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**境外学者发表的结核病英文文章摘要**

**（121篇）**

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

**1. Virulence. 2025 Aug 16:2547326. doi: 10.1080/21505594.2025.2547326. Online ahead of print.**

Description of bacterial RNA transcripts detected in mycobacterium tuberculosis

- Infected cells from peripheral human granulomas.

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Mycobacterium tuberculosis (Mtb) remains a global human health threat. However,

understanding effects of the microbe on cellular interactions in infected tissue

has been hindered by inability to discriminate between infected versus

un-infected cells. We included the H37Rv Mtb reference genome when assembling

scRNA seq libraries from fine needle aspirate samples of peripheral nodal TB

patients. Using the 10X Genomics Cell Ranger tool to align sequencing reads, we

consistently detected bacterial small and large ribosomal subunit RNA sequences.

We interpret Mtb reads associated with a cell's UMI and transcriptome to

indicate infection of that individual host cell. This provides a new window into

the status of infected cells in the context of the bystander cells in the

infected tissue. We investigated these Mtb transcripts to explore their clinical

utility. The Mtb transcripts showed frequent sequence variation from the

reference genome, with greater than 90 percent of the rrs or rrl reads from many

clinical samples having at least one sequence difference. The highly conserved

nature of the rrs and rrl gene sequences limited the ability to assign bacterial

lineage based solely transcriptome analysis. However, rapid improvements in

sequencing depth may soon allow transcriptome analysis of infecting microbes and

improved certainty regarding their lineage, drug resistance and virulence

factors.

DOI: 10.1080/21505594.2025.2547326

PMID: 40817758

**2. BMC Microbiol. 2025 Aug 15;25(1):509. doi: 10.1186/s12866-025-04213-y.**

Investigation of delamanid, bedaquiline, and linezolid resistance rates and

related gene mutations in multidrug-resistant Mycobacterium tuberculosis in

regional tuberculosis reference laboratories of Iran.

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**INTRODUCTION:** So far, there are scarce data on resistance to delamanid (DLM),

bedaquiline (BDQ), and linezolid (LZD) antibiotics and related gene mutations in

multidrug-resistant Mycobacterium tuberculosis (MDR M. tuberculosis) from Iran.

Hence, this study aimed to investigate the DLM, BDQ, and LZD resistance rates

and related gene mutations in MDR M. tuberculosis in regional tuberculosis

reference laboratories of Iran.

**METHODS:** In this cross-sectional study, MDR M. tuberculosis isolates (resistant

to antibiotics rifampicin and isoniazid) were collected from sputum samples of

tuberculosis patients referred to several regional tuberculosis reference

laboratories in Iran. The resistance against DLM, BDQ, and LZD antibiotics was

evaluated using the proportion method on the Middlebrook 7H11 agar culture

medium. The minimum inhibitory concentration (MIC) of three antibiotics was

evaluated using the broth microdilution method. Mutations in genes that

contributed to resistance to antibiotics DLM (fbiA, fbiC, ddn, fgd1), BDQ (atpE,

pepQ, Rv0678), and LZD (rrl and rplC) were investigated by polymerase chain

reaction (PCR) and sequencing.

**RESULTS:** This study examined 29 clinical MDR M. tuberculosis isolates. These

isolates were collected from 68.9% (20/29) males and 31.1% (9/29) females with a

mean age of 40 years (ranged 30–70 years). The resistance rate to DLM, BDQ, and

LZD was 27.6% (n = 8/29), 0.0% (n = 0/29), and 6.8% (n = 2/29), respectively.

The range of MIC for DLM was 0.12–0.48 µg/ml. Meanwhile, the 2 LZD-resistant

isolates showed MIC of 2.0 µg/ml. All MDR M. tuberculosis isolates with

phenotypic resistance to DLM (8 isolates) contained mutations in one of the

fgd1, fbiA, and fbiC genes. A mutation was identified in the 1090 bp fragment of

the fgd1 gene at position 839 in five isolates. Additionally, the 2386 bp

fragment of the fbiC gene revealed mutations at positions 266 and 952 in three

isolates. Also, two DLM-resistant isolates exhibited two mutations at position

145 and 960 in the 1136 bp fragment of fbiA. No genetic mutations were detected

in ddn, atpE, pepQ, and Rv0678 genes. Two LZD-resistant isolates exhibited

mutations in the rplc gene at position 460 within the 933 bp fragment, and in

the rrl gene at positions 2576 and 2814 within the 1772 bp fragment.

**CONCLUSION:** This study found multiple mutations in the fgd1, fbiA, fbiC, rplc,

and rrl genes that were responsible for the development of DLM and LZD

resistance in MDR M. tuberculosis isolates in Iran. More research is needed to

understand the underlying mechanisms of resistance to these antibiotics.

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**3. Trials. 2025 Aug 15;26(1):291. doi: 10.1186/s13063-025-08973-w.**

ACTG A5409 (RAD-TB): Study protocol for a phase 2 randomized, adaptive,

dose-ranging, open-label trial of novel regimens for the treatment of pulmonary

tuberculosis.

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**BACKGROUND**: The standard of care (SOC) treatment for drug-susceptible pulmonary

tuberculosis (DS-TB) consists of isoniazid, rifampicin, pyrazinamide, and

ethambutol (HRZE). New treatment regimen options for DS-TB are needed as HRZE is

long in duration (6 months), associated with frequent adverse events,

unforgiving of adherence lapses, and complicated by rifamycin-based drug-drug

interactions. The recent resurgence of TB drug development, particularly in the

context of drug-resistant TB, offers promise for additional regimens for persons

with DS-TB, provided they are sufficiently effective and well-tolerated. We

spotlight wave 1 of the RAD-TB platform trial (ACTG A5409, NCT06192160) that

will investigate new chemical entities for the treatment of DS-TB.

**METHODS:** In wave 1 of the RAD-TB platform, adult participants initiating

treatment for DS-TB will be randomized to SOC (HRZE, Arm 1) or one of five

experimental arms for the 8-week intensive phase. The experimental treatment

arms will consist of a bedaquiline and pretomanid backbone (BPa) in combination

with one of three oxazolidinones. Arm 2 will study linezolid (BPaL) at a dose of

600 mg daily, Arms 3A and 3B will study TBI-223 at 1200 mg and 2400 mg daily,

respectively, and Arms 4A and 4B will study sutezolid at 800 mg and 1600 mg

daily, respectively. The primary efficacy objective is to compare sputum culture

time to positivity (TTP) slope over the first 6 weeks of treatment for each

experimental treatment arm to SOC. The primary safety objective is to compare

new Grade 3 or higher adverse events over the first 8 weeks of treatment for

each experimental treatment arm to SOC. After the intensive phase, all

participants will receive the standard isoniazid and rifampicin (HR)

continuation phase for 18 weeks. Participants will be followed for 52 weeks

after TB treatment initiation to assess long-term outcomes.

**DISCUSSION:** Wave 1 of the RAD-TB platform aims to identify the optimal

oxazolidinone(s), with regard to both efficacy and safety, to combine with the

BPa backbone for the treatment of DS-TB. Subsequent waves of this platform trial

may add a fourth drug to the regimen, study new diarylquinolines to substitute

for bedaquiline, or study novel agents from other TB drug classes.

TRIALS REGISTRATION: ClinicalTrials.gov NCT06192160 . Registered on January 5,

2024.

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**4. Respir Med. 2025 Aug 13:108309. doi: 10.1016/j.rmed.2025.108309. Online ahead of print.**

Characteristics and In-Hospital Outcomes of Clinically Diagnosed Tuberculosis

Patients in a High-Burden Setting: A Five-Year Retrospective Analysis.

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**BACKGROUND:** The 2016 National TB Prevalence Survey revealed that TB prevalence

was 2.5 times higher than routine surveillance indicated and half of all

patients receiving treatment were missing from the national registry. Clinically

diagnosed tuberculosis (CD-TB), duly recognized in the national TB guidelines

when microbiological confirmation is unattainable, remains understudied despite

its relevance in the TB diagnostic and surveillance program.

**METHODS:** This retrospective study analyzed 1,187 hospitalized CD-TB patients

(2015-2019) at a Philippine tertiary hospital. Statistical analyses identified

mortality predictors via binary logistic regression (p<0.05 significant).

**RESULTS:** Patients (mean age 47.2±17.3 years; 70% male) faced significant

resource constraints: only 7.3% received GeneXpert testing, and 52.7% of

extrapulmonary TB cases lacked required imaging. Advancing age reduced

improvement likelihood (OR=0.9889/year, 95% CI 0.9815-0.9963, p=0.003).

Pulmonary TB decreased improvement odds by 60% (OR=0.40, 95% CI 0.23-0.68,

p<0.001). Respiratory failure depicts disease severity, with patients on

supplemental oxygen (OR=0.60, 95% CI 0.40-0.89, p=0.011) and mechanical

ventilation (OR=0.14, 95% CI 0.08-0.25, p<0.001) reduced improvement by 40% and

86%, respectively. Conversely, incentive spirometry (OR=3.59, 95% CI 1.19-10.86,

p=0.024) and surgical intervention (OR=3.10, 95% CI 1.84-5.23, p<0.001) tripled

improvement odds.

**CONCLUSION AND RECOMMENDATIONS:** Age, pulmonary TB, and respiratory failure

predict mortality in hospitalized CD-TB patients. Incentive spirometry and

surgery significantly improve outcomes. Findings provide input into the

Philippine Acceleration Action Plan for TB (PAAP-TB 2023 - 2025): scale

pulmonary rehabilitation and surgical pathways, address diagnostic gaps

(imaging, GeneXpert), and integrate screening into poverty-alleviation programs

(DSWD/4Ps).

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**5. J Glob Health. 2025 Aug 15;15:04230. doi: 10.7189/jogh.15.04230.**

Exploring potential barriers and facilitators to integrate tuberculosis,

diabetes mellitus, and tobacco control programmes in India.

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**BACKGROUND:** Co-integrating tuberculosis (TB), diabetes mellitus (DM), and

tobacco control (TC) programmes in India could help address the triple burden of

these diseases. However, limited information exists regarding the feasibility

and determining factors of such integration. We explored potential barriers and

facilitators to integrating TB, DM, and TC programmes in Ambegaon Block of Pune

District, Maharashtra, and Ballabgarh Block of Faridabad District, Haryana, in

India.

**METHODS:** We conducted a qualitative study based on in-depth interviews with

health workers, programme managers, and stakeholders involved in TB, DM, and TC

programme implementation whom we enrolled using purposive and snowball sampling.

The interview guide was based on World Health Organization's Health System

Strengthening framework. We collected the data between November 2022 and March

2023 and analysed it through the rapid analysis method.

**RESULTS:** We interviewed 32 participants. The major challenge for integration,

according to the participants' perspectives, relates to the level of service

delivery, which is primarily attributed to inadequate implementation of all the

programmes. Themes that emerged as facilitators were well-designed programmes

with robust guidelines and ample space for infrastructure, while those seen as

barriers included inadequate referral systems, insufficient infrastructure,

limited resources, a shortage of trained staff, and a lack of essential drugs

and equipment, all of which impeded the uptake and coverage of services.

**CONCLUSIONS:** Our findings highlight the critical importance of addressing

barriers and facilitators to implementing programmes in India for tackling the

triple burden of TB, DM, and TC. A multidimensional approach and targeted

strategies are needed for overcoming these challenges. Sensitising the health

system staff, implementing feedback and referral systems, and developing

cross-programme digital platforms will offer a roadmap for policymakers and

healthcare system managers.

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**6. J Microbiol Immunol Infect. 2025 Aug 10:S1684-1182(25)00152-5. doi:**

**10.1016/j.jmii.2025.08.004. Online ahead of print.**

NADPH Oxidase 4 Deficiency Enhances Dendritic Cell-mediated IL-12 Production and

Th1 Responses in Mycobacterium tuberculosis Infection.

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**BACKGROUND:** Mycobacterium tuberculosis (Mtb) infection triggers oxidative

stress, necessitating host mechanisms to maintain redox balance. The NADPH

oxidase (NOX) family, which produces reactive oxygen species, plays an integral

part in this process. While the protective role of NOX2 in Mtb infection is

well-studied, the function of NOX4 remains unclear.

**METHODS:** To investigate the impact of NOX4, we infected C57BL/6 wild-type (WT)

and NOX4-deficient (Nox4-/-) mice with the Mtb K strain, assessing bacterial

burdens, lung pathology, and immune responses. Then, we analyzed cytokine

production and signaling pathways to explore the interaction between dendritic

cells (DCs) and T cells.

**RESULTS:** Nox4-/- mice exhibited reduced bacterial burden and milder lung

pathology compared to WT mice, accompanied by increased DC infiltration and a

higher frequency of CD4+ T cells of the Th1 subset that secrete interferon-gamma

(IFN-γ) in the lungs. Interestingly, ex vivo experiments showed no significant

difference in IFN-γ production by T cells from WT and Nox4-/- mice when

activated using antibody-coated beads. However, Mtb-infected bone marrow-derived

DCs (BMDCs) from Nox4-/- mice markedly enhanced IFN-γ production in WT T cells.

Further investigation into the role of NOX4 in DCs revealed that BMDCs from

Nox4-/- mice infected with Mtb produced significantly higher levels of IL-12.

This elevation was attributed to enhanced activation of IRF1, mediated by the

AKT/GSK-3β signaling pathway.

**CONCLUSION:** NOX4 negatively regulates IL-12 production in Mtb-infected DCs,

suppressing Th1-mediated immunity. Its absence enhances Th1 responses, improves

immune control of Mtb. Targeting NOX4 may improve tuberculosis outcomes by

strengthening host immunity.

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**7. BMJ Glob Health. 2025 Aug 14;10(8):e017923. doi: 10.1136/bmjgh-2024-017923.**

Corticosteroids for reducing tuberculosis mortality in persons living with HIV:

a systematic review and meta-analysis using reconstructed individual patient

data.

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**OBJECTIVE:** To assess the effect of adjunctive corticosteroids on mortality in

persons living with HIV (PLHIV) being treated for tuberculosis (TB).

**DESIGN:** Systematic review and meta-analysis.

**DATA SOURCES:** PubMed, CENTRAL and EMBASE through 31 December 2023 STUDY

**SELECTION:** Randomised placebo-controlled trials (RCTs) with published

Kaplan-Meier survival curves comparing corticosteroids versus placebo in PLHIV

receiving TB treatment.

**QUALITY ASSESSMENT, DATA EXTRACTION AND ANALYSIS:** Three reviewers independently

assessed study quality and extracted data. Reconstructed individual patient data

were derived from published Kaplan-Meier survival curves, and a one-stage

mixed-effects Cox regression model was used to estimate HRs for all-cause

mortality.

**RESULTS:** Four trials involving 873 PLHIV with three forms of TB (618 meningitis,

197 pleural and 58 pericarditis) were included. Over a median follow-up of 19.3

months (IQR, 15.1-30.2), 367 (42%) participants died. At 12 months after

randomisation, corticosteroids were associated with a 67% reduction in mortality

(HR 0.33, 95% CI 0.26 to 0.41; p<0.0001) compared with placebo. This benefit was

maintained during the full follow-up period, with a 17% reduction in mortality

(0.83, 0.68-0.99; p=0.0477). In subgroup analyses, a non-significant trend

towards benefit was seen for TB meningitis (HR 0.84, 0.67-1.05; p=0.061, two

trials), with unclear effect for pleural (HR 0.90, 0.57-1.41; p=0.643, one

trial) and TB pericarditis (HR 0.40, 0.15-1.17; p=0.100, one trial).

**CONCLUSION:** Adjunctive corticosteroids were associated with reduced mortality

among PLHIV treated for TB in this meta-analysis of four RCTs. Further clinical

trials are needed to confirm this finding and inform guidelines on the use of

adjunctive corticosteroid in this population.

PROSPERO REGISTRATION NUMBER: CRD42024500865.

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**8. Pediatrics. 2025 Aug 15:e2024069274. doi: 10.1542/peds.2024-069274. Online ahead of print.**

Tuberculosis in Children, Adolescents, and Young Adults in California,

2000-2023.

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**OBJECTIVES:** To identify trends in pediatric tuberculosis (TB) epidemiology in

California and measure progress in reducing health disparities.

**METHODS:** Demographic, clinical, and neighborhood health support data in persons

younger than 25 years with TB during 2000-2023 in California were analyzed

across age groups.

**RESULTS:** A total of 8249 individuals younger than 25 years were identified with

active TB. Half (45.8%) were US-born. Incidence rates were highest among Asians,

residents of the San Diego region, and those living in the

least-health-supportive neighborhoods. The highest TB rates occurred among 18-

to 24-year-olds in 6 regions and among children younger than 5 years in 2

regions. TB rates declined across the period; 2 regions had rate increases

during 2020-2023. During 2020-2023, compared with white persons, the rate of TB

disease was 20.2 (95% CI, 13.2-29.4) times higher among Asian, 10.8 (95% CI,

7.1-15.4) among Hispanic, and 8.5 (95% CI, 5.1-13.4) among Black persons.

Central nervous system (CNS) TB did not decrease; deaths among individuals with

CNS TB were 9.5 times greater (95% CI, 5.6-16.2) than among those with other

forms of TB. After controlling for age, the incidence rate of CNS TB in US-born

individuals was 2.9 (95% CI, 1.9-4.7) times that for non-US-born individuals

younger than 18 years.

**CONCLUSIONS:** Despite falling TB rates among persons younger than 25 years in

California, disparities were found by age, race and ethnicity, region, and

health-supportiveness of neighborhood type. The incidence of CNS TB has not

declined. Increased partnership between public health and primary care providers

is needed to identify children and young adults at risk for TB.

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**9. J Infect Chemother. 2025 Aug 12:102792. doi: 10.1016/j.jiac.2025.102792. Online ahead of print.**

Association between Allergic Bronchopulmonary Aspergillosis or Aspergillus

sensitization and Tuberculosis: A Systematic Review of 607 cases.

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**INTRODUCTION:** Although allergic bronchopulmonary aspergillosis (ABPA) is

classically described in asthma and cystic fibrosis, pulmonary tuberculosis

(PTB) with post-tubercular lung disease (PTLD) has been reported as a likely

predisposing factor. It , however, has not been reviewed systematically, which

we aimed to achieve in the current systematic review.

**METHODS:** We screened the available literature from PubMed, Embase, SCOPUS and

Web of Science databases for studies reporting association between ABPA and PTB

from the beginning of time to June 30, 2023 and collated the data on association

of ABPA and tuberculosis.

**RESULTS:** 1176 articles were identified from the initial search, of which 60

articles (27 original articles and 33 case reports) were included in the final

analysis. . Four patterns were described: ABPA in patients with previous TB

(151, 24.9%), co-existent ABPA and TB (16, 2.6 %), Aspergillus sensitization in

patients with prior or current TB (91, ∼15%) and ABPA misdiagnosed as TB (349,

57.5%). There was significant heterogeneity in diagnostic criteria used for ABPA

andpulmonary TB. From limited individual data, which could be

extracted,observations were: 1) Central bronchiectasis (24.8%), cavity (19.6%),

fungal ball (10.9%), mucus plug/high attenuation mucus (HAM) (7.6%) and

centrilobular nodules (6.5%) were the most common radiographic abnormalities. 2)

96.4% received steroids,11% received antifungals mostly for relapse or

inadequate response. 3) Adequate treatment response was noted in the limited

cohort where it was reported.

**CONCLUSIONS:** ABPA is commonly misdiagnosed as TB, but Aspergillus sensitization

/ABPA can develop in patients with prior TB. However, significant heterogeneity

in diagnostic criteria limits generalizability. Future well-designed studies are

required to confirm these associations.

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Infectious Diseases, and Japanese Society for Infection Prevention and Control.

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**10. J Pharm Sci. 2025 Aug 12:103952. doi: 10.1016/j.xphs.2025.103952. Online ahead of print.**

Pulmonary drug delivery of clofazimine: A route of administration and

pharmacokinetics guided repositioning strategy against drug resistant

tuberculosis informed by use for other disease indications.

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Current oral therapeutic regime of Clofazimine (CFZ) in tuberculosis treatment

is limited by poor pharmacokinetics, long t1/2, and especially exposure-related

systemic toxicity. This review critically evaluates pulmonary administration as

a targeted delivery approach to reduce the dose and improve therapeutic

efficacy. From the primarily anti-leprotic indication, CFZ has evolved for

treatment of multidrug-resistant tuberculosis (MDR-TB), nontuberculous

mycobacterial (NTM) diseases, small-cell lung cancer, and programmed cell death

protein 1 (PD-1) and cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4) in

cancer patients. Despite broad-spectrum activity, clinical effectiveness is

constrained by its poor physicochemical and pharmacokinetic properties. Due to

its high lipophilicity, orally administered CFZ has a high volume of

distribution (1470 L) and tends to accumulate in fatty tissues, resulting in

long times to reach steady state concentrations, sub-therapeutic drug levels at

the infection site, increased risk of systemic toxicity and triggering drug

resistance over time. Although novel delivery systems administered through the

oral route are also explored extensively, they are inadequate to address the

concerns of sustained systemic exposure. Pulmonary delivery enables direct

deposition at the diseased site, provides higher local concentrations and

reduces off-target effects. Poor solubility and high lipophilicity are principal

biopharmaceutical disadvantages of CFZ for oral formulation development.

However, these properties are advantageous for pulmonary delivery in

facilitating prolonged lung retention and reduced dosing frequency. This review

evaluates the current advantages and challenges of CFZ inhalation versus oral

formulations, discusses their pharmacokinetic profiles, and explores pulmonary

macrophage uptake strategies to optimize tuberculosis treatment outcomes.

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DOI: 10.1016/j.xphs.2025.103952

PMID: 40812596

**11. Antimicrob Agents Chemother. 2025 Aug 14:e0026625. doi: 10.1128/aac.00266-25. Online ahead of print.**

Quality control and considering systematic MIC shifts are key when evaluating

the role of mmpR5 (Rv0678) frameshifts in bedaquiline resistance.

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DOI: 10.1128/aac.00266-25

PMID: 40810668

**12. J Antimicrob Chemother. 2025 Aug 14:dkaf274. doi: 10.1093/jac/dkaf274. Online**

**ahead of print.**

Studying intrapulmonary pharmacokinetics for tuberculosis treatment: a

systematic review of methodology.

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**OBJECTIVES:** Drug concentrations at the site of disease in pulmonary tuberculosis

(TB) remain limitedly available, while adequate exposures of anti-TB drugs in

the lungs are required for sterilization of lesions. Intrapulmonary

concentration data could benefit TB treatment optimization. We conducted a

systematic review to identify methods that can be used for sampling,

quantifying, describing and predicting intrapulmonary pharmacokinetics of

anti-TB drugs in humans.

**METHODS:** Two systematic search strategies were conducted in databases Embase and

PubMed, last searched on 18 July 2024. In total, 253 studies were identified,

and their applied methods were classified into three different categories: (i)

sampling techniques, (ii) quantitative analysis and (iii) modelling methods. All

types of pulmonary diseases were included in the search.

**RESULTS:** Sputum sampling was reported as sampling method in nine studies, tissue

biopsy in 51, bronchoalveolar lavage in 115, bronchoscopic microsampling in

eight, bronchoabsorption in one and microdialysis in 12 studies. LC-MS/MS, the

gold standard for drug quantification in biological samples, was used in 67

studies. Other quantification methods included positron emission tomography,

reported in 12 studies and matrix-assisted laser desorption ionization mass

spectrometry on lung tissue in three studies. For prediction and description of

(pre)clinical intrapulmonary concentration data, population pharmacokinetic

modelling was reported in 32 studies and physiologically based pharmacokinetic

modelling in 35 studies.

**CONCLUSIONS:** Many of the identified methods are associated with considerable

limitations including invasiveness, complexity, cost and lack of

standardization. Most importantly, the method of choice must provide adequate

representation of site of disease pharmacokinetics. Determining the best

approach for studying intrapulmonary pharmacokinetics involves careful

consideration of all these factors.

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Society for Antimicrobial Chemotherapy.

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**13. Nanoscale. 2025 Aug 12. doi: 10.1039/d5nr01498k. Online ahead of print.**

Ti(3)C(2)O(2) MXene as a dual-action modulator of inflammatory and tuberculosis

signaling: structural and in vitro insights.

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The growing threat of antimicrobial resistance and tuberculosis (TB)

necessitates innovative therapeutics capable of modulating both infection and

host immune responses. In this study, we report the dual anti-tubercular and

anti-inflammatory activity of oxygen-functionalized Ti3C2O2 MXene, a

two-dimensional nanomaterial synthesized via selective HF etching of Ti3AlC2

followed by ethanol-assisted delamination. Structural characterization by XRD

and Raman spectroscopy confirmed successful conversion to the MXene phase, with

an increased interlayer spacing of 9.87 Å. SEM and TEM analyses revealed uniform

sheet-like morphology, and AFM confirmed few-layer thickness (∼1.5 nm).

Biological assays using lipopolysaccharide (LPS)-stimulated murine macrophage

cell line RAW 264.7 macrophages demonstrated significant downregulation of

pro-inflammatory mediators- inducible nitric oxide synthase (iNOS), Tumor

necrosis factor (TNF)-α, and Interleukin-6 (IL-6)-with IC50 values of 23.2,

26.1, and 21.6 μg mL-1, respectively. Western blot analysis further validated

suppression of inflammatory pathways at the protein level. In parallel, Ti3C2O2

exhibited robust anti-tubercular activity against Mycobacterium tuberculosis

H37Rv, achieving complete inhibition at 4.0 μg mL-1. Computational studies

revealed strong and specific interaction of Ti3C2O2 with the TB inflammatory

target protein (PDB ID: 5V3Y), forming stable hydrogen bonds with His185,

Gln186, and Asp219. Molecular dynamics simulations over 3000 ns confirmed a

highly stable protein-MXene complex (RMSD: 2.41 Å; ΔGbind: -78.54 kcal mol-1).

Comparative simulations with streptomycin revealed weaker binding and greater

structural fluctuation. ADMET predictions suggested favorable pharmacokinetic

properties, including high volume of distribution, low toxicity, and absence of

major cytochrome P450 or cardiotoxic liabilities. These findings establish

Ti3C2O2 MXene as a promising nanoplatform for dual-function immunomodulation and

antimicrobial therapy, offering mechanistic and structural insight into its

bioactivity.

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PMID: 40808616

**14. BMC Infect Dis. 2025 Aug 13;25(1):1012. doi: 10.1186/s12879-025-11430-3.**

The role of IFN-γ + 874T/A and IL-12 + 16974A/C polymorphisms in susceptibility

to tuberculosis infection in a Sudanese population: a case-control study.

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**BACKGROUND:** Tuberculosis (TB) is a top infectious disease killer worldwide. The

susceptibility to infectious diseases, including tuberculosis, has been linked

to several cytokine gene polymorphisms.

**METHOD:** A case-control study was conducted at Abu Anja Chest Hospital, Omdurman,

Khartoum state, using PCR-RFLP in 200 Sudanese patients with pulmonary

tuberculosis and 200 healthy controls between February 2018 and February 2021.

Data analysis was done using the IBM SPSS software package version 20.0.

(Armonk, NY: IBM Corp).

**RESULT:** The mutant and heterozygous genotypes of IL-12+16974 A/C polymorphism

were associated with an almost four-fold [P-value <0.001 OR= 3.703(2.243-

6.115), 95% CI] increased risk of TB in the Sudanese population. No

statistically significant differences were found in the genotype and allele

frequencies of the IFN-γ+874T/A gene between patients and controls.

**CONCLUSION:** These findings suggest, for the first time in Sudan, the significant

risk of TB in people carrying the mutant and heterozygous genotypes of

IL-12+16974 A/C genes.

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**15. BMJ Open. 2025 Aug 12;15(8):e100927. doi: 10.1136/bmjopen-2025-100927.**

ThiPhiSA: new pathways to TB prevention from community screening - a

household-randomised controlled trial in KwaZulu-Natal, South Africa.

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**INTRODUCTION:** Tuberculosis (TB) remains the leading cause of infectious disease

deaths, particularly among people living with HIV (PWH). Despite being

preventable, TB preventive therapy (TPT) uptake is low in high-burden regions

like South Africa, where new guidelines have expanded TPT eligibility and

introduced shorter, more effective regimens like 3 months of weekly rifapentine

and isoniazid (3HP). As differentiated service delivery models for HIV care have

proven effective, there is increasing recognition that decentralising TPT

delivery may improve coverage and completion. This study explores whether a

community-based TPT delivery strategy can enhance uptake and completion of TPT

compared with traditional clinic-based services.

**METHOD AND ANALYSIS:** We will conduct a household-randomised, non-blinded,

controlled trial. Persons eligible for TPT will be recruited from the TB

TRIAGE+Trial study, a community-based household TB screening study. Households

containing at least one person eligible for TPT will be randomised 1:1 to either

community-based TPT or standard-of-care clinic referral for TPT. At enrolment,

all participants will be provided with a 2-week supply of TPT in the community.

Participants randomised to the community arm will receive the entire course of

TPT in a single dispense (12 weeks of 3HP or 6 months of isoniazid, if 3HP is

contraindicated). Clinic-arm participants will be referred to their local clinic

for the remainder of their course of TPT and will collect TPT refills on the

clinic-determined schedule. Our primary outcome is the proportion of

participants who complete a course of TPT. Secondary outcomes include overall

adherence to TPT, predictors of adherence with TPT, participant satisfaction

with the assigned TPT delivery method and adverse events.

**ETHICS AND DISSEMINATION:** The study and its tools were approved by the Human

Sciences Research Councils Research Ethics Committee (approval number:

2/25/10/23), based in Pretoria, Gauteng, South Africa, as well as the University

of Washington Institutional Review Board (Study 00018448). Study findings will

be shared through the community advisory group and local stakeholder meetings,

relevant international and local meetings/conferences and peer-reviewed

publications.

**TRIAL REGISTRATION NUMBER:** NCT06214910. Date and version: 3.0, 30 July 2024.

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**16. BMJ Open. 2025 Aug 12;15(8):e099124. doi: 10.1136/bmjopen-2025-099124.**

Patient-cost studies on self-administered treatment (SAT) for drug-sensitive

tuberculosis compared to facility-based directly observed treatment,

short-course (DOTS): a protocol for a systematic review.

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**INTRODUCTION:** Many patients with tuberculosis (TB) suffer from a huge economic

burden, even though TB services are often provided free of charge at the point

of care. Costs can create significant barriers, hindering patients' access to TB

treatment. These costs include direct medical costs (such as consultation fees),

direct non-medical costs (such as transportation costs) and indirect costs (such

as wages foregone). This systematic review aims to synthesise the best available

evidence on economic evaluations of patient-cost studies on self-administered

treatment (SAT) for drug-sensitive TB compared with facility-based directly

observed treatment, short-course (FB DOTS), globally.

**METHODS AND ANALYSIS:** We will conduct a systematic review following the

Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols

guidelines and search PubMed, Academic Search Complete, Scopus, CINAHL Plus

(EBSCO) and Google Scholar for articles published up to 2025, without date

restrictions. Eligible studies must be full or partial (cost analyses without

effectiveness data) economic evaluations conducted globally, comparing SAT to FB

DOTS regarding TB patient costs. Grey literature will be included. Exclusion

criteria include studies not reporting patient costs between SAT and FB DOTS,

and non-economic evaluations (non-original research). Two independent reviewers

will conduct the screening, data extraction and quality assessment. A quality

assessment will be performed using the Consolidated Health Economic Evaluation

Reporting Standards statement, the Consensus on Health Economic Criteria

checklist and the ROBINS-I tool.

**ETHICS AND DISSEMINATION:** Ethics approval is not required for this systematic

review because it does not use individual patient data. Instead, we will use

publicly available economic evaluation research studies. Findings will be

presented at international and national conferences and published in

open-access, peer-reviewed journals.

PROSPERO REGISTRATION NUMBER: CRD42024591221.

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**17. Trop Med Int Health. 2025 Aug 13. doi: 10.1111/tmi.70013. Online ahead of print.**

Effects of Communication Strategies on Treatment Adherence and Success in

Tuberculosis: A Systematic Review and Meta-Analysis.

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**INTRODUCTION:** Tuberculosis, although curable, presents challenges related to

treatment adherence, which compromises treatment effectiveness. Individual,

social and structural barriers interfere with patients' ability to properly

follow the therapeutic regimen, thereby impacting treatment outcomes. Given the

limitations of the conventional healthcare model, which relies primarily on

in-person consultations and standard treatment protocols without additional

adherence support technologies, new approaches have been explored to improve

patient outcomes. This study seeks to identify effective communication

approaches in this context.

**OBJECTIVE:** To identify the most effective communication strategies to optimise

treatment adherence and improve therapeutic success in patients diagnosed with

tuberculosis.

**METHODS:** A systematic review with meta-analysis was conducted. We included

studies available in the MEDLINE (via PubMed), EMBASE and SCOPUS databases, with

publication dates between January 2005 and December 2024. The primary outcomes

were adherence to and success in tuberculosis treatment.

**RESULTS:** This systematic review included 17 studies on tuberculosis treatment

adherence. Of these, 12 were included in the meta-analysis for adherence and 8

for treatment success. The most effective strategies for adherence were

community education (2 studies; RR: 0.25, 95% CI: 0.11-0.56) and video observed

therapy (VDOT) (2 studies; RR: 0.29, 95% CI: 0.21-0.40). The combination of

electronic devices with SMS also showed positive results (3 studies; RR: 0.53,

95% CI: 0.37-0.77). SMS alone (5 studies) and electronic devices alone (3

studies) were not effective. For treatment success, only the combination of

electronic devices with SMS (RR: 0.31, 95% CI: 0.17-0.55) and community

education (RR: 0.51, 95% CI: 0.40-0.64) were effective.

**CONCLUSION:** The combination of electronic devices with SMS and community

education is an effective strategy for improving adherence and therapeutic

success in tuberculosis treatment. Isolated interventions with SMS or electronic

technologies did not show significant results. Adapting approaches to local

realities is crucial for optimising outcomes.

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**Online ahead of print.**

Lung epithelial cells in the defense against tuberculosis: an essential

neglected activity.

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The human lungs are perpetually exposed to a myriad of potential pathogens that

necessitate neutralization and elimination. Within the airways, innate immune

mechanisms are employed to achieve this objective. A pivotal mechanism is the

epithelial cell barrier, which encompasses nearly the entirety of the pulmonary

area and the respiratory tract. The cellular variability within the respiratory

tract is significant not only structurally but also functionally. For instance,

the epithelial barrier is composed of different cell types, while some

participate mainly in gas exchange, such as type 1 pneumocytes, other cell types

are mainly responsible for the production of pulmonary surfactants and serve as

the first line of defense against xenobiotics and pathogens, such as type 2

pneumocytes. The immunological defense mechanisms associated with the epithelial

barrier include the secretion of mucus, chemokines, cytokines, and antimicrobial

peptides, among others. The functionality of these epithelial cells is crucial

for maintaining respiratory health; however, external factors such as pathogens

can disrupt their operations, leading to diseases like tuberculosis-a global

health concern due to its high morbidity and mortality rates. This review

briefly examines the immunological pathways associated with the epithelial cell

barrier and explores factors that interfere with their function, with a focus on

tuberculosis disease.

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**19. Biomed Pharmacother. 2025 Aug 12;191:118464. doi: 10.1016/j.biopha.2025.118464. Online ahead of print.**

The repurposed STAT3 inhibitor pyrimethamine controls mycobacterial

infection-induced vascular permeability and mycobacterial burden.

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Infection-induced vascular pathologies are a side effect of the immune response

to contact with a range of pathogens. Mycobacteria, including Mycobacterium

tuberculosis, are particularly adept at co-opting vascular leakiness as a

survival mechanism to shape the host immune response and impede the delivery of

antibiotics to sites of infection. Here using the zebrafish-Mycobacterium

marinum infection model, we confirm a critical role for Signal transducer and

activator of transcription 3 (STAT3) in mediating infection-induced vascular

permeability, and demonstrate the ability of FDA-approved drugs atovaquone

(Mepron) and pyrimethamine (Daraprim) to restore vascular barrier function

without compromising innate immune control of mycobacterial infection. We find

an additional antibiotic effect of pyrimethamine against M. marinum and M.

tuberculosis. Together our findings suggest pyrimethamine could be used as

adjunctive therapy against mycobacterial infection and explain the protective

effect of Daraprim prophylaxis against tuberculosis diagnosis in HIV positive

populations.

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**20. EBioMedicine. 2025 Aug 12;119:105885. doi: 10.1016/j.ebiom.2025.105885. Online ahead of print.**

Ultra-sensitive urinary lipoarabinomannan (LAM) immunoassay for tuberculosis

detection: a performance evaluation.

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**BACKGROUND:** The development of rapid non-sputum tests remains a global priority

to accelerate Tuberculosis (TB) diagnosis and treatment initiation. The only

WHO-recommended rapid diagnostic test (RDT), the Alere Determine TB

Lipoarabinomannan Ag (AlereLAM) has suboptimal sensitivity. A laboratory-based

electrochemiluminescence LAM assay (EclLAM) is the current sensitivity benchmark

for RDT development and the gold standard for urinary LAM detection. We assessed

the diagnostic accuracy of an ultra-sensitive, Plasmonic Fluor-linked

Immunosorbent LAM assay (PFLISA-LAM) compared to Sputum Xpert MTB/RIF, sputum

culture and urine EclLAM.

**METHODS:** We developed and evaluated the assay performance of PFLISA-LAM. Two

sub-studies were conducted using banked urine samples: 1. Preclinical study

using 337 well-characterised urine samples for cutoff determination and initial

evaluation of the performance of PFLISA-LAM compared to sputum Xpert MTB/RIF and

culture. 2. A Diagnostic accuracy assessment study using 77 blinded samples to

evaluate the performance of PFLISA-LAM compared to EclLAM versus microbiological

reference standard (MRS, Xpert positive and/or culture positive).

**FINDINGS:** PFLISA-LAM has a limit of detection (LOD) of 0.84 ± 0.9 pg/mL when

detecting purified LAM spiked in urine. In the preclinical study, the optimal

assay cutoff was determined to be 1.7 pg/mL. The sensitivities of PFLISA-LAM and

sputum Xpert MTB/RIF compared to culture were 51% (95% confidence interval [CI]:

43%-59%) and 62% (95% CI: 53%-70%). The specificities of PFLISA-LAM and Xpert

MTB/RIF were 99% (95% CI: 96%-100%) and 100% (95% CI: 100%-100%). Combining

PFLISA-LAM and Xpert MTB/RIF test data, an improved sensitivity of 76% (95% CI:

69%-83%) can be achieved. In the diagnostic study, the sensitivities of EclLAM

and PFLISA-LAM assays were 42% (95% CI: 27%-59%) and 73% (95% CI: 56%-85%). The

specificities of EclLAM and PFLISA-LAM were 95% (95% CI: 85%-99%) and 98% (95%

CI: 88%-100%).

**INTERPRETATION:** With better analytical and diagnostic sensitivity compared to

EclLAM, PFLISA-LAM can better detect urinary LAM in TB-positive cases.

PFLISA-LAM assay also demonstrated the capability to increase the diagnostic

value in detecting urinary LAM, complementing molecular tests, achieving

improved diagnostic outcome.

FUNDING: We report no external financial support for conducting the study.

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**21. PLoS Pathog. 2025 Aug 13;21(8):e1013350. doi: 10.1371/journal.ppat.1013350.**

**Online ahead of print.**

Infection with Mycobacterium tuberculosis alters the antibody response to HIV-1.

Zeeb M(1)(2), Kusejko K(1)(2), Hartnack S(3), Pasin C(1)(2), Abela IA(1)(2),

Rusert P(2), Liechti T(2), Kadelka C(2), Notter J(4), Eichenberger A(5),

Hoffmann M(6), Hirsch HH(7)(8)(9), Calmy A(10)(11), Cavassini M(12), Labhardt

ND(13)(14), Bernasconi E(11)(15)(16), Günthard HF(1)(2), Kouyos RD(1)(2), Trkola

A(2), Nemeth J(1); Swiss HIV Cohort Study.

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**BACKGROUND:** Co-infection with Mycobacterium tuberculosis (MTB) differentially

modulates untreated HIV-1 infection, with asymptomatic MTB reducing HIV-1

viremia and opportunistic infections and active tuberculosis (TB) accelerating

AIDS progression. Here, we investigate antibody (Ab) responses to HIV-1 in

people with HIV (PWH) without MTB, with asymptomatic MTB, and with later

progression to active TB to elucidate MTB-associated effects on HIV-1 immune

control.

**METHODS:** Using the Swiss HIV Cohort Study (SHCS), we conducted a retrospective

study that included 2,840 PWH with data on MTB status and HIV-1-specific plasma

binding-/neutralizing-responses. We evaluated associations between MTB status

and binding-/neutralizing-responses while adjusting for key disease and

demographic parameters.

**RESULTS:** Among the included 2,840 PWH, 263 PWH had asymptomatic MTB based on

either a positive TST-/IGRA-test at the baseline (time of HIV-1 Ab measurement)

or on later progression to active TB. Compared to PWH without MTB infection, PWH

with asymptomatic MTB infection showed reduced HIV-1 Ab levels, both for Env

binding (e.g., IgG1 BG505 trimer antigen, p = 0.024) and neutralization of a

diverse panel of HIV-1 viruses (p = 0.012). Conversely, PWH (n = 32) who later

progressed to active TB (>180 days after baseline) demonstrated a significant

shift towards IgG3 in their HIV-1 Ab repertoire (p = 0.011), detectable in

median 3.8 years (IQR 2.4 - 8.7) before active TB onset.

**CONCLUSION:** Our data indicate that asymptomatic MTB infection and active TB

exert profound heterologous effects on HIV-1 specific Ab development. These

findings advance our understanding of host-pathogen dynamics and may have

implications for new diagnostic approaches in predicting future active TB.

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PMID: 40802847

**22. Rev Soc Bras Med Trop. 2025 Aug 8;58:e02162025. doi:**

**10.1590/0037-8682-0216-2025. eCollection 2025.**

The Tuberculosis Response and the Role of the BRICS in the Current Global

Emergency.

Kritski A(1)(2), Arcêncio R(3)(2), Tavora E(4), Chimara E(5)(2), Silva

PEA(6)(2), Silva JRLE(1)(2), Oliveira MM(7)(2), Andrade MK(1)(2), Trajman

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DOI: 10.1590/0037-8682-0216-2025

PMCID: PMC12333615

PMID: 40802433

**23. Rev Bras Epidemiol. 2025 Aug 8;28:e250041. doi: 10.1590/1980-549720250041.**

**eCollection 2025.**

Trends and clusters of tuberculosis treatment interruption among people

experiencing homelessness in Brazil: influence of individual, social and

programmatic factors.

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Endêmicas e Micobactérias Não Tuberculosas - Brasília (DF), Brazil.

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(SP), Brazil.

**OBJECTIVE:** To analyze temporal trends and state-level clusters of tuberculosis

treatment interruption indicators among the homeless population in Brazil.

**METHODS:** This is an ecological study, in which treatment interruption among

homeless people with tuberculosis was assessed from 2015 to 2023. Joinpoint

regression was used for trend analysis, stratified by sociodemographic and

epidemiological variables. State clusters were identified by k-means clustering

analysis, based on socioeconomic and programmatic indicators.

**RESULTS:** Tuberculosis treatment interruption increased among: men (average

quarterly percent change - AQPC=0.15; 95% confidence interval - 95%CI

0.04-0.29), individuals aged 40-59 years (AQPC=0.38; 95%CI 0.25-0.53), tobacco

users (AQPC=0.72; 95%CI 0.61-0.82), beneficiaries of social programs (AQPC=4.59;

95%CI 3.69-6.02), those without directly observed treatment (AQPC=0.49; 95%CI

0.39-0.63), without HIV coinfection (AQPC=0.38; 95%CI 0.30-0.51), and in the

North (AQPC=1.51; 95%CI 0.96-2.21) and Midwest (AQPC=0.83; 95%CI 0.17-1.59)

regions. According to the cluster analysis, cluster A had the lowest treatment

interruption rate, low AIDS incidence, and better programmatic indicators.

Cluster B had high poverty and low level of education and income, but strong

primary health care performance. Cluster C stood out for its higher human

development, better social indicators, and lower inequality. Cluster D

concentrated the worst outcomes: higher treatment interruption, greater

inequality, higher AIDS incidence, and weaker primary health care.

**CONCLUSION:** Socioeconomic and programmatic inequalities were evident in access

and attachment to tuberculosis treatment among people experiencing homelessness

in Brazil.

DOI: 10.1590/1980-549720250041

PMCID: PMC12333893

PMID: 40802343

**24. Public Health Chall. 2025 Aug 12;4(3):e70108. doi: 10.1002/puh2.70108.**

**eCollection 2025 Sep.**

Geospatial Distribution of Tuberculosis Incidence and Determinants of

Tuberculosis Treatment Outcomes in Nzema East Municipality, Ghana.

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(2)Ghana Health Service Accra Ghana.

**BACKGROUND:** Ghana has seen a notable rise in tuberculosis (TB) cases with mired

treatment outcomes. However, evidence suggests disparities in the incidence of

TB and its treatment outcomes across the country. Nzema East Municipality

specifically reported a 62.34% increase in TB incidence in 2023 compared to

2022. The study, therefore, aims to determine the geospatial distribution of TB

incidence and predictors of TB treatment outcomes in Nzema East Municipality.

**METHODS:** The study used a retrospective cohort with a quantitative approach,

utilising health records of 545 TB cases from 2018 to 2023 in Nzema East. Data

were processed with Microsoft Excel and analysed using ArcGIS Pro version 3.3.2,

Joinpoint Regression Programme 5.2.0 and STATA MP version 17.

**RESULTS:** The Moran's index was 0.03 (p < 0.001). All the subdistricts had at

least one settlement with 2-26 TB cases per square kilometre. Significant TB

hotspots were identified in the population-dense communities and mining

communities. Overall, the successful TB treatment outcome was 76.70%. There was

a significant decline in successful TB treatment outcomes from 2018 to the end

of 2020 and through 2023 (p = 0.03 and p < 0.001), respectively. Having at least one follow-up lab (aRR = 0.43; 95% CI = 0.32, 0.58) and having a treatment supporter (aRR = 0.56; 95% CI = 0.40, 0.79) lessens the risk of having an unsuccessful TB treatment outcome. Having started the TB treatment in 2020 increases the chances of having an unsuccessful outcome (aRR = 1.97; 95%

CI = 1.13, 3.43).

**CONCLUSION:** TB incidence in Nzema East was spatially dependent, with

statistically significant higher incidence in the highly populated and mining

communities. The overall successful treatment outcome is suboptimal, which

demands targeted intervention to mitigate these menaces.

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PMID: 40800027

**25. Protein Pept Lett. 2025 Aug 11. doi: 10.2174/0109298665398349250728195645.**

**Online ahead of print.**

F18 Promiscuous Epitope of Acr1 Protein of Mycobacterium tuberculosis Induces

the Secretion of IL-10 and Tregs But Not IL-6.

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**INTRODUCTION:** Mycobacterium tuberculosis (Mtb) is a Gram-positive bacterium that

causes tuberculosis (TB). It remains viable for extended periods within host

macrophages by entering a dormant state. Alpha crystallin 1 (Acr1) is a 16 kDa

protein of Mtb and is reported to be highly upregulated in latent TB. Acr1

suppresses the host's immune system by impairing the differentiation and

maturation of dendritic cells and macrophages. We hypothesize that Mtb

judiciously utilizes its Acr1 protein to paralyse the immune system of the host

by inducing the release of IL-10 and generating an immunosuppressive

environment.

**METHODS:** We employed in silico tools to identify highly promiscuous,

IL-10-inducing and IL-6- non-inducing epitopes of Mtb. Moreover, the selected

epitope was synthesized and tested for its suppressive activity and generation

of Tregs.

**RESULTS:** We identified the presence of a specific epitope in Acr1 (F18) that is

responsible for bolstering the release of IL-10 and Tregs through in silico

tools and verified the activity by in vitro assays. In hPBMCs, the F18 epitope

could suppress the proliferation of CD4 T cells stimulated with PHA and expand

the pool of Tregs in a dose-dependent manner.

**DISCUSSION:** The F18 epitope from Mtb's Acr1 protein promotes IL-10 and Treg

responses without triggering pro-inflammatory IL-6, suggesting a potential

immunoregulatory role. While it holds potential for treating autoimmune

diseases, its impact on infection tolerance in tuberculosis should be further

investigated.

**CONCLUSION:** Our findings suggest that the F18 epitope induces IL-10 production

and Treg differentiation while inhibiting CD4+ T cell proliferation and IL-6

secretion, thereby promoting an immunosuppressive environment. Furthermore, this

study highlights the potential of Acr1 and its immunosuppressive epitope F18 as

therapeutic agents for inducing suppressive Tregs in the management of

autoimmune diseases.

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epub@benthamscience.net.

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PMID: 40798978

**26. Sci Rep. 2025 Aug 12;15(1):29586. doi: 10.1038/s41598-025-14734-1.**

Pyrazolopyridine pyrimidone hybrids as potential DprE1 inhibitors, design,

synthesis and biological evaluation as antitubercular agents.

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Tuberculosis (TB) remains a major global health challenge. This study presents

the design, synthesis, and evaluation of some novel

pyrazolo[3,4-b]pyridine-pyrimidone derivatives targeting Mycobacterium

tuberculosis (Mtb). The compounds were assessed for anti-tubercular activity

using the Microplate Alamar Blue Assay (MABA) against the Mtb H37Rv strain. Key

derivatives (8 and 14) showed significant activity with minimum inhibitory

concentration (MIC) values of 3.12 µg/mL, 12.5 µg/mL, respectively, comparable

to the standard drugs and are nontoxic at their effective concentration as

anti-TB agents. Molecular docking studies demonstrated strong binding

interactions with DprE1 and Mtb-DHFR enzymes, suggesting inhibition of these

critical proteins. Further computational analyses, including density functional

theory (DFT) and molecular dynamics simulations, confirmed the binding stability

of the compounds to the target proteins. Overall, these

pyrazolo[3,4-b]pyridine-pyrimidone derivatives are potential leads for further

development as future therapeutics for treating drug-resistant TB.

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DOI: 10.1038/s41598-025-14734-1

PMCID: PMC12343961

PMID: 40797008

**27. Sci Rep. 2025 Aug 13;15(1):29617. doi: 10.1038/s41598-025-15093-7.**

Genomic decoding of drug-resistant tuberculosis transmission in Thailand over

three decades.

Thawong N(#)(1)(2), Srilohasin P(#)(3), Phelan JE(1), Phornsiricharoenphant

W(4), Tongsima S(4), Suriyaphol P(3), Prammananan T(4), Faksri K(5), Sawaengdee

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Thailand has a high burden of tuberculosis, with control efforts hindered by

drug-resistant Mycobacterium tuberculosis (Mtb). The increasing use of

whole-genome sequencing (WGS) of Mtb offers valuable insights for clinical

management and public health surveillance. WGS can be used to profile drug

resistance, identify circulating sub-lineages, and trace transmission pathways

or outbreaks. We analysed WGS data from 2,005 Mtb isolates collected across

Thailand from 1994-2020, including 816 retrieved and 1,189 newly sequenced

samples, with most isolates being multidrug-resistant (MDR-TB). Most isolates

are lineage two strains (78·3%), primarily the Beijing sub-lineage (L2.2.1).

Drug resistance profiling revealed substantial isoniazid and rifampicin

resistance, and 67·3% classified as MDR-TB. Phenotypic and genotypic drug

susceptibility testing showed high concordance (91·1%). Clustering analysis

identified 206 transmission clades (maximum size 288), predominantly with

MDR-TB, especially in Central and Northeastern regions. One cluster (n = 22)

contains the ddn Gly81Ser mutation, linked to delamanid resistance, with some

members pre-dating drug roll-out. In the largest cluster (n = 288), containing

isolates spanning two decades, we applied transmission reconstruction methods to

estimate a mutation rate of 1·1 × 10-7 substitutions per site per year. Overall,

this study demonstrates the value of WGS in uncovering TB transmission and drug

resistance, offering key data to inform better control strategies in Thailand

and elsewhere.

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PMCID: PMC12344131

PMID: 40796628

**28. Transplant Proc. 2025 Aug 11:S0041-1345(25)00365-3. doi:**

**10.1016/j.transproceed.2025.07.018. Online ahead of print.**

Kidney Transplantation From a Brain-Dead Deceased Donor With Active

Tuberculosis.

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Tuberculosis is one of the most common infections on a global scale. While in

the 21st century it is practically endemic in some parts of the world, it poses

as a constant threat to immunocompromised transplant patients. Apart from

standards ways of transmission, transplant patients face another cause of

transmission, infected donors. We present a case depicting two kidney

transplantations from the same brain-dead deceased donor with active pulmonary

tuberculosis.

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PMID: 40796391

**29. Clin Infect Dis. 2025 Aug 12:ciaf451. doi: 10.1093/cid/ciaf451. Online ahead of print.**

Retrospective Cohort Analysis for Identification of Discordant

Rifampicin-resistant Xpert MTB/RIF Assay Results in South Kivu, Eastern

Democratic Republic of the Congo, a High Burden Tuberculosis Setting.

Bisimwa BC(1)(2)(3)(4), Kiselinova M(5), Cuella I(3), Rigouts L(3)(6), Bulabula

ANH(1), Byela V(1)(2), Chirambiza JP(7), Mulume E(7), Birembano F(7), Katoto

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**BACKGROUND:** The Xpert assay has revolutionized the rapid detection of resistance

to rifampicin. However, Xpert has its pitfalls. We explored potential

determinants of false-positive rifampicin resistance when using Xpert, aiming to

refine the precision of TB diagnostics and subsequently contribute to better

patient outcomes.

**METHODS:** This is a retrospective cross-sectional analysis of archived Xpert

files from the South Kivu province, used to diagnose MTB between 2013 and 2018.

Xpert cycle threshold was extracted for each molecular beacon probe and ΔCt was

calculated. We used the MTBDRplus line probe assay, which covers the same 81bp

RRDR, as reference test.

**RESULTS:** Of 1900 samples positive for MTB, 220 (11.2%) were rifampicin

resistant. Of the 141 patients' sputum samples that had results for both Xpert

and MTBDRplus, 45 (31.9%) showed discordant results with Xpert, indicating

rifampicin resistance while MTBDRplus indicated rifampicin susceptibility,

suggesting false-positive rifampicin resistance detection by Xpert,

predominantly in samples with very low (Ct>28, OR 2.23, 95% CI 1.30-3.82) or low

(Ct 22-28, OR 1.81, 95% CI 1.21-2.71) bacterial loads. Probe E was the most

frequently missed probe, followed by multiple probe dropouts or absence of probe

binding (OR 1.5, 95% CI 0.731-3.076).

**CONCLUSION:** Our findings indicate that low and very low MTB bacterial loads in

sputum is strongly associated with discordant rifampicin resistance results when

using Xpert. Further research into underlying mechanisms is needed to establish

causality definitively.

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**30. Lab Med. 2025 Aug 11:lmaf046. doi: 10.1093/labmed/lmaf046. Online ahead of**

**print.**

Comparison of active and dormant Mycobacterium tuberculosis DosR/DevR regulon

polymerase chain reaction-restriction fragment length polymorphism patterns.

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**INTRODUCTION:** This retrospective cross-sectional study aimed to evaluate the

differences between the restriction fragment length polymorphism (RFLP) patterns

of the dormancy survival regulator (DosR) regulon in latent tuberculosis vs

active disease.

**METHODS:** Sputum samples from 90 patients with active Mycobacterium tuberculosis

infection were collected. The presence of the devR, devS, and dosT genes in

active and induced dormant M tuberculosis infection was evaluated using

polymerase chain reaction (PCR). In addition, the differences between the

restriction enzyme digestion of these genes were determined using the RFLP

method.

**RESULTS:** The devR gene was much more prevalent in dormant than in active

samples, with statistical significance set at P = .033. The PCR-RFLP patterns

obtained from the effect of the AciI endonuclease on devR, the EaeI and HincII

endonucleases on devS, and the HaeIII and AciI endonucleases on dosT showed a

statistically significant difference between the active and dormant groups

(P = .001, P = .01, P = .008, P = .001, and P = .001, respectively), and this

difference was associated with more diverse patterns in the active group.

**DISCUSSION:** Results suggested that the DosR regulon may have more nucleotide

variations at the active stage. This study is the first to investigate the devR,

devS, and dosT genes using PCR-RFLP as a cost-effective and straightforward

method.

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**31. Clin Microbiol Infect. 2025 Aug 10:S1198-743X(25)00392-1. doi:**

**10.1016/j.cmi.2025.08.001. Online ahead of print.**

Systematic investigation of baseline nosocomial transmission of tuberculosis in

the Kyrgyz Republic, Central Asia.

Hoffmann H(1), Utpatel C(2), Iskakova A(3), Ahmedov S(4), Antonenka U(5), Dreyer

V(2), Sahalchyk E(5), Kadyrov A(6), Corbett C(7), Niemann S(2), Kalmambetova

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**OBJECTIVES:** Controlling tuberculosis (TB) transmission is of paramount

importance for combating the TB pandemic. Although TB hospitals are considered

hotspots of transmission, systematic longitudinal studies examining the

underlying incidence and possible risk factors of nosocomial TB transmission are

lacking. The objectives of this study were to detect nosocomial transmission

events over a 20 month period using whole genome sequencing (WGS) of

Mycobacterium tuberculosis complex (MTBC) isolates collected from 563 patients

with pulmonary TB hospitalized in the Kyrgyz Republic.

**METHODS:** Whole genome sequencing (WGS) was performed on 698 Mycobacterium

tuberculosis complex (MTBC) isolates, including 563 first isolates recovered

from participants within four weeks of hospitalization and 135 follow-up

isolates from treatment control samples collected at least four weeks apart. All

participants' roommates were recorded over the whole study period.

**RESULTS:** The cohort represented >95% of TB patients hospitalized at the study

sites during the follow-up period of 53,372 hospitalization days. Genome-based

cluster analysis revealed that 173 of the 563 (30.7%) first isolates fell into

56 clusters (<5 SNPs). Two nosocomial TB transmissions from index cases to their

roommates were proven. In addition, five potential transmissions were observed

between patients who shared time, but not a room, in the hospital or where the

index case was not identified. Most transmitted strains were more resistant than

the previous one.

**CONCLUSION:** Within-community transmission of MTBC is highly active in

Kyrgyzstan. With 13.7 per 1000 patient years (95%-CI: 1.6-49.5), we observed

markedly higher rates of nosocomial transmission than reported in previous

WGS-based studies.

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PMID: 40796011

**32. Br J Clin Pharmacol. 2025 Aug 12. doi: 10.1002/bcp.70195. Online ahead of print.**

Model-based evaluation of the interaction between ritonavir-boosted atazanavir

and rifampicin in Ugandan adults with HIV.

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D'Avolio A(4), Atoyebi S(5), Wiesner L(1), Svensson EM(6)(7), Waitt C(2)(5),

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(5)Department of Women's and Children's Health, University of Liverpool,

Liverpool, United Kingdom.

(6)Department of Pharmacy, Uppsala University, Uppsala, Sweden.

(7)Department of Pharmacy, Radboud University Medical Center, Nijmegen,

Netherlands.

**AIM:** Concomitant treatment of tuberculosis (TB) and human immunodeficiency virus

(HIV) is complicated by drug-drug interactions (DDI). This analysis aimed to

characterize the DDI between ritonavir-boosted atazanavir (ATV/r) and rifampicin

in plasma and peripheral blood mononuclear cells (PBMC).

**METHODS:** The DERIVE study (NCT04121195) recruited Ugandan adults with HIV (not

TB) on ATV/r-based second-line antiretroviral therapy, and collected intensive

plasma and PBMC pharmacokinetic samples during four visits: (i) standard-dose

ATV/r 300/100 mg QD, (ii) same ATV/r regimen adding rifampicin 600 mg QD, (iii)

doubling ATV/r to BID with rifampicin 600 mg QD and (iv) ATV/r 300/100 mg BID

with rifampicin increased to 1200 mg QD. ATV/r plasma and PBMC concentrations

were analysed with population pharmacokinetic modelling in NONMEM.

**RESULTS:** Twenty-six participants (23 female) were enrolled, with median age and

weight of 44 years and 67 kg, respectively. A two-compartment model with an

effect-compartment effectively described atazanavir concentrations in plasma and

PBMC. Rifampicin increased atazanavir clearance threefold, while decreasing its

bioavailability and absorption rate. Doubling dosing frequency of ATV/r largely

mitigated the interaction with rifampicin, restoring the proportion of simulated

participants achieving the targeted trough atazanavir concentration of

0.014 mg/L to 99%. Rifampicin did not affect the ratio of atazanavir

concentration between PBMCs and plasma.

**CONCLUSION:** Metabolic induction by rifampicin accounts for the decrease in

plasma exposure of ATV/r. Doubling the ATV/r dosing frequency to BID effectively

mitigated this interaction. The plasma exposure of ATV/r mirrored that in PBMCs,

suggesting that for these drugs, plasma concentrations provide a reliable

reflection of site-of-action exposures.

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Wiley & Sons Ltd on behalf of British Pharmacological Society.

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PMID: 40796001

**33. Comput Biol Med. 2025 Aug 11;196(Pt C):110858. doi:**

**10.1016/j.compbiomed.2025.110858. Online ahead of print.**

Mathematical model for analysing the interplay between income, nutrition, and

tuberculosis dynamics.

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This paper presents a mathematical framework to investigate the impact of

socio-economic factors, specifically income and nutrition on the transmission

dynamics of TB. Inadequate nutrition, driven by the unaffordability of a healthy

diet in low and middle income countries, is a major barrier to achieve the WHO's

End Tuberculosis (TB) strategy. To address this issue, the authors have

developed a compartmental model by incorporating transmission rate β̃(M),

recovery rate γ̃(N), and TB-related mortality rate μ̃tb(N), as functions of

income and nutrition levels. The model captures the dynamical interaction

between these factors and their influence on disease spread, and mortality. In

this work, the authors have calculated the reproduction number which quantifies

the contagious nature of the disease by using next generation matrix approach

and analysed its sensitivity using normalized forward sensitivity index

approach. Through numerical simulations, the authors have analysed various

scenarios such as including voluntary and mandatory nutrition uptake, as well as

varying nutrition and income levels within the population. The results of the

present model show that improved nutrition and higher income significantly

reduce TB transmission and mortality, but the disease burden can only be fully

alleviated when both factors are simultaneously addressed. The sensitivity

analysis for the reproduction number highlights that reducing the transmission

rate is essential for bringing the reproduction number R0 below the crucial

threshold of 1. This study emphasizes the necessity of holistic interventions

that improve both nutrition and socio-economic conditions for effective TB

control.

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DOI: 10.1016/j.compbiomed.2025.110858

PMID: 40795476

**34. J Immunol. 2025 Aug 8:vkaf186. doi: 10.1093/jimmun/vkaf186. Online ahead of**

**print.**

Single-cell profiling of blood and cerebrospinal fluid in tuberculous

meningitis.

Tram TTB(1), Garner LC(2), Thai LNH(1), Nhat LTH(1), Thu DDA(1), Nghia HDT(3),

Van LH(1), Thwaites GE(1)(4), Ha VTN(1), Klenerman P(2)(5)(6), Thuong NTT(1)(4).

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Tuberculous meningitis (TBM) is the most severe form of tuberculosis, with a

fatality rate of 20% to 50% in treated individuals. Although corticosteroid

therapy can increase survival in HIV-negative people with TBM, better

antimicrobial and host-directed therapies are required to improve outcome. There

is, therefore, a need to better understand local immunopathologic pathways.

Despite its power in identifying disease-specific cellular profiles, single-cell

RNA sequencing (scRNA-seq) has been underutilized in cerebral samples in brain

infection. We employed scRNA-seq to analyze fresh pretreatment cerebrospinal

fluid (CSF) from 4 TBM patients, along with paired PBMCs. While 29 cell subtypes

were present in both tissues, their relative abundance varied significantly. In

particular, CSF was enriched with highly inflammatory microglia-like

macrophages, GZMK+CD8+ effector-memory T (TEM) cells, and CD56bright NK cells.

The latter 2 subsets exhibited reduced cytotoxicity compared with their

blood-enriched counterparts, namely cytotoxic GNLY+CD8+ TEM and CD56dim NK

cells, respectively. Across multiple cell types, inflammatory signaling pathways

were increased and oxidative phosphorylation was decreased in CSF compared to

PBMCs. This study highlights the value of scRNA-seq for exploring CSF

immunopathogenesis in TBM patients and offers a resource for future studies

investigating the pathophysiology of TBM and other brain infections, including

potentially targetable cell populations linked with immune-mediated pathology.

© The Author(s) 2025. Published by Oxford University Press on behalf of The

American Association of Immunologists.

DOI: 10.1093/jimmun/vkaf186

PMID: 40795373

**35. J Trop Pediatr. 2025 Aug 8;71(5):fmaf034. doi: 10.1093/tropej/fmaf034.**

Comparison of Xpert® MTB/RIF and Xpert® MTB/RIF Ultra in pediatric pulmonary

tuberculosis diagnosis.

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The World Health Organization (WHO) recommends Xpert® MTB/RIF (Xpert) and its

advanced version, Xpert® MTB/RIF Ultra (Xpert Ultra), as first-line diagnostic

tests for detecting pulmonary tuberculosis (PTB) and rifampicin resistance in

children suspected of having the disease. Respiratory specimens (gastric

lavage/bronchoalveolar lavage/sputum/endotracheal aspirate) obtained from 116

children with presumptive PTB were simultaneously processed using liquid medium

culture, Xpert assay, and Xpert Ultra assay. Among the specimens from 116

children, six were excluded due to culture contamination (n = 5) or error in

Xpert Ultra results (n = 1). Among the remaining 110 specimens, 20 were positive

by liquid culture. The former and latter, of the two comparator tests gave a

sensitivity of 90% and 95%, respectively. The respective specificity was 93.3%

and 88.9%. Xpert Ultra showed a statistically significant slightly higher

sensitivity than Xpert. Xpert Ultra showed slightly higher sensitivity than

Xpert, with a minimal loss in specificity, partly due to the inclusion of trace

results, which help detect paucibacillary cases.

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PMID: 40795255

**36. PLoS Negl Trop Dis. 2025 Aug 12;19(8):e0013355. doi:**

**10.1371/journal.pntd.0013355. Online ahead of print.**

Perception of cattle owners towards risk of raw milk consumption for bovine

tuberculosis transmission in Hosanna, Central Ethiopia: A community-based

cross-sectional study.

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Central Ethiopia.

**INTRODUCTION:** Zoonotic diseases account for more than 61% of human diseases. Raw

milk is a major source of bovine tuberculosis (BTB) infection. However, there is

a lack of comprehensive information on the community's perception of the risks

associated with raw milk consumption for BTB transmission in Ethiopia. This

study aimed to investigate the awareness of cattle farmers in Hosanna, southern

Ethiopia, regarding the risk of bovine tuberculosis transmission through the

consumption of raw milk.

**METHODS:** We conducted a community-based cross-sectional study among a randomly

selected sample of households (n = 462) in Hosanna Town. We used pre-tested and

structured questionnaires to collect data. The perception of the risk of bovine

tuberculosis transmission due to raw milk consumption was assessed using the

mean score of each outcome. Scoring above the mean on the four constructs of the

Health Belief Model (HBM) is equivalent to having a high level of awareness of

the risk of BTB transmission from raw milk consumption. 95% confidence intervals

(CI) of the corresponding estimates were set to indicate significance.

**RESULTS:** The analysis results showed that 65.0% of the cattle farmers in the

study area had a low awareness of the risk of BTB transmission from drinking raw

milk. The perception of the risk of BTB transmission due to raw milk consumption

was significantly lower in males (adjusted odds ratio (AOR): 2.6 CI 1.51, 4.68)

and widowed (AOR: 3.7, CI 1.43, 9.92) participants.

**CONCLUSION:** In conclusion, the perception of the risk of raw milk consumption

for BTB transmission is low in this study. Thus, it is worthwhile to include

measures to enhance the perception of cattle owners toward the risk of raw milk

consumption as a fundamental practice to control BTB transmission.

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the original author and source are credited.

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PMID: 40794787

**37. Metabolomics. 2025 Aug 12;21(5):118. doi: 10.1007/s11306-025-02320-5.**

Mycobacterium tuberculosis curli pili facilitates pathogenicity by modulating

central carbon metabolism.

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**INTRODUCTION:** Strategies specifically targeting the initial host-pathogen

interactions, hold great promise in the identification of accurate biomarkers

for tuberculosis (TB) prevention interventions. Mycobacterium tuberculosis (Mtb)

curli pili (MTP) (encoded by mtp/Rv3312A), a surface adhesin utilised by the

pathogen to interact with host receptor cells, has been reported as a suitable

target for TB diagnostic and therapeutic strategies. Previous "omics" studies

highlighted the role MTP potentially plays in Mtb central carbon metabolism

(CCM). However, its precise contribution to metabolism remains unknown.

**OBJECTIVES:** This study aimed to examine the role of MTP in the bioenergetic

metabolism of Mtb, using bedaquiline (BDQ) to inhibit ATP production through

oxidative phosphorylation (OXPHOS), extracellular flux analysis, Mtb wildtype

(WT), ∆mtp deletion mutant, and mtp-complemented strains. The role of MTP in

regulation of CCM was assessed using 13C6-metabolic flux analysis.

**RESULTS:** MTP was associated with increased bacterial respiration and decreased

carbon catabolism via glycolysis in response to the inhibition of ATP synthase

by BDQ. The dependence of Mtb Δmtp on OXPHOS for energy production was

demonstrated to be greater than the WT and mtp-complemented strains. In

addition, metabolic flux profiles revealed that in the Δmtp mutant, CCM was

dysregulated by decreasing flux through glycolysis, tricarboxylic acid cycle,

glyoxylate and dicarboxylate metabolism, and the pentose phosphate pathway in

comparison to the WT.

**CONCLUSION:** These novel findings show that MTP is associated with the regulation

of bioenergetics and metabolism pathways and substantiate MTP as a potential

biomarker for TB diagnostics/therapeutics, and a novel target for vaccine/drug

development.

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DOI: 10.1007/s11306-025-02320-5

PMCID: PMC12343700

PMID: 40794122 [Indexed for MEDLINE]

**38. bioRxiv [Preprint]. 2025 Aug 8:2025.07.15.664002. doi:**

**10.1101/2025.07.15.664002.**

Spatial profiling reveals TREM2+ macrophages as central to Mycobacterium

tuberculosis pathogenesis in human pulmonary tuberculosis.

Teles RMB, Benabdessalem C, Perrie J, Wei C, West J, de Andrade Silva BJ,

Andrade PR, Mansky L, Divakar P, Fischbacher L, Lam K, Ma F, Rategh K, Pillai A,

French SM, Romdhane E, Barbouche MR, Klechevsky E, Colonna M, Steyn AJC,

Bensinger S, Barber DL, Rammeh S, Dulai PS, Bryson BD, Pellegrini M, Belisle JT,

Bloom BR, Modlin RL.

Tuberculosis (TB) remains a major global health challenge. While organized

granulomas have long been the focus of TB pathogenesis research, the early

development of TB pneumonia typically preceding granuloma formation has been

underexplored. Using spatial transcriptomics, high-resolution proteomics, and

scRNA-seq on human pulmonary TB lesions, we reveal a striking

compartmentalization of immune responses between early pneumonia and mature

granulomas. The immunologic composition of granulomas was distinct from the

pneumonia; granulomas are enriched for antimicrobial gene expression in both

macrophages and T cells and show reduced bacterial antigen burden. In contrast,

TREM2-expressing foamy macrophages are the predominant cell type occupying

alveolar spaces in TB pneumonia with T cells infrequent. These TREM2⁺

macrophages exhibit a lipid-associated gene program, accumulate lipid droplets,

and harbor Mycobacterium tuberculosis antigens and mRNA corresponding to

increased bacterial viability in vitro. We further show that the M. tuberculosis

virulence lipids, PDIM and mycolic acids, potently induce and activate TREM2

signaling in TREM2-expressing macrophages, promoting an intracellular

environment permissive for bacterial growth. These findings establish TREM2⁺

macrophages as an early niche for M. tuberculosis survival and implicate TB

pneumonia as a critical stage in disease transmission. Targeting this foamy

macrophage population may offer opportunities to interrupt early TB progression

and transmission.

DOI: 10.1101/2025.07.15.664002

PMCID: PMC12338719

PMID: 40791339

**39. BMC Med Inform Decis Mak. 2025 Aug 11;25(1):301. doi:**

**10.1186/s12911-025-03139-9.**

Risk factors for tuberculosis treatment outcomes: a statistical learning-based

exploration using the SINAN database with incomplete observations.

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**BACKGROUND:** Understanding early predictors of treatment outcomes allows better

outcome prediction and resource allocation for efficient tuberculosis (TB)

management.

**OBJECTIVES:** This study aimed to predict treatment outcomes of TB patients from a

real-world population-wide health record dataset with a significant rate of

incomplete observations. In addition, potential risk factors associated with

death during TB treatment were investigated.

**METHODS:** We exploited the upweighting approach and multiple imputation analysis

(MIA) to address the extreme imbalance in responses and missing data. Three

algorithms were employed for TB treatment outcome prediction, including logistic

regression (LOGIT), random forest, and stochastic gradient boosting. The three

models exhibited similar performance in predicting the treatment outcomes.

Moreover, an interpretation of LOGIT was conducted, adjusted odds ratios (aORs)

were computed, and the interpretation results were compared between MIA and

complete case analysis (CCA).

**RESULTS:** MIA was an appropriate method for coping with missing data. In

addition, compared to CCA, the interpretation results of the MIA-derived LOGIT

showed more statistically significant covariates associated with TB treatment

outcomes. In MIA, factors such as TB clinical form involving both pulmonary TB

and extrapulmonary TB [aOR = 3.077, 95% confidence interval (CI) = 2.994-3.163],

retreatment after abandonment (aOR = 2.272, 95% CI = 2.209-2.338), and the

absence of isoniazid (aOR = 2.072, 95% CI = 1.892-2.269) or rifampicin

(aOR = 1.968, 95% CI = 1.746-2.218) in the treatment regimen were associated

with increased odds of death.

**CONCLUSION:** In conclusion, our results shed light on the potential risk factors

for death during TB treatment and suggest the use of simple yet interpretable

LOGIT for the prediction of TB treatment outcomes.

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**40. Trials. 2025 Aug 11;26(1):285. doi: 10.1186/s13063-025-08978-5.**

Community and Universal Testing for TB among close contacts of microbiologically

confirmed pulmonary TB patients in two high TB burden countries: a protocol for

a pragmatic cluster-randomised control trial.

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Lalashowi J(4), Matete M(5), Kubeka G(2), Tsope L(2), Mukora R(2), Mudzengi

D(2), Nielson T(2), Lönnroth K(6), Niemann S(7), Rangaka M(3), Velen K(2),

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**BACKGROUND:** Tuberculosis (TB) symptom screening and testing using either smear

microscopy or GeneXpert MTB/RIF Ultra (Xpert Ultra) have been the mainstay for

diagnosing TB disease in case finding. Reliance on symptom-based TB screening

results in missed TB cases, and universal TB testing approach might be more

suitable to find missing TB cases in high-risk populations. Universal TB testing

involves testing for TB disease regardless of TB symptoms in those at risk of

TB. However, limited evidence exists to support its adoption including

cost-effectiveness. In this study, we will evaluate the effectiveness of

universal TB testing for detection of TB and uptake of TB preventive therapy

(TPT) among eligible household and community contacts in high TB settings as per

country guidelines.

**METHODS:** This is a pragmatic cluster-randomised trial conducted in Lesotho and

Tanzania. Drug-sensitive TB (DS-TB) index patients aged ≥ 18 years, who have at

least one contact, will be enrolled if they are microbiologically confirmed with

TB within ≤ 6 weeks of diagnosis at the time of recruitment by study team at

health facilities in selected districts or regions. Each TB index patient and

their contact(s) will be randomised into either universal TB testing or standard

TB screening arms. Household and community contacts listed by each TB index case

will be enumerated and invited to participate in the study after providing

informed consent or assent during household visits. The study has four

sub-studies including health economics and modelling, paediatrics, microbiology,

and socio-behavioural. A preparatory cross-sectional study will be conducted

before delivery of the pragmatic cluster-randomised trial. It will determine the

prevalence of TB infection (TBI), TPT eligibility in household contacts (HHCs),

and compare the performance of QuantiFERON-TB-Gold-Plus (QFT-Plus) and QIAreach

for diagnosing TBI among HHCs of TB index patients. Cluster-randomised trial and

community contact tracing will be conducted in phase II.

**SIGNIFICANCE:** This trial will provide evidence for a more intensive approach

which is hypothesised to increase cost-effectiveness of TB case finding. In

addition, it will provide evidence for high TB burden countries with inherently

different cost structures compared to intermediate and low burden settings where

previous cost-effectiveness analyses have been undertaken.

**CLINICAL TRIAL REGISTRATION NUMBER:** BMC Trial Registry ISRCTN10003903.

Registered on December 22, 2020. Protocol version number and date. Version 1.2,

dated 15 January 2023. Date recruitment began. 1 March 2022. Estimated date of

recruitment completion. 31 July 2025.

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**41. J Med Case Rep. 2025 Aug 11;19(1):402. doi: 10.1186/s13256-025-05455-0.**

Incidental diagnosis of Bardet-Biedl syndrome in a case of abdominal

tuberculosis: a case report.

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**BACKGROUND:** Bardet-Biedl syndrome is a rare autosomal recessive disease

occurring due to a ciliopathic genetic defect. It is caused by mutations in

genes encoding proteins vital for the BBSome complex. This complex is essential

for ciliary function and cellular signaling. It has multisystem involvement and

presents with a variety of phenotypes.

**CASE PRESENTATION:** A 30-year-old adult male patient, Indian by ethnicity,

presented with a 2-week history of ascites and dyspnea. The ascitic fluid

analysis confirmed abdominal tuberculosis. However, the patient showed other

symptoms and signs of a syndromic nature. The patient has been entirely blind

since the age of 9 years, with confirmed retinitis pigmentosa. The other

complaints were progressive weight gain and cognitive impairment. Examination

showed central obesity, almond-shaped eyes, moon-shaped face, and hexadactyly in

the left lower limb. Liver functional tests, renal function tests, lipid

profile, and ultrasonography of the abdomen were abnormal. Beales diagnostic

criteria confirmed Bardet-Biedl syndrome. The patient was treated for abdominal

tuberculosis, and psychosocial support and nutritional counseling were provided.

**CONCLUSION:** Effective treatment of Bardet-Biedl syndrome requires genetic

counseling and a personalized care plan that includes a multidisciplinary team,

regular monitoring, and supportive services such as neuropsychological and

psychiatric care and family support. This case also increases clinicians'

awareness of the presentation of Bardet-Biedl syndrome and the diagnosis in

settings without advanced diagnostic modalities.

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DOI: 10.1186/s13256-025-05455-0

PMCID: PMC12341301

PMID: 40790500 [Indexed for MEDLINE]

**42. Gut Pathog. 2025 Aug 11;17(1):59. doi: 10.1186/s13099-025-00736-x.**

Gut microbiota profile in newly diagnosed pulmonary tuberculosis patients: an

exploratory pilot study in southern India.

Baral T(1), Fayaz SMA(2), Manu MK(3), Kudru CU(4), Singh J(5), Mukhopadhyay

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Emerging evidence suggests the link between pulmonary tuberculosis (PTB) and gut

microbiota dysbiosis. This is the first study from the southern Indian

population that characterized the gut microbiota of PTB patients using 16 S

amplicon sequencing. The analysis revealed a significant reduction in gut

microbial diversity among PTB patients, with particularly lower alpha diversity

(Chao1 index, p ≤ 0.0001) than healthy controls (HC). This was further depleted

during antitubercular therapy (ATT). Beta diversity indicated distinct

clustering in all the groups (p < 0.05). Subgroup analyses showed that

supplementation of probiotics with ATT improved microbial richness and

diversity. However, broader shifts in composition were not observed. At the

genus level, specific taxa were upregulated or downregulated in PTB patients

compared to HC. Functional analysis showed a depletion in biosynthesis pathways

in PTB patients. Short-term probiotic supplementation had a partial effect on

microbial recovery but did not fully restore gut microbial diversity. These

findings highlight persistent dysbiosis in PTB patients, even after ATT.

Large-scale studies are needed to evaluate the role of microbiome-targeted

therapies to address this dysbiosis.

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DOI: 10.1186/s13099-025-00736-x

PMCID: PMC12337371

PMID: 40790221

**43. BMC Biotechnol. 2025 Aug 11;25(1):81. doi: 10.1186/s12896-025-01019-8.**

Nano delivery of MiR-146a and its effect study on genes involved in apoptosis

and autophagy pathways in lung cancer and tuberculosis.

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**BACKGROUND:** Tuberculosis (TB) and lung cancer (LC) are among the leading causes

of death worldwide and present serious challenges in diagnosis and treatment.

Therefore, developing new strategies for their treatment is crucial. MicroRNAs

(miRNAs) are biological molecules that play a critical role in regulating

essential processes, such as apoptosis and autophagy, in TB and LC by targeting

specific genes. Recently, carbon nanotubes functionalized with Polyethyleneimine

(CNT-PEI) to deliver miRNAs to target cells have been investigated to enhance

therapeutic effects.

**METHODS:** In this study, miR-146a was transfected into LC (A549), macrophages

infected with TB (THP1), and healthy lung cells (MRC5) using CNT-PEI. Then, the

expression of miR-146a and its target gene, TNF receptor-associated factor-6

(TRAF6), and other genes involved in apoptosis and autophagy pathways including

BCL-2, IL-6, tumor necrosis factor-alpha (TNFα), were measured using Real-Time

PCR. Finally, the effect of overexpression of miR-146a on these genes was

investigated in all three cell lines.

**RESULT:** The results showed successful transfection of miR-146a using the CNT-PEI

nano delivery system in LC and TB cell models. Then, increased expression of

miR-146 increased apoptosis and autophagy by targeting the TRAF6 gene and

affecting other genes such as BCL-2, IL-6, and TNFα through the NF-kB signaling

pathway.

**CONCLUSION:** The findings suggest an important role for miR-146a in TB and LC,

which regulates inflammatory responses and treats these diseases. However,

further studies are needed on using CNT-PEI in vivo, as well as the balance

between local anti-inflammatory and non-inflammatory factors.

© 2025. The Author(s).

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PMCID: PMC12337501

PMID: 40790202 [Indexed for MEDLINE]

**44. BMC Genomics. 2025 Aug 11;26(1):741. doi: 10.1186/s12864-025-11893-3.**

First whole-genome sequence of Mycobacterium avium subsp. silvaticum isolated

from a diseased Egyptian goose (Alopochen aegyptiaca).

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**BACKGROUND:** Among the non-tuberculous mycobacteria, Mycobacterium (M.) avium are

important pathogens for humans and/or animals. Currently, there are four M.

avium subspecies: subsp. hominissuis (Mah), subsp. paratuberculosis (Map),

subsp. avium (Maa), and subsp. silvaticum (Mas). While sufficient data is

available for the first three mentioned, only few reports exist on the

isolation, epidemiology and even less on the genetic equipment of Mas.

**RESULTS:** Here, Mas was isolated from an Egyptian goose that died of avian

tuberculosis. Subspecies identification was based on the presence of IS901 and

IS1245 as well as Mycobacterial Interspersed Repetitive Units-Variable Number

Tandem Repeat analysis demonstrating Mas specific profile INMV99 profile. During

cultural isolation, Mas showed preference for media with mycobactin

supplementation but was not limited to mycobactin-containing media. A closed

genome sequence was assembled using short- and long-read sequencing technology.

The genome sequence consisted of one circular chromosome of 4.84 Mb (GC content

69.3%) and no plasmid. It was highly similar to the only other available Mas

sequence (ANI 99.98%, GGDC 99.7%) and eight Maa sequences (ANI ≥99.88%, GGDC

≥98.9%), although all Maa genomes were larger (approx. 5 Mb). In silico

prediction of the metabolic pathways and gene content found that all Maa but no

Mas should be able to synthetize ergothioneine and the carotenoid neurosporene.

The analysis of the mycobactin cluster mbt-1 made it obvious that in Mas two of

the eleven mbt genes (mbtB and mbtE) were probably dysfunctional due

frameshift-based disruptions.

**CONCLUSIONS:** The first complete, high quality, closed genome sequence of a Mas

isolate closes a knowledge gap. Even if the collection of further genome

sequences is considered necessary, the now existing data set already enables a

deeper analysis of M. avium. The found differences in the Mas gene content

compared to the closest relative Maa seem to be stable and independent of

spatial (France, UK, Germany) and temporal (>40 years) differences on their

isolation. These data thus call into question the demand for merging the two

subspecies Maa and Mas into one, but further genome sequences from other Mas

strains are needed to answer this question conclusively.

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PMID: 40790159 [Indexed for MEDLINE]

**45. Metabolomics. 2025 Aug 11;21(5):107. doi: 10.1007/s11306-025-02304-5.**

Exploratory investigation of urinary alkanes and other volatile organic

compounds in paediatric patients with tuberculous meningitis.

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**BACKGROUND:** Tuberculous meningitis (TBM) is a disease caused by Mycobacterium

tuberculosis (M. tb) infection of the brain. Alkanes and other volatile organic

compounds (VOCs) are biologically important metabolites that are used by

infectious mycobacteria species for growth and survival strategies.

**OBJECTIVE:** This study investigated the altered alkanes and other VOCs in the

urine from paediatric cases with TBM.

**METHOD:** We used untargeted gas chromatography coupled with time-of-flight mass

spectrometry (GC-TOFMS) to analyse and compare all volatile, underivatised

compounds present in the urine from 27 confirmed cases of paediatric TBM over a

treatment period of six months, as well as a control group (n = 13).

**RESULT:** Four elevated alkanes (pentadecane, 5,7-dimethyl-undecane,

4,7-dimethyl-undecane, and 2,6-dimethyl-undecane), three alkenes (decreased

2,5-dimethyl-2-hexene and 4,4-dimethyl-1-pentene, and increased

3-methoxy-1-pentene), and three other VOCs of biological interest (decreased

2-butenoic acid methyl ester and 3-heptanone, and increased 2-pyrrolidinone)

were identified as statistically significant. These volatile compounds remained

perturbed during the TBM treatment.

**CONCLUSION:** This study discovered new systemic metabolic information about M. tb

in the host and the role of alkanes and VOCs in the potential persistence of M.

tb. We demonstrate the value of targeting alkanes and other VOCs for future

metabolomics studies of M. tb.

© 2025. The Author(s).

DOI: 10.1007/s11306-025-02304-5

PMCID: PMC12339628

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**46. BMJ. 2025 Aug 11;390:r1709. doi: 10.1136/bmj.r1709.**

UK's tuberculosis crisis deepens as doctors report rise in prison cases.

Bowie K(1).

Author information:

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DOI: 10.1136/bmj.r1709

PMID: 40789603

**47. Nat Prod Bioprospect. 2025 Aug 11;15(1):52. doi: 10.1007/s13659-025-00533-8.**

Harnessing Actinobacteria secondary metabolites for tuberculosis drug discovery:

Historical trends, current status and future outlooks.

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Tuberculosis (TB) is a leading infectious disease killer and one of the major

causes of deaths worldwide. Although TB is a curable and preventable disease, in

2023, approximately 10.8 million people fell ill with TB and there were an

estimated 1.25 million of deaths worldwide. Despite some research progress for

new drug candidates, drug repurposing, and new regimens, there is still an

urgent need for the new medicins to treat TB, especially due to the growing

cases of multidrug and extensively drug-resistant (MDR/XDR) strains. Drug

resistance is a challenging obstacle to TB care and prevention globally, making

TB harder and longer to treat, often with poorer outcomes for patients. The

Actinomycetota encompass Gram-positive bacteria that produce a milieu of

bioactive metabolites, including antibiotics, antiproliferative drugs,

immunosuppressive agents, and other important medical molecules. Actinomycetota

have a special place in the therapeutic arsenal to fight TB, as rifamycins,

aminoglycosides, and cycloserine are derived from Streptomyces species, one of

the most important genera in this phylum. Furthermore, hundreds of

antimycobacterial metabolites have been isolated from Actinomycetota and can

serve as effective drugs or useful agents for the discovery of new lead

compounds to combat TB. The present review covers more than 171 isolated

substances as potential antimycobacterial agents discovered between the years

1972 to 2024. Among the most potent compounds, with MIC in the submicromolar

range, steffimycins, ilamycins/rufomycins, nosiheptide, actinomycins, lassomycin

and boromycin are the most promising compounds. These compounds represent highly

promising candidates for development of new antitubercular drugs. Additionally,

some of these substances also demonstrated activity against resistant

Mycobacterium tuberculosis (Mtb) strains, which is particularly relevant given

the difficulty of treating MDR and XDR strains. Thus, actinobacteria have played

and continue to play an important role in fight TB, remaining a promising source

of antibiotic metabolites. Their unique metabolic diversity enables the

production of metabolites with innovative mechanisms of action, making them a

strategic reservoir for discovering therapies against untreatable forms of the

disease.

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DOI: 10.1007/s13659-025-00533-8

PMCID: PMC12339860

PMID: 40788464

**48. J Postgrad Med. 2025 Aug 11. doi: 10.4103/jpgm.jpgm\_126\_25. Online ahead of**

**print.**

Laboratory perspective of tuberculosis diagnosis -Test principles and report

interpretation.

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DOI: 10.4103/jpgm.jpgm\_126\_25

PMID: 40788279

**49. mSphere. 2025 Aug 11:e0003625. doi: 10.1128/msphere.00036-25. Online ahead of print.**

Characterization of PPE19 as a novel mediator of Mycobacterium

tuberculosis-macrophage interactions.

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Mycobacterium tuberculosis (Mtb) is a highly adapted human pathogen capable of

manipulating host immunity. This study demonstrates that PPE19, a member of the

PE/PPE protein family, facilitates Mtb adhesion to, and invasion of murine

macrophages. PPE19-coated microspheres showed enhanced uptake by macrophages

compared to control beads, while Mtb overexpressing ppe19 (Rv1361c) was

phagocytosed at a significantly greater rate than WT Mtb. ppe19 is identified as

pH responsive and displays reduced expression following macrophage entry. CRISPR

interference-mediated knockdown of two highly related PPE proteins, ppe18

(Rv1196) and ppe60 (Rv3478), revealed an additive reduction in Mtb's ability to

invade host macrophages, indicating a potential functional relationship.

Furthermore, the absence of an in vivo phenotype following murine infection with

a ppe19 knockout strain suggests functional redundancy within this PPE protein

family. Finally, PE13 has been identified here as a binding partner for PPE19,

characterizing another relationship presumed important for successful PPE

secretion. These findings reveal PPE19 as a secreted effector protein used by

Mtb to modulate important early interactions with the innate immune system,

enhancing entry into host macrophages.IMPORTANCETuberculosis remains a leading

infectious disease killer worldwide, with approximately one-quarter of the

global population infected with Mycobacterium tuberculosis (Mtb). Understanding

how this pathogen initially establishes infection is crucial for developing more

effective vaccines and treatments. This study identifies PPE19, a previously

uncharacterized bacterial protein, as a key factor that helps Mtb invade and

colonize human immune cells called macrophages during the earliest stages of

infection. The research shows that PPE19 acts like a molecular "key" that

facilitates bacterial entry into host cells but is then downregulated once the

bacteria are safely inside. Importantly, PPE19 belongs to a family of similar

proteins that can compensate for each other, explaining why targeting individual

members may not be sufficient for treatment. These findings provide new insights

into tuberculosis pathogenesis and suggest that early infection factors like

PPE19 could serve as targets for next-generation vaccines designed to prevent

initial infection rather than just disease progression.

DOI: 10.1128/msphere.00036-25

PMID: 40787981

**50. Br J Clin Pharmacol. 2025 Aug 11. doi: 10.1002/bcp.70197. Online ahead of print.**

Adverse drug reactions, particularly liver disorders, drive interruptions in

anti-tuberculosis treatment: A retrospective cohort study.

Dixon EG(1)(2), Biraua E(3), Brencsēns E(3), Pašuks V(3), Riekstina V(3),

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**AIMS:** Adverse drug reactions (ADRs) are a key driver of missed doses of

anti-tuberculosis (TB) therapy. We aimed to determine the relative burden of

ADR-driven missed doses, the missed dose patterns associated with ADRs, and the

association between specific ADRs and missed doses.

**METHODS:** In this retrospective cohort study, adults (≥18 years) who began the

standard 6-month drug-sensitive anti-TB regimen in an outpatient facility in

Riga, Latvia (May 2015-September 2022) and missed at least one dose of treatment

were included. Data were collected from medical records and observed therapy

records. Missed doses were subdivided into early discontinuation or sporadically

missed. Descriptive analyses and lasagne plots were used.

**RESULTS:** Across 174 patients, 54 (31.0%, CI: 24.2-37.9%) missed doses due to

ADRs. Of 31 320 doses, 4217 (13.5%, CI: 13.1-13.9%) were missed, 20.9%

(880/4217, CI: 19.6-22.1%) were due to ADRs. Eighteen (10.3%) of the 174

patients discontinued treatment early, two of which (11.1%) were due to ADRs.

Doses missed due to ADRs caused longer yet less frequent periods of sporadic

missed doses: 56.4% (479/849) of sporadic missed doses were 1 day in length vs.

only 9.1% (7/77) for ADR-related ones. Hepatobiliary disorders were the leading

ADR group causing missed doses. Hepatobiliary ADRs caused long median durations

of missed doses (median 15.0, CI: 13.0-22.0).

**CONCLUSION:** Our study underscores the importance of ADRs as a cause of missed

doses of treatment, particularly hepatobiliary disorders. Regimens that are less

prone to ADRs and strong healthcare system support structures for patients with

ADRs are required to minimize missed doses, reducing unfavourable outcomes.

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PMID: 40785321

**51. Pract Neurol. 2025 Aug 10:pn-2025-004634. doi: 10.1136/pn-2025-004634. Online**

**ahead of print.**

Brain abscess with concurrent infection: tuberculosis and aspergillosis.

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Brain abscess is rarely caused by coinfection with different pathogens. A

middle-aged immunocompetent woman developed right-sided focal motor seizures

with Todd's palsy. Brain imaging identified a frontal ring-enhancing lesion for

which she started antitubercular therapy and corticosteroids. However, on

tapering the corticosteroids, she developed a right-sided hemiparesis with

increased lesion size. Excision biopsy identified coinfection with Mycobacterium

tuberculosis and Aspergillus spp She recovered well with antitubercular and

antifungal agents. Coinfections with multiple pathogens pose diagnostic

challenges due to overlapping or non-specific clinical and radiological

features. This case underscores the importance of tissue diagnosis to enable

appropriate therapy.

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PMID: 40784749

**52. Int J Infect Dis. 2025 Aug 8:108003. doi: 10.1016/j.ijid.2025.108003. Online**

**ahead of print.**

Impact of age-stratified latent tuberculosis treatment on disease burden of

active tuberculosis: A mathematical modeling study in an aging country with a

high disease burden.

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**BACKGROUND:** The Republic of Korea has the highest tuberculosis (TB) incidence

among OECD countries, with older adults at elevated risk of reactivation.

However, latent TB infection (LTBI) control strategies often exclude individuals

over 65 due to potential side effects, such as hepatotoxicity. Identifying

optimal age groups for intervention is critical.

**METHODS:** We developed an age-structured dynamic transmission model to simulate

TB and LTBI progression in Korea. The model was calibrated using TB case data

(2011-2018) from the Korea Disease Control and Prevention Agency and the Health

Insurance Review and Assessment Service. We projected TB cases averted over 30

years by evaluating LTBI treatment strategies with varying coverage and success

rates across age groups.

**RESULTS:** Targeting LTBI treatment in adults aged 35-64 resulted in the greatest

reduction in TB incidence. A four-fold increase in the LTBI treatment rate in

this group averted 32,814 cases-compared to 11,564 and 5,689 cases in the 19-34

and ≥65 age groups, respectively. Increasing the probability of treatment

success had a smaller but similar effect.

**CONCLUSION:** Prioritizing LTBI treatment in the 35-64 age group may substantially

reduce TB burden and supports age-stratified strategies for national TB control.

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DOI: 10.1016/j.ijid.2025.108003

PMID: 40784588

**53. NPJ Syst Biol Appl. 2025 Aug 10;11(1):90. doi: 10.1038/s41540-025-00572-4.**

Generalized linear modeling of flow cytometry data to analyze immune responses

in tuberculosis vaccine research.

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Tuberculosis (TB) caused by Mycobacterium tuberculosis (Mtb) kills ~1.3 million

people annually. Accordingly, vaccines and sophisticated analytical tools are

necessary to evaluate their effectiveness. To address these challenges, we

created a Generalized Linear Model (GLM) framework to evaluate high-dimensional

flow cytometry data and the multivariable influences on immune responses,

accommodating proportional and non-normal data, and violations of assumptions

set by classical statistical evaluations. In naïve mice vaccinated with BCG

boosted with ID93-GLA-SE, we used GLMs to assess the impact of sex, vaccination,

and days post-infection on probabilities of immune cell phenotypes following Mtb

challenge. We demonstrate enhanced T cell responses in the lung following

BCG + ID93-GLA-SE compared to BCG or ID93-GLA-SE alone, with notable sex

differences in humoral immunity. This framework highlights GLMs in assessing

complex datasets while enhancing our comprehension of independent continuous and

categorical variables on vaccine efficacy, and serves as a foundation for

deeper, more complex scenarios.

© 2025. The Author(s).

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**54. Health Secur. 2025 Aug 8. doi: 10.1089/hs.2024.0109. Online ahead of print.**

Enhancing India's Health Security Efforts Against Mycobacterium Tuberculosis :

Gaps and Opportunities.

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Ministry of Science and Technology, Government of India, New Delhi, India.

India bears a quarter of the world's tuberculosis (TB) burden. In 2018, the

country set an ambitious goal to eliminate TB by 2025-5 years ahead of the

global target. While India has launched several large-scale public health

initiatives, including Pradhan Mantri TB Mukt Bharat Abhiyan and Ni-kshay Poshan

Yojana, several challenges persist that threaten progress toward elimination.

These include data transparency issues, overburdened healthcare systems, and an

unrealistic timeline for achieving elimination. In this article, we highlight

underaddressed health security challenges-including multidrug-resistant TB, weak

biosafety infrastructure, relapse without posttreatment monitoring,

environmental contributors like air pollution, and a lack of targeted strategies

for tribal populations and undocumented immigrants-and call for a revised

approach to TB elimination aligned with the global 2030 goal, emphasizing

evidence-based policy, improved surveillance, workforce support, multisectoral

coordination, and environmental and technological interventions.

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**55. BMC Infect Dis. 2025 Aug 8;25(1):1004. doi: 10.1186/s12879-025-11439-8.**

Prevalence and contributing factors of drug-resistant tuberculosis (DR-TB) in

iran: a systematic review.

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**INTRODUCTION:** Drug-resistant tuberculosis (DR-TB) is an increasing public health

concern in Iran, with multidrug-resistant tuberculosis (MDR-TB) posing

significant challenges to disease control efforts. This study examines the

prevalence of DR-TB in Iran from January 2000 to October 2023.

**METHODS:** A comprehensive systematic search was conducted across multiple

databases, including PubMed, Scopus, Google Scholar, EMBASE, BioMed Central, and

Web of Science. The search utilized specific keywords such as "drug-resistant

tuberculosis," "DR-TB," "MDR-TB," "XDR-TB," "Iran," "prevalence," and "risk

factors," among others. Boolean operators (AND/OR) were employed to refine the

search results. Only articles published between January 2000 and October 2023

were considered for inclusion. The search strategy followed the PRISMA

guidelines, and the review questions were formulated based on the PICO model.

The initial search identified 750 records. After removing duplicates and

screening the titles, abstracts, and full texts, a total of 9 articles that met

the inclusion criteria were included in the systematic review.

**RESULTS:** Between 2000 and 2023, the prevalence of MDR-TB in Iran ranged from 5.1

to 11.3% among general TB cases, increasing to 36% among retreatment cases and

18.5% in border provinces such as Sistan-Baluchestan. Retreatment patients had a

sixfold higher risk of MDR-TB compared to new cases. Comorbidities such as

diabetes (OR: 2.3) and HIV (OR: 3.1), along with male sex and older age, were

significant contributing factors-particularly in XDR-TB cases. Despite the

rising trend in drug resistance, diagnostic and laboratory limitations remain

major challenges. Key risk factors include a history of previous treatment,

diabetes mellitus, limited access to healthcare, and socioeconomic barriers.

Diagnostic difficulties, including inadequate laboratory capacity and

underutilization of molecular diagnostic tools, further complicate TB control

and management.

**CONCLUSION:** Addressing the rising prevalence of DR-TB in Iran requires urgent

public health interventions, including strengthening healthcare infrastructure,

improving access to diagnostic services, and implementing community-based

education programs to reduce stigma and enhance treatment adherence. Without

these measures, the burden of DR-TB is likely to increase, further complicating

efforts to control this public health crisis.

© 2025. The Author(s).

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**56. Sci Rep. 2025 Aug 9;15(1):29130. doi: 10.1038/s41598-025-14460-8.**

Application of causal forest double machine learning (DML) approach to assess

tuberculosis preventive therapy's impact on ART adherence.

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Adherence to antiretroviral therapy (ART) is critical for HIV treatment success,

yet the impact of tuberculosis preventive therapy (TPT) remains inadequately

understood. Using observational data from 4152 HIV patients in Ethiopia

(2005-2024), we applied causal inference methods, including Adjusted Logistic

Regression, Propensity Score Matching, and Causal Forest Double Machine Learning

(DML), to estimate TPT's effect on ART adherence. The DML approach (leveraging

Random Forests and orthogonalization) provided the most precise estimates after

model comparison. We found TPT initiation reduced adherence probability by 3.14

percentage points on average (ATE =  - 0.0314; 95% CI - 0.0373, - 0.0254;

p < 0.001). While most patients experienced negligible effects, substantial

heterogeneity existed: individuals with advanced WHO stage, longer ART duration,

higher BMI, or older age showed better adherence responses, whereas those with

higher CD4 counts, functional impairment, or cotrimoxazole prophylaxis use faced

greater risks. Subgroup analyses revealed consistent effects across clinical

strata but greater variability among non-TPT initiators. These findings support

personalized TPT deployment, prioritizing patients with advanced disease while

monitoring vulnerable subgroups and highlighting the need for adherence support.

Future research should validate results in multi-site cohorts using longitudinal

and psychosocial data.

© 2025. The Author(s).

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**57. PLoS One. 2025 Aug 8;20(8):e0329984. doi: 10.1371/journal.pone.0329984.**

**eCollection 2025.**

Spatial epidemiology of tuberculosis diagnostic delays, healthcare access

disparities, and socioeconomic inequities in Nairobi County, Kenya.

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Juja, Kenya.

**INTRODUCTION:** Kenya ranks among the top 30 countries with a high tuberculosis

(TB) burden globally. With a TB prevalence of 558 per 100,000, only 46% of TB

cases are diagnosed and treated, leaving 54% undiagnosed and at risk of

spreading the disease. This study analyzed the spatial distribution of

tuberculosis diagnostic delays and their association with health care

accessibility and socioeconomic inequalities in Nairobi County, Kenya.

**MATERIALS AND METHODS:** The cross-sectional study included 222 newly diagnosed

bacteriologically confirmed Mycobacterium tuberculosis (Mtb) patients from

Mbagathi County Hospital (MCH), Mama Lucy Kibaki Hospital (MLKH), and Rhodes

Chest Clinic (RCC) in Nairobi County, Kenya. Patients were recruited

consecutively through census sampling and categorized into two groups: delayed

diagnosis (≥21 days from symptom onset) and non-delayed (<21 days) as defined by

the WHO cutoff point. Patients' residential locations were georeferenced using

handheld GPS devices and captured digitally via Kobo Collect. Spatial analyses

were performed using ArcGIS Pro, version, where Global Moran's I statistic was

used to assess spatial autocorrelation in the distribution of TB cases.

**RESULT:** Spatial analyses identified 28 statistically significant clusters of

delayed TB diagnoses within Nairobi County. Spatial autocorrelation analysis

using Moran's I revealed a significant clustered distribution (Moran's Index =

0.471, z-score = 3.370, p < 0.001). Hotspot analysis with the Getis-Ord Gi\*

statistic detected high-delay clusters (z > 2.58, p < 0.001) in informal

settlements.

**DISCUSSION AND CONCLUSION:** The study revealed significant spatial clustering of

delayed TB diagnoses in Nairobi County, particularly in informal settlements. In

contrast, timely diagnoses were predominantly clustered in high-income areas

like Lang'ata and Karen. These clusters were significantly associated with lower

household income and increased travel time to health facilities which

underscored the need for targeted implementation of TB diagnostic services and

control measures in the wards with the highest delays.

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original author and source are credited.

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**58. Infection. 2025 Aug 8. doi: 10.1007/s15010-025-02579-9. Online ahead of print.**

Diagnostic performance of adenosine deaminase for extrapulmonary tuberculosis in

a higher-prevalence area of mainland France: a 10-year retrospective study.

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**PURPOSE:** Diagnosing extrapulmonary tuberculosis (EPTB) - including pleural,

peritoneal, pericardial, meningeal forms - remains challenging due to the

insufficient sensitivity of smear microscopy (SM), mycobacteriological culture,

and nucleic acid amplification test (NAAT). The Adenosine Deaminase (ADA) assay

has potential as a diagnostic tool for EPTB, but its performance in high-income

countries is poorly documented. This study aimed to evaluate the diagnostic

performance of ADA for microbiologically confirmed EPTB in such a setting.

**METHODS:** We retrospectively analyzed data from all patients undergoing ADA

testing in our hospital network in Paris area between May 2014 and April 2024.

Microbiological confirmation (positive SM, culture, or NAAT) from the same

sample site served as the reference standard.

**RESULTS:** Among 363 ADA assays (352 patients), 69% were pleural fluid, 18%

peritoneal, < 1% pericardial, 11% CSF. For pleural fluid, ADA at a threshold of

30 U/L demonstrated 92% sensitivity (CI 80-98%), 75% specificity (CI 68-81%),

47% PPV (CI 37-57%), and 97% NPV (CI 94-99%). For peritoneal fluid, sensitivity,

specificity, PPV, and NPV were 77% (CI 46-95%), 81% (CI 69-91%), 50% (CI

27-73%), and 94% (CI 82-99%), respectively. Raising the ADA threshold to 60 U/L

improved specificity to 92% in pleural fluid (CI 87-95%) and 85% in peritoneal

fluid (CI 73-93%). Combining ADA with other biomarkers showed no added

diagnostic value.

**CONCLUSION:** ADA testing is a rapid and practical tool for EPTB diagnosis. In

pleural and peritoneal fluids, a threshold < 30 U/L effectively excludes EPTB,

while a threshold > 60 U/L supports initiating treatment pending culture

results.

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**59. Chem Biodivers. 2025 Aug 8:e01727. doi: 10.1002/cbdv.202501727. Online ahead of print.**

Phytoconstituents and Immunological Responses in Tuberculosis: Insights Into

Network Pharmacology.

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Pulmonary tuberculosis (TB), caused by the Mycobacterium tuberculosis (MTB)

bacterium, remains a significant health problem worldwide, intensified by the

emergence of multidrug-resistant (MDR) and highly resistant (XDR) strains. The

current treatment protocols, related side effects, and the increasing incidence

of drug resistance limit the efficacy of conventional therapeutic strategies.

Traditional medicinal constituents rich in diverse phytoconstituents offer

multi-target action with reduced toxicity, minimal risk of resistance, and

immunomodulatory properties. Network pharmacology (NP), an integrated approach

merging systems biology and computational modeling, facilitates understanding

complex interactions among phytochemicals, molecular targets, and signaling

pathways. Integrating modern pharmacology principles with traditional wisdom, NP

provides a logical framework for developing new plant-based anti-TB agents and

advancing adjunctive therapies. Combining protein-protein interaction networks,

pathway enrichment analyses, multi-combinational data, and molecular docking

studies offers insights into how phytoconstituents affect the immune response,

block efflux pumps, and reduce resistance. This review provides a detailed

analysis of NP-based methods for the identification of active compounds (e.g.,

alkaloids, flavonoids, terpenoids, polyphenols) and their related molecular

targets involved in the pathogenesis of TB, including tumor necrosis

factor-alpha (TNF-α), Toll-like receptors (TLR), nucleotide-binding

oligomerization domain (NOD)-like receptor, and Janus kinase/signal transducer

and activator of transcription (JAK-STAT) pathway.

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**60. Arch Pharm (Weinheim). 2025 Aug;358(8):e70074. doi: 10.1002/ardp.70074.**

Exploration of New Dihydroindazole Derivatives as Promising Anti-TB Agents:

Design, Synthesis, In Silico, and Biological Evaluation.

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Bellapukonda SM(1), Devi A(3), Bhale NA(4), Dikundwar AG(4), Nanduri S(1),

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The escalating threat of drug-resistant Mycobacterium tuberculosis (Mtb)

necessitates the discovery of novel chemotherapeutic agents. In this study, a

series of dihydroindazole-based derivatives were designed, synthesized, and

evaluated for their antimycobacterial potential. Among the synthesized

compounds, 8u exhibited the most potent in vitro activity against Mtb H37Rv with

a minimum inhibitory concentration (MIC) of 2 µg/mL, while 8i and 8q showed

moderate activity (MIC = 8 µg/mL). Several analogs demonstrated MICs in the

range of 16-32 µg/mL. 8u also displayed enhanced activity against

single-drug-resistant Mtb strains, outperforming ethambutol and rifampicin.

Structure-activity relationship analysis indicated that both the hydrazide

linker and heteroaryl substitutions significantly influenced antimycobacterial

activity. 8u was non-cytotoxic to Vero cells (CC₅₀ > 100 µg/mL), yielding a

selectivity index (SI) > 50. Time-kill kinetics confirmed its bactericidal

nature. Mechanistic investigations using molecular docking and 100-ns molecular

dynamics simulations identified InhA as the probable molecular target. In silico

ADMET predictions (QikProp and ProTox-3.0) supported favorable pharmacokinetic

and toxicity profiles. Collectively, these findings highlight 8u as a promising

lead for the development of next-generation anti-TB agents.

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PMID: 40817577

**61. Immunol Rev. 2025 Aug;333(1):e70055. doi: 10.1111/imr.70055.**

Tertiary Lymphoid Structures in Tuberculosis: Persistence, Protection, and

Pathology.

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Tuberculosis (TB), caused by Mycobacterium tuberculosis (Mtb), is a major public

health burden responsible for over a million deaths each year. A deeper

understanding of the mechanisms that balance protective immunity and

immunopathology is essential for developing more effective therapeutics. This

review focuses on the dynamic interplay between CD4+ T cells and B cells in the

lung, with an emphasis on their interactions in tertiary lymphoid structures

(TLS). TLS are immune cell aggregates that arise in inflamed, nonlymphoid

tissues, range from loosely to highly organized clusters, and serve as localized

hubs for immune cell interaction, activation, and diversification. Drawing on

insights from other disease contexts, including infections, cancer, and chronic

inflammatory conditions, we examine the molecular signals and cellular

interactions involved in TLS formation, maintenance, and function during Mtb

infection. Additionally, we explore the anatomical and functional integration of

TLS with the lymphatic and vascular systems, and how this spatial organization

may influence bacterial persistence and dissemination. Clarifying the functional

role of TLS in TB-whether they support protective immunity, contribute to lung

pathology, or both-could inform novel approaches to modulate local immune

responses and improve TB disease outcomes.

© 2025 The Author(s). Immunological Reviews published by John Wiley & Sons Ltd.

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**62. J Family Med Prim Care. 2025 Jul;14(7):2915-2919. doi: 10.4103/jfmpc.jfmpc\_6\_25. Epub 2025 Jul 21.**

Comparative analysis of tuberculosis drug consumption data in public and private

sectors across selected districts of Madhya Pradesh.

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Sciences, Chhindwada, Madhya Pradesh, India.

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(7)State TB Officer, Bhopal, Madhya Pradesh, India.

**OBJECTIVES:** This study aimed to compare drug consumption rates in public and

private healthcare sectors between 2018 and 2022 in the Tikamgarh, Datia, and

Niwari districts of Madhya Pradesh.

**DESIGN:** A community-based survey methodology was employed, alongside an analysis

of program data and evaluation of anti-TB drug sales and utilization from both

healthcare sectors.

**MATERIALS AND METHODS:** Data were collected from district hospitals in both the

public and private sectors. Hospital records and pharmacy logs were reviewed to

assess anti-TB medication consumption rates from 2018 to 2022. Sputum samples

from patients with chest symptoms or a history of anti-TB treatment were tested

using Xpert/Rif/TrueNat. The analysis compared drug consumption rates based on

hospital records and calculated according to pharmacy sales data.

**RESULTS:** The mean patient months in the public sector (10,354 months, SD =

8,780) significantly exceeded those in the private sector (4,820 months, SD =

9,519). Public sector drug sales varied, with Tikamgarh declining sharply from

38,304 patient months in 2018 to 8,810 in 2019, while Datia remained more

stable. The private sector, particularly in Datia, peaked at 30,238 patient

months in 2020. One-way ANOVA showed no significant differences between sectors

for patient months (F = 2.74, P = .109). Linear regression identified patient

months as a significant predictor of calculated patients (estimate = 0.16529, P

< .001).

**CONCLUSION:** Aligning drug consumption patterns across healthcare sectors is

vital for effective tuberculosis management. Addressing disparities in drug

consumption rates is crucial for accurate TB incidence estimates.

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**63. J Family Med Prim Care. 2025 Jul;14(7):3025-3027. doi:**

**10.4103/jfmpc.jfmpc\_54\_25. Epub 2025 Jul 21.**

Rare cause of extrapulmonary tuberculosis in an immunocompetent elderly patient.

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Hindu University, Varanasi, Uttar Pradesh, India.

Tubercular hepatic abscesses in the geriatric population are rare and often

misdiagnosed, frequently leading to delayed or presumptive treatment based on

tissue biopsy findings. Early and accurate diagnosis using advanced diagnostic

tools is crucial for improving prognosis. We present the case of a 65-year-old

immunocompetent male who reported a three-month history of fever and one month

of right hypochondrial pain. Diagnosis of a tubercular hepatic abscess was

confirmed using a cartridge-based nucleic acid amplification test (CBNAAT),

which isolated Mycobacterium tuberculosis sensitive to rifampicin. The patient

was treated successfully with a standard anti-tubercular regimen. Although cases

of tubercular liver abscesses have been documented, using CBNAAT for direct

identification from pus samples is rare. Misidentification of such abscesses as

bacterial or neoplastic often results in inappropriate treatment, increasing the

risk of mortality. This case highlights the importance of early diagnosis and

prompt initiation of appropriate therapy to improve outcomes.

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**64. J Family Med Prim Care. 2025 Jul;14(7):3084-3085. doi:**

**10.4103/jfmpc.jfmpc\_1662\_24. Epub 2025 Jul 21.**

Does the risk factor assessment help to reduce drug-resistant tuberculosis?

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Research Centre, Dr. D. Y. Patil Vidyapeeth, Pimpri, Pune, Maharashtra, India.

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**65. J Family Med Prim Care. 2025 Jul;14(7):2997-3002. doi:**

**10.4103/jfmpc.jfmpc\_129\_25. Epub 2025 Jul 21.**

Estimate of TB incidence and a critical analysis of programmatic data of TB

score from Sub national Certification survey of district Niwari, M.P., India.

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**BACKGROUND:** India accounted for 26% of the global tuberculosis (TB) burden in

2023, with 27 lakh cases reported and 89% treatment coverage. Madhya Pradesh, a

high-burden state, reported 28,299 cases in 2023. The Government of India aims

to eliminate TB by 2025 through the Strategic National Campaign (SNC),

emphasizing surveillance, early diagnosis, and comprehensive care. This study

evaluates TB management trends in the Niwari district, Madhya Pradesh, a tribal

region, from 2018 to 2022.

**OBJECTIVES:** To estimate TB incidence, validate claims for TB-free status during

SNC surveys, and analyze TB score trends in the Niwari district.

**MATERIALS AND METHODS:** This retrospective, cross-sectional study utilized data

from the National Tuberculosis Elimination Programme (NTEP), including records

from the District Tuberculosis Officer (DTO), treatment cards, laboratory

registers, and the Ni-kshay portal. Seven TB score parameters were analyzed:

notification, HIV screening, UDST, and treatment success. TB incidence was

calculated per 100,000 population over five years (2018-2022). Ethical clearance

was obtained.

**RESULTS:** TB notification improved from 59.6% to 83.3%, with 97% HIV screening by

2022. UDST peaked at 112.5% in 2020. Treatment success rates ranged from 80.6%

to 87.6%. However, Nikshay Poshan Yojana beneficiary payments declined from

87.5% in 2021 to 49.4% in 2022. TB incidence fluctuated, from 129 per lakh

(2018) to 143 per lakh (2022), reflecting improved detection post-COVID-19.

Verified data closely matched reported data by 2022.

**CONCLUSION:** Niwari district has made significant progress in TB management,

particularly in notification and HIV screening, but challenges persist in

sustaining financial support and addressing operational inefficiencies.

Continued community engagement, advocacy, and SNC rounds are crucial for

achieving TB elimination by 2025.

Copyright: © 2025 Journal of Family Medicine and Primary Care.

DOI: 10.4103/jfmpc.jfmpc\_129\_25

PMCID: PMC12349803

PMID: 40814457

**66. J Clin Tuberc Other Mycobact Dis. 2025 Jun 17;40:100543. doi:**

**10.1016/j.jctube.2025.100543. eCollection 2025 Aug.**

Improving tuberculosis infection treatment completion among pregnant and

postpartum women.

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DOI: 10.1016/j.jctube.2025.100543

PMCID: PMC12348338

PMID: 40809674

**67. Open Forum Infect Dis. 2025 Aug 1;12(8):ofaf452. doi: 10.1093/ofid/ofaf452.**

**eCollection 2025 Aug.**

Epidemiological Analysis of Tuberculosis Transmission, Risk Factors, and

Subclinical Tuberculosis Management in a High School Outbreak, South Korea.

Choi Y(1), Park SJ(1), An HS(1), Kim HM(1), Yoo JY(1), Pyo SW(2), Song JS(3),

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**BACKGROUND:** Tuberculosis (TB) remains a significant public health concern,

particularly in congregate settings such as schools, where adolescents are at

increased risk transmission. This study aimed to investigate the epidemiological

characteristics, transmission dynamics, and control strategies during a TB

outbreak in a South Korean high school.

**METHODS:** A retrospective epidemiological investigation was conducted using data

from the Korea Tuberculosis Network and official outbreak reports. A total of

935 individuals-including students, staff, and household contacts-underwent

screening through chest X-rays, interferon-gamma release assays (IGRAs), and

chest computed tomography (CT). Genotyping of Mycobacterium tuberculosis

isolates was performed using spoligotyping and whole-genome sequencing (WGS).

Logistic regression identified risk factors associated with TB infection.

**RESULTS:** Among 935 contacts, 133 (14.2%) tested positive for TB infection. In

total, 30 cases of TB disease and 66 cases of latent TB infection were

identified among 762 student contacts. Prolonged exposure exceeding 10 hours per

week was associated with a significantly increased risk of TB infection

(adjusted odds ratio = 5.91, 95% confidence interval: 3.06-11.40, P < .001).

Notably, subclinical TB accounted for 74.2% of active TB cases, with most

detected via chest CT. WGS and phylogenetic analysis identified a distinct

genomic cluster of the Beijing clade, indicating a likely single transmission

chain within the school setting.

**CONCLUSIONS:** This outbreak highlights the importance of rapid TB diagnosis,

targeted screening for high-risk groups, and advanced diagnostic tools such as

IGRA and CT in identifying subclinical cases. Strengthened contact

investigations and expanded preventive strategies, including household contacts,

are essential for effective outbreak control.

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Infectious Diseases Society of America.

DOI: 10.1093/ofid/ofaf452

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PMID: 40809392

**68. Front Immunol. 2025 Jul 30;16:1608104. doi: 10.3389/fimmu.2025.1608104.**

**eCollection 2025.**

BCG and beyond: unlocking new frontiers in TB vaccine development.

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like to use, ensuring that the word-count remains at approximately 100 words for

best accessibility results. Further information on Alt-Text can be found

here.With over 10 million new cases and 1.6 million deaths annually,

tuberculosis (TB) continues to be a significant worldwide health-burden. To

assist in curbing the spread of TB, the century-old BCG, which is a

live-attenuated vaccine, is now the only licensed TB vaccine used in humans.

However, BCG's limited efficacy and poor antigenicity in adults have evoked the

need to design new vaccines against TB. The limited parameter is the

availability of potent antigens; as a consequence, it is imperative to study the

Mycobacterium tuberculosis (Mtb)-specific antigens that can provide a stronger

immune response if included in vaccine candidates. Through this review, we aim

to concentrate on the progress of current vaccine-candidates undergoing

preclinical and clinical-studies. Moreover, it is not the pathogen but the

genetics of the host that plays an essential role in fine-tuning the

immune-response and susceptibility to TB. Over the past 50 years, a systematic

approach to treating TB patients has overlooked factors like pharmacokinetics,

immune-response, and treatment duration. Henceforth, this review highlights the

precision medicine-guided approach considering genetic-makeup and host immunity

that could influence clinical management choices. The consolidated review will

shed light on advancements in vaccine-candidates, which can be harnessed in

prophylactic development against TB.

Copyright © 2025 Shaji, Verma, Bhaskar and Dwivedi.

DOI: 10.3389/fimmu.2025.1608104

PMCID: PMC12343704

PMID: 40808947

**69. J Clin Med. 2025 Jul 28;14(15):5327. doi: 10.3390/jcm14155327.**

Elevated Serum TNF-α/IL-1β Levels and Under-Nutrition Predict Early Mortality

and Hospital Stay Burden in Pulmonary Tuberculosis.

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Tudorache E(4), Bratosin F(6), Rosca O(6), Bogdan I(6), Tofolean DE(1)(2),

Preotesoiu I(1)(2), Zamfir V(1)(2), Dantes E(1).

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**Background/Objectives:** Romania remains a tuberculosis (TB) hotspot in the

European Union, yet host-derived factors of poor outcomes are poorly

characterised. We quantified circulating pro-inflammatory cytokines and examined

their interplay with behavioural risk factors, the nutritional status, and the

clinical course in adults hospitalised with pulmonary TB. We analysed 80 adults

with microbiologically confirmed pulmonary TB and 40 respiratory symptom

controls; four TB patients (5%) died during hospitalisation, all within 10 days

of admission. **Methods:** A retrospective analytical case-control study was

conducted at the Constanța regional TB referral centre (October 2020-October

2023). Patients with smear- or culture-confirmed TB were frequency-matched by

sex, 10-year age band, and BMI class to culture-negative respiratory controls at

a 2:1 ratio. The patients' serum interferon-γ (IFN-γ), interleukin-1α (IL-1α),

interleukin-1β (IL-1β), and tumour-necrosis-factor-α (TNF-α) were quantified

within 24 h of admission; the neutrophil/lymphocyte ratio (NLR) was extracted

from full blood counts. Independent predictors of in-hospital mortality were

identified by multivariable logistic regression; factors associated with the

length of stay (LOS) were modelled with quasi-Poisson regression. Results: The

median TNF-α (24.1 pg mL-1 vs. 16.2 pg mL-1; p = 0.009) and IL-1β (5.34 pg mL-1 vs. 3.67 pg mL-1; p = 0.008) were significantly higher in the TB cases than in

controls. TNF-α was strongly correlated with IL-1β (ρ = 0.80; p < 0.001), while

NLR showed weak concordance with multiplex cytokine patterns. Among the patients

with TB, four early deaths (5%) exhibited a tripling of TNF-α (71.4 pg mL-1) and

a doubling of NLR (7.8) compared with the survivors. Each 10 pg mL-1 rise in

TNF-α independently increased the odds of in-hospital death by 1.8-fold (95% CI

1.1-3.0; p = 0.02). The LOS (median 29 days) was unrelated to the smoking,

alcohol, or comorbidity load, but varied across BMI strata: underweight, 27

days; normal weight, 30 days; overweight, 23 days (Kruskal-Wallis p = 0.03). In

a multivariable analysis, under-nutrition (BMI < 18.5 kg m-2) prolonged the LOS

by 19% (IRR 1.19; 95% CI 1.05-1.34; p = 0.004) independently of the disease

severity. **Conclusions:** A hyper-TNF-α/IL-1β systemic signature correlates with

early mortality in Romanian pulmonary TB, while under-nutrition is the dominant

modifiable determinant of prolonged hospitalisation. Admission algorithms that

pair rapid TNF-α testing with systematic nutritional assessment could enable

targeted host-directed therapy trials and optimise bed utilisation in

high-burden settings.

DOI: 10.3390/jcm14155327

PMCID: PMC12347169

PMID: 40806949

**70. Healthcare (Basel). 2025 Jul 29;13(15):1846. doi: 10.3390/healthcare13151846.**

A Systematic Review of Tuberculosis Stigma Reduction Interventions.

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Kazakhstan.

**BACKGROUND:** Stigma associated with tuberculosis (TB) continues to undermine

patient well-being, treatment adherence, and public health goals and objectives.

This study aims to systematically review the literature to identify and

synthesize TB stigma reduction interventions published between 2015 and 2025.

**METHODS:** Following the PRISMA guidelines, we conducted a comprehensive

literature search across PubMed, Scopus, Science Direct, ProQuest, and Google

Scholar. Eligible studies included those with qualitative, quantitative, and

mixed-methods designs that focused on interventions related to TB-related

stigma. We categorized the studies into three groups: (1) intervention

development studies, (2) TB treatment programs with stigma reduction outcomes,

(3) stigma-specific interventions. Data extraction and quality appraisal were

conducted independently by two reviewers using the Mixed Methods Appraisal Tool

(MMAT).

**RESULTS:** A total of 15 studies met the inclusion criteria. Five studies focused

on co-developing stigma interventions, which incorporated multi-level and

multicomponent strategies targeting internalized, enacted, anticipated, and

intersectional stigma. Two studies assessed TB treatment-related interventions

(e.g., home-based care, digital adherence tools) with incidental stigma

reduction effects. The remaining seven studies implemented stigma-targeted

interventions, including educational programs, video-based therapy, peer-led

support, and anti-self-stigma toolkits. Interventions addressed stigma across

individual, interpersonal, institutional, community, and policy levels.

**CONCLUSIONS:** This review highlights the evolution and diversification of TB

stigma interventions over the past decade. While earlier interventions

emphasized education and support, recent strategies increasingly integrate peer

leadership, digital platforms, and socio-ecological frameworks. The findings

underscore the need for comprehensive, contextually grounded interventions that

reflect the lived experiences of people affected by TB.

DOI: 10.3390/healthcare13151846

PMCID: PMC12346600

PMID: 40805879

**71. Cien Saude Colet. 2025 Jul;30(7):e15972023. doi:**

**10.1590/1413-81232025307.15972023. Epub 2024 Jun 21.**

Temporal and spatial persistence of tuberculosis cases in Brazilian

municipalities between 2001 and 2022.

[Article in English, Portuguese; Abstract available in Portuguese from the

publisher]

Souza NKM(1), Machado LDS(2), Alves DF(3), Silva Filho LAD(4), Silva VMD(1).

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The objective was to analyze the association between socioeconomic variables and

the temporal and spatial persistence of TB rates reported in Brazilian

municipalities between the years 2001 and 2022. An ecological study of time

series and spatial analysis was conducted using secondary data from public

sources. Spatial correlation was sought between TB rates and socioeconomic

variables in Brazilian municipalities and their direct and indirect effects on

these rates. Global and Local Moran's Indices, both univariate and bivariate, as

well as the Durbin spatial error model, were used. The results show that an

increase in per capita GDP and health expenditure impacts the reduction of TB

cases. Additionally, there is a direct correlation between TB rates and

demographic density and the rate of healthcare professionals. It was concluded

that, despite its multifactorial nature, poverty is a strong determinant in the

increase of TB rates. The reduction of TB cases in Brazilian municipalities

depends on public health policies and intersectoral actions that are targeted to

each geographical area based on its specific characteristics.

DOI: 10.1590/1413-81232025307.15972023

PMID: 40802323

**72. Cureus. 2025 Jul 13;17(7):e87828. doi: 10.7759/cureus.87828. eCollection 2025**

**Jul.**

Laryngeal Tuberculosis Mimicking Laryngeal Carcinoma: A Case Report.

Yammouri Z(1), Chaouche S(2), Alami G(2), Harmouch F(3), Alami B(1), Lamrani

Y(1), Hammas N(4), Boubbou M(5), Maaroufi M(1).

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Laryngeal tuberculosis (LTB) is a rare form of extrapulmonary tuberculosis that

can clinically and radiologically resemble laryngeal carcinoma, leading to

potential misdiagnosis. We report the case of a 53-year-old man with a history

of chronic smoking, no known tuberculosis or BCG vaccination, who presented with

progressive dyspnea, dysphonia, and significant weight loss. Laryngoscopy

revealed ulcerative lesions involving the anterior commissure, right ventricular

strip, arytenoid fold, and epiglottis. CT imaging suggested malignancy, but a

biopsy confirmed LTB with pulmonary involvement. The patient responded favorably

to anti-tuberculous therapy, with near-complete resolution after two months.

This case highlights the diagnostic challenge of differentiating LTB from

malignancy. Awareness of this rare presentation is essential, especially in

tuberculosis (TB)-endemic regions, to avoid unnecessary surgical intervention

and ensure prompt medical treatment.

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DOI: 10.7759/cureus.87828

PMCID: PMC12341445

PMID: 40799900

**73. Open Forum Infect Dis. 2025 Jun 24;12(8):ofaf345. doi: 10.1093/ofid/ofaf345.**

**eCollection 2025 Aug.**

Stool-Based Molecular Tuberculosis Treatment Monitoring: A Faster Means for

Detecting Persistent Mycobacteria Compared to Phenotypic Culture.

Adu Gyamfi CG(1)(2)(3)(4), Seeger A(1), Mulengwa D(1)(2), Vasiliu A(1),

Carratala-Castro L(5)(6), Mtafya B(7), Maphalala N(1)(2), Munguambe S(6),

Saavedra B(6), Ness T(1), Maphalala G(8), Acacio S(6), Mambuque E(6), Ehrlich

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**BACKGROUND:** Tuberculosis (TB) treatment monitoring is hindered by the lack of a

rapidly measured biomarker that accurately predicts clinically relevant

outcomes. Symptom screening poorly correlates with bacillary burden. Although

culture is a direct measure of viable bacillary burden, the long turnaround time

makes it clinically irrelevant.

**METHODS:** The TB treatment monitoring potential of stool-based, quantitative

polymerase chain reaction (qPCR) was prospectively assessed among 231

participants of all ages from Eswatini, Tanzania, and Mozambique with

microbiologically confirmed TB. Stool qPCR results were compared to sputum

culture, persistent symptoms, drug resistance, and World Health Organization TB

outcomes.

**RESULTS:** Quantitative bacillary burden measured by stool qPCR strongly

correlated with sputum culture at baseline (Spearman correlation r s = 0.79; P <

.001). Stool was successfully collected at >90% of all timepoints, while sputum

collection decreased to <50% at the end of therapy. Participants with isoniazid

or rifampin resistance demonstrated decreased bacillary clearance by sputum

culture and stool qPCR during the first 2 weeks of treatment. Participants who

remained culture positive at 2 months had a slower decrease in bacillary burden

measured by stool qPCR compared to those who were culture negative by 2 months.

The odds of a participant being culture positive at 2 months was associated with

a lower initial qPCR cycle threshold (odds ratio [OR], 0.792; P = .004), and a

smaller absolute difference between the qPCR cycle threshold measured at 2 weeks

and baseline (OR, 0.72; P = .0006). Neither sputum culture, sputum Xpert Ultra,

or stool qPCR was associated with resolution of symptoms or in-treatment death.

**CONCLUSIONS:** Stool-based TB treatment monitoring correlates with sputum culture

but provides results faster, leverages a more accessible specimen, and

identifies patients with TB who are at risk for drug resistance and persistent

2-month culture positivity. None of the quantitative tests of bacillary burden

singularly could predict symptom resolution or death.

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Infectious Diseases Society of America.

DOI: 10.1093/ofid/ofaf345

PMCID: PMC12342930

PMID: 40799783

**74. Open Forum Infect Dis. 2025 Jul 21;12(8):ofaf433. doi: 10.1093/ofid/ofaf433.**

**eCollection 2025 Aug.**

Economic Burden of TB Deaths in India (2021): A Retrospective Cross-sectional

Study.

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Tuberculosis, Chennai, Tamil Nadu, India.

**BACKGROUND:** We aimed to estimat the economic burden of TB deaths in terms of

gross domestic product (GDP) across Indian states, regions, and different

demographic groups.

**METHODOLOGY:** Using the Human Capital Approach, we estimated the non-health GDP

losses due to TB deaths in India for 2021 at subnational level. The total

monetary value for the years of life lost due to TB deaths was calculated.

**RESULTS:** In 2021, 0.393 million TB deaths occurred in India, which would reduce

the non-health GDP by US$9.1 billion. North, West, South, and North Eastern

states of India incurred 33.5%, 25.6%, 18.5%, and 9.3% of that economic loss

respectively. Each TB death resulted in non-health GDP loss of US$23 161. The

economic burden was highest among youngr males (20.5%) followed by males aged

>75 years (17.3%). The economic cost was minimal among male adolescents and

youth accounting for 3.4%.

**CONCLUSIONS:** Finndings underscore the urgent need for concerted multisectoral

efforts, sustained investments and strategies to reduce TB deaths, and mitigate

the resulting economic losses at sub-national level.

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Infectious Diseases Society of America.

DOI: 10.1093/ofid/ofaf433

PMCID: PMC12343098

PMID: 40799778

**75. bioRxiv [Preprint]. 2025 Aug 4:2025.08.04.668387. doi:**

**10.1101/2025.08.04.668387.**

Minimal immune cell subset differences in a cohort of close contacts of

tuberculosis index cases.

Panda S, Cheng C, Hillery N, Catanzaro DG, Ciobanu N, Crudu V, Rodwell T,

Catanzaro A, Burel JG, Peters B, Arlehamn CSL.

Understanding the perturbations in immune response across the spectrum of TB

infection is still unclear. In this study, we followed a cohort of close

contacts of pulmonary TB patients with serial QFT testing at 0, 3, 6, and 12

months, and stratified them into six subgroups: QFT-increasing (low/high), QFT

converters (QFT- to QFT+), QFT+ stable, and QFT- individuals. Despite these

distinct QFT trajectories, we observed minimal differences in immune cell

frequencies, activation profiles, and T helper subset distributions among the

QFT subgroups, suggesting limited immunological stratification based on QFT

dynamics alone. Ex vivo immune phenotyping, including analysis of CD4, CD8, and

NKT cell frequencies, memory T cell subsets, and activated T cells

(HLA-DR⁺CD38⁺), failed to distinguish between QFT subgroups. Antigen-specific

CD4 T cell responses assessed by the activation-induced marker (AIM) assay were

elevated in QFT+ compared to QFT- individuals. These findings suggest that

blood-based immune profiling may not capture subtle immunological transitions

among QFT converters or individuals with increasing QFT responses. In contrast,

individuals with active TB (ATB) showed clear immune perturbations. ATB patients

at diagnosis exhibited significantly elevated frequencies of antigen-specific

CD4 T cells, increased activated T cells, and higher frequencies of intermediate

monocytes and NK cells compared to QFT+/QFT- contacts. Many of these immune

features declined with treatment, indicating therapy-associated immune

resolution. Additionally, shifts in T helper subsets and effector memory

populations were observed over the course of treatment. These results suggest

that while ex vivo immune profiling can robustly distinguish active TB from

non-diseased states, it lacks the resolution to differentiate QFT subgroups

based on QFT dynamics alone. This could reflect either immunological similarity

among close contacts regardless of QFT status or limitations of blood-based

phenotyping in detecting early or subclinical immune shifts. Our study

highlights the challenge of immunologically distinguishing QFT-defined subgroups

within close contacts using conventional ex vivo profiling approaches.

DOI: 10.1101/2025.08.04.668387

PMCID: PMC12340800

PMID: 40799590

**76. bioRxiv [Preprint]. 2025 Aug 6:2025.08.04.668403. doi:**

**10.1101/2025.08.04.668403.**

Sterilizing activity of spectinamide MBX-4888A when replacing linezolid in the

Nix- TB regimen in the relapsing BALB/c mouse model of tuberculosis.

Peroutka-Bigus N, Sherman MS, Kaya F, Waidyarachchi SL, Liu J, Rushefsky J,

Butler MM, Bowlin T, Meibohm B, Gonzalez-Juarrero M, Lenaerts AJ, Zimmerman M,

Lee RE, Robertson GT.

Spectinamides have garnered interest as experimental tuberculosis therapeutics

owing to their safety profile and efficacy as partner agents when used in

conjunction with established regimens in mice. The Nix-TB regimen of

bedaquiline, pretomanid, and linezolid represents a short, effective regimen

recommended for treatment of pre-extensively drug-resistant tuberculosis.

However, linezolid administration is associated with severe adverse events which

limits its use. Here we present preclinical data that spectinamide MBX-4888A can

replace linezolid in Nix-TB.

DOI: 10.1101/2025.08.04.668403

PMCID: PMC12340861

PMID: 40799565

**77. PNAS Nexus. 2025 Jul 29;4(8):pgaf242. doi: 10.1093/pnasnexus/pgaf242.**

**eCollection 2025 Aug.**

Mechanism of the dual action self-potentiating antitubercular drug

morphazinamide.

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N(1), Aldrich CC(2), Baughn AD(1).

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Pyrazinamide (PZA) is a cornerstone of first-line antitubercular drug therapy

and is unique in its ability to kill nongrowing populations of Mycobacterium

tuberculosis through disruption of coenzyme A (CoA) metabolism. Unlike other

drugs, PZA action is conditional and requires potentiation by host-relevant

environmental stressors, such as low pH and nutrient limitation. Despite its

pivotal role in tuberculosis therapy, the durability of this crucial drug is

challenged by the emergent spread of drug resistance. To advance drug discovery

efforts, we characterized the activity of a more potent PZA analog,

morphazinamide (MZA). Here, we demonstrate that like PZA, MZA acts in part

through impairment of CoA metabolism. Unexpectedly, we find that, in contrast to

PZA, MZA does not require potentiation and maintains bactericidal activity

against PZA-resistant strains due to an additional mechanism involving aldehyde

release. Further, we find that the principal mechanism for resistance to the

aldehyde component is through promoter mutations that increase expression of the

mycothiol oxidoreductase MscR. Our findings reveal a dual-action synergistic

mechanism of MZA that results in a faster kill rate and a higher barrier to

resistance. These observations provide new insights for the discovery of

improved therapeutic approaches for addressing the growing problem of

drug-resistant tuberculosis.

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**78. Front Oncol. 2025 Jul 29;15:1607025. doi: 10.3389/fonc.2025.1607025. eCollection 2025.**

Case Report: Unveiling the hidden: a rare case of endometrial tuberculosis

presenting as peritoneal carcinomatosis.

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**BACKGROUND:** Endometrial tuberculosis (TB) is a rare form of extrapulmonary TB,

particularly uncommon in postmenopausal women. Its atypical presentation,

characterized by nonspecific symptoms, often leads to misdiagnosis, particularly

when it is confused with malignancies. Moreover, peritoneal tuberculosis,

although rare, can further complicate the diagnostic process due to its clinical

manifestations that resemble those of various cancerous conditions. The

coexistence of both endometrial and peritoneal TB in the same patient is

particularly unusual and presents a significant diagnostic challenge.

**CASE PRESENTATION:** We report the case of a 49-year-old perimenopausal woman who

presented with chronic pelvic pain, ascites, and postmenopausal bleeding.

Initial imaging raised suspicion for peritoneal carcinomatosis. However,

histopathological and microbiological investigations confirmed the diagnosis of

endometrial and peritoneal tuberculosis. The diagnosis was established by the

detection of acid-fast bacilli and granulomas in the biopsies from the

endometrium and peritoneum. The patient was successfully treated with a standard

anti-TB regimen, showing a favorable clinical response and gradual resolution of

symptoms.

**CONCLUSION:** This case underscores the importance of considering tuberculosis in

the differential diagnosis of pelvic pathologies, particularly in endemic

regions where TB is prevalent. It highlights the need for thorough investigation

in cases of atypical pelvic symptoms in patients with risk factors, even in the

absence of clear pulmonary symptoms. Including tuberculosis in the differential

diagnosis could prevent misdiagnosis and allow for more prompt and appropriate

management.

Copyright © 2025 Garci, Makni, Abdelmoula, Abdeljabbar, Babay, Ben Saada, Dhieb,

Hadj Kacem, Mathlouthi, Belghith and Slimani.

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PMCID: PMC12340403

PMID: 40799242

**79. Clin Infect Dis. 2025 Aug 7:ciaf426. doi: 10.1093/cid/ciaf426. Online ahead of print.**

Preventing multidrug resistant tuberculosis: the dawn of a new era.

Churchyard GJ(1)(2)(3), Swindells S(4), Gupta A(5), Shah NS(6), Hughes M(7), Kim

S(7), Fox GJ(8), Harrington M(9), Chaisson RE(5), Hesseling AC(10).

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Multidrug resistant tuberculosis (MDR-TB) remains a global health threat and

accounts for a quarter of deaths due to antimicrobial resistance. Individuals

infected with MDR-TB are at risk of progressing to TB disease. Treatment of

drug-resistant TB infection to prevent progression to disease and avert the

associated morbidity and mortality is a global priority. Randomised evidence to

inform TB preventive treatment guidelines have been lacking. Two recently

completed trials provide the first randomized evidence that treatment of

household contacts exposed to patients with MDR-TB with daily levofloxacin for

six months is safe and efficacious in preventing TB. Based on these results, the

World Health Organization updated its TB preventive treatment guidelines to make

a strong recommendation for use of levofloxacin for six months in MDR-TB exposed

contacts. Novel, shorter regimens in development will usher in a new era for the

treatment of MDR-TB infection if shown to be safe and efficacious.

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PMID: 40795178

**80. J Infect Dis. 2025 Aug 7:jiaf418. doi: 10.1093/infdis/jiaf418. Online ahead of print.**

TB prevalence in people tested is a strong predictor of Xpert specificity in

community and risk group screening.

McCreesh N(1), Govender I(1)(2), Grant AD(1)(2), Khan PY(1).

Author information:

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(2)Africa Health Research Institute, School of Laboratory Medicine & Medical

Sciences, College of Health Sciences, University of KwaZulu-Natal.

DOI: 10.1093/infdis/jiaf418

PMID: 40795121

**81. J Infect Dis. 2025 Aug 7:jiaf406. doi: 10.1093/infdis/jiaf406. Online ahead of print.**

Impact of Case Detection and Covid-19-Related Disruptions on Tuberculosis In

Vietnam: A Modelling Analysis.

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BH(3)(4), Do HN(3)(4), Ha TS(5), Fox GJ(6)(7), Trauer JM(1).

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(7)The Woolcock Institute for Medical Research, Glebe, New South Wales,

Australia.

**BACKGROUND:** Vietnam, a high-burden tuberculosis (TB) country, experienced marked

declines in TB notifications during the COVID-19 pandemic. We assessed the

impact of pandemic-related disruptions on TB case detection and transmission

using a dynamic transmission model calibrated to local demographic and

epidemiological observations.

**METHODS:** We developed an age-structured compartmental TB transmission model to

estimate COVID-19's impact on TB in Vietnam. Four model assumptions reflecting

reductions in detection and/or transmission were calibrated to notification

data, with the best-fitting assumption used for future projections and to

evaluate the effects of enhanced case detection scenarios.

**RESULTS:** COVID-19 significantly disrupted TB services in Viet Nam, resulting in

an estimated 2,000 additional TB episodes (95% credible interval [CrI]:

200-5,100) and 1,100 TB-related deaths (95%CrI: 100-2,700) in 2021.By 2035, the

cumulative impact of these disruptions could reach 22,000 additional TB episodes

(95%CrI: 2,200-63,000) and 5,900 deaths (95%CrI: 600-16,600) by 2035. We

predicted two hypothetical scenarios of enhancing TB case detection. Under the

ambitious scenario, enhancing TB case detection could mitigate these potential

impacts by preventing 17.8% of new TB episodes (95%CrI: 13.1%-21.9%) and 34.2%

(95%CrI: 31.5%-37.0%) of TB-related deaths by 2035, compared to no enhancement.

**CONCLUSIONS:** COVID-19-related disruptions have hindered TB detection in Vietnam,

likely causing long-term increases in new TB episodes and deaths. However, the

uncertainty around these effects is considerable. Sustained investment in

diagnostics, system resilience, and patient-centric policies have the potential

to achieve benefits that are substantially larger than these pandemic-related

setbacks.

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DOI: 10.1093/infdis/jiaf406

PMID: 40795091

**82. J Infect Dis. 2025 Aug 6:jiaf401. doi: 10.1093/infdis/jiaf401. Online ahead of print.**

Deriving Dosages for Levofloxacin Tuberculosis Preventive Treatment for Young

People Exposed to Rifampicin-Resistant Tuberculosis.

Solans BP(1)(2), Miyakawa R(1)(2), Shin M(1)(2), Hesseling AC(3), White Y(1)(2),

Masini T(4), Kanchar A(4), Falzon D(4), Savic RM(1)(2).

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Faculty of Medicine and Health Sciences, Stellenbosch University, Stellenbosch,

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(4)Global Tuberculosis Programme, World Health Organization, Geneva,

Switzerland.

**BACKGROUND:** Tuberculosis (TB) is the leading single bacterial cause of death

worldwide. In 2023, approximately 400 000 people developed multidrug- and

rifampicin-resistant TB (MDR/RR-TB), which complicates treatment. TB preventive

treatment (TPT) is a critical strategy to prevent the progression from TB

infection to TB disease among those at risk. In February 2024, based on data

from 2 randomized controlled trials, levofloxacin was strongly recommended by

the World Health Organization (WHO) as a TPT option in people of all ages

exposed to MDR/RR-TB. There are uncertainties about the optimal dosing of

levofloxacin in children and adolescents when using dispersible and solid

formulations. We used pharmacokinetic modeling and simulations to determine the

best dosing strategy in people aged up to 19 years for both formulations of

levofloxacin.

**METHODS:** A previously developed population pharmacokinetic model of levofloxacin

in children (0.2-16.8 years) was used and applied to new WHO harmonized weight

bands. Simulations were conducted using demographic data from countries with the

highest incidence of RR- or MDR-TB. Two currently available levofloxacin

formulations (100 mg pediatric, dispersible tablets and 250 mg solid tablets)

were considered.

**RESULTS:** A dosing regimen by weight band was developed for levofloxacin when

used as TPT in people aged 0-19 years exposed to MDR/RR-TB. Doses correspond to

8-33 mg/kg for the 100 mg dispersible tablets and 10-42 mg/kg for 250 mg solid

tablets. These doses achieve adequate adult target exposure levels.

**CONCLUSIONS:** Pragmatic, weight-band dosing strategies help simplify the

administration of MDR/RR-TB TPT and have been included in WHO guidance.

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Infectious Diseases Society of America.

DOI: 10.1093/infdis/jiaf401

PMID: 40794705

**83. J Infect Dis. 2025 Aug 5:jiaf415. doi: 10.1093/infdis/jiaf415. Online ahead of print.**

The emerging role of immunothrombosis in the control and pathogenesis of

Mycobacterium tuberculosis.

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(2)Department of Infectious Diseases, St James's Hospital, Dublin, Ireland.

Greater understanding of the immunopathogenesis of tuberculosis is critical for

developing novel therapies. Here, we propose that immunothrombosis plays an

important role in the immune response to Mycobacterium tuberculosis. This

interplay between macrophages, neutrophils, and platelets leads to

microthrombosis at the site of infection, trapping the mycobacterium to prevent

dissemination. We explore how dysregulated immunothrombosis might contribute to

tuberculosis pathogenesis; with excessive microthrombosis driving drug

resistance, leading to lung damage and venous thromboembolism. Further research

into these poorly understood mechanisms could identify options for host-directed

therapies to ameliorate immunothrombosis, with its attendant tissue destruction,

and reduce the burden of resistance.

© The Author(s) 2025. Published by Oxford University Press on behalf of

Infectious Diseases Society of America.

DOI: 10.1093/infdis/jiaf415

PMID: 40794553

**84. Cureus. 2025 Jul 12;17(7):e87769. doi: 10.7759/cureus.87769. eCollection 2025**

**Jul.**

Empirical Tuberculosis Treatment in Human Immunodeficiency Virus

(HIV)-Associated Fever of Unknown Origin: A Case-Based Rationale.

Antonioli M(1), Antonioli SH(1), Aisenberg GM(1).

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Fever of unknown origin (FUO) in people living with human immunodeficiency virus

(PLHIV) is clinically defined as recurrent fever lasting more than four weeks in

the outpatient setting or more than three days during hospitalization, despite a

thorough diagnostic evaluation. This evaluation typically includes a

comprehensive medical history, physical examination, imaging studies (such as

chest radiography), and an extensive range of laboratory tests, including

complete blood counts, blood and urine cultures, and metabolic panels. Among the

many possible causes, tuberculosis (TB) stands out as a leading concern, given

its disproportionate burden in PLHIV. However, whether to initiate empirical

anti-tubercular therapy in HIV-positive patients presenting with FUO remains a

matter of clinical debate. The variability in regional TB prevalence and

resource availability makes universal recommendations difficult to apply. In

this context, we review the available evidence supporting the use of empirical

TB treatment in PLHIV with FUO, aiming to guide clinical decision-making in

settings where diagnostic certainty is elusive.

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DOI: 10.7759/cureus.87769

PMCID: PMC12337587

PMID: 40792312

**85. Radiol Case Rep. 2025 Aug 1;20(10):5271-5275. doi: 10.1016/j.radcr.2025.06.108. eCollection 2025 Oct.**

Pott's disease: A case of multilevel vertebral tuberculosis with spinal

deformity.

Crawford CK(1), Arshad H(1), Chu LC(1), Fishman EK(1).

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Baltimore, MD, USA.

Spinal tuberculosis (TB), also known as Pott's disease, occurs in 1%-5% of TB

patients. Spine is the most common musculoskeletal extrapulmonary site of

infection in TB, with the thoracolumbar region affected the most. Spinal

involvement leads to significant deterioration of the vertebrae, paraspinal

abscesses, spondylodiscitis and may involve the spinal cord leading to

neurologic deficits. Nonspecific signs and symptoms of back pain often delay and

complicate the diagnosis. Computed tomography (CT) and magnetic resonance

imaging (MRI) are the commonly used modalities for diagnosis as each can

identify early bone destruction and abscess formation. MRI is highly sensitive

for detecting disc and cord involvement. We present a case of a 29-year-old male

with long standing back pain, diagnosed to be Pott's disease, discussing the

role of imaging through computed tomography (CT) and MRI in diagnosis and

management of the disease.

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Washington.

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PMCID: PMC12337656

PMID: 40791959

**86. medRxiv [Preprint]. 2025 Jul 15:2025.07.14.25331510. doi:**

**10.1101/2025.07.14.25331510.**

Pharmacokinetics of dexamethasone in tuberculosis meningitis.

Calderin JM, Resendiz-Galvan JE, Abdelgawad N, Davis A, Stek C, Wiesner L,

Meintjes G, Wilkinson RJ, Denti P, Wasserman S.

**INTRODUCTION:** Dexamethasone is recommended as adjunctive therapy for

tuberculosis meningitis (TBM). Co-administration with rifampicin is expected to

reduce dexamethasone exposure in TBM, an effect that may be more pronounced with

the higher rifampicin doses currently being evaluated in clinical trials.

**METHODS:** This pharmacokinetic study was nested in a randomised controlled trial

comparing the safety of high-dose rifampicin (oral, 35 mg/kg; intravenous, 20

mg/kg) plus linezolid, with or without aspirin, vs standard-dose rifampicin (10

mg/kg) for adults with HIV-associated TBM. All participants received adjunctive

oral dexamethasone every 12 hours starting at a dose of 0.4 mg/kg/day.

Dexamethasone concentrations were measured on intensively sampled plasma on day

3 after study enrolment and analysed using nonlinear mixed-effects modelling.

**RESULTS:** In total, 261 dexamethasone concentrations from 43 participants were

available for model development. Eight (18%) participants were on

efavirenz-based ART and five (11%) were on a lopinavir/ritonavir-based regimen.

The median duration of rifampicin therapy at the time of pharmacokinetic

sampling was 4 days (range: 0-7). Dexamethasone pharmacokinetics was best

described by a one-compartment disposition model with first-order absorption and

elimination. Typical oral clearance (CL/F) was 131 L/h, reduced to 11.5 L/h with

concomitant lopinavir/ritonavir. High-dose rifampicin had no significant

additional effect on dexamethasone pharmacokinetic parameters compared with the

standard-dose.

**CONCLUSIONS:** In adults with HIV-associated TBM, there was high dexamethasone

clearance, likely related to a drug-drug interaction with rifampicin. High-dose

rifampicin had no additional effect on dexamethasone exposure.

40-WORD SUMMARY OF THE ARTICLE’S MAIN POINT: This pharmacokinetic analysis of

dexamethasone in adults with HIV-associated tuberculosis meningitis found high

oral clearance (131 L/h), likely due to a drug-drug interaction with rifampicin.

High-dose rifampicin had no additional effect on dexamethasone exposure compared

with standard dose.

DOI: 10.1101/2025.07.14.25331510

PMCID: PMC12338885

PMID: 40791718

**87. medRxiv [Preprint]. 2025 Jul 16:2025.07.15.25331513. doi:**

**10.1101/2025.07.15.25331513.**

Energy dense nutritional supplements improve weight gain among malnourished

adults with drug-sensitive pulmonary tuberculosis: an open-label randomized

controlled trial in Faridabad, India.

Kumar R, Sinha P, Krishnan A, Singh M, Singh A, Guleria R, Singh UB.

This open-label randomized controlled trial in India assessed the impact of a

peanut-based energy-dense nutritional supplement (EDNS) on weight gain among

undernourished adults with drug-susceptible pulmonary tuberculosis in India.

EDNS significantly improved weight gain compared to standard care, offering a

scalable solution for targeted nutritional support.

DOI: 10.1101/2025.07.15.25331513

PMCID: PMC12338934

PMID: 40791711

**88. medRxiv [Preprint]. 2025 Jul 15:2025.07.14.25331509. doi:**

**10.1101/2025.07.14.25331509.**

High treatment success among individuals with rifampicin-resistant tuberculosis

in Botswana: A retrospective cohort study.

Mogashoa T, Ngom JT, Choga OT, Loubser J, Sabone P, Molefi T, Makhondo T,

Stephen O, Makhema JM, Musonda RM, Fane K, Gaseitsiwe S, Warren RM, Moyo S,

Dippenaar A, Streicher EM.

**BACKGROUND:** The study reports on tuberculosis (TB) treatment outcomes among

individuals diagnosed with rifampicin-resistant TB (RR-TB) and assesses

predictors associated with treatment outcomes.

**METHODS:** We conducted a retrospective study to analyse treatment outcomes of 162

individuals with RR-TB from 2016 to 2023. Treatment outcome proportions were

estimated using the binomial exact method with 95% confidence intervals (CI).

Predictors of treatment outcomes were assessed using logistic regression models.

**RESULTS:** Of the 162 individuals, 102 (62.7%) were male with a median age of 39

(interquartile range (IQR): 29-50). Most individuals, 78 (48.1%), were from the

Greater Gaborone health district, and 88 (54.3%) were people living with HIV

(PLWH). Among these individuals, 137 (84.6%, 95% CI [78.2, 89.7]) were

successfully treated. Males had higher odds of unfavourable treatment outcomes

compared to females (OR = 1.70; 95% CI [0.73, 3.98]). Among those cured, a

slightly higher proportion was observed among PLWH (71.8%, 95% CI [62.1, 80.3])

compared to people not living with HIV (PNLWH) (69.2%, 95% CI [58.7, 78.5]).

However, the mortality rate was higher in PLWH (10.7%; 95% CI [5.5, 18.3])

compared to PNLWH (6.6%; 95% CI [2.5, 13.8]). Those with a history of TB

treatment had 1.03 odds of unfavourable treatment outcomes (95% CI [0.40,

2.73]); however, this association was not statistically significant.

**CONCLUSION:** Our study shows a high success rate of treatment among individuals

with RR- TB, with no significant difference based on sex, TB treatment history,

or HIV status. Higher mortality among PLWH highlights the need for targeted

interventions among high-risk groups.

DOI: 10.1101/2025.07.14.25331509

PMCID: PMC12338906

PMID: 40791701

**89. medRxiv [Preprint]. 2025 Jul 14:2025.07.11.25331385. doi:**

**10.1101/2025.07.11.25331385.**

Informing People-Centered Target Product Profiles for TB Diagnostics: A

Multi-Country Qualitative Study.

Castro MDM, Le H, Manoj Kumar K, Mamani-Mategula E, Nakaweesa A, Dalay V, Shah

K, Venter R, Christopher DJ, Yu C, Theron G, Worodria W, Nahid P, Cattamanchi A,

Denkinger CM, Kerkhoff AD, West N, Phan H.

**BACKGROUND:** Timely and accurate tuberculosis (TB) diagnosis remains a key

challenge in high-burden settings. The World Health Organization (WHO) has

developed Target Product Profiles (TPPs) to guide diagnostic development, which

have largely reflected the perspectives of experts, with limited input from

people affected by TB. This qualitative study explored preferences and

experiences to inform people-centered TB diagnostic strategies.

**METHODS:** We conducted 75 semi-structured interviews with adults undergoing TB

evaluation at outpatient clinics in India, the Philippines, South Africa,

Uganda, and Vietnam. Participants were purposively sampled to ensure diversity

in sex, TB status, age and treatment. Thematic analysis was utilized.

**FINDINGS:** Preferences were shaped by five interrelated domains: perceived

diagnostic accuracy, sample collection experience, time-to-results,

affordability, and testing location. Diagnostic accuracy was consistently

prioritized, with many expressing willingness to trade comfort and convenience

for more trustworthy results. Sputum and blood were widely trusted despite

collection challenges, whereas tongue swabs and urine were easier to provide but

perceived as less accurate. Rapid, same-day turnaround was valued for minimizing

emotional distress, financial and logistical burdens. Although testing was

typically free, indirect costs such as transport and lost income, remained

barriers. Hospital-based testing was preferred due to trust in staff and

infrastructure, though some acknowledged the appeal of community-based

approaches if reliability and privacy were ensured.

**CONCLUSION:** People seeking TB care prioritize accuracy and trustworthiness, even

at the expense of comfort or convenience. These preferences can inform WHO

policy updates, especially regarding the adoption of novel sample types and

testing strategies, to support uptake and equitable access to novel diagnostics.

DOI: 10.1101/2025.07.11.25331385

PMCID: PMC12338892

PMID: 40791696

**90. medRxiv [Preprint]. 2025 Jul 16:2025.07.15.25331566. doi:**

**10.1101/2025.07.15.25331566.**

Diagnostic accuracy of tongue swab testing in persons with sputum Xpert Ultra

Trace results.

Shapiro AE, Dalmat RR, Mukwatamundu J, Kamoga C, Ngwane MW, Steadman A, Budiawan

E, Stein G, Nalutaaya A, Mukiibi J, Nantale M, Biché P, Visek C, Sung J, Magcaba

Z, Ngcobo N, Morton JF, Lenn M, Aucock S, Draper R, Ganguloo A, Wilson D,

Katamba A, Kendall EA, Drain PK.

**BACKGROUND:** Molecular amplification of tongue swab samples is a non-sputum-based

investigational approach to diagnose pulmonary tuberculosis (pTB). An improved

manual qPCR method for tongue swabs recently achieved >90% sensitivity overall

in diagnosing TB, compared to a sputum microbiologic reference standard.

Performance characteristics in persons with low-positive results on sputum

molecular tests are unknown.

**METHODS:** Adults in South Africa and Uganda with sputum Xpert MTB/RIF Ultra Trace

(TR+) results were recruited for confirmatory evaluation and follow-up. They

underwent symptom evaluation, examination, chest X-ray, further sputum testing

(repeat Xpert Ultra and two solid and liquid mycobacterial cultures), and two

tongue swabs. Tongue swabs were tested using qPCR amplification of the IS6110

gene. A single copy detected on >=1 swab was considered TB-positive. TR+ persons

not diagnosed with TB at baseline were re-evaluated at 1 and 3 months. We

determined the sensitivity and specificity of tongue swabs against TB culture

alone, a microbiologic reference standard (MRS: any positive result from Xpert

Ultra or TB culture) and a composite reference standard (CRS: a clinical

recommendation for TB treatment or any positive culture) at baseline.

**RESULTS:** 225 enrolled TR+ participants (115 (51%) women, median age 38 [IQR

30-47], 130 (58%) people living with HIV (PWH)) provided at least 1 tongue swab

at baseline. With a culture reference standard, 45 (20%) were positive for TB at

baseline testing; 58 (26%) were positive for TB by MRS and 83 (37%) by CRS.

Sensitivity and specificity of tongue swabs against culture were 25% [95% CI

13-40%] and 94% [90-97%], vs. MRS were 25% [95% CI 14-38%] and 96% [91-98%], and

vs. CRS were 16% [9-26%] and 94% [89-98%].

**CONCLUSION:** Tongue swabs had low sensitivity and moderately high specificity for

TB in persons with a Trace Xpert Ultra result. Tongue swabs have limited value

for diagnosing people with low-positive molecular test results of uncertain

clinical significance.

DOI: 10.1101/2025.07.15.25331566

PMCID: PMC12338924

PMID: 40791694

**91. medRxiv [Preprint]. 2025 Jul 15:2025.07.14.25331384. doi:**

**10.1101/2025.07.14.25331384.**

Cumulative TB disease burden following sputum Xpert Ultra 'Trace' results in

clinical settings: Results from a multi-site observational clinical study.

Dalmat RR, Visek C, Budiawan E, Stein G, Nalutaaya A, Mukiibi J, Nantale M,

Biché P, Sung J, Magcaba Z, Ngcobo N, Morton JF, Lenn M, Aucock S, Shapiro AE,

Steadman A, Draper R, Ganguloo A, Wilson D, Katamba A, Kendall EA, Drain PK.

**BACKGROUND:** Highly sensitive molecular tests, like Xpert Ultra, are reshaping TB

diagnosis-detecting paucibacillary TB but sometimes creating uncertainty when

they detect DNA in extremely low quantities that may not signal disease. This

ambiguity also complicates the evaluation of novel diagnostic strategies. We

sought to monitor adults with a 'Trace' result on an Xpert Ultra test to

estimate the risk of tuberculosis disease up to 24 months later.

**METHODS:** We conducted a multi-site clinical observational study in South Africa

and Uganda, where we enrolled ambulatory participants aged >=15 years with a

sputum Xpert Ultra Trace result who had not yet initiated TB treatment. All

participants underwent comprehensive clinical evaluation and repeated, standard

sputum TB testing. Clinicians deferred treatment recommendations if TB status

remained uncertain after evaluation. Untreated participants were followed

regularly until TB diagnosis and/or treatment initiation. We estimated

cumulative incidence of TB disease, defined by three reference standards.

**RESULTS:** Of 311 participants with Trace results (50% male, 57% PLHIV, 37%

treated for TB within the last 5 years), 24% were positive for TB within 12

months by culture, 37% by sputum Xpert or culture, and 54% by culture or

clinical diagnosis. After excluding those diagnosed with TB at baseline,

patients identified at baseline as having recent TB history, abnormal chest

x-ray, or positive tongue swab, had higher risk of TB diagnosis (hazard ratios:

2.6, 2.4, 4.5, respectively) during follow-up. This hazard was highest in the

first three months after the negative baseline evaluation (0.22 [95% CI:

0.19-0.26] per person-month) and decreased to 0.01 [95% CI: 0-0.02] per

person-month in both the 3-6 and 6-12-month intervals.

**CONCLUSION:** Approximately half of adults and adolescents with a sputum Trace

result were diagnosed with TB disease within twelve months. Although most TB

diagnoses were made within 3 months, risk remained higher than estimated

population incidence rates through the follow-up period. Individuals with sputum

Trace results should receive close clinical monitoring, despite initial clinical

treatment decision.

**SUMMARY RESULTS:** Xpert Ultra "Trace" results detect low quantities of TB DNA,

creating diagnostic uncertainty that complicates both clinical decisions and

diagnostics evaluation. This clinical observational cohort study followed

untreated patients with Trace results for twelve or more months, using survival

analysis to estimate actual tuberculosis disease risk and identify risk factors.

DOI: 10.1101/2025.07.14.25331384

PMCID: PMC12338891

PMID: 40791690

**92. bioRxiv [Preprint]. 2025 Jul 17:2025.07.17.665241. doi:**

**10.1101/2025.07.17.665241.**

Increased vaccine efficacy against tuberculosis with a recombinant BCG

overexpressing the STING agonist cyclic di-AMP.

Singh DK, Um P, Arora G, Alvarez X, Shivanna V, Dick E, Mehra S, Bishai WR.

Tuberculosis (TB) remains the leading cause of death due to infection globally.

Bacillus Calmette Guérin (BCG), a live attenuated bacterial strain, is the only

available TB vaccine, but it has poor efficacy in preventing pulmonary TB in

adults. There are advantages associated with the BCG platform however, including

a remarkable safely profile, billions of administered doses and a public health

ecosystem associated with its production, administration and care. A

recombinant/modified BCG (rBCG/modBCG) anti-TB vaccine candidate would be able

to leverage these advantages while improving on efficacy. BCG-STING is a

recombinant BCG strain which overexpresses the mycobacterial diadenylate cyclase

disA gene leading to the release of ∼15-fold greater levels of the endogenous

small molecule STING agonist cyclic di-AMP. We evaluated vaccination with

BCG-STING compared to its parental BCG-WT strain in rhesus macaques challenged

with virulent Mycobacterium tuberculosis (Mtb). BCG-STING given intradermally

was well-tolerated, and during life serial BAL samples showed that BCG-STING

vaccinated animals had lower Mtb CFU counts than those receiving BCG-WT. At

necropsy, BCG-STING vaccinated animals had significantly lower Mtb lung CFU

counts, and a higher percentage of sterile lobes and granuloma lesions than the

BCG-WT recipients. The enhanced protection observed in BCG-STING vaccinated

animals was associated with significant elevations of antigen-specific CD4 + and

CD8 + T cells. Modifying BCG to overexpress a small molecule recognized by the

innate immune system significantly improves protection and cell-mediated immune

responses against TB the non-human primate (NHP) model.

DOI: 10.1101/2025.07.17.665241

PMCID: PMC12338612

PMID: 40791536

**93. bioRxiv [Preprint]. 2025 Jul 14:2025.07.14.664820. doi:**

**10.1101/2025.07.14.664820.**

Increased proportion of growth-arrested bacilli in acidic pH adaptation promotes

Mycobacterium tuberculosis treatment survival.

Chung ES, Johnson WC, Kamkaew M, McNellis ME, Smith TC, Vijay S, Thuong NTT, Tan

S, Aldridge BB.

The ability of Mycobacterium tuberculosis (Mtb) to adapt its growth behavior in

response to host environments promotes survival against immune and drug

stressors. However, how these behaviors shift at the single-cell level remains

poorly understood. Here, we show that Mtb adapts to acidic conditions by

increasing the proportion of bacteria in a growth-arrested state, rather than

uniformly slowing the growth rate of the entire population. This non-growing

subpopulation exhibits greater tolerance to ethambutol. Clinical strains

displayed higher proportions of growth-arrested cells under both neutral and

acidic conditions, suggesting that growth arrest serves as a bet-hedging

strategy during infection. Though the PhoPR two-component system contributes to

regulating this non-growing state, we show that it is a partial regulator of the

non-growing bacterial subpopulation and that additional transcriptional

regulators are involved. Our study demonstrates that non-growing subpopulations

of Mtb provide fitness benefits and are an active adaptation to environmental

cues and not a passive consequence of stressors.

DOI: 10.1101/2025.07.14.664820

PMCID: PMC12338602

PMID: 40791516

**94. bioRxiv [Preprint]. 2025 Jul 16:2025.07.16.665149. doi:**

**10.1101/2025.07.16.665149.**

An activator of a two-component system controls cell separation and intrinsic

drug resistance in Mycobacterium tuberculosis.

McDonough LD, Li S, Munsamy-Govender V, Gwin CM, Rock JM, Rego EH.

Unlike commonly studied rod-shaped bacteria, mycobacteria grow from their poles,

requiring precise coordination between division and initiation of new pole

growth. The mechanisms that mediate this transition are largely unknown, but

likely represent a rich source of drug targets for the treatment of

mycobacterial infections, including tuberculosis. Here, we identify TapA

(MSMEG\_3748/Rv1697) as a key regulator of this transition. TapA interacts with

the sensor kinase MtrB at the septum to initiate a signaling cascade that

ultimately results in the expression of the essential peptidoglycan hydrolases

RipAB, amongst others, at the end of division. Loss of TapA disrupts division,

dysregulates pole formation, and sensitizes Mycobacterium tuberculosis and other

mycobacteria to several first and second-line TB antibiotics, establishing TapA

as a potential therapeutic target, and defining a new link between cell cycle

progression, envelope remodeling, and intrinsic antibiotic resistance in

mycobacteria.

DOI: 10.1101/2025.07.16.665149

PMCID: PMC12338722

PMID: 40791357

**95. Ann Med Surg (Lond). 2025 Jul 10;87(8):4713-4717. doi:**

**10.1097/MS9.0000000000003548. eCollection 2025 Aug.**

Pakistan's path forward in DR-TB management: insights from global implementation

of BPaL/BPaLM regimen.

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Drug-resistant tuberculosis (DR-TB) is a serious public health threat, and

Pakistan is one of the most impacted nations. The long treatment duration of

traditional regimens puts a great burden on healthcare systems, especially in

resource-constrained environments. Accordingly, the World Health Organization

launched the Bedaquiline, Pretomanid, and Linezolid (BPaL)/Bedaquiline,

Pretomanid, Linezolid, and Moxifloxacin (BPaLM) regimen - a 6-month, all-oral

therapy consisting of BPaLM. With stated success rates as high as 90%, these

regimens present an exciting alternative to traditional treatments. Yet, their

integration into current treatment programs is hindered by policy lags, poor

diagnostic infrastructure, and difficulty in maintaining patient compliance.

This brief communication explores the promise of BPaL/BPaLM to enhance DR-TB

cure rates while pinpointing major hurdles to its use in Pakistan. Enhancing

diagnostic capacity, upgrading healthcare infrastructure, and accelerating

policy adjustment are crucial steps toward maximizing DR-TB management in

high-burden countries.

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DOI: 10.1097/MS9.0000000000003548

PMCID: PMC12333698

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**96. Ann Med Surg (Lond). 2025 Jul 16;87(8):5311-5315. doi:**

**10.1097/MS9.0000000000003576. eCollection 2025 Aug.**

Isolated renal tuberculosis presenting as staghorn calculi and hydronephrosis -

a case report and literature review.

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**INTRODUCTION AND IMPORTANCE:** TB, a major health concern caused by Mycobacterium

tuberculosis, primarily affects the lungs but can also manifest as

extrapulmonary TB (EPTB). Genitourinary tuberculosis (GUTB) ranks third among

extrapulmonary TB cases, following lymphatic and pleural involvement.

**CASE PRESENTATION:** A 45-year-old female from Amahra, Ethiopia presented with

long-standing flank pain, constitutional symptoms, and lower urinary tract

symptoms. She had no significant comorbidities. Physical examination was

unremarkable except for left costovertebral angle tenderness. Abdominal imaging

revealed normal renal parenchyma, left hydronephrosis, and a staghorn calculus.

A unilateral nephrectomy was performed, and surprisingly, pathological analysis

suggested renal tuberculosis. The patient was subsequently treated with a

6-month course of antituberculosis therapy.

**CASE DISCUSSION:** Isolated renal tuberculosis (RTB) is a rare and often

difficult-to-diagnose form of TB due to its nonspecific symptoms. Presentations

range from asymptomatic to severe, including complications like staghorn calculi

or masses. Rena; TB, while typically associated with certain risk factors, can

occur even in their absence, as in this case where the patient only resided in a

high TB burden area. Mycobacterium tuberculosis usually reaches the kidneys via

hematogenous spread from the lungs, though direct spread is also possible, but

isolated renal involvement is rare. Diagnosis of isolated renal tuberculosis is

challenging, often requiring histopathology after nephrectomy or biopsy, as

urine cultures may be unrevealing. Imaging findings vary with the disease stage,

with CT best for calcifications and CT IVP offering broader sensitivity.

Treatment involves anti-tuberculosis medications guided by WHO and national

guidelines. While medications are often sufficient, advanced cases may require

surgical interventions like nephrectomy, with the choice dependent on factors

like disease extent and renal function.

**CONCLUSION:** Isolated renal tuberculosis (RTB) is rare and can be difficult to

diagnose due to its varied symptoms Early detection and treatment with anti-TB

drugs are key to preventing irreversible kidney damage and nephrectomy.

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**97. J Orthop Case Rep. 2025 Aug;15(8):150-153. doi: 10.13107/jocr.2025.v15.i08.5920.**

Isolated Scapular Spine Involvement: A Rare Presentation of Osteoarticular

Tuberculosis.

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(1)Department of Orthopaedics, St. Stephen's Hospital, New Delhi, India.

**INTRODUCTION:** Tuberculosis (TB) is an endemic disease worldwide, especially in

the Indian subcontinent. Most common locations for osteoarticular TB are the

vertebral column and the hip. TB of flat bones, such as the scapula, is an

extremely rare entity.

**CASE REPORT**: The following case report describes a rare case of TB of the spine

of the scapula in a young adult presenting with vague pain over the right

scapular region and an osteolytic lesion over the spine of the scapula. After a

suspicious magnetic resonance imaging scan, the diagnosis was finally confirmed

on biopsy and culture. The patient was successfully managed with a four drug

antitubercular regimen.

**CONCLUSION:** Diagnosis is often delayed due to a lack of awareness among

clinicians and a nonspecific radiological picture. TB should be a differential

diagnosis in isolated scapular pain, particularly in an endemic region, and

biopsy may be helpful in cases of doubtful radiological presentation.

Copyright: © Indian Orthopaedic Research Group.

DOI: 10.13107/jocr.2025.v15.i08.5920

PMCID: PMC12328986

PMID: 40786776

**98. Gynecol Minim Invasive Ther. 2025 Jun 16;14(3):268-271. doi:**

**10.4103/gmit.GMIT-D-24-00046. eCollection 2025 Jul-Sep.**

Surgical Management of Cervical Canal Stenosis with Clinical Tuberculosis Using

Foley's Catheter Stent: A Case Report.

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Uterine cervical canal stenosis can lead to significant complications,

particularly in the context of active clinical tuberculosis. This case study

discusses a 25-year-old woman with undiagnosed clinical tuberculosis who

presented with amenorrhea and persistent abdominal pain. Further evaluation

revealed uterine cervical canal stenosis and frozen pelvis. Surgical

intervention was necessary after confirming the diagnosis through clinical

assessment. A laparotomy with hysterotomy was performed, during which a Foley's

catheter was used to create a patent uterocervical channel. This innovative

approach successfully alleviated her abdominal pain and restored her menstrual

function. The patient's recovery was smooth, and her symptoms improved markedly.

This case underscores the importance of recognizing cervical stenosis as a

potential consequence of tuberculosis and demonstrates the effectiveness of

surgical treatment in managing complex cases without resorting to hysterectomy

or bilateral salpingo-oophorectomy, thereby preserving reproductive potential

for women of childbearing age.

Copyright: © 2025 Gynecology and Minimally Invasive Therapy.

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PMCID: PMC12334098

PMID: 40786676

**99. Wellcome Open Res. 2025 May 28;10:282. doi: 10.12688/wellcomeopenres.24237.1.**

**eCollection 2025.**

Multimorbidity in tuberculosis (TB) and its impact on patient care (MITICare): a

cross-sectional study nested within a prospective cohort study protocol.

Hill K(1), Owori R(2), Naisanga M(3), Owarwo N(2), Mills S(1), Stagg HR(4),

Mpagama S(5), Sekaggya-Wiltshire C(2), Sloan D(1).

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Multimorbidity, defined as two or more co-existing long-term health conditions,

is increasing in low- and middle-income countries, overlapping with ongoing high

tuberculosis (TB) incidence. It is known that there is a high prevalence of

multimorbidity in patients with TB in South Africa, but our understanding of how

common TB-multimorbidity is in other African countries, and its effect on the

trajectories of TB care, is limited. This cross-sectional study nested within a

prospective cohort (co-designed between the Infectious Diseases Institute,

Uganda and the University of St Andrews, United Kingdom) aims to describe the

burden and evaluate the consequences of multimorbidity among patients with TB

disease in Kampala, Uganda. The primary objective is to describe the prevalence

of multimorbidity at the start of treatment for TB. The secondary objectives are

to determine the effect of multimorbidity on clinical characteristics at the

start of treatment, progress through TB care, and end of TB treatment outcomes.

254 adults commencing treatment for TB shall be recruited. Multimorbidity shall

be assessed using structured questionnaires, simple examination and blood

analysis. Th clinical characteristics of TB shall be determined using health and

quality of life scores and, in patients with pulmonary TB, the degree of chest

X-ray abnormalities and sputum bacillary burden. Patients shall be followed-up

at two and six months and their response to treatment determined. The analysis

of the prevalence of multimorbidity at baseline shall be reported using a

proportion and 95% confidence interval. For the secondary objectives, regression

models adjusting for confounders identified through directed acyclic graphs will

be used. This study has been developed in close collaboration with a core

patient and public involvement group, who will also be actively involved in the

dissemination of study results. Ugandan and St Andrews University ethical

approval has been prospectively granted (IDI-REC-2023-82, MD17720 and HS3888ES).

Copyright: © 2025 Hill K et al.

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PMCID: PMC12335725

PMID: 40786601

**100. Bioorg Med Chem. 2025 Aug 6;129:118341. doi: 10.1016/j.bmc.2025.118341. Online ahead of print.**

Synthesis of 1,3-diaryl substituted pyrazole-based imidazo[1,2-a]pyridine

carboxamides and evaluation of their antitubercular activity.

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The rise of drug-resistant tuberculosis (TB) has created an urgent need to

discover and develop new anti-mycobacterial agents. Herein, we report the

synthesis and evaluation of a library of 1,3-diaryl substituted pyrazole-based

imidazo[1,2-a]pyridine carboxamides as promising anti-TB agents. In preliminary

screening, 10 out of 26 compounds displayed potent in vitro inhibition against

Mtb H37Rv with a MIC value of 0.03 μg/mL, which is 17-fold more potent than the

first-line TB drug streptomycin, 33-fold more potent than ethambutol, and

equipotent with isoniazid and rifampicin. Encouragingly, most of these compounds

exhibited a selectivity index (SI) >3333.3 and CC₅₀ values >100 μg/mL against

Vero cells, indicating they are over 3000 times more toxic to M. tuberculosis

than to mammalian cells and demonstrate absence of cytotoxicity at

concentrations effective against TB (MIC = 0.03 μg/mL). Among them, 12a, 14a,

and 14d demonstrated remarkable activity against drug-resistant strains of Mtb

with an MIC of 0.03 μM. Time-kill kinetic studies revealed that 12a, 14a, and

14d exhibited bacteriostatic properties. Furthermore, 12a, 14a, and 14d

demonstrated synergistic effects with the FDA-approved anti-TB drugs rifampicin

(ƩFIC 0.093), ethambutol (ƩFIC 0.061), and moxifloxacin (ƩFIC 0.154-0.281),

exhibiting bactericidal time-kill properties in combination with these drugs.

Additionally, 12a, 14a, and 14d exhibited acceptable metabolic stability (CLint

11.49-14.62 μL/min/mg microsomal protein), indicating effective drug levels and

bioavailability. Also, 12a, 14a, and 14d showed stable interactions with QcrB in

docking studies. These findings highlight 12a, 14a, and 14d as potential

candidates for in vivo evaluation and further development as novel

anti-tubercular drugs.

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**101. J Infect Public Health. 2025 Aug 5;18(11):102920. doi:**

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Re-visiting the surgical role in treating chemotherapeutic-resistance pulmonary

tuberculosis: Results from a systematic review and meta-analysis.

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**BACKGROUND:** The incidence and prevalence of multi-drug-resistant and extensively

drug-resistant pulmonary tuberculosis are increasing, posing profound health

concerns; therefore, surgical intervention is gaining popularity again. However,

the effectiveness of surgical treatment needs to be reassessed. This study

attempted to determine the efficacy of surgical treatment and chemotherapy

compared to chemotherapy alone among patients with pulmonary tuberculosis.

**METHODS:** A systematic search and meta-analysis were conducted from inception to

June 2025 of the existing databases, including PubMed, EMBASE, Cochrane Central

Register of Controlled Trials, and Google Scholar. All double-arm studies

available in English published between 2005 and August 2019 were included. Among

618 studies, 468 were selected based on abstract review. Eight out of 468

(8/468) studies were double-arm retrospective cohorts and observational studies,

which included 1929 persons who matched the inclusion criteria. To measure the

success of the surgical intervention, we used the pooled rate ratio, loss of

patient follow-up, and the incidence of mortality using the random effects

heterogeneity model.

**RESULTS:** Overall, there was no statistically significant difference in the

treatment success rate (RR=1.24 (0.98-1.56), p = 0.07) and mortality rate

(RR=1.82 (0.31-10.63, p = 0.51) between the two groups. Interestingly, the

summary rate ratio (RR=0.41 (0.18-0.93), p = 0.03) showed that the surgical

group had a considerably lower loss rate to follow-up than the non-surgical

group. There was no evidence of heterogeneity amongst the trials (I2 =0 %,

τ2 =0.00, df=2, p = 0.36).

**CONCLUSIONS**: The current meta-analysis was the first to use a factor of loss of

follow-up collected from several reports as a predictive tool to assess the

effectiveness of surgical participation in treating drug-resistant tuberculosis

patients. The rate of patient loss to follow-up in the surgical group suggested

that the combination approach of surgery and chemotherapy showed a potential

superiority over chemotherapy alone.

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Adherence to tuberculosis infection treatment and its impact on prevention of

tuberculosis reactivation: A retrospective cohort study from Taiwan.

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Branch, Hsinchu, Taiwan.

**BACKGROUND:** Treatment for tuberculosis infection (TBI) is often discontinued

owing to adverse drug effects. The impact of treatment completion on TB

reactivation remains poorly understood.

**METHODS:** We conducted a retrospective analysis of 1432 patients at one medical

centre in Taiwan from 2016 to 2021. Patients with TBI were divided into three

groups: non-initiation (N), incomplete treatment (IC), and complete treatment

(C). Those exposure to TB but without TBI formed a control group. TB

reactivation was analysed using multivariable Cox regression models, with

follow-up for up to three years.

**RESULTS:** The overall TB reactivation rate was 2.3 % (34/1432), ranging from

6.1 % in the TBI (N) group (n = 378), 2.1 % in the TBI (IC) group (n = 330),

0.5 % in the TBI (C) group (n = 430), and 0.7 % in the control group (n = 294).

TBI treatment was independently associated with a reduced risk of TB

reactivation. The adjusted hazard ratio (aHR) for TBI (IC) versus TBI (N) was

0.32 (95 % CI 0.12-0.85, p = 0.022), and for TBI (C) versus TBI (N), the aHR was

0.05 (95 % CI 0.01-0.29, p < 0.001). Each 10 % increase in treatment adherence

rate resulted in a 23 % reduction in the risk of TB reactivation (aHR 0.77, 95 %

CI 0.67-0.88, p < 0.001).

**CONCLUSIONS:** TBI treatment, prescribed to 67 % and completed by 38 % of

patients, significantly reduces TB reactivation risk, especially with high

adherence. Enhancing adherence, particularly among elderly patients and those

with comorbidities, is crucial for improving the effectiveness of TBI treatment.

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**Online ahead of print.**

Validation and clinical application of an LC-MS/MS method designed to

simultaneously measure seven second-line TB drugs and two metabolites in human

lung tissue.

Foster KK(1), Pooran A(2), van der Merwe M(1), Castel S(1), Joubert A(1),

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We developed and validated a novel bioanalytical method for the simultaneous

quantification of levofloxacin, linezolid, moxifloxacin, delamanid, bedaquiline,

clofazimine, and pretomanid, along with the metabolites of delamanid (DM-6705)

and bedaquiline (N-desmethyl-bedaquiline, M2), in human lung tissue samples.

Following homogenization by bead beating and extraction by protein

precipitation, the analytes were separated on an Agilent 1260 Infinity II HPLC

system using a Poroshell 120 C18 EC (2.1 mm×50 mm, 2.7 µm) column with gradient

elution, applying a mobile phase consisting of 0.1 % formic acid in water and

0.1 % formic acid in a mixture of acetonitrile and methanol. Detection and

quantification of the analytes and their stable isotope labelled internal

standards were performed on a Sciex API 5500 QTrap mass spectrometer using

positive electrospray ionization and multiple reaction monitoring. Validation

according to the guidelines of the FDA and EMA proved the method to be precise,

accurate, and robust with no significant influence of matrix components. The

application of the method to the analysis of clinical samples demonstrated the

feasibility of quantifying the second-line anti-tuberculosis drugs in human lung

tissue and the potential to provide insights into the drug distribution across

the infection sites in the lung.

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DOI: 10.1016/j.jpba.2025.117093

PMID: 40782709

**104. Diagn Microbiol Infect Dis. 2025 Jul 26;113(4):117008. doi:**

**10.1016/j.diagmicrobio.2025.117008. Online ahead of print.**

The clinical profile of patients with indeterminate Xpert rifampin resistance

results in a single tertiary level institution.

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Philippine General Hospital, Manila, Philippines.

The significance of indeterminate rifampin resistance (RR) Xpert results remains

unclear. Databases from 2016 to 2023 were reviewed, leading to inclusion of 31

cases. Majority were male, newly-diagnosed, symptomatic, and had comorbidities.

On culture, ten were rifampin-susceptible, and two rifampin-resistant.

Indeterminate results cannot be interpreted, and final TB cultures should be

followed-up.

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DOI: 10.1016/j.diagmicrobio.2025.117008

PMID: 40782415

**105. Cell Rep Med. 2025 Aug 5:102286. doi: 10.1016/j.xcrm.2025.102286. Online ahead of print.**

Host-intrinsic and host-extrinsic factors modulate immunity to Mtb infection,

reinfection, and noncanonical vaccination routes.

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Tuberculosis (TB) disease states and outcomes are highly heterogeneous. While

this makes TB difficult to diagnose, monitor, and treat, it also presents

opportunities to identify correlates of protection or disease severity that can

be used as biomarkers and help inform future interventions. Immunological

priming due to primary Mycobacterium tuberculosis (Mtb) infection can protect

against subsequent reinfection; thus, comparing primary infection with

reinfection can provide insights into features associated with host control.

Here, we examine paradigms of natural and vaccine-induced immunity and examine

how host-intrinsic and -extrinsic factors modulate the immune response to

protect against infection and reinfection. We propose that the TB granuloma is a

quasi-homeostatic system, building this model on findings from Mtb reinfection

and successful prophylactics, which suggest that protective immunity depends on

a balance of pro- and anti-inflammatory cellular phenotypes and that this

balance can mitigate pathophysiological processes at the tissue and organismal

level.

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DOI: 10.1016/j.xcrm.2025.102286

PMID: 40780201

**106. Vaccine. 2025 Aug 7;62:127564. doi: 10.1016/j.vaccine.2025.127564. Online ahead of print.**

Pediatric tuberculosis and BCG vaccine in Japan.

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Children's Medical Center, Tokyo, Japan. Electronic address:

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Nagasaki University, Nagasaki, Japan.

Tuberculosis (TB) was a significant public health concern in Japan for over a

century. While archaeological evidence suggests its presence as early as

1800 years ago, TB spread rapidly during Japan's modernization in the late 19th

century. Initial control measures focused on patient isolation and the

establishment of sanatoriums, later supported by the Tuberculosis Prevention

Law. After World War II, public health interventions-such as mandatory case

reporting, mass BCG vaccination, and the introduction of antimycobacterial

agents like streptomycin-contributed to a marked decline in TB incidence and

mortality. Treatment outcomes further improved with the development of multidrug

chemotherapy. Mass BCG vaccination began in 1949, with universal childhood

vaccination implemented in 1974. Japan employs a distinctive intradermal "stamp"

method with multiple needles of BCG administration for less complication of a

skin ulcer. The current strain, BCG Tokyo-172-1, developed in 1981, is used

nationally and distributed globally through WHO-UNICEF programs. Pediatric TB

has become rare, with fewer than 100 new cases annually. Most are identified

through adults contact investigations; others are diagnosed based on clinical

symptoms or screening. In recent years, the proportion of TB cases-including

pediatric cases-among individuals born outside Japan, particularly from

high-burden countries, has increased. As Japan transitions to a low TB burden

setting, the continuation of universal BCG vaccination is under review.

Selective vaccination of high-risk infants and enhanced screening among adults

may offer more targeted and effective approaches.

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DOI: 10.1016/j.vaccine.2025.127564

PMID: 40780094

**107. Biochem Biophys Res Commun. 2025 Aug 7;779:152447. doi:**

**10.1016/j.bbrc.2025.152447. Online ahead of print.**

Structural insight into an intertwined homodimer of the N-terminal domain of

hypothetical protein Rv1421 from Mycobacterium tuberculosis H37Rv.

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Mycobacterium tuberculosis Rv1421 (MtRv1421) is a hypothetical protein that may

participate in the nucleotide-sugar metabolism for cell wall homeostasis. Our

previous studies have suggested that MtRv1421 may be involved in the regulatory

device mediated by uridine diphosphate N-acetylglucosamine (UDP-GlcNAc), a

precursor in peptidoglycan synthesis. However, the detailed molecular functions

of MtRv1421 are unclear due to a lack of structural information. To elucidate

its functional domain structure, we have constructed the truncated MtRv1421

containing the N-terminal domain (MtRv1421-NTD) and determined its crystal

structure at a resolution of 1.7 Å. The overall structure of MtRv1421-NTD showed

an intertwined homodimer in which the β5 strand and α6 helix of one subunit were exchanged with those of the other. In addition, the crystal structure of

MtRv1421-NTD contained an atypical kinase fold caused by an open conformation of

the hinge region between the α4 and α5 helices of each subunit. Our results

provide structural insights into the molecular understanding of MtRv1421,

including interactions between its functional domains and the binding of

UDP-GlcNAc to the putative ligand-binding pocket of MtRv1421-NTD.

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DOI: 10.1016/j.bbrc.2025.152447

PMID: 40779981

**108. medRxiv [Preprint]. 2025 Jul 25:2025.07.25.25332013. doi:**

**10.1101/2025.07.25.25332013.**

Tuberculosis infection screening recommendations for targeted immunotherapies:

comparison of U.S. prescribing information, clinical resources and quality

measures.

Murrill MT(1)(2), Velásquez GE(2)(3), Szumowski JD(4), Phillips A(4), Kim A(5),

Yazdany J(6)(7), Roberts ET(6), Habib AR(1), Batlle HR(8), Salazar J(3), Minter

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**BACKGROUND:** Targeted immunotherapies have transformed the treatment of many

diseases. However, some increase the risk of tuberculosis (TB) disease. We

sought to develop a comprehensive list of targeted immunotherapies with TB

infection screening recommendations in U.S. Food and Drug Administration

(FDA)-approved prescribing information and compare these recommendations to

clinical resources and quality measures.

**METHODS:** Through a grey literature review, we identified TB clinical resources

and U.S. quality measures. We created a list of targeted immunotherapies and TB

infection screening recommendations by analyzing four FDA databases. We then

evaluated the consistency of screening recommendations in prescribing

information, TB clinical resources and quality measures.

**RESULTS:** We identified six TB clinical resources and one quality measure for TB

infection. While TB infection screening recommendations for tumor necrosis

factor (TNF) inhibitors were consistently included, recommendations for other

therapies were less consistent. Through FDA database analyses, we identified 269

targeted immunotherapies, 35 (13%) of which had TB infection screening

recommendations in prescribing information, including all therapies targeting

TNF and several interleukins (IL); however, therapies targeting IL-6,

Janus-associated kinase and others had variable recommendations. Significant

discordance in screening recommendations for immunotherapies were further

identified when comparing prescribing information, clinical resources and

quality measures.

**CONCLUSIONS:** The number and targets of immunotherapies are rapidly evolving

resulting in challenges with creating, up-to-date and consistent TB infection

screening recommendations. Inconsistent recommendations in clinical resources

may contribute to gaps in TB preventive care. Harmonized recommendations and

additional epidemiologic studies of TB disease risk with the use of these agents

are needed.

DOI: 10.1101/2025.07.25.25332013

PMCID: PMC12330402

PMID: 40778184

**109. medRxiv [Preprint]. 2025 Jul 23:2025.07.22.25331806. doi:**

**10.1101/2025.07.22.25331806.**

UShER-TB: Scalable, Comprehensive, Accessible Phylogenomic Analysis of

Mycobacterium tuberculosis.

Karim LM, Martínez-Martínez FJ, O'Farrell A, Hinrichs AS, Sanderson T, Iqbal Z,

Kozyreva VK, Bell JM, López MG, Comas I, Corbett-Detig R.

Mycobacterium tuberculosis, the bacterium responsible for the Tuberculosis (TB)

disease, remains a leading global infectious disease killer, and genomic

epidemiology is essential for understanding its transmission dynamics.

Computational limitations prevent comprehensive phylogenetic analysis of the

publicly available Mycobacterium tuberculosis genomes. Here, we create UShER-TB,

a comprehensive pipeline for scalable phylogenomic MTB analysis. We processed

129,312 MTB genomes to construct a comprehensive global phylogeny capturing

unprecedented genomic diversity. UShER-TB achieved high accuracy in transmission

cluster reconstruction. The comprehensive phylogeny also facilitated

identification of putative novel lineages and sublineages, and successful

placement of ancient DNA samples. The UShER-TB platform enables real-time

phylogenomic analysis of new genomes, revealing transmission hotspots and

introduction patterns at global scales. Our approach overcomes longstanding

computational barriers, providing researchers with efficient tools for TB

genomic surveillance especially for resource-limited settings where TB burden is

highest.

DOI: 10.1101/2025.07.22.25331806

PMCID: PMC12330463

PMID: 40778146

**110. Afr Health Sci. 2024 Sep;24(3):69-74. doi: 10.4314/ahs.v24i3.10.**

Molecular identification of Mycobacterium bovis in patients with tuberculosis

attending a tertiary care hospital in South India.

Jamir I(1), Joseph NM(1), Kannambath R(1), Kumar P(1).

Author information:

(1)JIPMER, Microbiology.

**BACKGROUND:** Mycobacterium (M.) bovis is a member of Mycobacterium tuberculosis

complex (MTBC). Clinical infection caused by M. bovis is indistinguishable from

other MTBC and could pose a potential challenge for control of TB epidemic due

to its zoonotic nature. Availability of reliable molecular diagnostic methods

such as Genotype MTBC based on line probe assay (LPA) paves way for reliable

differentiation of M. bovis from other MTBC.

**OBJECTIVE:** To determine the proportion of Mycobacterium bovis among the

Mycobacterium tuberculosis complex isolates from patients with tuberculosis.

**METHODS:** In our study, we analysed MGIT positive cultures and performed Line

probe assay (LPA) for identification of MTBC isolates. Total of 206 patient

samples were taken, 104 pulmonary and 102 from extrapulmonary sites.

**RESULTS:** M.tuberculosis/M.canettii was isolated in all pulmonary specimens

(100%). Among 102 extrapulmonary samples, 99 % was identified as

M.tuberculosis/M.canettii, and 1 % as M. bovis BCG.

**CONCLUSION:** Our study suggests that zoonotic TB by M. bovis may not be as

prevalent in India and hence may not constitute a significant risk to public

health in India.

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DOI: 10.4314/ahs.v24i3.10

PMCID: PMC12327116

PMID: 40777939 [Indexed for MEDLINE]

**111. Iran J Public Health. 2025 Jul;54(7):1339-1349. doi: 10.18502/ijph.v54i7.19113.**

Community Empowerment through Cadres in the Tuberculosis Program: A Scoping

Review.

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Soepraoen, Malang, Indonesia.

**BACKGROUND:** Tuberculosis (TB) remains a global public health problem with high

morbidity and mortality rates, especially in low- and middle-income countries.

Community-based approaches, including empowerment of health cadres, have been

recognized as a key strategy to improve the success of TB control programs. This

review systematically identifies research that has been carried out to determine

the contribution of cadres in tuberculosis control programs in various

countries.

**METHODS:** This scoping review used five electronic databases, namely PubMed,

Scopus, Medline-Ebscohost, ProQuest, and Cochrane, to identify the contribution

of cadres in TB programs. Article selection was based on PCC (Population,

Concept, Context) criteria with a limitation of 2014-2024 and only

English-language articles.

**RESULTS**: Out of 793 initial articles, 20 articles met the eligibility criteria.

Studies show that empowering cadres is effective in detecting TB cases,

improving patient adherence to treatment, and overcoming stigma through

culture-based education. However, challenges such as lack of training,

incentives, and access to diagnostic tools often hinder cadre performance.

**CONCLUSION:** Health cadres play an important role in bridging the gap between

formal health services and the community. With the support of structured

training, resource allocation, and community empowerment, cadres can maximize

their impact in TB control programs.

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Sciences.

DOI: 10.18502/ijph.v54i7.19113

PMCID: PMC12325868

PMID: 40777896

**112. Front Vet Sci. 2025 Jul 24;12:1628812. doi: 10.3389/fvets.2025.1628812.**

**eCollection 2025.**

Field evaluation of the P22 ELISA for diagnosis of caprine tuberculosis in an

endemic area.

Velasco C(1)(2), Ortega J(1), Alvarez J(1)(2), Infantes Lorenzo JA(3), Moreno

JC(4), Sanz C(4), Romero B(1)(2), de Juan L(1)(2), Dominguez L(1)(2), Dominguez

M(5), Moreno I(5), Roy A(6), Bezos J(1)(2).

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Spain.

Animal tuberculosis (TB) affects a wide range of domestic species, including

goats. TB eradication programs in goats are based on cell-based techniques such

as the single and comparative intradermal tuberculin test (SITT and CITT,

respectively). In recent years, an ELISA technique based on the P22 protein

complex (P22 ELISA), has emerged as a valuable tool for TB diagnosis. The aim of

the study was to evaluate the performance of the P22 ELISA in the context of a

caprine TB eradication program using serum, individual milk and bulk tank milk

(BTM) samples in order to define its usefulness in classifying herds compared to

SITT and CITT. Samples from 53 herds categorized based on the detection of CITT

reactors (16 high-risk herds, with one or more CITT reactors, and 37 low-risk

herds, with only CITT-negative goats) were analyzed. Reactors in the P22 ELISA

were detected in a higher number of high-risk herds using both serum (87.5%) and

individual milk (81.3%) compared to SITT (75.0%) and CITT (31.3%), while the use

of BTM led to the detection of 33.3% of the herds. Individual apparent

prevalence was higher using the P22 ELISA in both serum (11.0%) and milk (15.0%)

compared to the SITT (6.8%) and CITT (2.5%), with also a significantly

(p < 0.001) higher number of reactors in individual milk compared with the

serum. Similarly, all six herds with MTBC confirmed infection showed reactors to

the SITT, CITT, and individual serum and milk P22 ELISA (2 out of 5 detected

using BTM), although the highest reactivity was observed using individual milk

samples. In the low-risk herds, a lower number of positive herds and animals

were found with the P22 ELISA using serum or individual milk (51.4%) compared to

SITT (59.5%) while using CITT only 2.7% of the herds were positive and none

reacted to the P22 ELISA in BTM samples. This study shows that the P22 ELISA,

using serum and especially individual milk samples, could be a complementary

tool for maximizing the sensitivity of intradermal testing within the framework

of a caprine TB eradication program.

Copyright © 2025 Velasco, Ortega, Alvarez, Infantes Lorenzo, Moreno, Sanz,

Romero, de Juan, Dominguez, Dominguez, Moreno, Roy and Bezos.

DOI: 10.3389/fvets.2025.1628812

PMCID: PMC12329796

PMID: 40777827

**113. Cureus. 2025 Jul 7;17(7):e87491. doi: 10.7759/cureus.87491. eCollection 2025**

**Jul.**

Successful Treatment of Post-tuberculosis Pulmonary Aspergillosis With Liposomal

Amphotericin B in a Patient After a Rare Event of Voriconazole-Associated

Hypotension: A Case Report.

Alsaeed A(1).

Author information:

(1)Infectious Disease Division, Internal Medicine Department, Dammam Medical

Complex, Dammam, SAU.

Pulmonary aspergillosis (PA) is a serious lung infection caused by Aspergillus

species, primarily affecting individuals with structural lung abnormalities.

Common risk factors include pulmonary tuberculosis (TB) and other chronic lung

diseases. Voriconazole, a second-generation triazole, is the preferred

first-line treatment for invasive PA, although few adverse events are reported.

Liposomal amphotericin B (LAmB) serves as an alternative treatment, particularly

in cases of azole resistance or intolerance. This case report describes a rare

occurrence of probable voriconazole-associated hypotension in a 52-year-old

immunocompetent male with post-TB aspergillosis. The patient, previously treated

for TB, presented with pleuritic chest pain, productive cough, and hemoptysis.

Initial treatment with voriconazole led to significant symptomatic relief but

was complicated by persistent hypotension, despite normal blood parameters. A

multidisciplinary team identified voriconazole as the cause of hypotension, and

treatment was switched to LAmB. Consequently, his blood pressure stabilized, and

the PA symptoms resolved without any adverse events. This case underscores the

importance of monitoring rare side effects during voriconazole therapy and

highlights LAmB as an alternative in voriconazole-intolerant scenarios and in

situations where the availability of other azoles (posaconazole and

itraconazole) is limited; however, further research is necessary to optimize

therapeutic strategies.

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DOI: 10.7759/cureus.87491

PMCID: PMC12329161

PMID: 40777692

**114. bioRxiv [Preprint]. 2025 Jul 21:2025.07.20.665812. doi:**

**10.1101/2025.07.20.665812.**

RNA polymerase-mediated regulation of intrinsic antibiotic resistance and

bacterial cell division.

Soni V, Zhu J, Patel Y, Helmann JD, Rubin EJ, Rhee KY.

Rifampin is a frontline antibiotic that inhibits the RNA polymerase of

Mycobacterium tuberculosis (Mtb), the causative agent of tuberculosis (TB).

Unlike most antibiotics, rifampin has an unusual ability to shorten the duration

of treatment needed to cure TB that is not simply explained by its antimicrobial

potency. We sought specific secondary effects of rifampin's inhibition of Mtb

RNA polymerase that may mediate this activity. We discovered that rifampin

elicited a cell division arrest that was mediated through its inhibition of RNA

polymerase. This arrest resulted in a downstream inhibition of the MtrAB

two-component regulatory system, a mediator of intrinsic antibiotic resistance

in Mtb. This inhibition is broadly conserved in other bacteria and represents a

novel form of antimicrobial activity, termed adjunctive sensitization, that can

mediate synergy and may contribute to rifampin's unusual treatment shortening

activity.

DOI: 10.1101/2025.07.20.665812

PMCID: PMC12330665

PMID: 40777489

**115. bioRxiv [Preprint]. 2025 Jul 24:2025.07.21.665984. doi:**

**10.1101/2025.07.21.665984.**

Distinct antibody-based signatures and functionality distinguish latent and

active pediatric tuberculosis.

Nziza N, Jung W, Chen T, Deng Y, Franken KLMC, Ottenhoff THM, Kiguli S,

Lewinsohn DA, Boom WH, Mayanja-Kizza H, Nsereko M, Fortune SM, Stein C, McNamara

R, Alter G, Lancioni CL.

**BACKGROUND:** Tuberculosis (TB), caused by Mycobacterium tuberculosis (Mtb), is

among the leading causes of death from an infectious agent among children

worldwide. Children represent a particularly vulnerable population due to the

greater challenges in diagnosis and the higher risk of progression to severe

forms of the disease. However, whether different pediatric outcomes relate to

distinct immunologic responses remains incompletely understood. Emerging data

suggest that Mtb-specific humoral immune responses represent a correlate of

protection against Mtb both following natural infection and vaccination.

**METHODS:** To determine if immune profiles can distinguish children across the

spectrum from Mtb infection to TB disease, as well as children with TB from

non-TB lower respiratory tract infection, we mapped the humoral immune response

across a panel of 4 dozen Mtb antigens across children presenting with symptoms

of active TB (ATB), children with evidence of latent TB infection (LTBI) and

children exhibiting non-TB lower respiratory tract infection (non-TB LRTI).

Using a custom Luminex assay, Mtb-specific antibody subclass/isotype, Fc

receptor (FcR) binding profiles, and functions were profiled across the

pediatric groups.

**FINDINGS:** A robust humoral immune response was observed in children with active

TB compared to non-TB LRTI, marked by a strong IgA response, that exhibited high

FcαR binding. Conversely, children with LTBI uniquely elicited Mtb-specific

antibodies with enhanced opsinophagocytic FcγR2A binding, as well as a higher

capacity to activate NK cells and neutrophils.

**INTERPRETATION:** There are significant differences in humoral immune profiles

across the landscape of pediatric TB, potentially contributing to differential

mycobacterial control, and highlighting biomarkers that could guide both

diagnostic and therapeutic approaches.

FUNDING: US National Institutes of Health.

DOI: 10.1101/2025.07.21.665984

PMCID: PMC12330548

PMID: 40777430

**116. bioRxiv [Preprint]. 2025 Jul 26:2025.07.23.664455. doi:**

**10.1101/2025.07.23.664455.**

Human iPSC derived alveolar macrophages reveal macrophage subtype specific

functions of itaconate in M. tuberculosis host defense.

Krebs A, Lazarov T, Reynolds A, Dill-McFarland KA, Xie A, Bean J, Du M, Levy O,

Buglino J, Zhong A, Neehus AL, Boisson-Dupuis S, Casanova JL, Kroon EE, Möller

M, Hawn TR, Zhou T, Finley LWS, Jean Juste MA, Fitzgerald D, Geissmann F,

Glickman MS.

Mycobacterium tuberculosis (Mtb) must survive within multiple macrophage

populations during infection, including alveolar macrophages (AM) and recruited

inflammatory macrophages. In mice, itaconate, produced in macrophages by ACOD1

mediated decarboxylation of aconitate, has direct antimicrobial activity,

modulates inflammatory cytokines, and is required for resistance to M.

tuberculosis (Mtb) infection. The role of itaconate in human macrophages is less

clear and whether itaconate mediates distinct effects in macrophage subtypes is

unknown. Here, we investigated the role of itaconate in human iPSC-derived

macrophages, either induced by GM-CSF to resemble alveolar macrophages (AM-Like

cells), or treated with M-CSF to generate control macrophages (MCDM cells). Both

types of human macrophages produce substantially less itaconate than mouse

macrophages and AM-Ls produced 4-fold less itaconate than MCDMs. Surprisingly,

ACOD1 deficient AM-L macrophages, but not MCDM macrophages, were permissive for

Mtb growth. Moreover, itaconate functioned to dampen the Mtb induced

inflammatory response in MCDMs, but not AM-L macrophages, affecting both the

Type I IFN and TNF pathways. These results indicate that itaconate is involved

in human macrophage responses to TB, with distinct roles in different macrophage

subsets. These results also show that genetically tractable hiPSC-derived

macrophages are a robust and versatile model to dissect cellular host pathogen

interactions.

DOI: 10.1101/2025.07.23.664455

PMCID: PMC12330731

PMID: 40777401

**117. Afr J Prim Health Care Fam Med. 2025 Jul 30;17(1):e1-e8. doi:**

**10.4102/phcfm.v17i1.4944.**

Access to tuberculosis care in South Africa during the COVID-19 pandemic: A

scoping review.

Appel K(1), Nackerdien F, Christian CS.

Author information:

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University of the Western Cape, Bellville. 3944771@myuwc.ac.za.

**BACKGROUND:**  Tuberculosis (TB) remains a major public health issue in South

Africa, a high-burden TB country. The coronavirus disease 2019 (COVID-19)

pandemic has exacerbated challenges in accessing essential TB services. This

scoping review explores how access to TB care was impacted during the pandemic.

AIM:  This research aimed to review original studies on access to TB care in

South Africa during the COVID-19 pandemic using a scoping review methodology.

**METHOD:**  A scoping review was conducted using the Preferred Reporting Items for

Systematic Reviews and Meta-Analyses for Scoping Reviews (PRISMA-ScR)

guidelines. Five databases were systematically searched for original

peer-reviewed research published between 2020 and 2022. Data were extracted and

synthesised using the Penchansky and Thomas framework of healthcare access.

**RESULTS:**  Three studies met the inclusion criteria. The review identified

significant disruptions in TB service delivery during the pandemic, including

reduced diagnostic capacity, healthcare facility closures and economic barriers.

Patients reported delayed diagnoses and increased stigma, while healthcare

workers faced resource shortages and operational challenges.

**CONCLUSION:**  The COVID-19 pandemic has exacerbated pre-existing barriers to TB

care in South Africa, highlighting critical gaps in healthcare delivery. This

review provides insights into the challenges faced and emphasises the need for

resilient health systems to sustain TB care during future health crises.

Contribution: This article highlights the impact of the COVID-19 pandemic on TB

care access in South Africa, identifying key barriers across healthcare access

dimensions and offering recommendations to improve TB care delivery during

public health emergencies.

DOI: 10.4102/phcfm.v17i1.4944

PMCID: PMC12339777

PMID: 40776715 [Indexed for MEDLINE]

**118. Eur J Immunol. 2025 Aug;55(8):e70004. doi: 10.1002/eji.70004.**

Granulysin Antimicrobial Activity Promotes Dormancy in Mycobacterium

tuberculosis.

Schmidiger S(1)(2), McCaffrey EF(3), Schmidt JM(4), Hameed OA(5), Mpina M(6),

Tumbo A(6), Mfinanga E(6), Haraka F(6), Hiza H(1)(2)(6), Sasamalo M(1)(2)(6),

Hella J(6), Walch M(5), Fellay J(7)(8)(9), Gagneux S(1)(2), Reither K(1)(2),

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Human tuberculosis (TB) caused by Mycobacterium tuberculosis (Mtb) remains a

global public health threat. Granulomas constitute a hallmark of TB pathogenesis

that can clear, contain, or exacerbate an infection. Containment is exploited by

Mtb as a hideout to persist in a dormant, antibiotic-tolerant state, only to

resuscitate upon immunosuppression. The immune determinants of a granulomatous

response driving Mtb persistence remain elusive. We here generated ex vivo

granuloma-like structures from peripheral blood mononuclear cell specimens of TB

patients and applied high-dimensional mass cytometry to elucidate immune factors

prompting Mtb dormancy. Compared with healthy controls, patient-derived

specimens rapidly forced Mtb to become dormant-like ex vivo. This observation

correlated with an enrichment in activated, innate (-like) cytotoxic lymphocytes

and required the presence of CD56+ lymphocytes or, more specifically, the

content of their granules. Finally, we demonstrated that direct exposure to

granulysin induces Mtb dormancy, thereby unravelling an immune escape mechanism

to cytotoxic lymphocyte activity.

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GmbH.

DOI: 10.1002/eji.70004

PMCID: PMC12332329

PMID: 40776481 [Indexed for MEDLINE]

**119. Stud Health Technol Inform. 2025 Aug 7;329:1550-1552. doi: 10.3233/SHTI251099.**

Evaluation of an AI-Assisted Platform to Support Tuberculosis Care Delivery.

Iribarren S(1), Yuwen W(2), Filienko D(3), Jakher H(1), Nizar M(3), Vidrio A(1),

Kwanin C(1), Galdamez D(1), Roberti J, De Cock M(3).

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The Tuberculosis Treatment Support Tools (TB-TST) will integrate a

Spanish-language AI-powered virtual assistant to enhance TB care. Leveraging

Large Language Models for real-time, empathetic, and clinically relevant

support, the system aims to improve treatment adherence, expand scalability, and

increase access to care while ensuring privacy, linguistic, and cultural

relevance.

DOI: 10.3233/SHTI251099

PMID: 40776117 [Indexed for MEDLINE]

**120. Vet Res. 2025 Aug 7;56(1):163. doi: 10.1186/s13567-025-01585-x.**

M. caprae in northern Italy: a comprehensive analysis through whole-genome

sequencing on the genetic variability in bovine herds.

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(#)Contributed equally

Mycobacterium (M.) bovis and M. caprae are the causative agents of bovine

tuberculosis (bTB), which is still a concern due to its health implications and

economic impact. Although M. caprae is less prevalent than M. bovis among bovine

tuberculosis cases, it has a significant impact on animal health especially in

Europe, where it has been isolated from a range of hosts. Starting from

spoligotyping and the MIRU-VNTR profile specifically associated with the Lechtal

subgroup we decided to process a selection of Italian M. caprae isolates using

whole genome sequencing (WGS) to define the phylogenetic relationships between

isolates and deepen the understanding of this public health issue. In this

study, 20 outbreaks of bovine tuberculosis caused by M. caprae in northern Italy

were retrospectively investigated by interpreting and validating WGS results

with available epidemiological information. Genomes of 34 Italian strains, with

a known and traditionally typed genotype, isolated between 2001 and 2022 from 21

bovine farms, with 12 isolates from Austria, were analyzed focusing on single

nucleotide polymorphisms (SNP) to derive evolutionary relationships, pairing

with the tracing of infections, suggested by the epidemiological contacts. The

results outline possible connections between outbreaks, which caused the spread

of the infection, obtaining two clusters differing by 6-16 SNP pairwise,

overlapping with the territory distribution of the herds between two different

Italian regions. Epidemiological information and phylogeny revealed that M.

caprae was probably introduced in northern Italy from Austria and/or Germany,

through separate and independent events for the two Italian clusters. The

complex approach of integrating WGS data with epidemiological information proved

to be useful in delineating likely transmission chains and identifying the

possible sources of infection, showing how NGS is a powerful tool to support

epidemiological investigations.

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DOI: 10.1186/s13567-025-01585-x

PMCID: PMC12330137

PMID: 40775653 [Indexed for MEDLINE]

**121. Am J Case Rep. 2025 Aug 16;26:e947502. doi: 10.12659/AJCR.947502.**

Successful Treatment of Multidrug-Resistant Tuberculous Meningitis in a Young

Chinese Woman: A Case Study From Japan.

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**BACKGROUND** Multidrug-resistant tuberculosis (MDR-TB) continues to pose a serious

public health challenge, especially when associated with tuberculous meningitis

(TBM), which complicates treatment due to the need for central nervous system

(CNS) penetration and non-oral administration routes. This case report describes

a 24-year-old woman with MDR pulmonary tuberculosis and tuberculous meningitis

(TBM) successfully treated with a combination of pyrazinamide, levofloxacin,

cycloserine, and linezolid. **CASE REPORT** A previously healthy 24-year-old woman

from Jilin Province, China presented with fever, headache, and impaired

consciousness. Chest computed tomography (CT) showed centrilobular nodules and

tree-in-bud appearances, while magnetic resonance imaging (MRI) revealed basal

meningeal enhancement and tuberculomas. Acid-fast bacilli (AFB) were detected on

smear microscopy of cerebrospinal fluid (CSF), and culture confirmed

Mycobacterium tuberculosis. Drug susceptibility testing confirmed MDR-TB. Due to

impaired consciousness, the treatment regimen was selected based on CNS

penetration and enteral administration compatibility. A combination of

pyrazinamide, levofloxacin, cycloserine, and linezolid was administered over 18

months. Bedaquiline and pretomanid were not used due to insufficient CNS

penetration data at the time and limited availability in Japan. The patient

required prolonged mechanical ventilation and was discharged in a minimally

conscious state after 541 days. **CONCLUSIONS** This case highlights the importance

of individualized drug selection for MDR-TB with CNS involvement. In managing

tuberculosis, especially in low-incidence countries, the epidemiological

background of the patient's country of origin should also be considered. Early

diagnosis and appropriate drug selection were critical to the patient's survival

despite severe neurological sequelae.

DOI: 10.12659/AJCR.947502

PMID: 40817574