, age, sex, and blood parameters-was subsequently evaluated. Up to

date, our findings show the absence of tuberculosis (TB) in all lynxes tested,

while they seem to be reservoirs of non-tuberculous mycobacteria (NTM), mainly

M. lentiflavum, the most isolated species. Nonetheless, these mycobacteria

appear to have no significant effect on the health condition of the animals.

DOI: 10.3390/vetsci12060527

PMCID: PMC12197730

PMID: 40559764

**72. Trop Med Infect Dis. 2025 May 24;10(6):149. doi: 10.3390/tropicalmed10060149.**

Assessing the 1918/19 Pandemic Influenza and Respiratory Tuberculosis

Interaction in Malta: Operationalizing a Syndemic During a Crisis Event.

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Studies have indicated that there was a disease interaction of pandemic

influenza with respiratory tuberculosis (TB) in Malta, which could explain the

heightened mortality recorded in young adults. We revisit the 1918/19 influenza

and TB syndemic potential on the island of Malta. Borrowing from crisis studies

that explore the harvesting effect, we used the method of assessing changes in

pre-pandemic, pandemic, fallow, and post-pandemic mortality/life expectancy to

reveal the syndemic experience. Pre-pandemic (1914-1917) life expectancy at

birth was significantly higher, at 37.91 years, than during the pandemic (1918),

when life expectancy dropped to 33.26 years (Z = 10.56, p < 0.0001).

Post-pandemic (1919) life expectancy rose to 43.49 years, which was an even

longer life expectancy than pre-pandemic (Z = 17.61, p < 0.0001). There were

significant changes in TB mortality death rates during the four periods in those

of reproductive age. Augmenting our framework for studies of syndemics involving

short-term events, we proposed the identification of contributing, driving, and

limiting factors. Underlying living conditions contributed to the syndemic. The

exacerbation of housing conditions, the economy associated with the First World

War, and meteorological measures-temperature, relative humidity, and

rainfall-were driving factors. The early implementation of mitigation

strategies, such as restrictions on mass gatherings, were limiting factors of

the syndemic.

DOI: 10.3390/tropicalmed10060149

PMCID: PMC12197708

PMID: 40559716

**73. Pathogens. 2025 Jun 19;14(6):602. doi: 10.3390/pathogens14060602.**

The Usefulness of the BD MAX MDR-TB Molecular Test in the Rapid Diagnosis of

Multidrug-Resistant Tuberculosis.

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Tuberculosis (TB), primarily caused by Mycobacterium tuberculosis complex

(MTBC), remains a global health challenge and can lead to severe pulmonary and

extrapulmonary complications. Multidrug-resistant TB (MDR-TB) poses additional

challenges, requiring advanced diagnostic and treatment strategies. This study

evaluates the BD MAX MDR-TB molecular test for a rapid diagnosis of MDR-TB,

detecting resistance to rifampicin (RIF) and isoniazid (INH). The BD MAX MDR-TB

test, utilizing real-time PCR, was used to analyze specimens collected from

TB-suspected patients, identifying MTB DNA and mutations associated with

rifampicin and isoniazid resistance. Results were compared with traditional drug

susceptibility testing, and 79 out of 638 samples tested were positive for MTB

DNA, with 65 showing a sufficient amount of genetic material for resistance gene

identification. The BD MAX test showed a 100% correlation with phenotypic

rifampicin resistance, though discrepancies were noted for isoniazid resistance,

with a 93% concordance. The BD MAX MDR-TB test is an effective tool for a rapid

diagnosis of MDR-TB, especially for rifampicin resistance. However, it may not

detect certain mutations related to isoniazid resistance. Complementary tests

like Xpert MTB/XDR or whole-genome sequencing could improve diagnostic accuracy

and support more effective TB control strategies.

DOI: 10.3390/pathogens14060602

PMCID: PMC12195635

PMID: 40559610 [Indexed for MEDLINE]

**74. Pathogens. 2025 Jun 16;14(6):592. doi: 10.3390/pathogens14060592.**

M72 Fusion Proteins in Nanocapsules Enhance BCG Efficacy Against Bovine

Tuberculosis in a Mouse Model.

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Mycobacterium bovis is the causative pathogen of bovine tuberculosis (bTB), a

disease that affects cattle and other mammals, including humans. Currently,

there is no efficient vaccine against bTB, underscoring the need for novel

immunization strategies. The M72 fusion protein, composed of three polypeptides

derived from Mycobacterium tuberculosis and M. bovis, has demonstrated

protective efficacy against M. tuberculosis in clinical trials when combined

with the AS01E adjuvant. Given the established efficacy of nanocapsule

formulations as vaccine delivery systems, this study evaluated a novel

immunization strategy combining BCG with either full-length M72 or a truncated

M72 fused to a streptococcal albumin-binding domain (ABDsM72). Both antigens

were encapsulated in chitosan/alginate nanocapsules and assessed in a murine M.

bovis challenge model. Priming with BCG followed by an M72 boost significantly

improved splenic protection compared to BCG alone, but it did not enhance

pulmonary protection. Notably, boosting with ABDsM72 further increased the

proportion of CD4+KLRG1-CXCR3+ T cells in the lungs of M. bovis-challenged mice,

a key correlate of protective immunity. These findings demonstrate that

chitosan/alginate-encapsulated antigens enhance BCG-induced immunity, supporting

their potential as next-generation vaccine candidates for bTB control.

DOI: 10.3390/pathogens14060592

PMCID: PMC12195942

PMID: 40559600 [Indexed for MEDLINE]

**75. Pathogens. 2025 Jun 4;14(6):559. doi: 10.3390/pathogens14060559.**

Tuberculosis and Impact of COVID-19 on Spread of Epidemics in Kazakhstan.

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This study examines the epidemiological situation of tuberculosis (TB) in the

regions of the Republic of Kazakhstan over the past seven years (2018-2024),

which cover the before-, during- and after-COVID-19 periods, with a focus on the

risks of its emergence and spread. The analysis revealed that while TB incidence

is declining, mortality remains high in the before- and during-COVID-19 periods,

indicating a general decline in population health. The concentration of TB

incidence in relation to geographic location was mainly in the northern, western

and southern regions. Before COVID-19, TB incidence reached 48.2 cases and

mortality reached a maximum of 2.4 cases per 100,000 people. In 2024, the

incidence and mortality of tuberculosis significantly decreased to 33.5 (30.5%)

and 1.0 (58.3%), respectively, reflecting an improvement in health indicators in

the post-pandemic period. In the after-COVID-19 period, in regions with high

unemployment, the incidence was higher than in the before- and during-COVID-19

periods. Nevertheless, it is important that the trend in tuberculosis incidence

shows positive improvement after the COVID-19 period. In addition, a comparative

analysis of tuberculosis incidence trends in different age groups and social

factor groups shows that the adult population remains the most vulnerable

category among the general population. The above-listed factors, as well as our

analysis of tuberculosis incidence, shows that TB incidence does not always

correlate with the level of vaccination in different regions of Kazakhstan,

indicating a multifactorial influence on the tuberculosis epidemic.

DOI: 10.3390/pathogens14060559

PMCID: PMC12195797

PMID: 40559567 [Indexed for MEDLINE]

**76. Pathogens. 2025 May 31;14(6):548. doi: 10.3390/pathogens14060548.**

Whole-Genome Sequence-Based Diversity of Mycobacterium tuberculosis Strains

Isolated from a Central Western Region of Mexico.

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Tuberculosis remains a significant health issue in Mexico, which has one of the

highest incidence rates in the Americas. This study aimed to analyze the

circulating sublineages, spoligotypes, drug resistance, and transmission

patterns of Mycobacterium tuberculosis in Mexico's Central Western region using

whole-genome sequencing. Seventy-seven Mycobacterium tuberculosis strains

underwent phenotypic drug susceptibility testing via MGIT. Genotypic resistance

was assessed with TB-Profiler and Mykrobe, while phylogenetic relationships were

reconstructed using Snippy and RaxML. SpoTyping identified circulating SITs and

families, with a 5-SNP threshold defining genomic transmission clusters. The

predominant sublineages were 4.1.1.3 (X-type, n = 19) and 4.1.2.1 (LAM, n = 11),

with rare sublineages (EAI5, EAI2-Manila, and Beijing) also observed. Resistance

to at least one first-line drug was found in 63.3% of strains, with streptomycin

mono-resistance (24.5%) being notable. Multidrug-resistant TB was identified in

16.3% (n = 8) of strains. Five genomic clusters, involving 18.7% of strains,

were identified. This study highlights the sublineage diversity in Mexico,

emphasizing its importance in global databases and resistance research. The

findings, such as SIT47 in GC1, underscore the value of localized genomic

studies for effective TB control.

DOI: 10.3390/pathogens14060548

PMCID: PMC12195799

PMID: 40559556 [Indexed for MEDLINE]

**77. Pathogens. 2025 May 22;14(6):517. doi: 10.3390/pathogens14060517.**

Evaluation of the Standard M10 MTB/NTM Molecular Test for the Rapid

Identification of Tuberculous and Nontuberculous Mycobacteria in Liquid

Cultures.

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Since 2013, the World Health Organization has recommended the use of rapid

molecular tests as the initial diagnostic step for Mycobacterium tuberculosis

(MTB) infection to enhance the control of tuberculosis. In recent years, the

prevalence of infections by non-tuberculous mycobacteria (NTM) in humans has

also risen, particularly in countries with low tuberculosis incidence, such as

Italy. Therefore, the rapid differentiation between NTM and Mycobacterium

tuberculosis complex is crucial for timely therapeutic decisions. This study

evaluates a new rapid molecular assay, Standard M10 MTB/NTM, designed to detect

MTB, NTM, or co-detection in Mycobacteria Growth Indicator Tube cultures from

different biological matrices. The assay was validated using 100 positive and 50

negative liquid mycobacteria cultures, already confirmed by specific real-time

PCR and Sanger sequencing. Following optimization of assay conditions for

culture sample processing and assessment of potential interference, Standard M10

demonstrated excellent sample stability, high specificity, and good sensitivity,

identifying all 50 MTB and 49 NTM samples. Some limitations included the

non-detection of M. celatum in one case and false positive results (MTB

co-infection) in two NTB cases. Nevertheless, overall, the adoption of this test

could be considered for laboratory management to enable rapid and effective

sample targeting for subsequent diagnostic evaluation and treatment

decision-making.

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PMCID: PMC12195744

PMID: 40559525 [Indexed for MEDLINE]

**78. Metabolites. 2025 May 28;15(6):355. doi: 10.3390/metabo15060355.**

Comparison of Pyrazinamide with Isoniazid for Their Effects on the Heme

Biosynthetic Pathway in Mouse Liver.

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**Background/Objectives:** Isoniazid (INH) and pyrazinamide (PZA) are first-line

drugs used to treat tuberculosis (TB), but their use is generally

contraindicated in patients with porphyria, a group of metabolic disorders

caused by defects in the heme biosynthetic pathway. To investigate the basis for

these contraindications, we compared the effects of INH and PZA on the heme

biosynthetic pathway in mouse liver. **Method:** We investigated the hepatic

expression and activity of the key enzymes involved in the heme biosynthetic

pathway, including aminolevulinic acid synthase 1 (Alas1) and ferrochelatase

(Fech). Additionally, we employed a metabolomic approach to analyze liver and

fecal samples from the mice treated with INH or PZA. **Result:** We found that INH,

but not PZA, significantly upregulated the expression and activity of Alas1, the

rate-limiting enzyme in heme biosynthesis, while concurrently downregulating

Fech, which converts protoporphyrin IX (PPIX) to heme. These changes resulted in

the accumulation of the toxic intermediate aminolevulinic acid (ALA) and PPIX in

the liver of INH-treated mice. In contrast, PZA had no measurable effect on the

expression or function of Alas1 or Fech. **Conclusions:** These findings provide

mechanistic insight into INH-induced porphyria exacerbation and suggest that PZA

may not carry the same risk, challenging its current contraindication.

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PMCID: PMC12195290

PMID: 40559379

**79. Diseases. 2025 May 30;13(6):173. doi: 10.3390/diseases13060173.**

Prevalence and Associated Factors of Latent Tuberculosis Infection Among

Healthcare Workers in a Mexican Tertiary Care Hospital.

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**BACKGROUND/OBJECTIVES:** Healthcare workers (HCWs) are globally recognized as a

high-risk group for tuberculosis (TB) infection. However, limited data exist on

the prevalence of latent TB infection (LTBI) and associated occupational risk

factors in the Mexican context. Identifying the burden of LTBI is essential for

effective prevention. This study aimed to estimate the prevalence of LTBI among

HCWs in a tertiary care hospital in Mexico and to explore associated risk

factors.

**METHODS:** An analytical cross-sectional study was conducted among 300 HCWs

(including physicians, nurses, and stretcher-bearers) at a tertiary-level

hospital in Mexico. Sociodemographic and occupational data were collected

through a structured questionnaire. LTBI screening was performed using the

tuberculin skin test (TST), with positive results confirmed via the

QuantiFERON-TB Gold assay. Associations between relevant variables and LTBI were

assessed using logistic regression models, adjusted for potential confounders.

**RESULTS:** The prevalence of LTBI was 16.7%. After adjusting for confounders, male

HCWs had significantly higher odds of LTBI compared to females (adjusted odds

ratio [aOR] = 2.02; 95% confidence interval [CI]: 1.06-3.80). Although elevated

odds of LTBI were also observed among physicians, stretcher-bearers, and those

with direct contact with TB patients, these associations were not statistically

significant.

**CONCLUSION:** LTBI represents a relevant occupational health issue among HCWs,

with nearly one in six workers affected. Early detection and prevention of TB in

healthcare settings are critical to protecting individual workers and public

health. These findings highlight the need to strengthen occupational TB

surveillance and prevention strategies in similar healthcare environments.

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**80. Diseases. 2025 May 27;13(6):171. doi: 10.3390/diseases13060171.**

Plasma Matrix Metalloproteinases Signature as Biomarkers for Pediatric

Tuberculosis Diagnosis: A Prospective Case-Control Study.

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Diagnosing tuberculosis (TB) in children presents significant challenges,

necessitating the identification of reliable biomarkers for accurate diagnosis.

In this study, we investigated plasma matrix metalloproteinases (MMPs) and

tissue inhibitors of metalloproteinases (TIMPs) as potential diagnostic markers.

A prospective case-control study involved 167 children classified into confirmed

TB, unconfirmed TB, and unlikely TB control groups. Plasma levels of MMPs (MMP

1, 2, 3, 7, 8, 9, 12, and 13) and TIMPs (TIMP 1, 2, 3, and 4) were measured

using multiplex assays. Elevated baseline levels of MMP-1, MMP-2, MMP-7, MMP-9,

TIMP-1, TIMP-2, TIMP-3, and TIMP-4 were observed in active TB cases compared to

unlikely TB controls. Receiver operating characteristics (ROC) analysis

identified MMP-1, MMP-2, MMP-9, and TIMP-1 as potential biomarkers with over 80%

sensitivity and specificity. A three-MMP signature (MMP-1, MMP-2, and MMP-9)

demonstrated 100% sensitivity and specificity. The findings suggest that a

baseline MMP signature could serve as an accurate biomarker for diagnosing

pediatric TB, enabling early intervention and effective management.

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PMID: 40558582

**81. Adv Respir Med. 2025 Jun 16;93(3):19. doi: 10.3390/arm93030019.**

Harnessing Natural Product Compounds to Target Dormancy Survival Regulator

(DosR) in Latent Tuberculosis Infection (LTBI): An In Silico Strategy Against

Dormancy.

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Dormancy occurs when Mycobacterium tuberculosis (Mtb) enters a non-replicating

and metabolically inactive state in response to hostile environment. During this

state, it is highly resistant to conventional antibiotics, which increase the

urgency to develop new potential drugs against dormant bacilli. In view of this,

the dormancy survival regulator (DosR) protein is thought to be an essential

component that plays a key role in bacterial adaptation to dormancy during

hypoxic conditions. Herein, the NP-lib database containing natural product

compounds was screened virtually against the binding site of the DosR protein

using the MTiopen screen web server. A series of computational analyses were

performed, including redocking, intermolecular interaction analysis, and MDS,

followed by binding free energy analysis. Through screening, 1000 natural

product compounds were obtained with docking energy ranging from -8.5 to -4.1

kcal/mol. The top four lead compounds were then selected for further

investigation. On comparative analysis of intermolecular interaction, dynamics

simulation and MM/GBSA calculation revealed that M3 docked with the DosR protein

(docking score = -8.1 kcal/mol, RMSD = ~7 Å and ΔG Bind = -53.51 kcal/mol)

exhibited stronger stability than reference compound Ursolic acid (docking score

= -6.2 kcal/mol, RMSD = ~13.5 Å and ΔG Bind = -44.51 kcal/mol). Hence, M3 is

recommended for further validation through in vitro and in vivo studies against

latent tuberculosis infection.

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**eCollection 2025 Mar.**

Tuberculosis Under Biotherapy in Patients with Spondyloarthritis: Data from the

Moroccan Biotherapy Registry (RBSMR) during 3 Years of Follow Up.

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**OBJECTIVE:** Biologics agents may lead to a significant risk of infection,

including tuberculosis, particularly in endemic countries. This study aims to

determine the incidence and characteristics of active tuberculosis in

spondyloarthritis patients undergoing biotherapies and estimate the rate of

reactivation of latent tuberculosis infection (LTBI).

**METHODS:** A prospective multicentre study was conducted based on 3-year data from

the Moroccan Register of Biotherapies (RBSMR). We determined the incidence rate

of tuberculosis during follow-up and performed a comparison with patients in

whom tuberculosis was not detected. Screening for LTBI prior to the initiation

of biotherapy was analysed, and the reactivation rate was determined at the

3-year follow-up.

**RESULTS:** 194 patients with SpA were included. 98.8% of the patients received

TNF-inhibitors, and 6.6% had a history of treated tuberculosis infection. After

3 years of follow-up, 10 cases of active tuberculosis were recorded with an

incidence of 17/1000 patient-years. All of these patients were on

TNF-inhibitors. diabetes was significantly higher in patients with active

tuberculosis (P=0.02), as was the prior use of at least two TNF-inhibitors

(P=0.03). Before initiating biotherapy, 22.6% of individuals were found to have

LTBI and received chemoprophylaxis. After a 3-year follow-up, only 2 (4.5%)

cases of active TB were noted in patients previously treated for LTBI whereas

the other 8 cases had negative screening.

**CONCLUSION:** This study suggests that patients undergoing biotherapy,

particularly TNF-inhibitors have a higher incidence of active tuberculosis

compared to the general population. Rheumatologists should be aware of both

reactivation LTBI and de novo tuberculosis.

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**83. Qatar Med J. 2025 Jun 9;2025(2):64. doi: 10.5339/qmj.2025.64. eCollection 2025.**

Endocrine manifestations of lung adenocarcinoma with epidermal growth factor

receptor mutation mimicking tuberculosis: A case report and literature review.

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**BACKGROUND:** Lung cancer is a leading cause of cancer-related mortality globally,

often presenting with diverse and challenging manifestations. This case report

discusses an unusual presentation of epidermal growth factor receptor

(EGFR)-mutated non-small-cell lung cancer (NSCLC) initially mimicking

tuberculosis (TB), complicated by pituitary involvement.

**CASE PRESENTATION:** A 30-year-old female presented with respiratory symptoms and

systemic complaints, initially suggestive of miliary TB. Further investigations

revealed metastatic lung adenocarcinoma with pituitary metastasis, causing

diabetes insipidus, hyperprolactinemia, adrenal insufficiency, and

hypothyroidism. Treatment with targeted therapy involving osimertinib resulted

in clinical improvement.

**CONCLUSION:** This case underscores the diagnostic challenges posed by atypical

presentations of lung cancer, which can masquerade as infectious diseases like

TB. The presence of pituitary metastasis further complicates the clinical

picture, emphasizing the importance of considering rare metastatic sites in the

differential diagnosis of lung adenocarcinoma. Timely recognition and

appropriate management are crucial for optimizing outcomes in such complex

cases, highlighting the need for a multidisciplinary approach in oncological and

endocrine care.

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**Online ahead of print.**

Chronic pulmonary histoplasmosis masquerading as tuberculoma: A case report and

literature review.

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**INTRODUCTION:** In endemic areas of Southeast Asia, particularly Indonesia,

histoplasmosis is one of the most common causes of fungal respiratory

infections. It can manifest in a variety of ways and has a wide range of

clinical symptoms.

**PRESENTATION OF CASE:** A 25-year-old woman who worked as a farmer and lived in a

cold, humid region presented with chronic pleuritic chest pain and was diagnosed

with pulmonary tuberculosis. She was treated with anti-tuberculosis drugs for

2 months, but there was no clinical or radiological improvement. Chest x-ray

revealed tuberculoma. Based on a multidisciplinary team discussion, surgery was

considered. Histopathological examination revealed histoplasmic fungal spores.

We determined that the patient had chronic pulmonary histoplasmosis, a

clinically suggestive form of lung nodule, based on the multidisciplinary

discussion. After receiving antifungal therapy, there was a noticeable

improvement in both clinical and radiological outcomes.

**DISCUSSION:** The fungus Histoplasma capsulatum is the principal cause of chronic

pulmonary histoplasmosis (CPH), a lung illness. On computed tomography (CT)

imaging, histoplasmosis pulmonary nodules frequently show up with features

similar to those of tuberculoma. When host variables (immunocompromising

diseases), relevant clinical symptoms, and mycological evidence are present, a

probable diagnosis of histoplasmosis can still be made, even though a conclusive

diagnosis requires culture or histopathologic confirmation.

**CONCLUSION:** Due to the low sensitivity of culture, several tests might be

necessary to confirm the diagnosis of chronic pulmonary histoplasmosis. Since

histoplasmosis symptoms frequently resemble those of pulmonary infections like

tuberculosis.

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Primary isolated laryngeal tuberculosis: A rare extrapulmonary manifestation.

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Laryngeal tuberculosis (TB) is a rare form of extrapulmonary tuberculosis and

its isolated presentation without concurrent pulmonary involvement is even rare

[1, 2] This poses significant diagnostic challenges as it can present with

nonspecific symptoms such as hoarseness, throat pain or dysphagia. In this

report, we highlight the case of a 42-year-old female who presented with a

history of a change in voice, which was eventually diagnosed as isolated primary

laryngeal tuberculosis post investigations.

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Disseminated Lupus Vulgaris Revealing Multifocal Tuberculosis in a Patient with

HIV: A Case Report.

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Lupus vulgaris is the most common type of cutaneous tuberculosis, known for its

diverse clinical presentations, particularly in association with human

immunodeficiency virus (HIV) infection. We report a case of disseminated lupus

vulgaris with plaques and ulcerative morphology. Despite negative smear and

culture results, histopathological examination revealed granulomatous reactions.

Further evaluation, including lymph node biopsy and cartridge-based nucleic acid

amplification test (CBNAAT), confirmed multifocal tuberculosis.

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Human Gut Bacteriophageome: Insights Into Drug Resistance Mechanisms in

Tuberculosis.

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Tuberculosis (TB), caused by Mycobacterium tuberculosis, remains a major global

health burden. The emergence of drug-resistant strains presents a critical

challenge in TB management. The recent research has explored the interaction

between TB and the human gut bacteriophage community (phageome). The gut

phageome plays a crucial role in regulating microbial diversity and

functionality, and its composition and function have been linked to various

health conditions. Examining the gut phageome through metagenomic analysis

provides insights into its composition, role in health, and interactions with

the host immune system. Exploring the interaction between the gut phageome and

M. tuberculosis may reveal how phages affect the bacterium's pathogenicity,

survival, and mechanisms of drug resistance. Understanding the gut phageome's

impact on TB drug resistance could inform novel therapeutic strategies, such as

phage therapy, and highlight the importance of microbiome-based interventions in

combating drug-resistant TB strains. This review explores the role of the gut

phageome in influencing drug resistance in TB, focusing on interaction

mechanisms and potential therapeutic implications, synthesizing current research

findings, and identifying knowledge gaps in this emerging field. This review

also synthesizes the current evidence on the gut phageome's role in TB drug

resistance, focusing on phage-mediated horizontal gene transfer (e.g., rpoB,

katG), immune modulation, and preclinical efficacy of mycobacteriophage

therapies. Key findings highlight phage cocktails (e.g., DS6A, D29 LysB) as

promising adjuncts to antibiotics, reducing M. tuberculosis burden in murine

models. These insights advocate for phage therapy as a complementary strategy

against drug-resistant TB, urging clinical validation to bridge the existing

knowledge gaps.

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Subacute Mastoiditis Without Verified Nontuberculous Mycobacteria-Still a

Clinical Challenge.

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University Hospital Stockholm Sweden.

(3)Department of Neuroradiology Karolinska University Hospital Stockholm Sweden.

**OBJECTIVE:** An indolent form of mastoiditis has gained increased attention

lately, challenging clinicians both regarding diagnosis as well as treatment.

The etiology behind this assumed infection herein named subacute mastoiditis

(SAM) is unknown; however, a link to nontuberculous mycobacteria (NTM)

infections has been seen. A survey on pediatric cases with SAM over 20 years was

performed to investigate the typical clinical features and to identify optimal

treatment strategies for this condition, causing aggressive temporal bone

destructions along with intratemporal and intracranial complications.

**METHODS:** A retrospective survey of pediatric patients (0-17 years) hospitalized

with SAM during 2003-2023 at Karolinska University Hospital, Sweden, was

conducted. Data collection included demographics, diagnostics (radiology,

microbiology, histopathology), treatment, and clinical outcome.

**RESULTS:** Sixteen cases (median age 7.5 years) with SAM were included.

Longstanding otorrhea from ventilation tubes preceded clinical signs of

mastoiditis in most cases. CT scan generally revealed cortical temporal bone

destructions close to the ear canal and sigmoid sinus. Histopathological

examination displayed a high incidence of granulomatous inflammation. Upon

microbiological testing, six cases revealed NTM infection. All cases underwent

mastoidectomy, and 11 cases received long-term mycobacteria-targeted

antibiotics. No deaths occurred, but seven cases had a delayed recovery or

relapsing disease, and several cases experienced complications. The long-term

outcomes were good. Two cases with Mycobacterium tuberculosis mastoiditis were

identified, entailing diagnostic challenges.

**CONCLUSION**: Histopathological and microbiological sampling along with CT scan is

crucial in diagnosing SAM. We suggest surgical intervention combined with

empirical long-term antimycobacterial treatment for optimal recovery and outcome

in SAM.

LEVEL OF EVIDENCE: 4.

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**10.1016/j.cmi.2025.06.017. Online ahead of print.**

Risk of tuberculosis disease among patients with inflammatory bowel disease and

inflammatory rheumatic disease treated with biologics in Denmark: a nationwide

cohort study.

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Colic A(7), Petersen I(2), Johansen IS(2).

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(7)Department of Rheumatology, Zealand University Hospital, Køge, Denmark.

**OBJECTIVES:** This nationwide retrospective cohort study estimates TB disease risk

in adults and children with inflammatory bowel disease (IBD) and inflammatory

rheumatic disease (IRD) treated with immunosuppressive biologics in Denmark,

including temporal trends and risk stratification by TB infection status and

country of birth.

**METHODS:** Patients diagnosed with IBD or IRD between 1994 and 2018 were

identified using the Danish National Patient Registry. Treatments with biologics

and diagnoses of TB disease were determined through ICD-10 codes and

microbiological records. Patient demographics, interferon-gamma release assay

(IGRA) results, and drug use data were collected from national databases.

Poisson regression was used to calculate TB incidence rates (IR) and assess

associations with biologic treatment, IGRA-status, country of birth, age, and

sex.

**RESULTS:** During 553,551 person-years of follow-up (PYFU), 117 patients with TB

disease were identified, with 71 cases occurring in biologic-naïve patients and

46 in biologic treated individuals. The crude IR was 39.3/100,000 PY (95% CI

29.4-52.4) for biologic treated individuals, compared to 12.4/100,000 PY (95% CI

9.2-16.8) for naive patients, yielding an incidence rate ratio (IRR) of 3.2

(95%CI 2.0-4.9). The TB risk was higher in IGRA-positive patients (vs. negative,

IRR 45.0, 95% CI 12.0-168.2) and those born in intermediate (vs. low incidence

country, IRR 7.9, 95% CI 3.3-18.9) or high TB-incidence countries (vs. low

incidence country, IRR 7.5, 95% CI 2.9-19.1).

**CONCLUSION:** The elevated risk of TB disease in patients with IRD and IBD treated

with biologics is strongly associated with IGRA positivity and country of birth.

These findings highlight the importance of comprehensive baseline TB risk

assessment, patient education in combination with personalized follow-up to

guide preventive strategies in this population.

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Diseases. Published by Elsevier Ltd. All rights reserved.

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**10.1016/S2213-2600(25)00168-7. Online ahead of print.**

Tuberculosis in Indonesia: challenges and future directions.

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DOI: 10.1016/S2213-2600(25)00168-7

PMID: 40550239

**91. J Vis Exp. 2025 Jun 6;(220). doi: 10.3791/68147.**

Matrix-based DNA Extraction for Targeted Next-Generation Sequencing on

Decontaminated Sputum Samples.

Williams J(#)(1), Steyn J(#)(2), Conceição EC(#)(3), Wells FB(4), Grobbelaar

M(4), Ismail N(4), Ghebrekristos Y(5), Opperman CJ(6), Singh S(5), Limberis

J(7), Naufal F(7), Mann BC(4), Colman RE(8), Rodwell T(#)(8), Warren RM(#)(4),

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(#)Contributed equally

Next-generation sequencing (NGS) is now recognized as a powerful tool for timely

and accurate drug-resistant tuberculosis (DR-TB) diagnosis. Targeted NGS (tNGS)

offers a streamlined approach by focusing on specific genes associated with drug

resistance, bypassing the need for traditional culture-based methods with

turnaround times ranging from weeks to months. The World Health Organization

(WHO) has recommended tNGS as a valuable strategy for improving tuberculosis

(TB) diagnosis to guide treatment and improve treatment outcomes, particularly

in resource-limited settings. Among the WHO-recommended tNGS assays, we have

selected a method that provides rapid and comprehensive drug susceptibility

testing, lineage determination, and strain typing. While standardized DNA

extraction methods are available, they can be time-consuming and

labor-intensive. To address this challenge, we optimized a simplified,

matrix-based DNA extraction protocol in combination with magnetic bead

purification. This method offers a rapid and efficient approach for extracting

DNA directly from decontaminated sputum sediments, enabling rapid downstream

tNGS analysis. By streamlining the DNA extraction process from sputum sediment,

this protocol could facilitate wider adoption of tNGS in routine clinical

settings, ultimately contributing to improved patient outcomes and lending to

global TB control efforts.

DOI: 10.3791/68147

PMID: 40549675 [Indexed for MEDLINE]

**92. Monaldi Arch Chest Dis. 2025 Jun 19. doi: 10.4081/monaldi.2025.3434. Online**

**ahead of print.**

Impact of patient counseling on medication adherence and drug resistance

patterns in tuberculosis patients.

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Mahavidyalaya, Shahapur, Belagavi, Karnataka.

Tuberculosis (TB) remains a primary global health concern, with non-adherence to

anti-TB therapy contributing to prolonged infectiousness, treatment failure, and

unfavorable outcomes. Despite established treatment protocols, adherence remains

suboptimal due to patient-related, healthcare system, and socioeconomic

barriers. This study aimed to identify key factors contributing to non-adherence

and to evaluate the impact of structured patient counselling on treatment

adherence. A cross-sectional observational study was conducted at Vivekananda

General Hospital, Hubballi, India, involving 80 hospitalized TB patients. Data

collection included demographic details and medication adherence scores,

measured before and one month after counseling using the Medication Adherence

Report Scale. Statistical analysis was performed using SPSS version 27.0, with

Pearson's correlation applied to assess changes in adherence. The mean adherence

scores significantly increased from 4.24±1.452 to 7.05±1.525 following

counseling (p=0.006). The most commonly reported barriers to adherence included

forgetfulness (62.5%), limited access to healthcare (50%), and poor

communication with healthcare providers (47.75%). These findings highlight the

effectiveness of structured counseling in improving adherence among TB patients.

Addressing both individual and systemic barriers through targeted counseling

interventions should be considered an integral component of TB care strategies.

DOI: 10.4081/monaldi.2025.3434

PMID: 40548472

**93. Monaldi Arch Chest Dis. 2025 Jun 19. doi: 10.4081/monaldi.2025.3545. Online**

**ahead of print.**

Interleukin-18 cytokine gene polymorphism 137G/C (rs187238) and susceptibility

to tuberculosis in north India.

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Tuberculosis (TB) regained its position globally as the leading cause of

mortality from a single infectious agent after being surpassed by COVID-19 for 3

years consecutively. Host genetic factors, particularly cytokine gene

polymorphisms, play a significant role in influencing susceptibility to TB.

Interleukin-18 (IL-18) is a proinflammatory cytokine involved in immune

regulation against Mycobacterium tuberculosis. This study aimed to evaluate the

association of IL-18 gene polymorphism (rs187238) with susceptibility to TB and

its effect on serum IL-18 levels in a north Indian population. A case-control

study was conducted with 100 newly diagnosed TB patients (pulmonary and

extrapulmonary) and 100 age- and gender-matched healthy controls. Serum IL-18

levels were measured using sandwich enzyme-linked immunosorbent assay, and the

IL-18 gene polymorphism at rs187238 was analyzed by polymerase chain

reaction-restriction fragment length polymorphism. The association between IL-18

polymorphism, TB susceptibility, and serum IL-18 levels was statistically

evaluated. Mean serum IL-18 levels were significantly elevated in TB patients

(400.42±149.58 pg/mL) compared to controls (96.05±40.67 pg/mL; p<0.01). The

distribution of IL-18 genotypes showed that individuals with GC/CC genotypes had

a significantly lower risk of developing TB compared to the GG genotype [odds

ratio (OR)=0.31; 95% confidence interval (CI)=0.20-0.88; p=0.0167].

Additionally, the C allele conferred a protective effect against TB (OR=0.33;

95% CI=0.22-0.51; p<0.0001). Serum IL-18 concentrations varied significantly

with genotype, with the highest levels observed in CC genotype carriers in both

cases and controls (p<0.01). Thus, our study suggests that IL-18 polymorphism at

rs187238 significantly influences susceptibility to TB in the north Indian

population. The C allele and GC/CC genotypes appear to confer a protective

effect, possibly through modulation of IL-18 serum levels. IL-18 rs187238

polymorphism may serve as an independent predictive marker for TB risk, though

larger studies are recommended for validation.

DOI: 10.4081/monaldi.2025.3545

PMID: 40548455

**94. Cureus. 2025 Jun 17;17(6):e86248. doi: 10.7759/cureus.86248. eCollection 2025**

**Jun.**

Characterizing Musculoskeletal and Neurological Toxicities Associated With the

BPaLM Regimen: A Clinical Evaluation of Arthralgia and Peripheral Neuropathy in

Patients With Multidrug-Resistant Tuberculosis (MDR-TB).

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**BACKGROUND:** Musculoskeletal and neurological toxicities are common side effects

of the BPaLM (bedaquiline, pretomanid, linezolid, and moxifloxacin) regimen, an

emerging treatment for multidrug-resistant tuberculosis (MDR-TB). These

toxicities, particularly arthralgia and peripheral neuropathy, can significantly

impair the quality of life of patients undergoing treatment. Despite the

promising therapeutic benefits of the BPaLM regimen, the prevalence and severity

of these side effects remain underexplored. Understanding these toxicities is

crucial to improving patient management strategies and ensuring better treatment

adherence.

**OBJECTIVE:** This study aims to determine how common and severe musculoskeletal

and neurological toxicities, particularly arthralgia and peripheral neuropathy,

are among MDR-TB patients treated with the BPaLM regimen.

**MATERIALS AND METHODS:** This prospective observational study was conducted at the

Programmatic Management of Drug-Resistant Tuberculosis in Mardan Medical Complex

between January 2024 and April 2025. Patients with MDR-TB undergoing treatment

with the BPaLM regimen were monitored for musculoskeletal and neurological

toxicities, specifically arthralgia and peripheral neuropathy. Clinical

evaluations included assessing the onset, severity, and impact of joint pain and

nerve damage, as well as evaluating the effectiveness of pain management and

physical therapy interventions. Data collection included demographic

information, comorbidities, and baseline physical activity levels. Statistical

analysis was performed using SPSS Statistics version 26 (IBM Corp. Released

2019. IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp.),

Python (Python Software Foundation, Beaverton, OR, USA), and R 4.4.5 (R

Foundation for Statistical Computing, Vienna, Austria) to identify significant

predictors of toxicity severity through descriptive statistics, chi-square

tests, and decision tree modeling. Kaplan-Meier survival analysis was also

conducted to assess the relationship between toxicity severity and treatment

outcomes.

**RESULTS:** Among the 44 MDR-TB patients, 35 (79.54%) experienced mild to moderate

arthralgia, with knee pain being most common (34, 77.27%). Peripheral neuropathy

was reported in 26 (59.09%) patients, with the lower limbs (20, 45.45%) being

most affected. Kaplan-Meier survival analysis revealed a significant difference

in survival times based on the severity of arthralgia and peripheral neuropathy,

with more severe symptoms correlating with reduced survival duration.

**CONCLUSIONS:** The findings underscore the importance of early identification,

regular monitoring, and personalized management strategies to mitigate the

burden of these toxicities and enhance patient outcomes.

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PMID: 40548154

**95. J Family Med Prim Care. 2025 May;14(5):2058-2061. doi:**

**10.4103/jfmpc.jfmpc\_1333\_24. Epub 2025 May 31.**

Orofacial tuberculosis mimicry of odontogenic abscess: A diagnostic dilemma!

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Orofacial tuberculosis is a rare extrapulmonary form of tuberculosis without

pathognomic signs and symptoms. Due to its unusual clinical presentation,

orofacial tuberculosis (TB) is more often misdiagnosed as other orofacial

pathologies and presents a diagnostic challenge in dentistry. One such case is

described in the present case report, where a paediatric patient presented with

extraoral submandibular swelling that mimicked an odontogenic infection

associated with a mandibular primary molar. The treatment plan was formulated

considering the condition as an odontogenic infection, and an incision and

drainage of the lesion was performed. However, the lesion showed no signs of

healing even after medication and surgical management. Eventually, an incisional

biopsy was performed, and the results suggested of Tuberculosis. Later, magnetic

resonance imaging (MRI) of the neck revealed Tubercular Lymphadenitis of the

left submandibular lymph node. As Paediatric Dentist, we should have a broad

vision while treating such patients, as many times dentists are the primary

health care providers to diagnose tuberculosis in a dental clinic setup through

proper history and examination. Tuberculosis, being an endemic problem in a

country like India, needs early diagnosis and management to prevent its spread

and reduce the health-related burden in the community.

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**96. J Family Med Prim Care. 2025 May;14(5):1716-1721. doi:**

**10.4103/jfmpc.jfmpc\_1352\_24. Epub 2025 May 31.**

Clinical and radiological profile of tuberculosis and treatment outcome in

patients ≤18 years: A prospective study.

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Bhubaneswar, Odisha, India.

**BACKGROUND:** Tuberculosis is an important cause of morbidity and mortality in

children, especially in endemic countries. The diagnosis of tuberculosis in

these patients is challenging due to various reasons. The outcome of treatment

in these patients is also varied.

**AIMS AND OBJECTIVES:** Our study aims to determine the various types of

presentations of tuberculosis; describe the clinical, radiological and

microbiological characteristics and also study the outcome of treatment in

patients ≤ 18 years of age.

**MATERIALS AND METHODS:** It was a prospective study. We included all newly

diagnosed consecutive cases of pulmonary or extra pulmonary TB in patients (up

to 18 years of age). After a detailed history and complete physical examination,

AFB smear and CBNAAT of samples and radiology were performed. Follow-up of all

cases was done at the end of intensive phase (IP) and at the end of treatment or

at any time as needed. All statistical analyses were performed using SPSS

version 19.0.

**RESULTS:** A total of 105 cases were included in our study. Most cases belonged to

the age group of 7-14 yrs. Pulmonary tuberculosis (PTB) was diagnosed in 37

cases (35.2%), followed by TB lymphadenitis (31.4%). Microbiological

confirmation could be obtained only in 53 cases (50.47%). Joint pain and a

derangement in liver function test were the most common adverse effects (4

cases) and 1 case developed optic atrophy.

**CONCLUSION:** A combination of history, signs and symptoms, and radiology may help

reach a diagnosis in children. The risk of serious adverse events in children

associated with the use of the recommended treatment regimens is also very low.

Children and their family members should be educated about TB and the importance

of completing treatment.

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**97. J Family Med Prim Care. 2025 May;14(5):2087-2088. doi:**

**10.4103/jfmpc.jfmpc\_1363\_24. Epub 2025 May 31.**

Does malnutrition play an essential role in developing drug-resistant

tuberculosis, and how can it be prevented?

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DOI: 10.4103/jfmpc.jfmpc\_1363\_24

PMCID: PMC12178514

PMID: 40547740

**98. IJID Reg. 2025 May 8;15:100665. doi: 10.1016/j.ijregi.2025.100665. eCollection 2025 Jun.**

Anti-tuberculosis drug-induced hepatotoxicity and associated risk factors among

patients with pulmonary tuberculosis at a tertiary care hospital in Thailand.

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**OBJECTIVES:** First-line anti-tuberculosis (TB) medications are effective for

drug-susceptible TB but are commonly associated with hepatotoxicity, which can

compromise treatment adherence and contribute to drug resistance. This study

aimed to determine the frequency of anti-TB drug-induced hepatotoxicity and

identify associated risk factors among patients at Chiang Mai University

Hospital.

**METHODS:** A retrospective cross-sectional study was conducted among patients with

drug-susceptible pulmonary TB receiving standard treatment. Liver function tests

were monitored biweekly during the first 2 months to detect hepatotoxicity. The

risk factors evaluated included body mass index (BMI), age, alcohol use,

N-acetyltransferase 2 (NAT2) acetylator status, and concomitant statin use.

Adverse drug reactions were assessed by physicians using severity grading.

Binary logistic regression and multivariate analysis were performed to identify

independent predictors of hepatotoxicity. Adjusted odds ratios (ORs), 95%

confidence intervals (CIs), and P-values were reported.

**RESULTS:** The incidence of hepatotoxicity was 41.97%. The multivariate analysis

showed significant associations between hepatotoxicity and the following: age

>70 years (OR = 41.72, P = 0.001), underweight BMI (OR = 56.48, P = 0.001),

current alcohol use (OR = 10.95, P = 0.001), and slow NAT2 acetylator status (OR

= 78.18, P = 0.001).

**CONCLUSIONS:** Hepatotoxicity is a common complication of TB treatment. Older age,

low BMI, alcohol use, slow NAT2 genotype, and statin co-administration

significantly increase risk. Targeted monitoring and consideration of NAT2

genotyping in high-risk patients may help prevent treatment interruptions and

improve clinical outcomes.

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PMID: 40547509

**99. Front Public Health. 2025 Jun 6;13:1529687. doi: 10.3389/fpubh.2025.1529687.**

**eCollection 2025.**

A mixed-method study to inform the design of a video observed therapy app to

monitor individuals with TB in the Dominican Republic.

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**Publisher: INTRODUCTION:** Video Observed-Therapy, a digital adherence

technologies (DAT), could improve patients’ adherence to tuberculosis (TB)

treatment. However, countries with high TB burden countries, such as the

Dominican Republic, struggle to adopt DAT as a control and prevention tool to

improve clinical outcomes. Objectives: To describe patients’ knowledge,

attitudes and behaviors towards digital technologies for TB control and

prevention in the Dominican Republic.

**METHODS:** A mixed-method study was implemented by organizing two Focus Group

Discussions (FGDs) and a survey with 137 TB patients. Qualitative data were

coded using the Integrated Behavior Model (IBM) and descriptive statistics were

used to analyze knowledge, attitudes, practices, and preferences. Data

integration was achieved by comparing convergent and divergent results.

**RESULTS:** Participants expressed a positive attitude towards using DAT to

facilitate communication with health personnel to support treatment adherence.

Participants noted the benefit of having an application that facilitates this

process while safeguarding data privacy.

**CONCLUSION:** This study demonstrates positive attitudes among individuals with TB

toward adopting digital tools in their follow-up. Current practices suggest that

intent to use DAT is prevalent, emphasizing the need to fully transition from

intention to adoption of DAT to improve TB treatment outcomes.

DOI: 10.3389/fpubh.2025.1529687

PMCID: PMC12179108

PMID: 40547466 [Indexed for MEDLINE]

**100. Colomb Med (Cali). 2025 Mar 30;56(1):e6005918. doi: 10.25100/cm.v56i1.5918.**

**eCollection 2025 Jan-Mar.**

Clinical practice guideline for the evaluation, treatment, and follow-up of

children in contact with patients with pulmonary tuberculosis in Colombia.

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**INTRODUCTION:** The available clinical practice guidelines on tuberculosis

infection are not exclusive to the pediatric population.

OBJECTIVE: To formulate evidence-based recommendations for the evaluation,

treatment, and follow-up of children in contact with patients with pulmonary

tuberculosis in Colombia.

**METHODS:** A multidisciplinary development panel (composed by clinical and field

experts, researchers, and methodologists who declared conflicts of interests),

including patient representatives, and decision-makers formulated 10 questions

and prioritized outcomes related to diagnosis (clinical evaluation, chest X-ray,

and interferon-gamma release assays-IGRA), treatment (efficacy of regimens in

different clinical scenarios), and follow-up (monitoring and strategies to

increase adherence) for children exposed to tuberculosis. We conducted

systematic literature reviews to identify guidelines, systematic reviews, and

primary studies. We assessed these sources' quality and risk of bias with

specific tools. We synthesized the evidence narratively and, in some cases,

performed de novo meta-analyses (diagnostic and network meta-analyses). We

evaluated the certainty of evidence using the GRADE system. We used the GRADE

evidence-to-recommendation framework to formulate the recommendations.

**RESULTS:** We recommend 1) the use of IGRA tests to identify tuberculosis

infection and chest X-rays to screen for active tuberculosis in children exposed

to tuberculosis, 2) short instead of extended regimens for children with and

without immunosuppression, 3) levofloxacin or susceptibility-guided regimens in

cases of contact with drug-resistant tuberculosis, 4) monthly clinical follow-up

during the treatment, 5) the implementation of comprehensive approaches to

identify barriers to encourage treatment adherence.

**CONCLUSIONS:** The guideline panel provides context-specific, evidence-based

recommendations for assessing and treating children exposed to tuberculosis in

Colombia.

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**eCollection 2025.**

Performance of eight serum cytokine/chemokine biomarkers in discriminating

between active and latent tuberculosis infection in Ghana.

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**INTRODUCTION:** The existing Interferon γ release assay (IGRA) tests for TB

infection, lacks utility in discriminating between active TB (ATB) and latent TB

infection (LTBI). This study evaluated the potential of eight serum

cytokines/chemokines in differentiating LTBI from ATB and as a surrogate marker

for TB treatment response.

**METHODS:** We quantified and compared the serum levels of pro-inflammatory

cytokines (TNF-α, IFN-γ, IL-12p70, IL-17A, Granzyme B) and anti-inflammatory

cytokines (IL-10, IL-6, IL-4) among LTBI, ATB, and healthy controls using the

Human Magnetic Luminex™ 200 system. Serum cytokine/chemokine levels were also

assessed at four timepoints before and during TB treatment.

**RESULTS:** Among ATB cases, there were twice as many males (69%) as females (30%),

with infectivity spanning a wide age range. IFN-γ, IL-6, IL-10, IL-4, and IL-17A

levels were higher in LTBI compared to ATB. IL-12p70 was found to be a good

discriminant between ATB and LTBI (21-fold increase in ATB compared to LTBI, p <

0.05) but it did not have a good predictive potential for treatment (follow up).

The predictive potential of TNF-α, IL-6, IL-10, IFN-γ, IL-4, IL-17A, Granzyme B and IL-12p70 to differentiate between ATB and LTBI using AUROC was 57%, 98 %,

91%, 100%, 100%, 97%, 66% and 100% respectively.

**DISCUSSION:** These findings confirm reports from other studies in different

settings that LTBI and ATB express differential cytokine profiles that can be

exploited as diagnostic biomarkers. Of note, the quantitative estimation of

IL-12p70 may serve as a valuable marker for monitoring disease progression and

treatment success in tuberculosis.

Copyright © 2025 Mensah, Amponsah, Alahaman, Anim-Baidoo, Tetteh, Addo and

Koram.

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The concentration of tuberculosis within Paraguay's Indigenous population,

2018-2022: a retrospective population-based study.

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**BACKGROUND:** While over the past decade global incidence rates of tuberculosis

(TB) have decreased, in Paraguay incidence has risen. A new reporting system

implemented in 2018 has not previously been used to characterise trends in TB

and identify areas to prioritise for the expansion of access to TB diagnostics

and treatment programmes.

**METHODS:** We conducted a retrospective study of all TB cases notified to the

Paraguay National Program for Tuberculosis Control (NPTC) from 2018 to 2022. We

quantified trends in case notifications spatially and in specific populations

identified as vulnerable by the NPTC and measured trends in access to GeneXpert

testing.

**FINDINGS:** Of the 13,725 TB cases notified in Paraguay from 2018 to 2022, 2337

(17%) occurred among incarcerated individuals and 1743 (12.7%) occurred among

self-identified Indigenous individuals. In 2022, the relative risk of TB was 87

and 6.39 (95% CI: 6.08-6.72) among persons deprived of liberty and Indigenous

populations, compared to those who are not persons deprived of liberty and

non-Indigenous populations respectively. We found significant heterogeneity in

TB incidence across Paraguay's 17 departments. While 45% of TB cases among the

Indigenous population occurred in the Chaco Region, in western Paraguay,

notification among the Indigenous population was highest (1127.4 per 100,000) in

the Capital, including the metropolitan area.

**INTERPRETATION:** TB cases are concentrated among Paraguay's incarcerated and

Indigenous populations, both of which have extremely high relative risk of TB.

Our findings highlight the urgency of expanding access to TB diagnosis,

treatment, and prevention across the country and specifically, to the

populations at heightened risk of TB.

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Epidemiological Trends and Treatment Outcomes: Findings of a TB Survey From

Selected Districts of Madhya Pradesh, India.

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**BACKGROUND AND OBJECTIVE:** Tuberculosis (TB) remains a significant public health

challenge in India, particularly in Madhya Pradesh. In this study, we aimed to

examine epidemiological trends and treatment outcomes in TB patients in the

Datia and Tikamgarh districts of Madhya Pradesh, from 2018 to 2022, to inform

targeted TB control strategies.

**METHODS**: We conducted a retrospective observational study using data from the

National TB Elimination Program (NTEP), accessed through the Nikshay portal (a

Government of India initiative). We analyzed trends in TB notifications, rates

of microbiological confirmation, treatment outcomes, and co-infections.

Statistical tests, including the Mann-Whitney U test, Kruskal-Wallis test, and

chi-square test, were employed, with a p-value of less than 0.05 indicating

statistical significance.

**RESULTS:** In Datia, the proportion of pediatric TB cases decreased from 6% to 3%

(p = 0.04), while extrapulmonary TB (EPTB) cases rose from 11.3% to 13.8% (p =

0.02). Notifications from the private sector significantly increased from 4% to

28% (p = 0.03), whereas drug-resistant TB (DR-TB) cases fell from 2% to 1% (p =

0.02). TB-related mortality rose from 3.28% to 3.93% (p = 0.008), with the

proportion of patients lost to follow-up remaining stable at 9%-10% (p = 0.02).

In Tikamgarh, pediatric TB rates declined from 7.7% to 6.3% (p = 0.04), and EPTB

cases increased from 4.77% to 9.37% (p = 0.02). Notifications from the private

sector surged from 1.13% to 20.75% (p = 0.03). DR-TB rates decreased from 4.33%

to 1% (p = 0.02), but TB-related mortality increased from 1.87% to 5.46% (p =

0.008). The rate of patients lost to follow-up improved slightly, decreasing

from 12.71% to 10.09% (p = 0.02).

**CONCLUSION:** The reduction in pediatric TB and DR-TB indicates progress in

diagnosis and treatment adherence. However, the rising incidence of EPTB and

increasing mortality rates highlight ongoing challenges. Enhancing private

sector involvement, improving patient adherence, and integrating HIV-TB care are

crucial for achieving India's TB elimination objectives.

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Vulval tuberculosis - A masquerade reveler.

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Genital tuberculosis (TB) in females is a chronic disease with low-grade

symptoms. It commonly occurs secondary to extragenital TB and rarely occurs

primarily by inoculation from male partners. Owing to its rarity and variability

of clinical presentation, along with its ability to mimic many other common

conditions, its clinical diagnosis poses a challenge for practitioners.

Histopathological examination plays a pivotal role in diagnosing such cases. One

such rare case of TB, reveling in the vulva, masquerading as a tumor is

presented here.

Copyright: © 2025 Indian Journal of Sexually Transmitted Diseases and AIDS.

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A Call to Action: Empowering Pharmacists in Drug-Resistant Tuberculosis

Management.

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Drug-resistant tuberculosis (DR-TB) continues to be a major global health

threat, and while advancements in drug therapies have been made, the role of

pharmacists in improving patient outcomes has not been fully optimized. This

review aims to describe the types, resistance mechanisms, and management

strategies of DR-TB, with a focus on discussing the critical role of pharmacists

in optimizing treatment outcomes for DR-TB patients. A narrative review approach

was adopted to provide an updated and evidence-based perspective. Additionally,

manual review of reference lists from the retrieved articles was performed to

identify additional relevant studies. The review identifies types of DR-TB,

including mono-, poly-, rifampicin-, multi-, pre-extensively, and

extensively-drug resistance. Resistance mechanisms are outlined, highlighting

mutations in key genes, such as those involved in rifampicin and isoniazid (INH)

resistance, which compromise treatment efficacy. The treatment regimens for

DR-TB include the INH-R regimen, Bedaquiline, Pretomanid, and Linezolid (with or

without Moxifloxacin) (BPaL(M) regimen, shorter oral regimen, and longer oral

regimen, each tailored to the specific resistance pattern and patient condition.

The challenges in managing DR-TB include complex treatment regimens and side

effects, social barriers such as stigma and adherence issues, and system-related

obstacles like limited resources and healthcare infrastructure. The review

underscores pharmacists' vital yet underutilized role in addressing challenges.

Pharmacists' contributions include patient counseling to improve adherence, and

optimizing regimens for vulnerable populations and therapeutic drug monitoring.

Addressing DR-TB requires a multifaceted approach, with pharmacists playing a

critical role in its management. Their contributions are key to improving

patient outcomes and overcoming the challenges associated with DR-TB management.

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Diagnostic Performance of Xpert MTB/RIF Assay in Adults with Presumed Pulmonary

Tuberculosis at Uyo, Nigeria.

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**BACKGROUND:** Tuberculosis (TB) is a disease of immense public health importance

in sub-Saharan Africa. Xpert MTB/RIF assay, a relatively recent, rapid molecular

testing modality offers potential solutions to most of the challenges associated

with TB diagnosis.

**OBJECTIVE:** This study determined the diagnostic performance of Xpert MTB/RIF

assay in adults with presumed pulmonary tuberculosis (PTB).

**METHODS:** This was a descriptive cross-sectional study involving consenting

adults with presumed PTB at the University of Uyo Teaching Hospital, Uyo,

southern Nigeria. A structured questionnaire was used to collect participants'

data. All participants submitted 2 sputum samples (spot and early morning).

Sputum smear microscopy, Xpert MTB/RIF assay and mycobacterial culture were

done. They also had chest radiography.

**RESULTS:** They were 230 participants in the study. Seventy-nine (34.3%) patients

were living with HIV. Xpert MTB/RIF assay detected MTB in 65 (28.3%) patients

with 2 (3.1%) of them having rifampicin resistance. M. tuberculosis was isolated

from sputum culture in 69 participants while the result was negative in 151

participants. The culture results of these 220 patients were used as the

reference standard for the determination of the sensitivity and specificity of

Xpert MTB/RIF assay. The overall sensitivity and specificity of the assay were

88.4% and 98.7% respectively. Younger age, longer duration of cough, weight

loss, low body mass index (BMI) and positive smear status were independent

factors associated with MTB detection using the assay.

**CONCLUSION:** Xpert MTB/RIF assay is a highly sensitive and specific modality for

pulmonary TB diagnosis when compared with mycobacterial culture, which is the

gold standard.

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Magnetic hyperthermia drastically enhances killing of Mycobacterium tuberculosis

by bacteriocin AS-48 grafted on biomimetic nanoparticles.

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Mycobacterium tuberculosis, the etiological agent of human tuberculosis, is an

intracellular pathogen responsible for one of the infectious diseases with

highest mortality rates. Its ability to replicate inside alveolar macrophages

and trigger the formation of granulomas, alongside the appearance of

multidrug-resistant strains, impose the employment of drugs that exacerbate

their toxic effects after the long therapies necessary to deal with the

infection. As an alternative to conventional drugs, this work proposes the use

of bacteriocin AS-48 immobilized on biomimetic magnetic nanoparticles (BMNPs) as

a nanoformulation capable of killing M. tuberculosis in infected THP-1

macrophages, which allows combination with magnetic hyperthermia to increase its

effectiveness. This work is a proof of concept of a nanosystem that could

potentially be magnetically directed to infected areas, where it could be

applied locally. Our results show that AS-48\_BMNP nanoassemblies used against M.

tuberculosis in vitro display a synergistic effect with magnetic hyperthermia

that can completely eradicate the bacteria from infected macrophages in four

days. This combined treatment represents a promising opportunity for the future

development of a local therapy for the treatment of M. tuberculosis.

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Fractional-order modeling of tuberculosis and diabetes mellitus co-existence

dynamics.

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This paper proposes a fractional-order model using the Atangana-Baleanu-Caputo

derivative to study the co-dynamics of tuberculosis and diabetes mellitus among

susceptible (S), TB-infected (I), DM-infected (D), and co-existence (C)

populations. The model's well-posedness is established via the Banach

fixed-point theorem, ensuring the uniqueness and positivity of solutions. Basic

reproduction numbers (R0TB,R0DM,R0) are derived, with values exceeding unity

indicating the instability of the disease-free equilibrium and progression

toward endemicity. Sensitivity analysis highlights key parameters

(β1,β2,δ1,δ3,δ5) affecting co-existence dynamics. Numerical simulation is

conducted over T=365 days (1 year) with a unit step h=1 day, using the

Adams-Bashforth method to reveal that lower fractional orders α∈(0,0.8] slow

disease decay. The model is validated against real data over 90 days at α=0.5

using logistic growth for C(t). Results underscore the effectiveness of

fractional calculus in modeling chronic co-existence and guiding control

strategies.

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