**2025年第31周**

**境外学者发表的结核病英文文章摘要**

**（102篇）**

**PubMed Publication date: 2025/7/28 --- 2025/8/3**

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

**1. Front Microbiol. 2025 Jul 4;16:1612354. doi: 10.3389/fmicb.2025.1612354.**

**eCollection 2025.**

Dictyostelium discoideum-Mycobacterium marinum infection model: a powerful

high-throughput screening platform for anti-infective compounds.

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Tuberculosis is among the world's deadliest diseases, causing approximately 2

million deaths annually. The urgent need for new antitubercular drugs has been

intensified by the rise of drug-resistant strains. Despite recent advancements,

most hits identified through traditional target-based screening approaches

exhibit limited efficacy in vivo. Consequently, there is a growing demand for

whole-cell-based approaches that utilize host-pathogen systems directly. The

Dictyostelium discoideum-Mycobacterium marinum host-pathogen system is a

well-established and powerful alternative model system for studying

mycobacterial infections. In this article, we present a phenotypic host-pathogen

assay protocol that monitors M. marinum during infection of the amoeba D.

discoideum. This assay is characterized by its scalability for high-throughput

screening, robustness, and ease of manipulation, making it an effective system

for compound screening. Notably, this system provides dual readouts: bacterial

load via a bioluminescent M. marinum strain and host survival and growth via a

fluorescent D. discoideum strain, enabling further host characterization by

quantifying growth inhibition and potential cytotoxicity. Finally, the assay was

benchmarked against selected antibiotics and anti-infectives, and IC50s and MIC

values were calculated where applicable, demonstrating its ability to

differentiate between antibiotics and anti-infective compounds.

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DOI: 10.3389/fmicb.2025.1612354

PMCID: PMC12271166

PMID: 40687854

**2. ACS Omega. 2025 Jul 2;10(27):29547-29557. doi: 10.1021/acsomega.5c02912.**

**eCollection 2025 Jul 15.**

Designing Novel InhA Inhibitors for Antituberculosis Agents Using ab Initio

Fragment Molecular Orbital Calculations.

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Tuberculosis is an ancient chronic disease caused by () and remains one of the

leading causes of death worldwide. InhA, an enoyl-ACP reductase in , plays a

crucial role in the biosynthesis of mycolic acids, essential constituents of the

mycobacterial cell wall. Therefore, InhA enzyme has been considered as a

promising target for the development of novel antitubercular drugs. In our

previous molecular simulations, we investigated the interactions between InhA

and a series of benzimidazole derivatives for the crystal structure of InhA (PDB

ID: 6R9W) using ab initio fragment molecular orbital (FMO) calculations. To

design highly effective benzimidazole derivatives as InhA inhibitors, we here

extended our molecular simulations to other derivatives and highlighted key

electronic-level interactions between InhA and these compounds. Indeed, we

strategically modified substituents at three sites of the 2,3-dihydro-1H-indene

ring of the most potent benzimidazole derivative, with the aim of facilitating

hydrogen bond formation to InhA residues. A total of 24 compounds were

rationally designed and virtually screened based on Lipinski's rule of five and

toxicity predictions, ultimately obtaining nine promising candidate compounds.

Using FMO calculations, specific interactions were elucidated between InhA and

the compounds to highlight key interactions for achieving high binding affinity

to InhA. Notably, the highest-affinity inhibitor exhibited strong hydrogen bond

interactions with the backbones of Gln100, Ala157, and Ile215, as well as

nicotinamide adenine dinucleotide of InhA. These findings provide valuable

structural insights for designing novel benzimidazole derivatives with improved

binding efficiency to InhA. Overall, our ab initio molecular simulations provide

crucial insights for the rational design of more effective InhA inhibitors,

potentially advancing tuberculosis chemotherapy.

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DOI: 10.1021/acsomega.5c02912

PMCID: PMC12268426

PMID: 40687024

**3. Turk J Med Sci. 2025 Apr 7;55(3):595-601. doi: 10.55730/1300-0144.6006.**

**eCollection 2025.**

One-year clinical follow-up of granulomatous lymphadenitis diagnosed via

EBUS-TBNA in a tuberculosis-endemic region.

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**BACKGROUND/AIM:** Granulomatous lymphadenitis is not a specific clinical

diagnosis. In regions where tuberculosis (TB) is endemic, differentiating

between various diseases presenting with granulomatous lymphadenitis poses a

significant clinical challenge. This study aims to evaluate the etiological

distribution of underlying conditions and to assess diagnosis changes observed

during at least one year of follow-up in patients diagnosed with granulomatous

lymphadenitis through endobronchial ultrasound-guided transbronchial needle

aspiration (EBUS-TBNA).

**MATERIALS AND METHODS:** A total of 4711 patients were included in the study, and

9353 lymph node samples were collected. Granulomatous lymphadenitis was

identified in 791 patients, from whom 1505 lymph node samples were obtained. A

cohort of 453 patients was monitored for at least 1 year, during which 873 lymph

node samples were collected. The medical records of these patients were

retrospectively reviewed in detail, and the final clinical diagnosis for each

patient was established at the conclusion of the 1-year follow-up period.

**RESULTS:** Sarcoidosis was the most common final diagnosis, accounting for 52.3%

of cases, while tuberculosis lymphadenitis was diagnosed in 42.6% of patients.

Diagnostic procedures, including acid-fast bacteria (AFB) staining, culture, and

TB-PCR, were performed in 94.3% of the cohort. Nonnecrotizing granulomatous

lymphadenitis was identified in 8 patients with a history of extrathoracic

malignancy; 5 were diagnosed with sarcoid-like reactions and 3 with TB

lymphadenitis. Additionally, during the 1-year clinical follow-up period, the

initial diagnosis was revised in 14 patients.

**CONCLUSION:** Long-term follow-up of clinical progression and treatment response

is crucial for precise diagnosis and management. The study findings suggest that

routine TB-PCR and AFB testing on EBUS-TBNA-derived lymph node samples could

enhance diagnostic precision.

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DOI: 10.55730/1300-0144.6006

PMCID: PMC12270314

PMID: 40686701 [Indexed for MEDLINE]

**4. Br J Nurs. 2025 Jul 17;34(14):713. doi: 10.12968/bjon.2025.0306.**

Tuberculosis: a public health challenge.

Peate I(1).

Author information:

(1)Editor in Chief, British Journal of Nursing.

DOI: 10.12968/bjon.2025.0306

PMID: 40686402

**5. Clin Infect Dis. 2025 Jul 18:ciaf397. doi: 10.1093/cid/ciaf397. Online ahead of print.**

Oral washes and tongue swabs for Xpert MTB/RIF Ultra-based tuberculosis

diagnosis in people with and without the ability to make sputum.

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**BACKGROUND:** Oral samples show promise for tuberculosis (TB) diagnosis, but data

from different sample types and sputum-scarce individuals remain limited.

**METHODS:** We evaluated Xpert MTB/RIF Ultra (Ultra) in symptomatic clinic

attendees (Cohort A, n=891) and people initiating antiretroviral therapy without

symptom screening (Cohort B, n=258). In Cohort A, we collected oral washes (OWs)

and, separately, tongue swabs (flocked or foam with heat). In Cohort B, we

collected OWs, three flocked tongue swabs (one heated, two pooled), and,

separately, buccal swabs and periodontal brushes. Sputum induction was offered,

and different culture methods applied to a subset of Cohort B tongue swabs.

**RESULTS:** In Cohort A, Ultra sensitivity was 80% (95% CI: 56-94) for OWs, 59%

(53-65) for flocked swabs, and 65% (58-72) for foam swabs, with high

specificity. Foam swabs detected more people with lower sputum semi-quantitation

categories than flocked swabs [53% (41-64) vs. 37% (29-46)]. In Cohort B, OWs

and single heated swabs had sensitivities of 71% (42-92) and 64% (35-87),

respectively. Pooled tongue swabs, buccal swabs, and brushes had lower

sensitivity. MGIT960 showed the highest sensitivity [64% (35-87)] among culture

methods. Oral sampling identified TB in sputum-scarce people: 25% (7/28)

positive by flocked or foam swabs (Cohort A); 18% (10/56) OW- and 23% (13/56)

single swab-positive (Cohort B). In Cohort B, this could double Ultra positivity

if induction were unavailable.

**CONCLUSION:** Ultra on OWs or foam swabs offers higher sensitivity than other oral

methods and effectively detects TB in sputum-scarce individuals.

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Infectious Diseases Society of America.

DOI: 10.1093/cid/ciaf397

PMID: 40686067

**6. Indian J Pediatr. 2025 Jul 25. doi: 10.1007/s12098-025-05682-9. Online ahead of print.**

Tuberculosis Preventive Treatment Coverage in India: An Ignored Yellow Alert?

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DOI: 10.1007/s12098-025-05682-9

PMID: 40711651

**7. Respir Med. 2025 Aug 1:108287. doi: 10.1016/j.rmed.2025.108287. Online ahead of print.**

Retrospective Evaluation of 5-Year Tuberculosis Cases in Bolu, Turkey (Before,

During and After the COVID-19 Pandemic).

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**INTRODUCTION:** Tuberculosis (TB) regained its position as the world's leading

cause of death in 2023, following the coronavirus disease 2019 (COVID-19)

pandemic. This study aims to analyze the diagnosis, treatment, and follow-up

processes of TB patients diagnosed in our province over a five-year period and

to assess the impact of the COVID-19 pandemic on TB.

**MATERIALS AND METHODS:** Demographic data, comorbidities, TB diagnosis, treatment,

and follow-up information for 144 patients monitored in the TB Unit between

January 2019 and December 31, 2023, were evaluated. The demographic

characteristics, case definitions, comorbidities, treatment approaches, and

outcomes of TB cases were compared over the five-year period. Patients were

categorized as either living or deceased, and their case characteristics were

analyzed accordingly.

**RESULTS:** When patient characteristics were compared across years, no significant

differences were observed, except for a notable increase (26.1%) in the use of

first- and second-line treatment options in 2022 compared to other years

(p=0.011). Compared to the living group, deceased patients were older, had a

higher frequency of first- and second-line treatment use, and showed a greater

prevalence of concurrent pulmonary and extrapulmonary TB.

**CONCLUSION:** Although the number of TB cases declined between 2020 and 2022, it

increased again in 2023 following the end of the pandemic. The pandemic did not

significantly impact demographic data, TB case definitions, disease

localization, or treatment outcomes, except for an increased use of first- and

second-line drugs in 2022.

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DOI: 10.1016/j.rmed.2025.108287

PMID: 40754265

**8. Eur J Pharm Sci. 2025 Aug 1:107219. doi: 10.1016/j.ejps.2025.107219. Online**

**ahead of print.**

Development, characterization and evaluation of antibacterial efficacy of

actively targeted gold-polydopamine nanoparticle formulations for tuberculosis

treatment.

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Tuberculosis (TB) is one of the oldest known diseases in the world and it

remains a significant public health challenge. The increasing resistance of

microorganisms to antibiotics underlines the necessity of appropriate use of

antibiotics and correct dosage in treatment. In some cases, frequent and

high-dose drug therapy is required, which can lead to serious organ damage in

the liver and kidneys in long-term treatment. However, this problem can be

overcome by using appropriate drug delivery systems that allow more effective

treatments at lower doses. Here, we developed a drug delivery system

specifically targeting tuberculosis using gold (Au)-polydopamine (PDA)

nanoparticles and modified with polyethylene glycol (PEG), a targeting agent

(antibody), and the antibiotic linezolid, resulting in

Au-PDA-PEG-Antibody-Linezolid nanoparticles. We successfully developed and

characterized these active targeted nanoparticles using UV-Vis absorbance

spectroscopy, Fourier-transform infrared spectroscopy (FT-IR), dynamic light

scattering (DLS), zeta potential measurements, and surface-enhanced Raman

spectroscopy (SERS) measurements. Additionally, the developed formulations were

compared with the commercial product through in vitro release studies, and

antibacterial efficacy studies were conducted on multidrug-resistant

tuberculosis (MDR-TB) strains. The targeted drug delivery system might be able

to reduce side effects by increasing treatment effectiveness at lower doses.

Additionally, our study is the one of the first example to feature actively

targeted nanoparticle formulations using the active ingredient linezolid and

PEGs with different chemical structures.

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DOI: 10.1016/j.ejps.2025.107219

PMID: 40754012

**9. BMC Infect Dis. 2025 Aug 2;25(1):974. doi: 10.1186/s12879-025-11344-0.**

Chest x-ray features and their associated factors among

rifampicin/multi-drug-resistant tuberculosis patients in drug-resistant

tuberculosis treatment initiating centers in Addis Ababa, Ethiopia: a

retrospective study.

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**INTRODUCTION:** Rifampicin/multi-drug resistant tuberculosis (RR/MDR-TB) treatment

regimen selection and its treatment duration are significantly influenced by the

degree of lung damage identified with baseline chest x-rays (CXR). Hence, this

study was aimed at determining baseline CXR features and their associated

factors in Addis Ababa, Ethiopia.

**METHODS:** The data was collected from 324 RR/MDR-TB patients who had baseline

chest x-rays. The data was collected using a structured checklist containing

socio-demographics, baseline chest x-rays, and other clinical variables. It was

entered into Epi Data 4.1 and then exported to SPSS version 25 for data cleaning

and analysis. A binary logistic regression model was fitted. Bivariate logistic

regression was done first, then variables with a p-value ≤ 0.2 were taken into

the multivariable logistic regression analysis. Variables with a p-value < 0.05

were reported as statistically significant.

**RESULTS:** Of the 324 study participants, nearly 74% (239) of them had abnormal

baseline CXR features. The most common abnormal CXR feature was cavitation,

followed by consolidation. In RR/MDR-TB patients with malnutrition, anemia, and

any previous TB treatment history, the most common abnormal radiologic feature

was cavitation. Daily laborer [AOR = 0.1 (95% CI: 0.01, 0.55)], BMI < 18.5 kg/m2

[AOR = 1.8 (95% CI: 1.02, 3.17)], HIV-positive [AOR = 0.41 (95% CI: 0.2, 0.86)],

and comorbidities [AOR = 0.32 (95% CI: 0.15, 0.67)] were significantly

associated with abnormal CXR features in RR/MDR-TB patients.

**CONCLUSIONS AND RECOMMENDATIONS:** In our study, the majority of RR/MDR-TB

patients had abnormal CXR features, of which cavitation was the most common.

Therefore, further study needs to be done prospectively at the multi-center

level since the extent of lung damage identified by CXR is one of the

determining factors for DR-TB treatment regimen selection, DR-TB treatment

duration, help diagnose DR-TB clinically, and TB sequelae.

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DOI: 10.1186/s12879-025-11344-0

PMID: 40753370 [Indexed for MEDLINE]

**10. Int J Tuberc Lung Dis. 2025 Aug 1;29(8):362-369. doi: 10.5588/ijtld.24.0610.**

Model-based evaluation of adherence to bedaquiline and clofazimine in adults

with drug-resistant TB.

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**BACKGROUND** There is a need for objective measures of adherence to fully-oral bedaquiline-based regimens for rifampicin- and multidrug-resistant tuberculosis (RR/MDR-TB). Due to their prolonged half-lives, bedaquiline (BDQ) and clofazimine CFZ) are appropriate for evaluating long-term treatment adherence using a model-based approach. **METHODS** We enrolled adults initiating a 9-month regimen that included BDQ and CFZ for RR/MDR-TB. Dried blood spot samples were taken at intervals and assayed for BDQ and CFZ concentrations. Demographic and clinical factors were used to predict drug concentrations using known pharmacokinetic models, assuming full adherence. Individual observed concentrations were compared to model-predicted values (1000 simulations). Observations were ranked, with those below the 5th percentile of simulated concentrations, indicating possible poor

adherence. **RESULTS** Adherence worsened over time, especially for BDQ (11, 21, 26, and 35% of the observations below the 5th percentile in the first, second, fourth, and sixth month respectively). CFZ observations under the 5th percentile were 10, 9, 7.5, 14, and 23% at months 1, 2, 4, 6, and 9. **CONCLUSION** Concentrations of BDQ and CFZ below the 5th percentile increased over time and this trend was more marked with BDQ. We hypothesise that the complexity of the thrice-weekly BDQ regimen increases the risk of suboptimal adherence.</sec>.

DOI: 10.5588/ijtld.24.0610

PMID: 40751208 [Indexed for MEDLINE]

**11. Int J Tuberc Lung Dis. 2025 Aug 1;29(8):340-348. doi: 10.5588/ijtld.24.0597.**

Drug management of TB in the intensive care setting: an international

multicentre study.

Tiberi S(1), Akkerman O(2), Sotgiu G(3), Saderi L(3), Kunst H(4), Carvalho

ACC(5), Muñoz-Torrico M(6), Lui GC(7), Rendon A(8), Cordeiro Dos Santos M(9),

Rosso RG(10), Mendes IC(11), Mendoza A(12), Borges MC(9), Kritski A(11), Marçôa

R(13), Vieira MA(11), Hernandez-Cardenas CM(5), Rahman A(14), Barrett J(14),

Shah K(15), Wagrell L(16), Johnson E(17), Hall J(18), Sabir N(19), Lynn W(20),

Zolfaghari P(17), Duarte R(21), Davies Forsman L(16), Whittington A(22),

Martin-Lazaro JF(23), White V(14), Chen C(14), Gray A(18), Brown M(18),

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**BACKGROUND** Individuals requiring admission to an intensive care unit (ICU) due to TB have complex clinical presentations and high mortality rates. There is a clear knowledge gap on how to optimally manage treatment. OBJECTIVE To evaluate the treatment outcomes of TB patients in ICU and explore the potential benefits of intravenous (IV) TB treatment regimens. **METHODS** A retrospective observational multicentre study was conducted by the International Severe TB and Rehabilitation Working Group of the Global Tuberculosis Network (GTN). The study included TB patients aged >15 years admitted to ICUs in Europe, Asia and Latin America from January 1, 2005 to December 31, 2018. Data on demographics, microbiology, clinical information and treatment outcomes were collected and analysed. **RESULTS** The study enrolled 434 cases. Over half were sputum smear-positive and 85.7% were culture-positive. Most required invasive mechanical ventilation, vasopressor support and steroids. Only 48.4% had TB medications initiated before or during ICU admission. The overall mortality rate was 54.8%, with 33.4% achieving treatment success. IV anti-TB drugs were administered to 43% of participants, with levofloxacin and amikacin being the most used. IV treatment longer than 10 days was associated with better outcomes. Individuals receiving IV rifampicin had a lower mortality rate (35.7%) compared to those who did not receive it (51.7%), p-value= 0.05. **CONCLUSIONS** High mortality rates in ICU indicate the need for improved management strategies. The use of IV TB drugs, especially IV rifampicin, show potential benefit, suggesting the need for further prospective studies. Early screening and standardized treatment protocols could improve patient outcomes in high-incidence areas.

DOI: 10.5588/ijtld.24.0597

PMID: 40751207 [Indexed for MEDLINE]

**12. Int J Tuberc Lung Dis. 2025 Aug 1;29(8):355-361. doi: 10.5588/ijtld.24.0685.**

Mycobacterium tuberculosis genotypes isolated from clinical specimens of

extrapulmonary TB.

Mollalign H(1), Beyene D(2), Moga S(3), Alemayehu DH(4), Ayele A(4), Melaku

K(4), Chala D(3), Getu M(3), Getahun M(3), Tola HH(5), Collins JM(6), Wassie

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**BACKGROUND** Ethiopia has reported a high rate of extrapulmonary TB (EPTB). We aimed to identify the epidemiology of TB (sub-) lineages and the transmission cluster of EPTB as understanding the driving genotypes helps to implement appropriate

intervention. **METHODS** In a cross-sectional study conducted between 2022-2023, whole genome sequencing was employed on microbiologically confirmed EPTB isolates. A bioinformatics pipeline MTBSeq was used to analyze genomic data. **RESULTS** The majority (98.1%) of study isolates belonged to the Mycobacterium tuberculosis (MTB) species, and the remaining 1.9% were identified as Mycobacterium bovis. The MTB species were further classified into 4 common lineages and 15 sub-lineages. The Euro-American lineage 4 (63.8%) and East African Indian lineage 3 (31.9%) were predominant. Lineage 4 was further branched into 11 sub-lineages, of which the group Clade1 (n = 78, 48.8%) was the highest, followed by the Haarlem branch (n = 19, 11.9%). The clustering rate and recent transmission index were 12.5% and

6.9% respectively. The risk of rifampicin resistance increases among (sub-)lineage 4.2.2 genotypes. **CONCLUSION** There was high genotype variability and low clustering rate among main MTBC genotypes and (sub-)lineages of EPTB. M.bovis was detected among EPTB patients in central urban areas.

DOI: 10.5588/ijtld.24.0685

PMID: 40751205 [Indexed for MEDLINE]

**13. BMJ Open Respir Res. 2025 Jul 31;12(1):e003088. doi:**

**10.1136/bmjresp-2024-003088.**

Temporal complexity in missed doses of rifampicin-sensitive anti-tuberculosis

treatment: a prospective cohort study in Tanzania.

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Tropical Medicine, London, UK.

**BACKGROUND:** Non-adherence to anti-tuberculosis (TB) regimens is not simplistic;

rather, doses are missed in complex patterns. In a cohort of individuals being

treated for rifampicin-sensitive pulmonary TB in Tanzania, we sought to examine

how doses were missed across the treatment course and within a day, as well as

the reasons for missed dose periods.

**METHODS:** 200 participants aged ≥18 years treated with the standard 6-month

regimen were recruited from March 2022 to June 2023. Missed doses were measured

using evriMED pillboxes and by pill count. The reasons for up to three missed

dose periods per month were collected. Patterns of missed doses-across treatment

and within a day-and their reasons were visualised and described.

**FINDINGS:** Two participants died early in treatment, leaving 198 with missed dose

data. The increase in the percentage of participants that missed any given dose

as time progressed was driven by early discontinuation (median doses missed 0.0%

in month 1 vs 6.7% in month 6) from treatment, as opposed to sporadic missed

doses (median doses missed 3.1% in month 1 vs 4.1% in month 6). There was a

median of one sporadic missed dose period (ranging between 0 and 42 doses in

length) per participant. Out of all the reported reasons for missed dose

periods, forgetting or forgetting and inconvenience were the most common

(59.6%).

**INTERPRETATION:** Missing doses of anti-TB treatment is a temporally complex

phenomenon and the result of the intersection of multifaceted day-to-day events

in an individual's life, with complicated implications for effective drug levels

across the treatment course. This complexity limits our ability to predict an

individual's missed doses at the start of treatment.

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by BMJ Group.

DOI: 10.1136/bmjresp-2024-003088

PMID: 40750254 [Indexed for MEDLINE]

**14. JACC Case Rep. 2025 Jul 30;30(21):104428. doi: 10.1016/j.jaccas.2025.104428.**

Pericardial Conundrum: Unmasking Tuberculosis as the Culprit.

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Southfield, Michigan, USA.

**BACKGROUND:** Tuberculosis, caused by Mycobacterium tuberculosis, primarily

affects the lungs but can involve other organs, termed extrapulmonary

tuberculosis. Tuberculous pericarditis (TBP) is a rare form, representing

approximately 1% of tuberculosis-related autopsies and 4% of acute pericarditis

cases in developed countries.

**CASE SUMMARY:** A 29-year-old healthy Indian man presented with fever, night

sweats, and weight loss. Imaging revealed a large pericardial effusion with

tamponade physiology. He underwent pericardiocentesis and a surgical pericardial

window, with biopsy confirming M. tuberculosis. He was treated with rifampin,

isoniazid, pyrazinamide, and ethambutol therapy, colchicine, and a steroid

taper, resulting in clinical improvement.

**DISCUSSION:** TBP is rare in developed regions and presents diagnostic challenges

because of nonspecific symptoms and delayed culture results. Early recognition

and intervention are critical to prevent progression to constrictive

pericarditis and improve outcomes.

**TAKE-HOME MESSAGE:** A high index of suspicion for TBP is essential in patients

with pericardial effusion to enable timely diagnosis and intervention,

optimizing clinical outcomes.

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DOI: 10.1016/j.jaccas.2025.104428

PMID: 40750148

**15. J Adv Res. 2025 Jul 30:S2090-1232(25)00585-5. doi: 10.1016/j.jare.2025.07.056.**

**Online ahead of print.**

Enhanced tuberculosis control via leveraging dendritic cell-mediated Th1

responses in preventive and immunotherapeutic vaccine strategies.

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**INTRODUCTION:** Insufficient vaccine efficacy of the Bacillus Calmette-Guérin

(BCG) and long, expensive tuberculosis (TB) treatments highlight the need for

better TB control measures.

**METHODS:** This study evaluated whether the adoptive transfer of dendritic cell

(DC)-based vaccines pulsed with culture filtrate antigens (CFA) of Mycobacterium

tuberculosis (Mtb) could enhance BCG efficacy and support anti-TB drug therapy.

**RESULTS:** In BCG-vaccinated mice, adoptive transfer of CFA-pulsed DCs promoted

swift T cell recruitment to the lung parenchyma, reducing bacterial load within

1 week post-infection, promoting the generation of tissue-resident T cells and

expansion of CD4+ T cells co-producing IFN-γ, IL-2, and/or TNF-α. The vaccine

efficacy persisted for a prolonged period post-infection, with protection found

in both high dose and low dose Mtb infection models. Additionally, CFA-DC

administration during chemotherapy enhanced treatment efficacy, maintaining CD4+

T cell responses. In latent TB models, mice were protected from Mtb reactivation

in both drug-sensitive and multidrug-resistant TB models.

**CONCLUSIONS:** DC-based prophylactic and immunotherapeutic vaccine strategies

enhance protective immunity during BCG vaccination and chemotherapy, offering

new insights into TB control strategies.

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DOI: 10.1016/j.jare.2025.07.056

PMID: 40749789

**16. J Med Chem. 2025 Aug 1. doi: 10.1021/acs.jmedchem.5c01331. Online ahead of**

**print.**

Design and Development of Lysyl tRNA Synthetase Inhibitors, for the Treatment of

Tuberculosis.

Davis SH(1), Mathieson M(1), Buchanan KI(1), Dawson A(1), Smith A(1), Cocco

M(1), Tamaki FK(1), Post JM(1), Baragaña B(1), Jansen C(1), Kiczun M(1),

Zuccotto F(1), Wood G(1), Scullion P(1), Ray PC(1), Epemolu O(1), Lopez-Román

EM(2), López LG(2), Engelhart CA(3), Kim J(3), Pino PA(3), Schnappinger D(3),

Read KD(1), Encinas L(2), Bates RH(2), Wyatt PG(1), Green SR(1), Cleghorn

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There is currently a public health crisis due to the rise of multidrug-resistant

tuberculosis cases, as well as the rise in the number of deaths from

tuberculosis. To achieve the United Nations Sustainable Development Goal of

ending the tuberculosis epidemic by 2030, new treatments are urgently required.

We previously reported the discovery of 49, a preclinical candidate that acted

through inhibition of the Mycobacterium tuberculosis lysyl tRNA synthetase

(LysRS). In this report, the full medicinal chemistry program is reviewed from

the original hit through to the optimized lead. The work was guided by the first

crystal structures of M. tuberculosis LysRS. The physicochemical and

pharmacokinetic properties were optimized to afford compounds suitable for

evaluation in mouse efficacy models of tuberculosis and with the potential for

clinical development.

DOI: 10.1021/acs.jmedchem.5c01331

PMID: 40749104

**17. PLoS Pathog. 2025 Aug 1;21(8):e1012980. doi: 10.1371/journal.ppat.1012980.**

**Online ahead of print.**

NK cell-macrophage interactions in granulomas correlate with limited

tuberculosis pathology.

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Primate Research Center (BPRC), Rijswijk, The Netherlands.

Development of novel vaccines and treatment approaches against tuberculosis are

hampered by limited knowledge of what constitutes a protective immune response

against Mycobacterium tuberculosis (Mtb). Granulomas are organized immune

aggregates that form in the lung in response to mycobacterial infection and are

an important site of pathogen-host interaction. The composition and cellular

microenvironment within the granuloma impacts the bacterial control capacity. To

identify protective responses in granulomas, imaging mass cytometry was used to

study archived lung tissue from low dose Mtb-infected non-human primates

presenting with various levels of disease. This approach revealed that granuloma

composition is correlated with the severity of lung pathology. Granulomas of

animals with limited lung pathology were enriched for NK cells showing increased

interactions with tissue macrophages. This work improves our understanding of

local immune interactions in the lung and how these correlate with severity of

tuberculosis disease.

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DOI: 10.1371/journal.ppat.1012980

PMID: 40749077

**18. PLOS Glob Public Health. 2025 Aug 1;5(8):e0004668. doi:**

**10.1371/journal.pgph.0004668. eCollection 2025.**

Prioritizing countries for TB vaccine readiness research using a global

stakeholder-centric approach.

Gill MM(1), Limaye R(2)(3), Pelzer PT(4), Frick M(5), Kerkhoff AD(6)(7).

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Francisco, California, United States of America.

The promise of new tuberculosis (TB) vaccine candidates prompts the need for

research on vaccine demand and health system readiness to help ensure effective

and equitable vaccine deployment. We developed an approach to prioritizing

countries for TB vaccine readiness research by combining stakeholder

preferences, elicited through best-worst scaling (BWS) with an analytical

hierarchy process (AHP) framework. We conducted a self-administered electronic

survey targeting TB vaccine stakeholders involved in vaccine development,

advocacy, and implementation across 23 of the 24 USAID TB priority countries,

and key stakeholders working globally. The survey included BWS to determine the

relative importance of 17 criteria for country selection. Stakeholders were

recruited using an existing email list, a 'snowball' approach, and TB experts'

recommendations. In a series of 13 choice tasks, respondents selected the most

and least important criteria from four randomly generated criteria. The weights

derived through BWS for each criterion were combined with country-specific

scores for each criterion using publicly available data to determine the overall

prioritization score for each country. Of 427 stakeholders, 115 (26%) completed

the survey; 88% were from TB priority countries. Sixteen of 17 criteria were

identified as 'important' using BWS. Overall country TB burden (weight = 11.1)

and TB-related political will (weight = 10.3) were the most important, followed

by burden of TB-related deaths (weight = 7.9), health systems strength

(weight = 7.5), and adult COVID-19 coverage (weight = 7.4). The five countries

with the highest prioritization scores were in sub-Saharan Africa. Three of them

were selected alongside the highest-scoring country from South Asia, Europe and

Central Asia, and East Asia as priority research settings in pursuit of regional

diversity. This study demonstrates the successful use of the AHP combined with

BWS, as a practical and transparent approach for prioritizing countries for TB

vaccine readiness research which could be applied to support other

evidence-based funding decisions in global public health.

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DOI: 10.1371/journal.pgph.0004668

PMCID: PMC12316289

PMID: 40749042

**19. PLoS One. 2025 Aug 1;20(8):e0329267. doi: 10.1371/journal.pone.0329267.**

**eCollection 2025.**

Epidemiological and clinical analysis, and outcomes of tuberculosis co-infection

among people living with HIV in Türkiye (2014-2024) ClinSurv HIV cohort: A large

case series.

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AF(7), Koç MM(8)(9)(10), Kayaaslan B(11)(12), Batırel A(13)(14), Gündüz A(10),

Nakir İY(4), Yörük G(5), Sevgi DY(2)(9), Kumbasar Karaosmanoğlu H(6)(9), Mete

B(7), Özçelik MN(4), Sarı ND(5)(9), Akkoyunlu Y(8), Tabak F(7).

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**BACKGROUND:** Tuberculosis (TB) is one of the most common opportunistic infections

in people living with HIV (PLHIV). Mycobacterium tuberculosis may cause more TB

in all stages of HIV infection than in the general population, with the

incidence of TB and the spread of pulmonary TB to other organs increasing as the

CD4 count decreases.

**OBJECTIVE:** In this HIV cohort study, we aimed to evaluate the clinical features,

diagnosis, and prognosis of TB among PLHIV in Türkiye.

MATERIALS AND METHODS: We conducted a retrospective cohort study to analyze

clinical outcomes and identify determinants of mortality among people living

with HIV (PLHIV) co-infected with tuberculosis. We included 264 patients

diagnosed and treated for TB across six centers in Türkiye. We extracted

clinical, demographic, laboratory, microbiological, and radiological data from

patient medical records. To identify independent predictors of mortality, we

performed multivariable logistic regression and reported the results as odds

ratios (ORs) with 95% confidence intervals (CIs).

**RESULTS:** Of the 9,687 PLHIV who were followed for 10 years, 2.7% (264

individuals) developed TB. The median age of these individuals was 40 years, and

89% were male. The prevalence of pulmonary TB only, extrapulmonary TB only, and

the coexistence of pulmonary and extrapulmonary TB were 42.4%, 48.8%, and 8.7%,

respectively. Opportunistic infections and cancers were found in 23% (62 out of

264) of patients with HIV/TB co-infection. Among patients with HIV/TB

co-infection, 42% showed lymphadenopathy, with 70% of these cases being

generalized. In patients who underwent chest CT scans (n=200), radiological

patterns revealed post primary TB in 46%, primary TB in 36%, and miliary TB in

18%. The positivity rates of Ehrlich-Ziehl-Neelsen staining (EZN), polymerase

chain reaction (PCR), and TB cultures in clinical samples were found to be

47.5%, 72.5%, and 53%, respectively. Most of our patients (95%) were given the

standard TB treatment regimen (HRZE), with a paradoxical reaction observed in

11.6% of cases and hepatotoxicity occurring in 18% of cases. Age, CD4 count

(<200 cells/mm3-late presenters), and thrombocytopenia were identified as

independent risk factors for mortality in the 58 patients (22%) who died after

diagnosis.

**CONCLUSION:** Even today, more than one fifth of patients with HIV-TB co-infection

in our cohort died. Mortality was higher among individuals who presented late

with tuberculosis disease, especially those with advanced immunosuppression (CD4

<200 cells/μL). These findings underscore the urgent need for early HIV

diagnosis and systematic TB screening to reduce co-infection-related mortality

and improve clinical outcomes.

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DOI: 10.1371/journal.pone.0329267

PMCID: PMC12316272

PMID: 40748951 [Indexed for MEDLINE]

**20. ACS Chem Biol. 2025 Aug 1. doi: 10.1021/acschembio.5c00330. Online ahead of**

**print.**

Systematic Determination of the Impact of Structural Edits on Peptide

Accumulation into Mycobacteria.

Dash R(1), Liu Z(1), Lepori I(2), Chordia MD(1), Ocius K(1), Holsinger K(1),

Zhang H(3)(4), Kenyon R(1), Im W(3)(4), Siegrist MS(2)(5), Pires MM(1)(6).

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Understanding the factors that influence the accumulation of molecules beyond

the mycomembrane of Mycobacterium tuberculosis (Mtb)─the main barrier to

accumulation─is essential for developing effective antimycobacterial agents. In

this study, we investigated two design principles commonly observed in natural

products and mammalian cell-permeable peptides: backbone N-alkylation and

macrocyclization. To assess how these structural edits impact molecule

accumulation beyond the mycomembrane, we utilized our recently developed

Peptidoglycan Accessibility Click-Mediated Assessment (PAC-MAN) assay for

live-cell analysis. Our findings provide the first empirical evidence that

peptide macrocyclization generally enhances accumulation in mycobacteria, while

N-alkylation influences accumulation in a context-dependent manner. We examined

these design principles in the context of two peptide antibiotics, tridecaptin

A1 and griselimycin, which revealed the roles of N-alkylation and

macrocyclization in improving both accumulation and antimicrobial activity

against mycobacteria in specific contexts. Together, we present a working model

for strategic structural modifications aimed at enhancing the accumulation of

molecules past the mycomembrane. More broadly, our results also challenge the

prevailing belief in the field that large and hydrophilic molecules, such as

peptides, cannot readily traverse the mycomembrane.

DOI: 10.1021/acschembio.5c00330

PMID: 40748788

**21. J Immigr Minor Health. 2025 Aug 1. doi: 10.1007/s10903-025-01744-4. Online ahead of print.**

Advocating for Change: Addressing Barriers To Tuberculosis Care for Immigrants

and Refugees in Canada.

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Tuberculosis (TB) disproportionately affects immigrants and refugees in Canada,

who accounted for 80% of active TB cases in 2023 despite making up only 23% of

the population. This commentary highlights the urgent need to address systemic

barriers that hinder access to timely and effective TB care across the cascade,

from screening and diagnosis to treatment completion. Drawing on recent policy

reports and emerging evidence, this paper focuses on four main intersecting

challenges: language barriers, limited cultural competency among providers,

healthcare system inefficiencies, and misinformation. These barriers not only

delay diagnosis, but also undermine treatment adherence and trust in the

healthcare system. This commentary calls for scalable, equity-driven

interventions including improved interpretation services, and tailored

community-based education to TB-specific training for healthcare providers. To

advance Canada's TB elimination goals, we must center the lived realities of

immigrants and refugees, whilst strengthening the responsiveness, accessibility,

and continuity of care within the Canadian healthcare system.

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Media, LLC, part of Springer Nature.

DOI: 10.1007/s10903-025-01744-4

PMID: 40748445

**22. Extremophiles. 2025 Aug 1;29(2):33. doi: 10.1007/s00792-025-01398-y.**

Actinomycetes from high altitude salt lake Tso-Kar of Ladakh offers bright

prospects for antimycobacterial drug discovery especially for drug resistant

mycobacteria.

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The rise of multidrug-resistant (MDR) strains of Mycobacterium tuberculosis (M.

tb) has driven the search for new antimycobacterial agents. Our study focused on

isolation and characterization of actinomycetes from the hypersaline Tso-Kar

Salt lake in Ladakh, India, to explore their antibacterial potential. We

isolated 145 bacterial isolates from various soil, salt and water samples and

found 23 actinomycete isolates effective against Mycobacterium smegmatis through

cross-streak screening. Molecular identification confirmed that these isolates

belonged to 14 genera of actinomycetes. Out of 23 extracts from these isolates,

15 ethyl acetate organic extracts exhibited strong antimycobacterial activities

against M. smegmatis, M. tb H37Ra, and M. tb H37Rv, with MIC values between 125

and 31.25 µg/mL. Importantly, all 15 extracts demonstrated bactericidal

activities at their respective MICs against M. tb H37Rv. The other 8 extracts

displayed comparatively weaker MIC and MBC ranging 500-250 µg/mL and 1000-500

µg/mL respectively. These extracts were equally effective against drug-resistant

and drug-susceptible M. tb clinical isolates. Furthermore, they showed broad

antibacterial activity against both gram-positive and gram-negative bacteria,

with MICs ranging from 500 to 31.25 µg/mL. The GC-MS analysis of the potent

extracts revealed that a wide range of compounds including Phenolics, Peptides,

Ergot alkaloids and their derivates may have contributed to anti-mycobacterial

activity. The genetic diversity and significant antimicrobial properties of

these actinomycetes from extreme environments highlight their potential for

developing new antituberculosis and general antibiotic agents, particularly

against MDR infections.

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DOI: 10.1007/s00792-025-01398-y

PMID: 40748406 [Indexed for MEDLINE]

**23. Org Lett. 2025 Aug 1. doi: 10.1021/acs.orglett.5c02803. Online ahead of print.**

Total Synthesis of Mycoplanecin A.

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The first total synthesis of mycoplanecin A, a potent antitubercular macrocyclic

depsipeptide natural product targeting the DnaN sliding clamp, is described.

Interesting key steps are the synthesis of the two trans-4-alkylated-l-prolines

via an iterative Matteson homologation and an O→N acyl shift observed during the

fragment coupling of the building blocks. The challenging macrocyclization of

the globally deprotected linear precursor was accomplished under optimized

high-temperature, high-dilution conditions. This work provides chemical access

to mycoplanecin A, enabling further biological investigation and analogue

development against the important pathogen Mycobacterium tuberculosis.

DOI: 10.1021/acs.orglett.5c02803

PMID: 40748198

**24. BMC Infect Dis. 2025 Jul 31;25(1):967. doi: 10.1186/s12879-025-11295-6.**

Pre-treatment loss to follow-up and associated factors among drug-resistant

tuberculosis patients diagnosed in Wakiso district, central Uganda.

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**BACKGROUND:** Tuberculosis ranks among the top ten causes of death worldwide. The

Sub-Saharan African region faces increasing trends of Drug-Resistant

Tuberculosis (DR-TB), further complicating the existing efforts for prevention,

control, and eradication. Pre-treatment loss to follow-up (LTFU) among diagnosed

DR-TB patients also signifies a setback in the timely prevention of disease

progression and transmission, especially in low-resource settings. This study

assessed the magnitude of and factors associated with pre-treatment LTFU among

DR-TB patients within Wakiso district, central Uganda.

**METHOD:** A sequential explanatory study design was adopted to analyze electronic

case-based surveillance (eCBSS) data between 2017 to 2022 from the Ministry of

Health, Uganda. Participants for qualitative data comprised of six (6) key

informant interviews and 2 focus group discussions among health workers and

DR-TB patients respectively.

**RESULTS:** Out of the 972 records retrieved from the eCBSS system for patients

treated at Mulago National Referral Hospital from 2017 to 2022; 253 were

analyzed. The majority of the participants, 62% (157/253), were male. The median

age of study participants was 34 years (range: 18- 85). The prevalence of

pretreatment LTFU was 13.4% (34/253). The qualitative findings reinforced and

provided context to the quantitative results, revealing how behavioral, social,

and system-level factors contribute to pre-treatment loss to follow-up (LTFU)

among DR-TB patients. Significant associations were observed in patients who

lacked a recorded telephone contact in TB register (adjusted PR = 0.47, 95% CI:

0.27-0.80) and those without documented home address (adjusted PR = 0.52, 95%

CI: 0.27-0.97); qualitatively, this was linked to patients' fear of stigma, lack

of trust in the health system, and unstable living conditions, leading them to

avoid being traced. The analysis also showed that tobacco use (adjusted

PR = 1.96, 95% CI: 1.00-3.87) and illicit drug use (adjusted PR = 4.00, 95% CI:

1.76-9.08) significantly increased the risk of LTFU, which was supported by

narratives describing substance use as contributing to hopelessness and neglect

of health. Furthermore, patients with a history of treatment failure had 2.4

times the risk of being lost to follow-up (adjusted PR = 2.40, 95% CI:

1.08-5.36), consistent with qualitative reports of discouragement, denial, and

lack of awareness about the severity of DR-TB. Relapse cases had 69% higher

prevalence of loss to follow-up (adjusted PR = 1.69, 95% CI 0.78-3.70) compared

to new cases. Although factors such as alcohol use and family support did not

reach statistical significance in the quantitative model, they were prominent in

the qualitative data, suggesting under-recognized barriers related to

psychosocial distress and poverty. Together, these findings demonstrate a strong

convergence between data strands while highlighting that some influential

factors particularly social and psychological may be underrepresented in routine

health data.

**CONCLUSION:** The study found a 13.4% prevalence of pre-treatment LTFU among DR-TB

patients in Wakiso District. Quantitative analysis identified significant

predictors, including lack of contact information, prior treatment failure,

tobacco use, and illicit drug use, while protective factors included having a

recorded home address and telephone contact recorded in relevant TB

registers/electronic systems. These findings were reinforced by qualitative

insights, which revealed that fear of stigma, denial of illness, substance

abuse, poor health system responsiveness, and lack of social support contributed

to patient disengagement. The integration of both data strands highlights the

need for a patient-centered approach that strengthens communication, addresses

behavioral health needs, and improves follow-up systems to reduce pre-treatment

LTFU and improve DR-TB outcomes.

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DOI: 10.1186/s12879-025-11295-6

PMCID: PMC12312580

PMID: 40745635 [Indexed for MEDLINE]

**25. Lancet Infect Dis. 2025 Jul 28:S1473-3099(25)00439-6. doi:**

**10.1016/S1473-3099(25)00439-6. Online ahead of print.**

Evaluation for fungal pulmonary infections is essential in suspected

tuberculosis relapse.

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DOI: 10.1016/S1473-3099(25)00439-6

PMID: 40744054

**26. J Am Nutr Assoc. 2025 Jul 31:1-8. doi: 10.1080/27697061.2025.2531086. Online**

**ahead of print.**

Effect of Probiotics Supplementation on Clinical, Humanistic, and Safety

Outcomes in Patients With Tuberculosis: A Prospective Cohort Study in a Tertiary

Healthcare Facility in South India.

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**OBJECTIVE:** This study aimed to assess the effect of probiotic supplementation on

multiple dimensions of tuberculosis (TB) care, including clinical, humanistic,

and safety outcomes.

**METHOD:** This study is a prospective cohort study. Data were collected for TB

treatment outcome, hematologic inflammatory indices, anti-tuberculosis treatment

(ATT)-induced adverse drug reactions (ADRs), and health-related quality of life

(HRQoL) using EuroQol 5-Dimension 5-level questionnaire to evaluate the effect

of probiotics supplementation.

**RESULTS:** In all, 177 patients with drug-sensitive pulmonary TB were enrolled. TB

treatment success rates in the study group (SG) and the reference group (RG)

were 85.1% and 84.6%, respectively (p = 1.000). Among hematologic inflammatory

indices, only the systemic inflammation response index (SIRI) showed a

statistically significant reduction after probiotic supplementation (p = 0.048).

No significant changes were observed in HRQoL scores at various time points.

ATT-induced ADRs were significantly lower in the SG than the RG (14.8% vs 61.3%;

p < 0.001).

**CONCLUSION:** Probiotic supplementation did not significantly influence TB

treatment success or HRQoL outcomes. However, it showed a favorable impact on

systemic inflammation and a significant reduction in the incidence of

ATT-induced ADRs, especially gastrointestinal side effects. These findings

suggest a potential role for probiotics as a supportive adjunct to ameliorate

ATT-induced ADRs. Future studies should focus on assessing long-term

supplementation effects to investigate humanistic outcomes.

DOI: 10.1080/27697061.2025.2531086

PMID: 40743501

**27. Antimicrob Agents Chemother. 2025 Jul 31:e0005225. doi: 10.1128/aac.00052-25. Online ahead of print.**

Pharmacokinetics of first-line tuberculosis drugs rifampin, isoniazid,

ethambutol, and pyrazinamide during pregnancy and postpartum with and without

efavirenz-based antiretroviral treatment: IMPAACT P1026s study.

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MF(2), Eke AC(6), Cressey TR(7), Wabwire D(8), Shapiro DE(4), Bacon K(9),

Knowles K(9), George K(10), Browning R(11), Chakhtoura N(12), Rungruengthanakit

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The pharmacokinetics (PK) of antituberculosis drugs may be altered by both

pregnancy-induced physiological changes and drug interactions in individuals

living with HIV who develop tuberculosis. Within the multicenter International

Maternal Pediatric Adolescent AIDS Clinical Trials Network P1026s study, we

assessed the PK of rifampin, isoniazid, ethambutol, and pyrazinamide during

pregnancy and postpartum (PP) in women on efavirenz-based antiretroviral therapy

(ART). Results were compared to a previously published non-HIV group and

described minimum targets. World Health Organization-recommended daily doses of

antituberculosis and ART medications were administered, followed by PK sampling

of all antituberculosis drugs over 24 h during the second trimester (2T), third

trimester (3T), and 2-8 weeks PP. PK parameters were characterized using

noncompartmental analysis, and comparisons were made among stages of pregnancy

and between groups using geometric mean ratios with 90% confidence intervals.

Twenty-two participants were enrolled, and PK data were available for 12, 20,

and 13 participants in 2T, 3T, and PP, respectively. While no significant

difference in rifampin exposure between pregnancy and postpartum was detected,

the median area-under-the-plasma-concentration-time-curve up to 24 h post-dose

(AUC0-24) and Cmax were below target during each period and were 42% and 35%

lower in 3T than the non-HIV group. No significant difference in isoniazid

exposure was found between pregnancy and PP or between the groups. Ethambutol

and pyrazinamide AUC0-24 and Cmax in 2T and 3T were similar between the groups.

In both groups, pyrazinamide Cmax was above target in all periods. The clinical

relevance of lower rifampin exposure in pregnant women requiring tuberculosis

treatment while on efavirenz should be determined.

DOI: 10.1128/aac.00052-25

PMID: 40741959

**28. Antimicrob Agents Chemother. 2025 Jul 31:e0036925. doi: 10.1128/aac.00369-25. Online ahead of print.**

A chlorinated diketopiperazine antibiotic targets Mycobacterium tuberculosis.

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Morrissette M(1), Ghiglieri M(1), Curtis T(1), Corsetti R(1), Son S(1), Sarkar

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We describe a novel macrocyclic peptide, speirobactin, produced by Photorhabdus

temperata that selectively kills Mycobacterium tuberculosis. A nonribosomal

peptide synthase containing two linear modules codes for the synthesis of

speirobactin. The biosynthetic operon contains a pentapeptide-repeat protein as

a resistance gene. Genomic analysis of speirobactin-resistant mutants of M.

tuberculosis led to the identification of DNA gyrase as the molecular target.

The mutations were recreated and show that DNA gyrase is the only target.

Transcriptome analysis of M. tuberculosis treated with antibiotics shows that

speirobactin clusters close to fluoroquinolones, supporting its action against

the DNA gyrase.

DOI: 10.1128/aac.00369-25

PMID: 40741954

**29. mBio. 2025 Jul 31:e0108325. doi: 10.1128/mbio.01083-25. Online ahead of print.**

Disulfide bonds are critical for stabilizing cell division, cell envelope

biogenesis, and antibiotic resistance proteins in mycobacteria.

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Mycobacteria, including Mycobacterium tuberculosis-the etiological agent of

tuberculosis-possess a unique and impermeable cell envelope that is critical for

survival and antibiotic resistance. The assembly and maintenance of this

envelope depend on properly folded proteins, yet the role of disulfide bond

formation in these processes remains poorly understood. Mycobacteria rely on two

membrane enzymes, disulfide bond formation protein A (DsbA) and vitamin K

epoxide reductase (VKOR), for introducing disulfide bonds into exported

proteins. In silico studies predict that ~64% of exported proteins contain even

numbers of cysteine residues and thence disulfide bonding; nevertheless,

substrates of the DsbA-VKOR pathway remain largely unknown. Here, we demonstrate

that DsbA and VKOR introduce disulfide bonds into substrate proteins and

identify several essential proteins that depend on oxidative folding in the

mycobacterial cell envelope. Using bioinformatics and cysteine profiling

proteomics, we uncover numerous exported proteins that require disulfide bonds

for stability. Cysteine derivatization in whole cells confirms that key

proteins, including LamA (MmpS3), PstP, LpqW, and EmbB, rely on disulfide bonds

for proper function. Furthermore, chemical inhibition of VKOR phenocopies vkor

deletion, thus highlighting its essential role in maintaining mycomembrane

integrity. These findings address a critical gap in understanding mycobacterial

cell envelope biogenesis and underscore the DsbA-VKOR system as a promising

target for disrupting cell envelope homeostasis in drug-resistant

Mycobacteria.**IMPORTANCE** This work addresses a major deficiency in understanding

mycobacterial cell envelope processes and highlights the biological and clinical

implications of oxidative protein folding in mycobacteria. This process, marked

by the formation of disulfide bonds, is essential for the stability of exported

proteins. While disulfide bond formation studies in Gram-negative bacteria

suggested a similar role in mycobacteria, the underlying consequences of

disulfide bonds remained unclear. Thus, we began investigating the diverse

physiological functions dependent on disulfide bonds in Mycobacteria using a

combination of bioinformatics, proteomics, and genetic and biochemical

approaches. We identified hundreds of proteins affected by oxidative protein

folding and validated essential substrates of this process. We show that

disulfide bonds are not only crucial for the stability and function of key

mycobacterial proteins but also represent a novel therapeutic target against

antimicrobial resistance. Our findings underscore the potential of targeting

disulfide bond formation to disrupt mycomembrane assembly, opening new avenues

for antimycobacterial drug development.

DOI: 10.1128/mbio.01083-25

PMID: 40741763

**30. Cureus. 2025 Jul 30;17(7):e89046. doi: 10.7759/cureus.89046. eCollection 2025**

**Jul.**

Development and Internal Validation of the Yuvarajan Sarcoidosis Diagnostic

Score (YSDS): A Retrospective Cohort Study.

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**BACKGROUND:** Sarcoidosis is a complex, multisystem granulomatous disease of

unknown etiology, often presenting a diagnostic challenge due to its highly

variable clinical manifestations and its overlap with infectious and neoplastic

diseases. This is especially problematic in regions with a high burden of

tuberculosis (TB), such as India, where the clinical and radiological features

of sarcoidosis and TB can be remarkably similar. Early, accurate diagnosis is

imperative to guide treatment and avoid inappropriate therapy, yet no

universally accepted diagnostic scoring system exists.

**OBJECTIVE:** The objective of this study was to develop and internally validate a

novel, composite clinical scoring tool named the Yuvarajan Sarcoidosis

Diagnostic Score (YSDS) to aid in the diagnosis of sarcoidosis using routinely

available clinical, radiologic, laboratory, and histopathologic parameters.

**METHODS:** A retrospective observational study was conducted at a tertiary care

hospital in South India. Medical records of 94 patients evaluated for suspected

sarcoidosis between January 2022 and January 2025 were reviewed. Patients were

categorized into sarcoidosis (n = 63) and non-sarcoidosis groups (n = 31) based

on histopathological confirmation, radiological features, and exclusion of

differential diagnoses. Multivariate logistic regression was used to identify

significant independent predictors of sarcoidosis. These predictors were used to

create a weighted diagnostic score, and their diagnostic accuracy was assessed

using receiver operating characteristic (ROC) curve analysis.

**RESULTS:** Five independent predictors were identified: bilateral hilar

lymphadenopathy (BHL) on chest imaging, elevated serum angiotensin-converting

enzyme (ACE) levels, histologic presence of non-caseating granulomas, negative

Mantoux test, and characteristic extrapulmonary manifestations such as uveitis,

parotid gland enlargement, or lupus pernio. Each parameter was assigned a score

based on the regression coefficient. The YSDS score ranged from 0 to 13, with a

cutoff ≥8 yielding a sensitivity of 87.3% (55/63), specificity of 83.9% (26/31),

positive predictive value (PPV) of 89.6% (55/61), negative predictive value

(NPV) of 80.6% (26/33), and an overall accuracy of 85.9% (81/94). The area under

the ROC curve was 0.90, indicating excellent discriminatory power.

**CONCLUSION:** The YSDS is a statistically robust, easy-to-implement clinical tool

that enhances diagnostic confidence in sarcoidosis, particularly in settings

where TB and other granulomatous diseases are prevalent. It offers a promising

strategy for standardized diagnostic assessment and warrants external validation

in larger, prospective cohorts.

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DOI: 10.7759/cureus.89046

PMCID: PMC12309321

PMID: 40741038

**31. Trop Doct. 2025 Jul 31:494755251362095. doi: 10.1177/00494755251362095. Online ahead of print.**

Geriatric Tuberculosis in India: Emerging challenges and practical perspectives.

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Geriatric tuberculosis (TB) is an emerging but under-recognized challenge in

India. Older adults often present with atypical or advanced disease, leading to

delayed diagnosis, treatment complications, and increased mortality. While

pulmonary TB is common, extrapulmonary and disseminated forms are also frequent.

Diagnosis is hindered by non-specific symptoms and reduced microbiological

yield, and treatment is complicated by co-morbidity, polypharmacy, and poor

adherence. Despite elevated risk, older adults are not prioritized under current

TB preventive strategies. This review highlights the unique clinical features,

diagnostic limitations, and management challenges of TB in older adults,

emphasizing the need for age-responsive TB control strategies.

DOI: 10.1177/00494755251362095

PMID: 40740031

**32. BMC Microbiol. 2025 Jul 30;25(1):462. doi: 10.1186/s12866-025-04196-w.**

Establishing translational performance standards for TB therapy using

rifampicin-based regimens in a male and female high-burden murine model.

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**BACKGROUND:** Establishing efficacy benchmarks in preclinical tuberculosis (TB)

models is essential for optimizing and prioritizing therapeutic regimens.

However, standardized classification methods for comparing high-performing

regimens are currently lacking. This study defines a quantitative framework

utilizing rifampicin-based regimens in a high-burden aerosol BALB/c mouse model,

incorporating both male and female mice to assess potential sex-specific

treatment responses.

**METHODS:** Mice were infected with Mycobacterium tuberculosis Erdman strain and

treated for 4 or 8 weeks with rifampicin (R), rifampicin plus pyrazinamide (RZ),

or rifampicin, isoniazid, and pyrazinamide (RHZ). Treatments were administered

orally five days a week. The bacterial burden in the lungs and spleens was

quantified by CFU enumeration. Pharmacokinetic analysis confirmed drug

exposures. To establish classification benchmarks, treatment efficacy was

evaluated using quartile performance thresholds and Cohen's d effect size

analysis.

**RESULTS:** All regimens reduced lung CFUs compared to controls. RHZ demonstrated a

high benchmark, achieving mean reductions of 3 ± 0.5 Log10 CFUs at 4 weeks and

4 ± 0.4 Log10 CFUs at 8 weeks, with clearance below detection limits in most

mice. The R and RZ regimens achieved intermediate reductions. No statistically

significant sex differences in bacterial clearance were observed.

Pharmacokinetic analysis confirmed equivalent drug exposures across sexes.

Quartile ranking (> 75th percentile) and Cohen's d calculations (Cohen's d > 15)

consistently classified RHZ as the benchmark high-performing regimen at both

time points, showing exceptional efficacy.

**CONCLUSION:** This study establishes a quantitative framework for evaluating TB

treatments in a preclinical high-burden BALB/c mouse model. The dual-metric

classification framework provides sex-inclusive, quantitative performance

criteria that enhance the translational relevance of preclinical efficacy

studies. This approach sets relative benchmarks that support the comparative

evaluation of novel regimens and helps to align preclinical performance with

clinical expectations.

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DOI: 10.1186/s12866-025-04196-w

PMCID: PMC12308929

PMID: 40739473 [Indexed for MEDLINE]

**33. Infection. 2025 Jul 30. doi: 10.1007/s15010-025-02613-w. Online ahead of print.**

Performance of whole blood interferon-γ release assays in SARS-CoV-2 and

tuberculosis is age dependent.

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**INTRODUCTION:** A lot of research has been done, mainly on tuberculosis (TB), on

the extent to which cellular immune protection as measured by interferon-γ

release assays (IGRA) is age-dependent. In a previous study we showed that

following an Omicron infection, adolescents with a hybrid immunity had a higher

probability of having a reactive SARS-CoV-2-specific IGRA than children.

Therefore, we examined in a large group of minors and adults whether age

influences cellular immunity as measured by IGRA in TB and SARS-CoV-2.

**METHODS:** Participants were recruited at 13 German study sites between September

and December 2022. Cellular immunity was analyzed using SARS-CoV-2 and

Tb-specific IGRA and humoral immunity against SARS-CoV-2 by measuring antibodies

against spike (S) and nucleocapsid protein. Analysis was done depending on

natural (convalescent, not vaccinated) or hybrid immunity (convalescent and

vaccinated).

**RESULTS:** Overall, 1401 adults and 392 minors were included. The amount of

interferon-γ released by T cells, as well as the probability of a positive

SARS-CoV-2 IGRA (OR 1.022) and a positive Tb IGRA (OR 1.047) were age dependent.

Sensitivity of SARS-CoV-2 IGRA in natural immunity was lower in minors (0.45),

especially in those less than 5 years (0.29) as compared to adults (0.66).

**CONCLUSION: T**he interferon-γ response to SARS-CoV-2 infections and/or

vaccinations and to Tb infections as measured by IGRA is in quality and quantity

dependent on age. The sensitivity of commercially available tests in young

children seems to be suboptimal, limiting their use as a diagnostic or research

tool in this age group.

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DOI: 10.1007/s15010-025-02613-w

PMID: 40739412

**34. Jpn J Infect Dis. 2025 Jul 31. doi: 10.7883/yoken.JJID.2025.058. Online ahead of print.**

COVID-19 Incidence and Mortality in Patients Recovered from Tuberculosis: A

Retrospective Cohort Analysis of the National Health Insurance in Republic of

Korea.

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Tuberculosis (TB) is an endemic respiratory disease in several countries,

including South Korea. The coronavirus disease 2019 (COVID-19) may pose greater

risks to individuals with pre-existing respiratory diseases, but there are few

reports on how the post-recovery state from TB affects COVID-19 infection and

mortality. This study aimed to investigate the susceptibility and mortality of

COVID-19 in patients with a history of TB. We retrospectively analyzed data from

the National Health Insurance Service of Korea. We extracted individuals with TB

from 2011 to 2019 and matched them with a population-based control group. The

main outcomes were COVID-19 incidence and death within 30 days of infection. The

study included 138,278 matched pairs of individuals with and without a history

of TB. COVID-19 incidence was slightly lower in the TB group (38.0% vs. 38.4%,

P-value = 0.023). Subgroup analysis showed significantly lower COVID-19

incidence in the pulmonary TB group compared to controls (P-value = 0.001).

However, the mortality rate was higher in the TB group (0.9% vs. 0.7%, P-value <

0.001). This study showed that TB has a slightly protective effect against

COVID-19 infection but increases the mortality rate. These findings will guide

future research on the interaction between TB and COVID-19.

DOI: 10.7883/yoken.JJID.2025.058

PMID: 40738665

**35. J Med Internet Res. 2025 Jul 30;27:e76742. doi: 10.2196/76742.**

User-Centered Refinement of a Digital Tool for Tuberculosis Treatment Support:

Iterative Mixed Methods Study.

Iribarren S(1), Aguilar Vidrio OA(1), Roberti J(2), Goodwin K(1), Chirico C(3),

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**BACKGROUND:** Despite the potential of digital adherence technologies to support

patient-centered monitoring for tuberculosis (TB), there is limited research on

incorporating indirect and direct adherence monitoring or assessing patients'

experiences with these technologies. The TB Treatment Support Tools (TB-TST)

includes a comprehensive mobile app for patients and health care providers and a

direct adherence metabolite test to report and monitor adherence.

**OBJECTIVE:** This paper describes the iterative refinement process of the TB-TST

intervention.

**METHODS:** To refine the TB-TST intervention, we used an iterative approach

involving multiple embedded mixed methods studies guided by the Information

Systems Research framework and Design Thinking Process. Embedded studies

included a randomized controlled pilot study, interviews, usability testing, and

surveys with patients and experts to inform ongoing refinements. The project

consisted of interface evaluation, high-level system design, and iterative

redesign.

**RESULTS:** The TB-TST intervention was refined through 3 iterative phases. In

Phase 1, based on feedback from pilot study participants and 4 experts in TB,

improvements included an in-app discussion board, submission confirmations, and

enhanced account recovery. Cultural adaptation was based on Hofstede's

dimensions. Phase 2 involved 4 Directed Research Groups and 19 stakeholders to

redesign user flows, simplify reporting, and transition the app to a progressive

web app, improving device compatibility. Phase 3 included usability testing

cycles with 48 participants (26 patients and 22 health care professionals),

yielding high satisfaction scores: patient app Mobile Health App Usability

Questionnaire, mean 5.96 (SD 0.46); provider mobile dashboard IT Usability

Evaluation Scale scores ranged from 5.83 to 6.23 out of 7, and optimization of

interface and dashboard. Refinements included larger icons, streamlined

onboarding, symptom summary enhancements, and a new cohort-level adherence

graph. These modifications improved navigation, usability, and remote monitoring

for patients with TB and providers in preparation for a multisite clinical

trial.

**CONCLUSIONS:** Combining multiple methods guided by the Information Systems

Research framework and elements of the Design Thinking Process can help

researchers and developers leverage the strengths of mixed methods iterative

designs to create highly personalized and effective digital health

interventions.

© Sarah Iribarren, Omar Alfonso Aguilar Vidrio, Javier Roberti, Kyle Goodwin,

Cristina Chirico, Hugo Telles, Barry Lutz, Fernanda Bornengo, Fernando

Rubinstein. Originally published in the Journal of Medical Internet Research

(https://www.jmir.org).

DOI: 10.2196/76742

PMCID: PMC12309858

PMID: 40737522 [Indexed for MEDLINE]

**36. J Exp Med. 2025 Oct 6;222(10):e20250161. doi: 10.1084/jem.20250161. Epub 2025**

**Jul 30.**

Early and opposing neutrophil and CD4 T cell responses shape pulmonary

tuberculosis pathology.

Gern BH(1)(2)(3), Klas JM(1), Foster KA(1)(4), Kanagy ME(1)(3), Cohen SB(1),

Plumlee CR(1), Duffy FJ(1), Neal ML(1), Halima M(1), Gustin AT(4), Stull SM(1),

Wilson JJ(4), Diercks AH(1), Aderem A(1)(2), Gale M Jr(4), Aitchison JD(1)(2),

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Pulmonary Mycobacterium tuberculosis (Mtb) infection results in a variety of

heterogeneous lesion structures, from necrotic granulomas to alveolitis, but the

mechanisms regulating their development remain unclear. Using a mouse model of

concomitant immunity and subsequent aerosol infection, we demonstrate that

counter regulation between neutrophils and CD4 T cells occurs very early during

infection and governs these distinct pathologies. In primary Mtb infection, a

dysregulated feed-forward circuit of neutrophil recruitment occurs, in which

neutrophils hinder CD4 T cell interactions with infected macrophages, cause

granuloma necrosis, and establish a replicative niche that drives a two-log

increase in lung bacterial burden. Conversely, the rapid recruitment and

activation of T cells due to concomitant immunity promotes local macrophage

activation and dampens detrimental neutrophil responses. Together, these studies

uncover fundamental determinants of tuberculosis lung pathology, which have

important implications for new strategies to prevent or treat tuberculosis.

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DOI: 10.1084/jem.20250161

PMCID: PMC12309470

PMID: 40736456 [Indexed for MEDLINE]

**37. Clin Infect Dis. 2025 Jul 30:ciaf309. doi: 10.1093/cid/ciaf309. Online ahead of print.**

Harmonization of Study Design and Reporting for Chronic Pulmonary Aspergillosis

in Tuberculosis Patients.

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DOI: 10.1093/cid/ciaf309

PMID: 40731380

**38. Sci Rep. 2025 Jul 29;15(1):27709. doi: 10.1038/s41598-025-13329-0.**

A computational approach to mycolic acid biosynthesis disruption in

mycobacterium tuberculosis via molluscan metabolites as KasA inhibitors.

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The ongoing global health challenge posed by Mycobacterium tuberculosis, the

causative agent of tuberculosis (TB), is exacerbated by the emergence of

drug-resistant strains. This study explores the potential of inhibiting the KasA

protein, a key component of the bacterium's type II fatty acid synthase system

(FAS-II) involved in mycolic acid biosynthesis. Inhibition of KasA could disrupt

the integrity of the mycobacterial cell wall, which is crucial for its survival

and virulence. In this study, we screened a library of 730 Molluscan metabolites

using molecular docking techniques via the Glide tool, identifying ten compounds

with significant binding affinities ranging from - 7.535 to -6.517 kcal/mol. The

ADMET profiles of these compounds were evaluated, revealing acceptable toxicity

levels for four selected candidates: CMNPD7125, CMNPD22991, CMNPD4542, and

CMNPD12265. Additionally, molecular dynamics simulations confirmed the stability

of these compounds within the KasA binding pocket, reinforcing their potential

as effective inhibitors. This integrated approach combining molecular docking,

ADMET analysis, and dynamic simulations advances the search for innovative

treatments against drug-resistant TB and supports rational drug design efforts

for future anti-tubercular agents.

© 2025. The Author(s).

DOI: 10.1038/s41598-025-13329-0

PMCID: PMC12307626

PMID: 40730846 [Indexed for MEDLINE]

**39. Mol Divers. 2025 Jul 29. doi: 10.1007/s11030-025-11300-9. Online ahead of print.**

Identifying dormancy-associated enzymes in Mycobacterium tuberculosis through a

computational pipeline integrating flux balance analysis and metabolic modeling.

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Tuberculosis, caused by Mycobacterium tuberculosis (Mtb), remains a critical

global health challenge due to rising drug resistance and the pathogen's ability

to persist in hostile host environments. Identifying novel molecular targets

that underlie Mtb's unique survival mechanisms is essential for developing more

effective therapies. In this study, we developed an integrative computational

pipeline combining genome-scale metabolic modeling, flux balance analysis (FBA),

comparative genomics, and network-based prioritization to uncover metabolic

vulnerabilities specific to Mtb. Comparative analysis with the reductively

evolved Mycobacterium leprae revealed significant differences in pathways

involved in pantothenate biosynthesis (PanB), peptidoglycan synthesis (GlmU),

and branched-chain amino acid metabolism (IlvN). These targets were prioritized

based on gene essentiality, dormancy-associated expression, druggability, and

absence of human homologs to maximize therapeutic selectivity. Molecular

docking, followed by MM-GBSA binding free energy calculations, identified

high-affinity ligands from LifeChemicals and ChEMBL libraries interacting

strongly with active-site residues. Molecular dynamics simulations were

performed to further validate target engagement and ligand retention, revealing

stable conformational behavior and persistent protein-ligand interactions across

300 ns. Similarly, metabolite flux analysis and pathway enrichment highlighted

adaptive rewiring in glycine, serine, pyruvate, and nitrogen metabolism,

reflecting Mtb's persistence strategies under host-imposed stress. This study

provides a robust, generalizable pipeline for pathogen-specific drug target and

ligand discovery and supports the rational development of new therapies against

drug-resistant tuberculosis.

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AG.

DOI: 10.1007/s11030-025-11300-9

PMID: 40730708

**40. BMJ Open. 2025 Jul 28;15(7):e105881. doi: 10.1136/bmjopen-2025-105881.**

Evaluating the accuracy of artificial intelligence-powered chest X-ray diagnosis

for paediatric pulmonary tuberculosis (EVAL-PAEDTBAID): Study protocol for a

multi-centre diagnostic accuracy study.

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**INTRODUCTION:** Diagnosing pulmonary tuberculosis (PTB) in children is challenging

owing to paucibacillary disease, non-specific symptoms and signs and challenges

in microbiological confirmation. Chest X-ray (CXR) interpretation is fundamental

for diagnosis and classifying disease as severe or non-severe. In adults with

PTB, there is substantial evidence showing the usefulness of artificial

intelligence (AI) in CXR interpretation, but very limited data exist in

children.

**METHODS AND ANALYSIS:** A prospective two-stage study of children with presumed

PTB in three sites (one in South Africa and two in Pakistan) will be conducted.

In stage I, eligible children will be enrolled and comprehensively investigated

for PTB. A CXR radiological reference standard (RRS) will be established by an

expert panel of blinded radiologists. CXRs will be classified into those with

findings consistent with PTB or not based on RRS. Cases will be classified as

confirmed, unconfirmed or unlikely PTB according to National Institutes of

Health definitions. Data from 300 confirmed and unconfirmed PTB cases and 250

unlikely PTB cases will be collected. An AI-CXR algorithm (qXR) will be used to

process CXRs. The primary endpoint will be sensitivity and specificity of AI to

detect confirmed and unconfirmed PTB cases (composite reference standard); a

secondary endpoint will be evaluated for confirmed PTB cases (microbiological

reference standard). In stage II, a multi-reader multi-case study using a

cross-over design will be conducted with 16 readers and 350 CXRs to assess the

usefulness of AI-assisted CXR interpretation for readers (clinicians and

radiologists). The primary endpoint will be the difference in the area under the

receiver operating characteristic curve of readers with and without AI

assistance in correctly classifying CXRs as per RRS.

**ETHICS AND DISSEMINATION:** The study has been approved by a local institutional

ethics committee at each site. Results will be published in academic journals

and presented at conferences. Data will be made available as an open-source

database.

STUDY REGISTRATION NUMBER: PACTR202502517486411.

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DOI: 10.1136/bmjopen-2025-105881

PMCID: PMC12306472

PMID: 40730400 [Indexed for MEDLINE]

**41. BMJ Open. 2025 Jul 28;15(7):e096709. doi: 10.1136/bmjopen-2024-096709.**

Incidence of QT interval prolongation in patients receiving bedaquiline for

drug-resistant tuberculosis in Sub-Saharan Africa: a protocol for systematic

review and meta-analysis.

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**INTRODUCTION:** Tuberculosis (TB) remains a major public health challenge in

Sub-Saharan Africa, exacerbated by the high prevalence of drug-resistant TB

(DR-TB) and its strong association with HIV. Bedaquiline (BDQ), approved by the

WHO in 2013, offers a promising treatment for DR-TB, including

multidrug-resistant TB (MDR-TB) and extensively DR-TB (XDR-TB). However, BDQ has

been associated with QT interval prolongation, a condition that can lead to

serious cardiac arrhythmias such as torsades de pointes. This systematic review

and meta-analysis aims to quantify the incidence of QT interval prolongation in

patients receiving BDQ for DR-TB in Sub-Saharan Africa and identify predictors

of this adverse effect.

**METHODS AND ANALYSIS:** We will conduct a comprehensive search of PubMed, Embase,

Cochrane Library, Web of Science and African Journals Online using medical

subject headings and keywords related to 'BDQ', 'DR-TB', 'QT interval

prolongation' and 'Sub-Saharan Africa'. Eligible studies will include randomised

controlled trials, cohort studies, case-control studies and observational

studies conducted in Sub-Saharan Africa. Study titles and abstracts will be

initially screened, and full texts will be retrieved and reviewed against

eligibility criteria. Relevant data will be extracted from the selected articles

and assessed for risk of bias. The primary outcome will be the pooled incidence

of QT interval prolongation. Data will be synthesised using a random-effects

model meta-analysis if significant heterogeneity is present; otherwise, a

fixed-effects model will be applied.

**ETHICS AND DISSEMINATION:** This study will use published data, requiring no

ethical approval. Findings will be disseminated through peer-reviewed

publications and conference presentations to inform clinical guidelines and

DR-TB treatment policies in Sub-Saharan Africa.

PROSPERO REGISTRATION NUMBER: CRD42024560368.

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DOI: 10.1136/bmjopen-2024-096709

PMCID: PMC12306456

PMID: 40730389 [Indexed for MEDLINE]

**42. Am J Trop Med Hyg. 2025 Jul 29:tpmd250048. doi: 10.4269/ajtmh.25-0048. Online**

**ahead of print.**

Addressing Stigma, Mental Well-Being, and Alcohol Use among People with

Tuberculosis in Sub-Saharan Africa: A Call for an Integrated Care Model.

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Tuberculosis (TB) remains a major public health challenge in sub-Saharan Africa

(SSA), with stigma, mental health issues, and alcohol use significantly

affecting treatment outcomes. Stigma delays TB diagnosis, reduces treatment

adherence, and disrupts care continuity. Mental health conditions, such as

depression and anxiety, further undermine adherence, whereas alcohol use

accelerates TB disease progression and leads to poor treatment outcomes. Current

TB care models in SSA lack integrated support for psychosocial and behavioral

health needs. This article advocates for a comprehensive care model that

integrates mental health screening, counseling, psychosocial support, alcohol

use disorder screening, and harm reduction strategies into TB programs.

Effective implementation requires collaboration among TB care providers, mental

health specialists, and alcohol use counselors supported by research, provider

training, and community engagement. By addressing stigma, mental health, and

alcohol use, this model can enhance treatment adherence and outcomes, advancing

the WHO's End TB Strategy in SSA.

DOI: 10.4269/ajtmh.25-0048

PMID: 40730178

**43. FEBS J. 2025 Jul 29. doi: 10.1111/febs.70202. Online ahead of print.**

Biophysical characterization and interaction study of WhiB6 protein of

Mycobacterium tuberculosis with espA.

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Tuberculosis is an intractable disease because of the peculiar nature of the

virulent properties of Mycobacterium tuberculosis (Mtb). The probable

transcriptional regulator WhiB6 protein plays a crucial role in the virulence

systems of Mtb. It regulates the expression of genes essential for the virulence

pathways by binding to their promoter region; espA (encoding ESX-1

secretion-associated protein EspA) is one such gene. Herein, we have used

biophysical methods, including steady-state intrinsic fluorescence spectroscopy,

circular dichroism (CD) spectroscopy, isothermal titration calorimetry (ITC),

and surface-enhanced Raman spectroscopy (SERS), to understand the interaction of

apo-WhiB6 protein with espA promoter DNA. For the first time, we report the

conformational details and biophysical parameters related to the

WhiB6-espA-promoter-DNA interaction. WhiB6 binds to the DNA with moderate

affinity, as revealed by ITC. It is an entropy-driven process, signifying the

importance of hydrophobic interaction and an increase in conformational

flexibility upon binding. Addition of salt changes the binding from endothermic

to exothermic, revealing the increase in electrostatic interaction between

protein and DNA with concomitant decrease in flexibility. CD and SERS studies

suggest subtle perturbation in the secondary conformation of the protein upon

binding to the DNA. ITC titration data of an arginine-to-leucine mutant in the

arginine-rich region (GRARAF) of WhiB6 suggest involvement of these residues in

the binding with DNA. Preventing the binding of WhiB6 with promoter DNA of the

virulence genes can hinder the functioning of Mtb and hence can act as an

effective therapeutic intervention for tuberculosis.

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DOI: 10.1111/febs.70202

PMID: 40729538

**44. Eur J Clin Microbiol Infect Dis. 2025 Jul 29. doi: 10.1007/s10096-025-05221-6. Online ahead of print.**

Rapid screening of mutations for second-line-drug-resistant genes in

Mycobacterium tuberculosis culture isolates by in-house developed DNA bio-chip.

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**BACKGROUND:** The rate of multidrug-resistant (MDR) and extensively drug-resistant

(XDR) tuberculosis (TB) has been steadily increasing and is a major setback to

TB control in India. The availability of quick and reliable methods for

detecting second-line drug resistance (SLDR) is vital to managing patients

satisfactorily. A rapid molecular technique to detect SLDR in Mycobacterium

tuberculosis (M. tuberculosis) has been developed using DNA biochip.

**METHODS:** Specific probes containing wild-type region or specific mutations were

designed for immobilization on DNA bio-chip. DNA bio-chip was developed in-house

on polycarbonate track-etched membranes (PC-TEM). DNA bio-chip allows the

identification of mutations in gyrA gene for fluoroquinolone (FQ) resistance, in

rrs gene and the eis promoter region for resistance to second-line injectable

drugs (SLID). An asymmetric multiplex PCR was standardized for gyrA, rrs and eis

genes. A chemiluminescence based biochip assay was optimized. Bio-chip was

tested on 112 M. tuberculosis clinical isolates with different resistance

spectra.

**RESULTS:** Isolates analyzed using bio-chip shows that 61 (61%) samples were

wild-type. Twelve samples show mutations in gyrA gene, 11 samples in rrs gene,

12 samples in eis gene and 4 samples show double mutation in rrs and eis genes.

The sensitivity and specificity of bio-chip for detection of FQ resistance

ranged from 75 to 100% and 96.7%-100%, respectively. The sensitivity and

specificity of SLID detection ranged from 90.9 to 100% and 96.7-100%

respectively. The analytical sensitivity of the bio-chip was ~ 250 genome copies

per assay.

**CONCLUSION:** The biochip has high sensitivity and specificity and could be useful

for clinical microbiology studies and epidemiological surveillance of drug

resistant (DR) M. tuberculosis. It is a highly accurate tool for screening for

SLDR, significantly reducing the time for phenotypic drug susceptibility test

(DST) results from weeks to a single day.

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DOI: 10.1007/s10096-025-05221-6

PMID: 40728715

**45. Cochrane Database Syst Rev. 2025 Jul 29;7(7):CD009593. doi:**

**10.1002/14651858.CD009593.pub6.**

Xpert MTB/RIF Ultra assay for pulmonary tuberculosis and rifampicin resistance

in adults and adolescents.

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Update of

 doi: 10.1002/14651858.CD009593.pub5.

**BACKGROUND:** Xpert MTB/RIF Ultra (Xpert Ultra) is a molecular World Health

Organization (WHO)-recommended rapid diagnostic test that simultaneously detects

tuberculosis and rifampicin resistance. This review updates a comparative

accuracy Cochrane review of Xpert MTB/RIF and Xpert Ultra as Xpert Ultra has

replaced Xpert MTB/RIF.

**OBJECTIVES:** To determine the diagnostic accuracy of Xpert MTB/RIF Ultra (Xpert

Ultra) for detecting pulmonary tuberculosis and rifampicin resistance in adults

and adolescents with presumptive tuberculosis based on signs or symptoms or with

an abnormal chest x-ray suggestive of tuberculosis.

**SEARCH METHODS:** We searched seven databases including CENTRAL, MEDLINE, and

Embase, plus two trial registers (ClinicalTrials.gov and the WHO ICTRP) to 16

October 2023 without language restrictions. A WHO Public Call for ongoing and

unpublished studies was made between 30 November 2023 and 15 February 2024.

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

randomised controlled trials that provided data on the diagnostic accuracy of

Xpert Ultra using respiratory specimens in adolescents (aged 10 to 14 years) and

adults (aged 15 years and older) with presumptive pulmonary tuberculosis. For

pulmonary tuberculosis detection, the reference standards were culture and a

composite reference standard. For rifampicin resistance, the reference standards

were culture-based phenotypic drug susceptibility testing with or without whole

**genome sequencing.**

**DATA COLLECTION AND ANALYSIS:** Two review authors independently extracted data

using a standardised form. We assessed risk of bias using QUADAS-2. We performed

meta-analyses using a bivariate model to produce summary sensitivities and

specificities, separately for pulmonary tuberculosis detection and rifampicin

resistance detection. We performed subgroup analyses by smear status, HIV

status, and history of tuberculosis. We summarised Xpert Ultra trace-positive

results.

**MAIN RESULTS:** Pulmonary tuberculosis detection For detection of pulmonary

tuberculosis, Xpert Ultra summary sensitivity and specificity against culture

were 90.7% (95% confidence interval (CI) 88.2 to 92.7) and 94.8% (95% CI 92.8 to

96.3) (32 studies, 12,529 participants; high-certainty evidence). Most studies

had low risk of bias in all QUADAS-2 domains. If the point estimates for Xpert

Ultra are applied to a hypothetical cohort of 1000 people, where 100 of those

presenting with symptoms have pulmonary tuberculosis, Xpert Ultra will miss nine

cases. The number of people wrongly diagnosed with pulmonary tuberculosis would

be 47. In people living with HIV, Xpert Ultra summary sensitivity and

specificity were 87.7% (82.0 to 91.7) and 95.3% (92.2 to 97.2) (11 studies, 1164

participants). Amongst people with smear-negative, culture-positive pulmonary

tuberculosis, Xpert Ultra summary sensitivity and specificity were 80.7% (75.4

to 85.0) and 94.0% (91.3 to 95.9) (16 studies, 6460 participants). In people

with a history of tuberculosis, Xpert Ultra summary sensitivity and specificity

were 84.8% (78.2 to 89.7) and 86.2% (78.9 to 91.3) (9 studies, 809

participants). The proportion of Ultra trace-positive results that were true

positives compared to the microbiological reference standard was 38.8%.

Reclassifying trace-positive results as Xpert Ultra-negative led to a reduction

in sensitivity and modest increase in specificity. Rifampicin resistance

detection For detection of rifampicin resistance, Xpert Ultra summary

sensitivity and specificity were 95.8% (93.2 to 97.4) and 98.3% (97.0 to 99.0)

(10 studies, 1644 participants; high-certainty evidence). Most studies had low

risk of bias in all QUADAS-2 domains. If the point estimates for Xpert Ultra are

applied to a hypothetical cohort of 1000 people, where 100 of those presenting

with symptoms have rifampicin resistance, Xpert Ultra will miss four cases. The

number of people wrongly diagnosed with rifampicin resistance would be 16 out of

the 900 who do not have rifampicin resistance. Xpert Ultra performed similarly,

for rifampicin resistance, in people with smear-positive and smear-negative

tuberculosis.

**AUTHORS' CONCLUSIONS:** Xpert Ultra has high sensitivity and specificity for

detection of pulmonary tuberculosis rifampicin resistance. Xpert Ultra for the

detection of pulmonary tuberculosis has lower sensitivity in people with

smear-negative/culture-positive tuberculosis and lower sensitivity and

specificity in people with a history of tuberculosis. Xpert Ultra trace-positive

results were common. Strengths of this review include the approach to

identifying relevant studies, the number of studies and participants included in

this systematic review, and that most studies were at low risk of bias. The

small number of studies (six) and participants who were adolescents is a

limitation to our accuracy estimates in this age group. Xpert Ultra testing

provides accurate results and can allow rapid initiation of treatment for

rifampicin-resistant and multiple-drug-resistant tuberculosis.

FUNDING: The WHO supported this systematic review. Liverpool School of Tropical

Medicine hosted the Cochrane Infectious Diseases Group (CIDG) editorial base,

which supported the authors in the development of this review update. The

Foreign, Commonwealth and Development Office funded the CIDG.

REGISTRATION: Generic protocol available on Open Science Framework via

https://osf.io/26wg7/wiki/home/. Previous protocol and review versions available

via DOI 10.1002/14651858.CD009593 and DOI 10.1002/14651858.CD009593.pub5.

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by John Wiley & Sons, Ltd. on behalf of The Cochrane Collaboration.

DOI: 10.1002/14651858.CD009593.pub6

PMCID: PMC12305759

PMID: 40728034 [Indexed for MEDLINE]

**46. Indian J Otolaryngol Head Neck Surg. 2025 Aug;77(8):2857-2866. doi:**

**10.1007/s12070-025-05592-4. Epub 2025 May 31.**

Head Neck Tuberculosis Amidst COVID Pandemic: An Assessment of Change in Disease

Dynamics.

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COVID 19 pandemic has had its effect on the entire world population. The purpose

of the study was to perform Epidemiological and Head Neck site wise assessment

of Tuberculosis (TB) presentation and investigation during and immediately after

the COVID 19 pandemic. The changing incidence and atypical presentations were

documented. Institution based retrospective study was conducted and the data of

Head Neck TB (HN- TB) was extracted from the patient registers of National

Tuberculosis Elimination Programme (NTEP) of the same institute during the

period of March 1st 2020 to 31st December 2022. Statistical analysis was done to

satisfy the investigative purpose. In the study period 2118 patients were

registered for TB. 279 patients were diagnosed with HN-TB as the primary site of

involvement. Cervical Lymph node TB was the predominantly involved site followed

by Head Neck Skin, Ear, Larynx, Ophthalmological structures, Facial bones, Oral

cavity and Oropharynx, Neck sinus. The Incidence of TB as a whole and HN- TB saw

uneven rise and fall with respect to its incidence during and after the

pandemic. There were definite variations in the incidence of site specific

involvement of HN- TB when compared to world literature. Changing disease

dynamics comes as a challenge before NTEP amidst the prevailing pandemic. No

particular investigation is full proof to detect tuberculosis and so, attempts

should be made to maximise the number of detection options. Lessons should be

learnt from the present situation to keep us prepared for the future.

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this article is solely governed by the terms of such publishing agreement and

applicable law.

DOI: 10.1007/s12070-025-05592-4

PMCID: PMC12297187

PMID: 40727207

**47. Int J Dermatol. 2025 Jul 28. doi: 10.1111/ijd.17988. Online ahead of print.**

Multifocal Tuberculosis in an Immunocompetent Patient.

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DOI: 10.1111/ijd.17988

PMID: 40722131

**48. BMJ Open. 2025 Jul 28;15(7):e093989. doi: 10.1136/bmjopen-2024-093989.**

Effectiveness and cost-effectiveness of community-based TB screening algorithms

using computer-aided detection (CAD) technology alone compared with CAD combined

with point-of-care C reactive protein testing in Lesotho and South Africa:

protocol for a paired screen-positive trial.

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M(7)(2), Tediosi F(7)(2), Verjans A(7)(2), Brugger C(7)(2), Harkare HV(7)(2),

Labhardt ND(8)(9), Bosman S(3), Kamele M(5), Keitseng M(5), Madonsela T(3),

Kurscheid J(7)(2), Muhairwe J(10), Keter AK(11), Murphy K(12), van Ginneken

B(12), Gils T(6)(13), Katende B(14), Gebresenbet RF(15), Erhardt RM(7)(2),

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**INTRODUCTION:** Tuberculosis (TB) remains a significant public health challenge in

many African communities, where underreporting and underdiagnosis are prevalent

due to barriers in accessing care and inadequate diagnostic tools. This is

particularly concerning in hard-to-reach areas with a high burden of TB/HIV

co-infection, where missed or delayed diagnoses exacerbate disease transmission,

increase mortality and lead to severe economic and health consequences. To

address these challenges, it is crucial to evaluate innovative, cost-effective,

community-based screening strategies that can improve early detection and

linkage to care.

**METHODS AND ANALYSIS:** We conduct a prospective, community-based, diagnostic,

pragmatic trial in communities of the Butha Buthe District in Lesotho and the

Greater Edendale area of Msunduzi Municipality, KwaZulu-Natal in South Africa to

compare two strategies for population-based TB screening: computer-aided

detection (CAD) technology alone (CAD4TBv7 approach) versus CAD combined with

point-of-care C reactive protein (CRP) testing (CAD4TBv7-CRP approach).

Following a chest X-ray, CAD produces an abnormality score, which indicates the

likelihood of TB. Score thresholds informing the screening logic for both

approaches were determined based on the WHO's target product profile for a TB

screening test. CAD scores above a threshold prespecified for the CAD4TBv7

approach indicate confirmatory testing for TB (Xpert MTB/RIF Ultra). For the

CAD4TBv7-CRP approach, a CAD score within a predefined window requires the

conduct of the second screening test, CRP, while a score above the respective

upper threshold is followed by Xpert MTB/RIF Ultra. A CRP result above the

selected cut-off also requires a confirmatory TB test. Participants with CAD

scores below the (lower) threshold and those with CRP levels below the cut-off

are considered screen-negative. The trial aims to compare the yield of detected

TB cases and cost-effectiveness between two screening approaches by applying a

paired screen-positive design. 20 000 adult participants will be enrolled and

will receive a posterior anterior digital chest X-ray which is analysed by CAD

software.

**ETHICS AND DISSEMINATION:** The protocol was approved by National Health Research

Ethics Committee in Lesotho (NH-REC, ID52-2022), the Human Sciences Research

Council Research Ethics Committee (HSRC REC, REC 2/23/09/20) and the Provincial

Health Research Committee of the Department of Health of KwaZulu-Natal

(KZ\_202209\_022) in South Africa and from the Swiss Ethics Committee Northwest

and Central Switzerland (EKNZ, AO\_2022-00044). This manuscript is based on

protocol V.4.0, 19 January 2024. Trial findings will be disseminated through

peer-reviewed publications, conference presentations and through communication

offices of the consortium partners and the project's website

(https://tbtriage.com/).

TRIAL REGISTRATION: ClinicalTrials.gov (NCT05526885), South African National

Clinical Trials Register (SANCTR; DOH-27-092022-8096).

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DOI: 10.1136/bmjopen-2024-093989

PMCID: PMC12306269

PMID: 40721262 [Indexed for MEDLINE]

**49. JMIR Public Health Surveill. 2025 Jul 28;11:e62881. doi: 10.2196/62881.**

Engagement With Digital Adherence Technologies as Measures of Intervention

Fidelity Among Adults With Drug-Susceptible Tuberculosis and Health Care

Providers: Descriptive Analysis Using Data From Cluster-Randomized Trials in

Five Countries.

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**BACKGROUND:** Digital adherence technologies (DATs) are promising tools for

supporting tuberculosis (TB) treatment. DATs can serve as reminders for people

with TB to take their medication and act as proxies for adherence monitoring.

Strong engagement with DATs, from both the person with TB and health care

provider (HCP) perspectives, is essential for ensuring intervention fidelity.

The Adherence Support Coalition to End TB (ASCENT) project evaluated 2 types of

DATs, pillboxes and medication labels (99DOTS), in cluster-randomized trials

across 5 countries.

**OBJECTIVE:** This study aims to investigate participant and HCP engagement with

DATs for TB treatment, stratified by DAT type and country.

**METHODS:** This study is a subanalysis of data generated through the ASCENT

trials, which enrolled adults with drug-susceptible TB. A digital dose was

defined as either a pillbox opening (for pillbox users) or a dosing confirmation

SMS text message sent by the participant (for label users), both of which were

recorded on the adherence platform. Descriptive analysis was used to provide an

overview of dose-day outcomes. DAT engagement was assessed from both participant

and HCP perspectives. To enhance participant engagement, we summarized the

frequency of digital engagement overall and by treatment phase, as well as the

frequency of consecutive days without engagement. For HCP engagement, we

summarized the frequency of doses added manually, the number of days between the

actual dose day and when a manual dose was added, and instances of consecutive

manual dosing lasting more than 3 and more than 7 days, where doses were added

more than 1 week after the dose day.

**RESULTS:** Of the 9511 participants included, 6719 (70.64%) were using the

pillbox, 3544 (37.26%) were female, and the median age was 40 years. Across DAT

types, there were 1,384,879 dose days, with 973,876 (70.32%) contributed by

pillbox users. Of all dose days, 1,165,195 (84.14%) were recorded as digital,

156,664 (11.31%) as manual, 59,045 (4.26%) had no information, and 3975 (0.29%)

were confirmed as missed. Digital dosing decreased slightly from the intensive

to the continuation phase. The percentage of digital dose days was higher among

pillbox users (851,496/973,876, 87.43%) compared with label users

(313,699/411,003, 76.33%). Among label users, manual dosing was most common in

the Philippines (37,919/171,786, 22.07%) and least common in Tanzania

(11,108/76,231, 14.57%). Among pillbox users, manual dosing was most common in

the Philippines (24,015/208,130, 11.54%) and Ukraine (13,209/111,901, 11.80%).

Overall, 512 out of 2792 (18.34%) label users and 588 out of 6719 (8.75%)

pillbox users experienced a run of more than 7 consecutive nondigital dose days

that were resolved more than 1 week after the dose day. The highest occurrence

was observed in the Philippines (368/1142, 32.22%, for label users and 224/1351,

16.58%, for pillbox users).

**CONCLUSIONS:** There was considerable variation in DAT engagement across countries

and DAT types, reflecting differences in how the intervention was implemented.

Further refinement of the intervention and improvements in its delivery may be

necessary to enhance outcomes.

© Jason Alacapa, Amare Worku Tadesse, Natasha Deyanova, Tanyaradzwa Dube, Andrew

Mganga, Rachel Powers, Job van Rest, Norma Madden, Egwuma Efo, Salome

Charalambous, Kristian van Kalmthout, Degu Jerene, Katherine Fielding.

Originally published in JMIR Public Health and Surveillance

(https://publichealth.jmir.org).

DOI: 10.2196/62881

PMCID: PMC12303541

PMID: 40720892 [Indexed for MEDLINE]

**50. PLoS Med. 2025 Jul 28;22(7):e1004666. doi: 10.1371/journal.pmed.1004666.**

**eCollection 2025 Jul.**

Rapid molecular testing or chest X-ray or tuberculin skin testing for household

contact assessment of tuberculosis infection: A cluster-randomized trial.

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D(5), Djohoun F(2), Oxlade O(5), Fregonese F(5), Affolabi D(2)(7), Kouchade

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Brazil.

**BACKGROUND:** The World Health Organization recommends evaluation of all household

contacts (HHC) of index tuberculosis (TB) patients for TB disease (TBD) and TB

infection (TBI). Tests to identify TBI and TBD are preferred but can be skipped

in persons living with HIV and children <5 years. There is equipoise on the need

for these tests in other HHC.

**METHODS:** We conducted a superiority, open label cluster-randomized trial in

Benin and Brazil to compare three strategies to evaluate HHC aged 5-50 of

persons newly diagnosed with drug susceptible pulmonary TBD: Standard:

tuberculin skin testing (TST) for TBI and if positive, chest X-ray (CXR) to rule

out TBD; rapid molecular test (RMT): same as Standard, except CXR replaced by an

RMT; and No-TST: CXR for all but no TST. Randomization was computer-generated

and stratified by country, in blocks of variable length. The primary outcome was

TB preventive therapy (TPT) initiation among HHC considered eligible (positive

TST, if done, and no evidence of TBD on CXR or RMT). Secondary outcomes were:

completion of investigations to detect TBI and TBD, detection of TBD, TPT

completion, severe adverse events, and societal costs.

**RESULTS:** Among 1,589 participating HHC enrolled from 29 January 2020, to 30

November 2022, 474 were randomized to the standard, 583 to the RMT, and 532 to

the no-TST strategies; all were included in the analyses. Of 848 HHC considered

eligible for TPT, 802 (94.6%) initiated TPT, with no difference between

strategies (95%, 94%, and 95% for the standard, RMT, and no-TST strategies,

respectively). Of the secondary outcomes, protocol-mandated investigations to

detect TBI and exclude possible TBD were completed for 93.4% overall, with

slight differences between arms (93%, 95%, and 93% for the standard, RMT, and

no-TST strategies, respectively). Adverse events resulting in discontinuation of

TPT occurred in 3 (0.4%) participants in total (with 1, 0, and 2 events among

participants in the Standard, RMT, and no-TST arms, respectively). The

proportion completing TPT was similar with Standard and RMT strategies but was

13% lower (95% confidence interval: 3% to 23% lower) with the No-TST strategy.

Societal costs per HHC completing investigations were $61 ($56-$65) with the

standard strategy, compared to $52 ($49-$55) with the RMT strategy and $74

($72-$77) with the no-TST strategy.

**CONCLUSION:** This randomized trial provides high-quality evidence that TST

followed by selected use of CXR or an RMT to exclude disease can achieve high

rates of TPT initiation at reasonable costs. A limitation of the trial is the

potential study effect, which may have affected adherence by providers and HHCs.

RMT could replace CXR in the management of HHC in resource limited settings.

REGISTRATION: clinicaltrials.gov NCT04528823.

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DOI: 10.1371/journal.pmed.1004666

PMCID: PMC12316388

PMID: 40720526 [Indexed for MEDLINE]

**51. J Infect Dev Ctries. 2025 Jul 28;19(7):1074-1082. doi: 10.3855/jidc.20731.**

Clinical misconceptions and diagnostic delays in extrapulmonary tuberculosis: an

evaluation on 89 cases.

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**INTRODUCTION:** Extrapulmonary tuberculosis (EPTB) has highly variable clinical

findings, and has a more difficult diagnostic process than pulmonary

tuberculosis (PTB). The aim of this study was to examine the difficulty of the

diagnostic process in 89 cases that applied to different clinics in our

hospital, with different complaints.

**METHODOLOGY:** A total of 89 patients diagnosed with EPTB between March 2020 and

March 2024 were included in the study. EPTB diagnosis was determined by

excluding patients with primary PTB.

**RESULTS:** The mean age of the cases was 47.84 ± 19.23 years, and 52 (58.4%) of

the patients were women. There was a significant relationship between the

affected area and gender (p < 0.001). The rate of peripheral lymphadenopathy

(LAP) involvement was much higher in women than that in men (85.2% vs. 14.8%).

Pleural involvement was 6.5-fold higher in men than in women (51.4% vs. 7.8%).

There was also a significant relationship between the affected area and the time

to diagnosis (p < 0.001). While peripheral LAP cases were diagnosed late,

patients with pleural involvement were diagnosed more quickly (p < 0.001). The

rate of smoking addiction was high in males with pleural involvement (79.9%).

Quinolone use was 77.4% in the early-diagnosed group and 54.9% in the

late-diagnosed group (p = 0.110).

**CONCLUSIONS:** Due to the difficulty of diagnosis, EPTB should be included in the

differential diagnoses of all relevant medical specialties, and insistence

should be made for the diagnosis in the presence of clinical suspicion.

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DOI: 10.3855/jidc.20731

PMID: 40720464 [Indexed for MEDLINE]

**52. QJM. 2025 Jul 28:hcaf169. doi: 10.1093/qjmed/hcaf169. Online ahead of print.**

Renal Tuberculosis Following Intravesical Bacillus Calmette-Guérin Therapy.

Oguni K(1)(2), Hagiya H(2), Otsuka F(1)(2).

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(2)Department of Infectious Diseases, Okayama University Hospital, Okayama,

Japan.

DOI: 10.1093/qjmed/hcaf169

PMID: 40719771

**53. Chem Commun (Camb). 2025 Jul 28. doi: 10.1039/d5cc02403j. Online ahead of print.**

Smartphone-assisted tuberculosis detection by a smart amplification process and

lateral flow immunoassay with a 3D-printed device.

Chen CA(1)(2), Ho NY(2), Yang CC(2), Hsiao HY(3), Huang TH(2), Hsieh MK(1)(2),

Lai PL(1)(2), Tsai TT(1)(2).

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(3)Department of Biomedical Sciences, Chang Gung University, Taoyuan, Taiwan.

A portably 3D-printed sensing platform combining a sunrise-biotin-labeled smart

amplification process (sb-SmartAmp) and stacking pad lateral flow immunoassay

(sLFIA) enables smartphone-assisted image analysis or naked-eye detection for

on-site TB diagnosis, validated with clinical TB samples beyond in vitro

testing.

DOI: 10.1039/d5cc02403j

PMID: 40719028

**54. Tuberculosis (Edinb). 2025 Jul 23;154:102674. doi: 10.1016/j.tube.2025.102674.**

**Online ahead of print.**

Incidence of infectious diseases in children with Mycobacterium tuberculosis in

Japan, 2007-2022.

Hamaguchi Y(1), Yamaguchi T(2), Yoshiyama T(3).

Author information:

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522-8522, Japan.

(3)The Research Institute of Tuberculosis, Japan Anti-Tuberculosis Association,

3-1-24 Matsuyama, Kiyose, Tokyo, 204-8533, Japan.

The objective of this study was to understand the descriptive epidemiology of

childhood tuberculosis (TB) in Japan under the 2013 Bacillus Calmette-Guérin

(BCG) immunization program modification. The median percentage of annual

vaccination coverage for infants aged <13 months was 97.0 % during follow-up

(2007-2022). The age at which most infants received their vaccinations was 3

months before 2013 and 5 months after 2013. During follow-up, the number of

childhood TB notifications and annual incidence declined by approximately 60 %

and 40 %, respectively. A multivariate-adjusted model analysis was performed by

birth year to determine the association between childhood TB and the 2013 BCG

immunization program modification. However, childhood TB was associated with age

and BCG vaccination history but not with the 2013 BCG immunization program

modification. This study represents a valuable resource for future research,

elucidating the efficacy of BCG as well as the impact of BCG policies.

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DOI: 10.1016/j.tube.2025.102674

PMID: 40752240

**55. J Pak Med Assoc. 2025 Jul;75(7):1135-1137. doi: 10.47391/JPMA.20719.**

Colorenal fistulae: A rare but fatal presentation of renal tuberculosis in a

paediatric patient.

Mahar NA(1), Mughal N(1), Mahar R(1), Channa MA(1), Hussain M(1).

Author information:

(1)Sindh Institute of Urology and Transplantation, Karachi, Pakistan.

Genitourinary Tuberculosis (GUTB) primarily occurs due to haematogenous

infection and represents the most prevalent form of extra-pulmonary

tuberculosis. It typically presents with non-specific symptoms and is rare in

children, making diagnosis challenging and, potentially, leading to

complications such as renal failure, pyonephrosis, nephrocutaneous fistulae, and

sepsis. We describe a unique case involving a four-year-old male child who

developed renal tuberculosis secondary to a renal stone, resulting in

pyonephrosis and colorenal fistulae.

DOI: 10.47391/JPMA.20719

PMID: 40751629 [Indexed for MEDLINE]

**56. Euro Surveill. 2025 Jul;30(30):2500210. doi:**

**10.2807/1560-7917.ES.2025.30.30.2500210.**

Early adopters of 6-month levofloxacin as rifampicin-resistant tuberculosis

preventive treatment regimen in the WHO European Region, 2023.

Felker I(1), Solovyeva A(2), Ciobanu A(2), Hovhannesyan A(2), Falzon D(3), Dadu

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Geneva, Switzerland.

Tuberculosis (TB) preventive treatment (TPT) is crucial for preventing infection

with Mycobacterium tuberculosis from progressing to TB disease, especially among

people in high-risk groups. The expansion of novel TPT regimens for

drug-susceptible TB is a notable advancement in TB care. However, managing

contacts of drug-resistant TB patients remains a major challenge, particularly

in Eastern Europe and Central Asia. In 2020, the World Health Organization (WHO)

recommended TPT for high-risk household contacts of multidrug-resistant (MDR) or

rifampicin-resistant (RR) TB patients; this was further reinforced in 2024 with

a recommendation of a 6-month levofloxacin (6-Lfx) regimen. This Perspective

discusses the early adoption of 6-Lfx for MDR/RR-TPT in the WHO European Region.

In 2023, 38 of 53 WHO European Region countries reported on 6-Lfx use, with only

eight confirming its use for MDR-TB contact persons. Accelerating the adoption

of the 6-Lfx regimen and other evidence-backed TPT regimens is crucial for

achieving TB elimination in the WHO European Region. Addressing challenges such

as slow uptake of the recommendations, low awareness in affected communities and

resource shortages are essential for success.

DOI: 10.2807/1560-7917.ES.2025.30.30.2500210

PMCID: PMC12315515

PMID: 40747573 [Indexed for MEDLINE]

**57. bioRxiv [Preprint]. 2025 Jul 18:2025.07.18.665318. doi:**

**10.1101/2025.07.18.665318.**

Early Antibody-Mediated Immunity to Tuberculosis in Mice Requires NLRP3.

Bouzeyen R, Sithole N, Watson A, Abramovitz L, Rakayev K, Fillion A, Dickson T,

MacAry PA, Darrah PA, Seder RA, Freund NT, Javid B.

While antibodies have emerged as potential mediators of protective immunity

against Mycobacterium tuberculosis (Mtb), their mechanisms of action remain

incompletely understood. Here, we demonstrate that immune complexes of Mtb and

monoclonal antibodies targeting the Mtb phosphate transporter subunit PstS1

robustly activate the NLRP3 inflammasome in human and murine macrophages,

leading to enhanced interleukin-1β secretion. Surprisingly, antibody-mediated

inflammasome activation occurred independently of cell-surface Fcγ receptors, as

confirmed using Fc-domain glycosylation mutant mAbs and macrophages from Fcγ

receptor-deficient mice. Crucially, NLRP3 is indispensable for early

antibody-mediated protection in vivo, as both pharmacological inhibition, and

genetic deletion of NLRP3 completely abolished protective effects of

PstS1-specific antibodies in Mtb-infected mice. This mechanism extends beyond

monoclonal antibodies, as polyclonal sera from intravenously BCG-immunized

rhesus macaques also required NLRP3 for protective efficacy. Our findings reveal

a previously unrecognized mechanism by which Mtb-specific antibodies enhance

host defense through inflammasome activation, potentially informing novel

approaches for tuberculosis vaccine development.

DOI: 10.1101/2025.07.18.665318

PMCID: PMC12312167

PMID: 40747430

**58. Cureus. 2025 Jun 30;17(6):e87077. doi: 10.7759/cureus.87077. eCollection 2025**

**Jun.**

Diverse Manifestations of Central Nervous System Tuberculosis: Magnetic

Resonance Imaging (MRI) Presentations and Laboratory Investigations in a Cohort

Study.

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(4)Yoga and Naturopathy, All India Institute of Medical Sciences, Jodhpur,

Jodhpur, IND.

**OBJECTIVES:** This study aims to evaluate and characterize the diverse MRI

findings in central nervous system (CNS) tuberculosis (TB) and the role of other

laboratory investigations to aid in early detection and appropriate management.

**MATERIALS AND METHODS:** This retrospective, cross-sectional study analyzed

clinical and imaging data from 43 patients with confirmed CNS TB. The diagnosis

was confirmed through cerebrospinal fluid (CSF) analysis, biopsy, or clinical

and radiological improvement post-antitubercular therapy (ATT). MRI findings

were categorized into meningeal and parenchymal forms, with further subtyping

based on lesion characteristics. Chi-square statistics were performed using IBM

SPSS Statistics for Windows, version 27 (IBM Corp., Armonk, New York, United

States) to correlate CNS TB with clinical parameters.  Results: The mean age of

the 43 patients was 33 years, and 58% were male. The most common clinical

symptoms were headache (86%) and fever (79%). MRI findings revealed meningeal TB

(leptomeningitis and pachymeningitis) and parenchymal TB (tuberculomas,

tubercular abscesses, cerebritis, rhombencephalitis, and encephalopathy).

Frequent observations included ring-enhancing lesions and perilesional edema.

Parenchymal tuberculomas showed varying stages. Advanced imaging techniques such

as magnetic resonance spectroscopy and perfusion imaging were useful in

differentiating tuberculomas from neoplastic and infectious differentials.

**CONCLUSION:** CNS TB presents with diverse MRI patterns, including both typical

and atypical manifestations. Accurate radiological assessment, combined with

clinical correlation, is essential for early diagnosis and management. Prompt

initiation of ATT is critical in preventing long-term neurological

complications. Future research should focus on refining imaging biomarkers to

improve diagnostic accuracy.

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DOI: 10.7759/cureus.87077

PMCID: PMC12311320

PMID: 40746790

**59. J Am Assoc Lab Anim Sci. 2025 Jul 1:1-6. doi: 10.30802/AALAS-JAALAS-25-057.**

**Online ahead of print.**

Characteristics of Tuberculosis Tests Performed during Postimport Quarantine of

Nonhuman Primates, United States, 2021 to 2024.

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Carroll A(1), Bravo DM(4), Langer AJ(3), Pieracci EG(1).

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Hepatitis, STD, and TB Prevention, CDC, Atlanta, Georgia; and.

(4)4National Veterinary Services Laboratories, USDA, Ames, Iowa.

Screening nonhuman primates (NHPs) for tuberculosis (TB) is important to protect

the health of NHP colonies and people who interact with them. Screening is

especially important for imported NHPs from countries where TB is prevalent and

biosecurity practices may be lax. There are a variety of testing methods

available for TB screening and diagnosis in NHPs; all have limitations, and

their performance in different settings is incompletely characterized. The US

Centers for Disease Control and Prevention (CDC) collects TB testing results as

part of its regulatory oversight of NHP importation. We collated the results of

tuberculin skin tests (TSTs), interferon-γ release assays (IGRAs), multiplexed

fluorometric immunoassay (MFIA), Mycobacterium tuberculosis complex PCR,

staining for acid-fast bacilli (AFB), and culture of bacteria from tissues for

imported NHPs in CDC-mandated quarantine during fiscal years 2021 to 2024. We

used these data to assess test performance and intertest agreement for the

different tests used. Among 107 imported NHPs tested, TST and IGRA were the most

common antemortem tests performed, but they agreed poorly with each other and

with culture. AFB staining and PCR exhibited moderate agreement and high

positive predictive values using culture as the gold standard. The most commonly

affected tissues were lungs and tracheobronchial lymph nodes, regardless of the

Mycobacterium sp. identified. Further research is needed to identify and

validate additional methods for TB testing in NHPs, particularly for antemortem

screening. Tissue acid-fast staining and PCR exhibited high positive predictive

values and could be useful to inform policies and clinical decisions about

colony management and occupational health while awaiting culture results.

DOI: 10.30802/AALAS-JAALAS-25-057

PMID: 40744447

**60. WHO South East Asia J Public Health. 2025 Jan 1;14(1):68. doi:**

**10.4103/WHO-SEAJPH.WHO-SEAJPH\_157\_24. Epub 2025 Jul 31.**

Exploring the Role of Health Systems Strengthening in Reducing the Burden of

Latent Tuberculosis among Healthcare Workers.

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DOI: 10.4103/WHO-SEAJPH.WHO-SEAJPH\_157\_24

PMID: 40743423

**61. Cureus. 2025 Jun 29;17(6):e87004. doi: 10.7759/cureus.87004. eCollection 2025**

**Jun.**

Anti-MDA5 Antibody-Positive Dermatomyositis-Associated Interstitial Lung Disease

With a False-Positive Tuberculosis-Targeted RNA Capture (TB-TRC) Result: A

Multimodal Management.

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Anti-MDA5 antibody-positive dermatomyositis often causes rapidly progressive

interstitial lung disease (RP-ILD) with high mortality. We present a 59-year-old

man with three weeks of fever and dyspnea whose chest CT images showed bilateral

subpleural ground-glass and reticular opacities. A markedly elevated anti-MDA5

titer and skin biopsy confirmed anti-MDA5 anti-positive

dermatomyositis-associated RP-ILD. Tacrolimus plus nintedanib was initiated.

Initial bronchoalveolar lavage fluid (BALF) testing on admission was

unexpectedly positive for Mycobacterium tuberculosis by targeted RNA capture

(TB-TRC), precluding cyclophosphamide and prompting plasma exchange, followed by

intravenous immunoglobulin (IVIG). Repeat BALF TB-TRC and all sputum cultures

remained negative for M. tuberculosis, confirming a false-positive result. On

day 28, tofacitinib replaced tacrolimus due to persistent hyperferritinemia. The

patient was discharged without home oxygen therapy on day 54. This case

highlights the importance of interpreting rapid assays in context and using

multimodal therapy - steroids, calcineurin inhibition, antifibrotics, plasma

exchange, IVIG, and Janus kinase (JAK) inhibition - for refractory anti-MDA5

RP-ILD.

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DOI: 10.7759/cureus.87004

PMCID: PMC12308046

PMID: 40741562

**62. Clin Exp Vaccine Res. 2025 Jul;14(3):210-228. doi: 10.7774/cevr.2025.14.e21.**

**Epub 2025 Mar 31.**

Multilevel systems biology analysis identifies key immune response profiles and

potential correlates of protection for M72/AS01E vaccine against tuberculosis.

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**PURPOSE:** Tuberculosis (TB) claims around 1.5 million lives annually. The

M72/AS01E vaccine candidate is an innovative effort demonstrating a 50%

reduction in the incidence of active TB in adults. However, optimization and

effective immunization strategies against TB depends heavily on precise

identification of specific molecular signatures active in vaccine protection.

**MATERIALS AND METHODS:** In this study, we employed weighted gene co-expression

network analysis, machine learning, and network biology to investigate the gene

expression patterns of peripheral blood mononuclear cells, identifying

transcriptomic markers of vaccine protection.

**RESULTS:** Our comprehensive exploration of publicly available gene expression

dataset comprising samples from subjects vaccinated twice with 10 μg of

M72/AS01E vaccine one day post-second dose (D31) and one week post-second dose

(D37) in a phase IIA clinical trial revealed intense induction of multiple gene

modules, indicative of acute/immediate immune response at D31 that subsided by

D37. Thirty-one hub genes with significant elevation/correlation with immune

protection were identified significantly mediating key events in immunity to TB.

The more selective profile at D37 involved additional adaptive immunity pathways

including T helper (Th) 1/Th2/Th17 differentiation, T cell receptor and cytokine

signaling. The functional relevance of these biomarkers in predicting vaccine

response was further analyzed using the Random Forest classifier demonstrating

high accuracy in distinguishing between vaccinated and non-vaccinated samples.

Additionally, the study pinpointed a miRNAs-transcription factors (TF)-target

regulatory network excavating key TF, miRNA, mRNAs mediating vaccine protection.

**CONCLUSION:** Our results provided new insights into M72/AS01E immunity,

warranting further study to optimize and guide future TB vaccine development.

© Korean Vaccine Society, Korean Society for Zoonoses.

DOI: 10.7774/cevr.2025.14.e21

PMCID: PMC12303709

PMID: 40741055

**63. Front Pharmacol. 2025 Jul 16;16:1606150. doi: 10.3389/fphar.2025.1606150.**

**eCollection 2025.**

A scoping review about smoking, smoking cessation and their effects on

anti-tuberculosis agents: insights into drug metabolisms, safety, and

effectiveness.

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D(6)(7)(8), Nailes JM(9), Shahbaz H(10)(11), Tanuwihardja RK(12), Mohan A(13),

Ceccarelli M(14), Bernardini R(1)(2), Marino A(#)(5), Cantarella G(#)(1).

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(#)Contributed equally

The World Health Organization (WHO) ranks tuberculosis (TB) as one of the top 10

causes of deaths worldwide. Notably, tobacco smoking represents a significant

promoting factor in TB progression, being associated with poorer treatment

outcomes, delayed conversion to negative smear or culture, and higher dropout

rates from treatment plans. Remarkably, high rates of smoking and TB frequently

overlaps in the same countries, warranting the need for targeted public health

interventions. Prioritising smoking cessation is essential for smokers with TB,

as sustained abstinence has been associated with reduced mortality and a more

successful cure. This review examines the intricate relationship between

cigarette smoking, smoking cessation therapies and anti-TB drugs, focusing on

the impact of tobacco smoking compounds on liver detoxifying systems, such as

influence of polycyclic aromatic hydrocarbons (PAHs) on hepatic cytochrome P450

(CYP450) enzymes mostly, and on metabolism of antituberculous medications.

Integrating smoking cessation and TB treatment programmes must also take into

account potential drug-drug interactions between smoking cessation medications

and anti-TB drugs, a critical area for patient safety and effective TB

management. This review article aims to provide healthcare professionals with

the knowledge to better support TB patients who smoke or are intending to quit,

to ensure tailored and effective treatment strategies, while highlighting gaps

in current research and advocating for further studies to fill these gaps.

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Gaudio, Nunnari, Campagna, Nailes, Shahbaz, Tanuwihardja, Mohan, Ceccarelli,

Bernardini, Marino and Cantarella.

DOI: 10.3389/fphar.2025.1606150

PMCID: PMC12308143

PMID: 40741006

**64. J Clin Tuberc Other Mycobact Dis. 2025 Jul 11;40:100551. doi:**

**10.1016/j.jctube.2025.100551. eCollection 2025 Aug.**

Defining the role for Mycobacterium tuberculosis PCR testing from stool samples.

Gaensbauer JT(1)(2), Buckwalter SP(3), Solon JA(4), Montoya J(5), Ang CF(5),

Antonios VS(6), Wengenack NL(3), Sia I(7).

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DOI: 10.1016/j.jctube.2025.100551

PMCID: PMC12275846

PMID: 40688756

**65. J Clin Tuberc Other Mycobact Dis. 2025 Jul 2;40:100549. doi:**

**10.1016/j.jctube.2025.100549. eCollection 2025 Aug.**

Factors influencing the risk of developing multidrug-resistant pulmonary

tuberculosis in Northeast Thailand.

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**BACKGROUND:** This study aimed to identify the factors influencing

Multidrug-Resistant Pulmonary Tuberculosis (MDR-TB) in Northeast Thailand.

**METHODS**: A case-control study was conducted by reviewing medical record and

collecting primary data using a structured questionnaire. The study population

comprised the case group of patients with MDR-TB and the control group consisted

of other pulmonary tuberculosis patients aged 18 years and over with ratio 1

case: 3 controls. The factors influencing MDR-TB in the Northeast of Thailand

were identified by multivariable analysis.

**RESULTS:** The results revealed that the majority of the cases and controls were

males (73.79 % and 59.87 %, respectively) with mean ages of 50.50 years and

56.30 years. Cases had more moderate self-care behaviors (40.78 %) compared with controls (17.15 %). Nearly half (48.54 %) of the cases had a limited level of health literacy. Multivariable analysis demonstrated that education level

(Adjusted Odd Ratio (AOR) = 1.12; 95 % CI = 1.14-1.96, p = 0.04), average

monthly family income (AOR = 1.78; 95 % CI = 1.19-2.97, p = 0.01), number of windows (AOR = 2.03; 95 % CI = 1.34-3.91, p = 0.001), being diagnosed with tuberculosis two or more times (AOR = 4.63; 95 % CI = 2.51-12.35, p < 0.001), poor attitude towards tuberculosis illness (AOR = 1.32; 95 % CI = 1.05-2.48, p = 0.03), mild to moderate self-care behavior levels (AOR = 1.47; 95 % CI = 1.14-3.05, p < 0.001), and inadequate to problematic levels of health literacy (AOR = 2.11; 95 % CI = 1.36-3.63, p < 0.001) were significant determinants of MDR-TB.

**CONCLUSIONS:** This study concluded that education level, monthly family income,

number of windows, recurrence of TB diagnosis, attitude towards TB illness,

self-care behavior level and limited health literacy level were risk factors of

MDR-TB. Inadequate health literacy was particularly associated with a high risk

of developing MDR-TB. In order to increase treatment success rates, the results

from this study should be used to improve targeted interventions and health

education strategies.

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DOI: 10.1016/j.jctube.2025.100549

PMCID: PMC12272133

PMID: 40688755

**66. J Clin Tuberc Other Mycobact Dis. 2025 Jun 26;40:100547. doi:**

**10.1016/j.jctube.2025.100547. eCollection 2025 Aug.**

Efficacy of mindful meditation in adjunct to a pulmonary rehabilitation program

in improving functional capacity and quality of life in post-treated pulmonary

tuberculosis patients: A randomized controlled trial (Study Protocol).

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Physiotherapy College, Datta Meghe Institute of Higher Education and Research

(DU), Sawangi, Meghe, Wardha, Maharashtra 442001, India.

**BACKGROUND:** Post-treated pulmonary tuberculosis (PTB) frequently leads to

long-term impairments in lung function, endurance, and mental well-being.

Pulmonary rehabilitation (PR) programs aim to restore functional capacity but

may not sufficiently address psychological distress. Mindful meditation, when

integrated with PR, may offer enhanced recovery by addressing both physical and

emotional deficits [1,2].

**METHODS:** We plan to conduct this study at a single hospital, where 51 people who

recently completed TB treatment will be invited to participate. Each person will

be randomly placed into one of two groups. One group will follow a regular rehab

program, while the other will follow the same program with added daily

meditation sessions. The rehab will last for four weeks. We'll check each

person's walking ability and quality of life [5,6], and also note changes in

their breathing, oxygen levels, and vital signs [7].Expected Results: People who

do both meditation and rehab are likely to feel and function better than those

who only do rehab. We hope this combined approach gives more balanced physical

and mental recovery [1,2].

**CONCLUSION:** If adding meditation works well, it could become part of rehab for

others recovering from TB. This might help patients feel more energetic and

positive after their illness [3,4].

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DOI: 10.1016/j.jctube.2025.100547

PMCID: PMC12271624

PMID: 40688753

**67. J Surg Case Rep. 2025 Jul 18;2025(7):rjaf546. doi: 10.1093/jscr/rjaf546.**

**eCollection 2025 Jul.**

Intestinal tuberculosis revealed by acute intestinal obstruction: a case report

and review of the literature.

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Tuberculosis is a major public health problem. It is an infectious disease

present in every country in the world and can occur at any age, with a higher

incidence in developing countries. Among the extra-pulmonary forms, the

intestinal form is rare and often misdiagnosed and/or lately at the stage of

complications such as occlusion, stricture, perforation, or hemorrhage.

Unfortunately, this contributes to the increased mortality and morbidity

associated with this benign disease. We report the case of a 78-year-old patient

who presented to our department with an acute intestinal obstruction, secondary

to an ileal mass. He had undergone bowel resection of the mass and hand sewn

end-to-end anastomosis. Histopathological examination of the specimen confirmed

intestinal tuberculosis.

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Ltd.

DOI: 10.1093/jscr/rjaf546

PMCID: PMC12273898

PMID: 40688381

**68. Lancet Reg Health West Pac. 2025 Jul 3;60:101604. doi:**

**10.1016/j.lanwpc.2025.101604. eCollection 2025 Jul.**

Overcoming barriers in tuberculosis control: a case study from a remote

community of South Australia.

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DOI: 10.1016/j.lanwpc.2025.101604

PMCID: PMC12271421

PMID: 40688172

**69. BMJ Public Health. 2025 Jun 26;2(Suppl 1):e001566. doi:**

**10.1136/bmjph-2024-001566. eCollection 2024 Jul.**

Assessing tuberculosis clinical presentation, diagnosis and treatment outcomes

among children under 5 years old: results from a cohort of children with

presumptive TB in Cameroon and Kenya.

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S(4), Goura AP(1), Ouma M(4), Petnga SJ(1), Tchakounté Youngui B(1), Zemsi A(1),

Zoung-Kanyi Bissek AC(6), Okomo G(7), Simo L(8), Casenghi M(9), Tchendjou P(1),

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**INTRODUCTION: T**he majority of paediatric tuberculosis (TB) cases remain

undiagnosed or unreported, with only 55% of the estimated 1.25 million

paediatric TB cases reported in 2023. We leveraged the INPUT study to

characterise the clinical presentations and factors associated with TB diagnosis

and treatment success in children under 5 years in Cameroon and Kenya.

**METHOD:** We conducted a prospective cohort analysis nested in the INPUT study,

implemented from May 2019 to June 2021 to assess the integration of paediatric

TB services into child healthcare services. All children presenting in

participating health facilities, presumed with TB and eligible to the INPUT

study, were enrolled and followed up from diagnosis to treatment initiation and

completion. We used multivariable logistic regression to explore factors

associated with TB diagnosis.

**RESULTS:** Of the 790 children enrolled in the cohort, 458 (58.0%) were aged <2

years; the most frequent suggestive TB symptoms were cough (76.5%), fever

(34.9%), night sweats (21.2%), loss of appetite (33.5%) and fatigue (35.9%).

Overall, 157 (19.9%) children were diagnosed with TB disease, including 13/157

(8.3%) bacteriologically confirmed and 84/157 (53.5%) with a chest radiography

evocative of TB. In multivariable analysis, living in rural area (aOR 1.9;

95% CI (1.1 to 3.5)), presenting with fever >10 days (aOR 1.8; 95% CI (1.1 to

3.1)), having HIV (aOR 3.9; 95% CI (1.7 to 8.9)), presenting with acute

malnutrition (aOR 2.8; 95% CI (1.5 to 5.2)), living with someone coughing in the

household for more than 2 weeks (aOR 1.8; 95% CI (1.0 to 3.0)) and presenting

with peripheral lymphadenitis (aOR 9.5; 95% CI (4.3 to 20.9)) were significantly

associated with TB diagnosis in children under 5 years with signs and symptoms

suggestive of TB. All children diagnosed with TB were initiated on treatment;

136 (86.6%) achieved treatment success according to WHO definition.

**CONCLUSION:** In the context of integrated, decentralised evaluation of paediatric

TB in the INPUT study, most TB diagnoses in children under 5 years old were made

clinically-radiologically. Decentralised strategies enhancing the clinical

diagnosis, including repeated capacitation of clinicians to the use of treatment

decision algorithms and increased access to chest radiography, could overcome

underdiagnosis of paediatric TB.

TRIAL REGISTRATION NUMBER: NCT03862261.

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BY-NC. Published by BMJ Group.

DOI: 10.1136/bmjph-2024-001566

PMCID: PMC12308155

PMID: 40740312

**70. Cell Syst. 2025 Jul 25:101348. doi: 10.1016/j.cels.2025.101348. Online ahead of print.**

Integration of multi-modal measurements identifies critical mechanisms of

tuberculosis drug action.

Johnson WC(1), Alivisatos A(2), Smith TC 2nd(3), Van N(2), Soni V(4), Wallach

JB(5), Clark NA(6), Fitzgerald TA(1), Whiteley JJ(7), Tan S(1), Sokolov A(8),

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Treatments for tuberculosis remain lengthy, motivating a search for new drugs

with novel mechanisms of action. However, it remains challenging to determine

the direct targets of a drug and which disrupted cellular processes lead to

bacterial killing. We developed a computational tool, DECIPHAER (decoding

cross-modal information of pharmacologies via autoencoders), to select the

important correlated transcriptional and morphological responses of

Mycobacterium tuberculosis to treatment. By finding a reduced feature space,

DECIPHAER highlighted essential features of cellular damage. DECIPHAER provides

cell-death-relevant insight into uni-modal datasets, enabling interrogation of

drug treatment responses for which transcriptional data are unavailable. Using

morphological data alone with DECIPHAER, we discovered that respiration

inhibition by the polypharmacological drugs SQ109 and BM212 can influence cell

death more than their effects on the cell wall. This study demonstrates that

DECIPHAER can extract the critical shared information from multi-modal

measurements to identify cell-death-relevant mechanisms of TB drugs. A record of

this paper's transparent peer review process is included in the supplemental

information.

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DOI: 10.1016/j.cels.2025.101348

PMID: 40738114

**71. Tuberculosis (Edinb). 2025 Jul 23;154:102675. doi: 10.1016/j.tube.2025.102675.**

**Online ahead of print.**

Population pharmacokinetics of levofloxacin in drug-susceptible and

drug-resistant tuberculosis patients: Optimal dose suggestion based on renal

function.

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**BACKGROUND:** Levofloxacin (LFX) has gained attention as an effective drug to

reduce treatment duration in tuberculosis (TB). We aimed to evaluate factors

related to interindividual variability (IIV) and describe the pharmacokinetics

(PK) of LFX in both DS- and DR-TB, as well as explore the optimal dose for TB

treatment.

**METHODS:** We included demographics, clinical information, and LFX concentrations

from multinational hospitals. All data were utilized for model establishment.

The population PK model was built using nonlinear mixed-effects method. Dose

simulation was carried out thereafter using Monte Carlo simulation.

**RESULTS:** A one-compartment model with allometric scaling described LFX PK

adequately. PK parameters were similar between DS- and DR-TB. eGFR significantly

affected CL/F, which decreased by 22 % and 48 % in mild and moderate-severe

renal impairment, respectively (normal CL/F: 6.6 L/h). Considering LFX's AUC/MIC

target of 146 and epidemiological cut-off value of MIC 0.5 μg/mL, doses of

1000 mg, 1250 mg, and 1500 mg may achieve 90 % probability of target attainment in patients with normal renal function weighing <40 kg, 40-70 kg, and >70 kg, respectively.

**CONCLUSION**: Renal impairment reduced LFX clearance. Doses equal to or greater

than 1000 mg may improve AUC/MIC target attainment but require cautious use

considering safety and clinical efficacy.

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DOI: 10.1016/j.tube.2025.102675

PMID: 40738019

**72. Diagn Microbiol Infect Dis. 2025 Jul 22;113(3):117006. doi:**

**10.1016/j.diagmicrobio.2025.117006. Online ahead of print.**

Accidental needle inoculation of bacillus Calmette-Guerin vaccine in medical

worker - TBC arthritis.

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Despite the increase of mycobacterial infection, the incidence of tuberculous

hand infection remains extremely low. We report a case of a 51-old pediatric

nurse, who inadvertently inoculated her index finger via needlestick, while

performing BCG immunization of the baby. Two days after the event, painful

swelling and erythema of the distal interphalangeal joint region of the index

finger appeared. Further diagnostic confirmed rare case of mycobacterial finger

joint infection. It is important that hospital stuff should be informed about

the possibility of BCG accident transmission to reduce the incidents of

percutaneous injuries.

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DOI: 10.1016/j.diagmicrobio.2025.117006

PMID: 40737817

**73. J Med Microbiol. 2025 Jul;74(7):002048. doi: 10.1099/jmm.0.002048.**

Dissecting rifampicin heteroresistance in Mycobacterium tuberculosis:

integrating whole-genome sequencing with phenotypic and clonal validation.

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Vargas-Ruiz AP(1), Coronel J(1), Torres A(3), Perez-Martinez JL(1), Ochoa-Ortiz

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Introduction. This study underscores the critical role of identifying

heteroresistant infections of Mycobacterium tuberculosis (Mtb) in enhancing the

diagnostics of tuberculosis (TB). These conditions complicate diagnostics and

treatment, underlining the need for advanced techniques to detect and

characterize resistant populations effectively.Hypothesis/Gap statement. Current

diagnostics may fail to identify heteroresistance and mixed infections, limiting

the understanding of their impact on treatment outcomes.Aim. This pilot study

aimed to phenotypically and genotypically characterize

rifampicin-heteroresistant clinical isolates and assess their genetic diversity

and resistance patterns.Methodology. A retrospective analysis of 2,917 Mtb

genomes from Peru (1999-2020) was conducted using MTBseq and TB-Profiler.

Techniques included indirect microscopic observation drug susceptibility, MIC

determination via tetrazolium microplate assay, agar proportion method and

sequencing. From each clinical isolate, three colonies were isolated from both

rifampicin-supplemented (1 µg mL-1) and drug-free media for subsequent

phenotypic and genotypic characterization, including rpoB sequencing.Results. Of

the 2,917 genomes analysed, 14.6% were classified as mixed infections, 3.8%

exhibited heteroresistance to at least 1 drug between 21 antibiotics analysed

and 0.79% were rifampicin-heteroresistant. Colonies from rifampicin-supplemented

media displayed high resistance (MIC >1 µg mL-1) with mutations such as S450L in

the RpoB protein. In contrast, those from drug-free media exhibited sensitivity

to rifampicin (MIC <1 µg ml-1), harbouring other RpoB mutations including D435Y,

L452P and L430P. Notably, some colonies retained WT RpoB sequences, suggesting a

diversity of subpopulations within isolates.Conclusion. Whole-genome sequencing

and phenotypic analysis confirmed the coexistence of rifampicin-susceptible and

rifampicin-resistant Mtb populations within single clinical isolates.

Subculturing in drug-free media favoured the selection of sensitive strains,

emphasizing the critical need for advanced diagnostic tools to accurately detect

and characterize heteroresistant and mixed infections. These findings pave the

way for more targeted treatment strategies to combat antimicrobial resistance in

TB.

DOI: 10.1099/jmm.0.002048

PMCID: PMC12310241

PMID: 40737173 [Indexed for MEDLINE]

**74. IDCases. 2025 Jun 19;41:e02295. doi: 10.1016/j.idcr.2025.e02295. eCollection**

**2025.**

Isolated splenic tuberculosis in a patient with rheumatoid arthritis.

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Isolated splenic tuberculosis (TB) is rare. Here, we report a case of isolated

splenic TB in a 70-year-old man with rheumatoid arthritis (RA). The patient

presented to the emergency department with a 3-day history of epigastric pain

and hematemesis. For RA treatment, a combination of methotrexate (8 mg) and

baricitinib (4 mg) had been initiated 2 years prior. Abdominal computed

tomography (CT) scan revealed upper gastrointestinal hemorrhage and intrasplenic

involvement. Following endoscopic hemostasis, we performed endoscopic

ultrasound-guided fine-needle aspiration via the stomach due to suspected

pancreatic cancer. At an outpatient follow-up visit 1 month later, fever and

elevated C-reactive protein (9.02 mg/dL) levels were observed. CT imaging showed

enlarged necrotic lymph nodes near the gastroesophageal junction, left mesentery

of the colon, and the greater curvature of the pylorus, along with an increased

low-density area in the spleen. Subsequently, upper gastrointestinal endoscopy

and ultrasound-guided percutaneous fine-needle aspiration cytology were

performed. Cultures from the abscesses tested positive for Mycobacterium

tuberculosis, which was susceptible to isoniazid, rifampicin, ethambutol, and

pyrazinamide. No lesions were identified, thus confirming a diagnosis of

isolated splenic TB. Oral anti-TB treatment with four drugs (isoniazid,

rifampicin, ethambutol, and pyrazinamide) was initiated. After 6 months of

treatment, the splenic lesions had shrunk. Nine months after completing therapy,

RA treatment was resumed without relapse. Therefore, early diagnosis and anti-TB

treatment can successfully manage splenic TB without requiring splenectomy.

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DOI: 10.1016/j.idcr.2025.e02295

PMCID: PMC12304717

PMID: 40735451

**75. Pathogens. 2025 Jul 11;14(7):684. doi: 10.3390/pathogens14070684.**

First Confirmed Case of Zoonotic Transmission of RR-TB from a Dog to a Human, a

Neglected Mode of Mycobacterium tuberculosis Infection-Case Report and Review of

the Literature.

Zmak L(1)(2), Gomercic Palcic M(2)(3), Obrovac M(1), Folnozic I(3), Strelec

D(4), Reil I(5), Miljan A(6), Zdelar-Tuk M(5), Duvnjak S(5), Mihalac D(7),

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Mycobacterium (M.) tuberculosis mostly spreads from active tuberculosis (TB)

patients to human contacts, although human-to-animal and animal-to-human

transmission has been described. Here, we present a rare case of

rifampicin-resistant tuberculosis (RR-TB) transmission from a companion dog to

its owner, highlighting the zoonotic potential of the pathogen. Namely, a

37-year-old Croatian man was diagnosed with RR-TB, with whole-genome sequencing

analysis revealing a close genetic link to the strain isolated from his dog,

which had died of miliary TB six years earlier. This case emphasizes the

complexity of TB transmission dynamics, particularly involving companion

animals, and underlines the importance of integrated "One Health" approaches for

TB control. Awareness of zoonotic TB risks is essential for the early detection

and prevention of cross-species transmission, especially in vulnerable

populations and households with close human-animal contact.

DOI: 10.3390/pathogens14070684

PMCID: PMC12298124

PMID: 40732730 [Indexed for MEDLINE]

**76. Indian J Hematol Blood Transfus. 2025 Jul;41(3):747-748. doi:**

**10.1007/s12288-024-01907-7. Epub 2024 Oct 17.**

Scarring Cutaneous Tubercular Abscess in a Patient with Lymphoblastic Lymphoma.

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DOI: 10.1007/s12288-024-01907-7

PMCID: PMC12267797

PMID: 40687443

**77. Medicina (Kaunas). 2025 Jul 9;61(7):1238. doi: 10.3390/medicina61071238.**

Full-Blood Inflammatory Ratios Predict Length of Stay but Not Early Death in

Romanian Pulmonary Tuberculosis.

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C(6), Tudorache E(6), Bratosin F(7), Rosca O(7), Bogdan I(7), Chisoi A(8),

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**Background and Objectives**: Blood-borne inflammatory ratios have been proposed as

inexpensive prognostic tools across a range of diseases, but their role in

pulmonary tuberculosis (TB) remains uncertain. In this retrospective

case-control analysis, we explored whether composite indices derived from

routine haematology-namely the neutrophil-to-lymphocyte ratio (NLR), the

platelet-to-lymphocyte ratio (PLR), the systemic immune-inflammation index (SII)

and a novel CRP-Fibrinogen Index (CFI)-could enhance risk stratification beyond

established cytokine measurements among Romanian adults with culture-confirmed

pulmonary T. **Materials and Methods:** Data were drawn from 80 consecutive TB

in-patients and 50 community controls. Full blood counts, C-reactive protein,

fibrinogen, and four multiplex cytokines were extracted from electronic records,

and composite indices were calculated according to standard formulas. The

primary outcomes were in-hospital mortality within 90 days and length of stay

(LOS). **Results:** Among TB patients, the median NLR was 3.70 (IQR 2.54-6.14), PLR

was 200 (140-277) and SII was 1.36 × 106 µL-1 (0.74-2.34 × 106), compared with

1.8 (1.4-2.3), 117 (95-140) and 0.46 × 106 µL-1 (0.30-0.60 × 106) in controls.

Those with SII above the cohort median exhibited more pronounced acute-phase

responses (median CRP 96 vs. 12 mg L-1; fibrinogen 578 vs. 458 mg dL-1), yet

median LOS remained virtually identical (29 vs. 28 days) and early mortality was

low in both groups (8% vs. 2%). The CFI showed no clear gradient in hospital

stay across its quartiles, and composite ratios-while tightly

inter-correlated-demonstrated only minimal association with cytokine levels and

LOS. **Conclusions:** Composite cell-count indices were markedly elevated but did

not predict early death or prolonged admission. In low-event European cohorts,

their chief value may lie in serving as cost-free gatekeepers, flagging those

who should proceed to more advanced cytokine or genomic testing. Although

routine reporting of NLR and SII may support low-cost surveillance, validation

in larger, multicentre cohorts with serial sampling is needed before these

indices can be integrated into clinical decision-making.

DOI: 10.3390/medicina61071238

PMCID: PMC12298156

PMID: 40731867 [Indexed for MEDLINE]

**78. Biochem Biophys Res Commun. 2025 Jul 25;778:152408. doi:**

**10.1016/j.bbrc.2025.152408. Online ahead of print.**

A heterologous prime-boost regimen using BCG and an mRNA encoding Ag85B

heightens immune response in mice.

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MG(5), Prompetchara E(6), Premchaiporn P(7), Chareanpat P(7), Yindeeyoungyeon

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The mRNA vaccine platform holds a great promise as novel tuberculosis vaccine.

In this study, the use of mRNA encoding Ag85B from M. tuberculosis (M. tb)

formulated in lipid nanoparticle (LNP) was investigated as a standalone vaccine

or a booster dose for BCG in mice. Two doses of Ag85 B mRNA/LNP induced robust

specific humoral response and Th1 response as measured by IFN-γ-producing T

cells and polyfunctional CD8+ T cells (IFN-γ, TNF-α, and IL-2) in spleens and

lungs. A heterologous BCG prime and mRNA/LNP boost regimen induced higher

response to broad M. tb antigens than one dose of BCG vaccine or homologous

prime-boost regimen by mRNA/LNP. This approach produced the highest

IFN-γ-producing T cells and polyfunctional CD4+ T cells, indicating that

mRNA/LNP provided help that enhanced the response to other antigens beyond

Ag85B. The mycobacterial growth inhibition assay showed that the heterologous

prime boost effectively reduced mycobacterial growth to the lowest level among

the groups tested in this study. Thus, by integrating the mRNA vaccine platform

into the tuberculosis vaccine development, it may be possible to provide an

effective strategy to control tuberculosis.

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DOI: 10.1016/j.bbrc.2025.152408

PMID: 40730090

**79. Tuberculosis (Edinb). 2025 Jul 22;154:102673. doi: 10.1016/j.tube.2025.102673.**

**Online ahead of print.**

Identification of non-tuberculous mycobacteria in slaughtered cattle from

Chennai, India.

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Non-tuberculous mycobacteria (NTM) are emerging pathogens in human and

veterinary medicine, with a globally increasing incidence. In India, sporadic

studies have identified an upward trend in NTM infections, but accurate

prevalence estimates are lacking due to the absence of nationwide surveillance.

Non-tuberculous mycobacteria have been reported in clinically healthy cattle and

wildlife globally, complicating tuberculosis (TB) diagnostics and surveillance.

This study aimed to characterize NTM species isolated from tissue samples of

slaughtered cattle in Chennai using culture and targeted hsp65 gene sequencing.

A total of 118 presumed NTM samples from 115 animals were processed, and 49

isolates were confirmed as NTMs by PCR. Sequencing identified 18 different

species, with Mycobacterium intracellulare (9/49) being the most frequent,

followed by Mycobacterium sp. strain 79\_MI18\_10584 (6/49) and Mycobacterium

elephantis (6/49). Several identified species, including M. intracellulare, M.

fortuitum (5/49), M. kansasii (4/49), and M. avium, have caused infections in

humans as well. NTMs in cattle lymph nodes without visible lesions suggest their

asymptomatic persistence, albeit there being a possibility of transient

colonization. Non-tuberculous mycobacteria complicate bovine tuberculosis (bTB)

diagnostics by inducing cross-reactive immune responses and forming

granulomatous lesions resembling those caused by Mycobacterium tuberculosis

complex (MTBC). This study highlights the presence and diversity of NTMs in

Indian cattle and emphasizes the need for better surveillance, improved

molecular characterization, and better understanding of their epidemiological

and immunological roles in both veterinary and public health contexts.

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DOI: 10.1016/j.tube.2025.102673

PMID: 40730079

**80. Biosens Bioelectron. 2025 Jul 24;288:117821. doi: 10.1016/j.bios.2025.117821.**

**Online ahead of print.**

Ultra-sensitive detection of mycobacterium cells on a smartphone through

enhanced emission of autofluorescence signals.

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Tuberculosis (TB) remains one of the deadliest infectious diseases of the 21st

century, affecting millions of people worldwide each year. Traditional

diagnostic methods primarily rely on light and fluorescence microscopy. However,

the low sensitivity of light microscopy and the high cost and complexity

associated with fluorescence microscopy limit their effectiveness in

resource-limited settings. This study presents the design of an alternative

sensing platform capable of detecting TB cells with enhanced sensitivity. The

system leverages the natural autofluorescence (AF) signal emitted from

Mycobacterium cells. The key innovation of the proposed platform is the

integration of an onboard heating element, that significantly amplifies the AF

signal, allowing detection at concentrations as low as 104 CFU/ml. The designed

platform is standalone, low-cost, and compact and built around a smartphone.

Housed within a 3D-printed enclosure, it ensures portability and ease of

use-making it suitable for deployment in resourced limited environment. The

proposed system holds promise to develop as an alternative platform for TB

diagnosis in areas where access to advanced healthcare facilities is still very

limited.

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DOI: 10.1016/j.bios.2025.117821

PMID: 40730069

**81. Open Forum Infect Dis. 2025 Jun 26;12(7):ofaf372. doi: 10.1093/ofid/ofaf372.**

**eCollection 2025 Jul.**

Donor-Derived Tuberculosis in 3 Solid Organ Transplant Recipients From the Same

Donor.

Vega P(1)(2), Newby R(1), Bender Ignacio RA(1)(2), Fisher CE(1)(2), Oken E(1),

Harbell JW(3)(4), Mour GK(4)(5), Shubeilat J(6), Ng YH(7), Li M(8), Bhattacharya

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Donor-derived tuberculosis is a rare complication following solid organ

transplantation, and tuberculosis screening is not a current transplant

prerequisite for most donors. Donor-derived tuberculosis usually presents sooner

than reactivation tuberculosis, and the most common finding is fever. We present

3 cases of donor-derived tuberculosis in the recipients of 2 kidneys and 1 liver

from the same donor, who presented with unexplained fevers occurring 4-5 weeks

after transplantation. Initial antibacterial therapy failed in all 3 patients,

leading to further testing, which identified Mycobacterium tuberculosis by

culture and molecular studies. All recipients successfully received tuberculosis

therapy but had significant morbidity and prolonged hospital stays.

Donor-derived tuberculosis should be among the differential diagnoses of

unexplained fever in solid organ transplant recipients in the first few months

after transplantation. Screening protocols should be implemented for donors with

an epidemiologic risk of tuberculosis, with special emphasis on deceased donors.

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

Infectious Diseases Society of America.

DOI: 10.1093/ofid/ofaf372

PMCID: PMC12301964

PMID: 40727571

**82. Pan Afr Med J. 2025 May 8;51:6. doi: 10.11604/pamj.2025.51.6.47259. eCollection 2025.**

Epidemiological surveillance of tuberculosis-HIV co-infection and genotypic

strains of the Mycobacterium tuberculosis complex in four departments at the

Centre Hospitalier Universitaire de Référence Nationale in N'Djamena, Chad.

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**INTRODUCTION:** the comorbidity of infectious diseases is a real public health

challenge in Chad. The main objective of this study is to determine the

prevalence rate of HIV/TB co-infection among patients of the Centre Hospitalier

Universitaire de Référence Nationale (CHU-RN), as well as the frequency of

circulating Mycobacterium tuberculosis complex (MTBc) genotypic strains within

the institution.

**METHODS**: a cross-sectional analytical and prospective study was conducted from

January to November 2024 in four departments of the CHU-RN in N'Djamena. Patient

samples were collected, decontaminated, and analyzed using techniques such as

the GeneXpert MTB/RIF test, MGIT culture, and spoligotyping.

**RESULTS**: one hundred and fifty-six (156) patients were included, with a majority

of men at 65% and an average age of 38.28 years. Approximately 69.2% of the

samples were positive for MTBc and the TB/HIV co-infection rate was 7.4%. The

MTBc Cameroon strain was the most represented, with 43%, followed by the

CAS-Delhi strain at 29%. Among the strains found at the CHU-RN, two lineages

were revealed: L3 and L4. Rifampicin resistance of MTBc was 13%.

**CONCLUSION:** the identification of MTBc genotypic strains shows high genetic

diversity with a predominance of certain strains involved in co-infection with

HIV at the CHU-RN. Targeted intervention is necessary to control the

transmission of tuberculosis.

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DOI: 10.11604/pamj.2025.51.6.47259

PMCID: PMC12296671

PMID: 40727521 [Indexed for MEDLINE]

**83. Pan Afr Med J. 2025 May 6;51:3. doi: 10.11604/pamj.2025.51.3.47431. eCollection 2025.**

Chronic tubercular thoracic empyema.

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DOI: 10.11604/pamj.2025.51.3.47431

PMCID: PMC12296667

PMID: 40727514

**84. J Glob Infect Dis. 2025 Jun 26;17(2):77-86. doi: 10.4103/jgid.jgid\_152\_24.**

**eCollection 2025 Apr-Jun.**

Clinical Presentations and Species Spectrum of Nontuberculous Mycobacteria in

Suspected Pulmonary Tuberculosis Cases.

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**INTRODUCTION:** The prevalence of nontuberculous mycobacteria (NTM) is on the rise

worldwide. The diagnosis of NTM lung disease (NTM-LD) is a dilemma. The 2020

guidelines jointly established by the American Thoracic Society (ATS) and

Infectious Diseases Society of America (IDSA) outline the criteria for

diagnosing pulmonary NTM disease. Herein, we report a series of cases with an

analysis of relevant literature to gain insight into the pathogenicity of NTM

species, the risk factors involved, and treatment strategies.

**METHODS:** This is a prospective observational study starting from April 2023 to

December 2023. A total of 370 suspected pulmonary tuberculosis (TB) patients

were included. Clinical specimens were processed for Ziehl-Neelsen staining,

GeneXpert Mycobacterium tuberculosis (MTB)/RIF assay, and culture.

Culture-positive mycobacteria were classified as MTB complex or NTM based on

detection of MPT64 antigen. The NTM isolates were speciated by line probe assay

using GenoType® Mycobacterium common mycobacteria (Hain Lifescience, Nehren,

Germany). The criteria of ATS/IDSA were applied to confirm NTM-LD.

**RESULTS:** Nine (n = 9) patients were diagnosed as cases of NTM-LD. Bronchiectasis

and previous TB were the most common comorbidities. Mycobacterium scrofulaceum

(n = 2), Mycobacterium szulgai (n = 2), Mycobacterium intracellulare (n = 1),

Mycobacterium kansasii (n = 1), Mycobacterium abscessus (n = 1), Mycobacterium

fortuitum (n = 1), and Mycobacterium interjectum (n = 1) were the species

involved. Specific therapeutic drug regimens were administered in four cases,

which resulted in clinical improvement.

**CONCLUSION:** People with comorbid (LDs) are at risk of NTM-LD. The severity of

NTM-LD and mortality also depend on the species involved. New guidelines with

evidence-based recommendations should be formulated to simplify the diagnosis

and treatment of NTM-LD caused by an array of more than 190 species.

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DOI: 10.4103/jgid.jgid\_152\_24

PMCID: PMC12294139

PMID: 40727500

**85. J Glob Infect Dis. 2025 May 15;17(2):108-111. doi: 10.4103/jgid.jgid\_111\_24.**

**eCollection 2025 Apr-Jun.**

Miliary Tuberculosis in an Immunocompetent Patient Presenting with Tuberculous

Meningoencephalitis Complicated by Hydrocephalus and Seizures.

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Miliary tuberculosis (MTB) is a disseminated form of tuberculosis (TB) arising

from the lymphohematogenous dissemination of Mycobacterium tuberculosis bacilli

followed by millet seed-sized tuberculous foci. It mainly affects

immunocompromised patients and can lead to severe complications or even death.

The clinical manifestation is diverse and depends on the organ affected, the

patient's immune status, and the possible involvement of the central nervous

system (CNS). Hence, this case report presents a case of an immunocompetent male

with a decreased level of consciousness and convulsions requiring admission to

the intensive care unit. The patient was diagnosed with MTB,

meningoencephalitis, hydrocephalus, and severe hyponatremia. He subsequently

improved after a short period of initiation of anti-TB medications. This report

also highlights the clinical features of MTB and reviews the literature on

associated CNS complications of MTB.

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DOI: 10.4103/jgid.jgid\_111\_24

PMCID: PMC12294149

PMID: 40727498

**86. Infect Drug Resist. 2025 Jul 23;18:3637-3646. doi: 10.2147/IDR.S513294.**

**eCollection 2025.**

Pharmacokinetic Profile of Isoniazid and Acetylator Status in Patients with

Systemic Lupus Erythematosus: Implications for Tuberculosis Prevention Therapy

in Indonesia.

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**INTRODUCTION:** Systemic Lupus Erythematosus (SLE) is a chronic autoimmune

inflammatory disease with a high risk of tuberculosis (TB) infection, especially

in those living in TB-endemic areas. Isoniazid (INH), an anti-tuberculosis drug,

is recommended as preventive therapy in TB susceptible groups, however, its use

in SLE is still controversial. SLE patients are more likely to have compromised

liver function which can influence the kinetic of INH. The aim of the study was

to explore the pharmacokinetic profile of INH and acetylator status in SLE

patients.

**METHODS:** This was a descriptive observational study with a purposive sampling

technique, including adult female SLE at Dr. Hasan Sadikin Hospital Bandung,

conducted in January - August 2023. Inclusion criteria were SLE patients in

remission with no TB infection; whereas the exclusion criteria were INH allergy,

liver or kidney disorders, pregnant or lactating patients, and malignancy.

Pharmacokinetic data was collected from six blood collection time points (0, 1,

2, 3, 4, and 8 hours) after 10 days of daily INH 300 mg administration on an

empty stomach.

**RESULTS:** In total, 20 female SLE patients were included. The Cmax value was 8.73

(2.55-18.27) mg/L and AUC0-24 was 28.01 (8.82-79.40) mg.h/L.

**CONCLUSION:** In terms of pharmacokinetic features, preventive isoniazid (INH)

daily use of 300mg in SLE is sufficient to provide the prospect of protection

from TB. These findings suggest that INH prophylaxis may be a viable strategy

for TB prevention in SLE patients, warranting further investigation into

long-term safety and efficacy.

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DOI: 10.2147/IDR.S513294

PMCID: PMC12301248

PMID: 40727383

**87. IJID Reg. 2025 Jun 23;16:100692. doi: 10.1016/j.ijregi.2025.100692. eCollection 2025 Sep.**

Non-tuberculous mycobacterial infections among patients with suspected or

confirmed pulmonary tuberculosis in Ethiopia: A systematic review and

meta-analysis.

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**OBJECTIVES:** This study reviews and analyzes non-tuberculous mycobacteria (NTM)

isolation from Ethiopian sputum samples, estimating prevalence, identifying

common species, and analyzing regional and temporal variations.

**METHODS:** This systematic review and meta-analysis aimed to determine NTM

prevalence among diseased individuals in Ethiopia. Using PubMed, Scopus, Web of

Science, Google Scholar, and African Journals Online, we conducted a

comprehensive literature search. Data extraction and quality assessment were

conducted using the Newcastle-Ottawa scale. Meta-analysis was performed using

STATA-18 software with a random-effects model and included subgroup analysis.

The protocol of this study was registered with PROSPERO (CRD420251000131).

**RESULTS:** In this review, a total of 5415 participants were involved, and 53.8%

were patients with suspected tuberculosis (TB), 37.6% were patients with

pulmonary TB, 4.0% were patients with multidrug-resistant TB, and 4.6% were

HIV-positive patients. The NTM prevalence was 3.8%, showing high heterogeneity

and regional species variability. The meta-analysis highlighted differences in

NTM prevalence across age groups and diagnostic tools, emphasizing the need for

enhanced diagnostics and continuous surveillance to improve patient outcomes and

inform public health strategies.

**CONCLUSIONS:** The review summarizes the epidemiology and geographical

distribution of NTM infections and common NTM species isolated from patients

with suspected pulmonary TB in Ethiopia, revealing regional variations and

clinical implications. Despite limited data, Ethiopia has a lower prevalence of

NTM compared with other African regions and the worldwide average.

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Infectious Diseases.

DOI: 10.1016/j.ijregi.2025.100692

PMCID: PMC12302293

PMID: 40727033

**88. IJID Reg. 2025 Jul 1;16:100697. doi: 10.1016/j.ijregi.2025.100697. eCollection 2025 Sep.**

Tuberculosis: The insidious threat that compromises health in post-Assad Syria.

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This perspective explores the state of tuberculosis (TB) after the prolonged

conflict in Syria and fall of the regime in December 2024; we discuss key

considerations in light of multiple competing health priorities within Syria's

borders and the recovering health system. During the conflict, the health system

fragmentation under differing geopolitical control led to unequal access to TB

prevention, diagnostics and management social determinants such as poverty,

malnutrition, inadequate water and sanitation, and lack of proper shelter, along

with risks associated with disadvantaged groups, including internally displaced

people, detainees, former detainees, and rural communities, not only increase

the risk of TB transmission and the activation of latent infections but also

hinder active case finding. Tackling these risks requires re-establishing the

National TB Program (NTP) across the country, which acts equitably across all

geographical areas to identify new cases, support robust surveillance

activities, ensure drug resistance is identified promptly, and monitor

treatment. Leadership from the Ministry of Health and the World Health

Organization, with support from other stakeholders e.g., humanitarian, civil

society or private sector can support the NTP and optimize health worker

education and referral pathways. Beyond this, addressing the social

determinants, which contribute to TB in Syria, is an essential component of TB

control in post-conflict Syria.

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DOI: 10.1016/j.ijregi.2025.100697

PMCID: PMC12302421

PMID: 40727030

**89. Cureus. 2025 Jun 28;17(6):e86906. doi: 10.7759/cureus.86906. eCollection 2025**

**Jun.**

The Clinical Spectrum of Cutaneous Tuberculosis: A Case Series Emphasizing

Prompt Recognition and Treatment.

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Cutaneous tuberculosis (CTB) represents a minor proportion of all cases of

extrapulmonary tuberculosis (EPTB), with lupus vulgaris (LV) and cervical

scrofuloderma (CS) being the most prevalent forms. Metastatic tuberculosis

abscesses (MTBA), tuberculids (TBDs), and tuberculosis verrucosa cutis (TBVC)

are less common variations. Since CTB frequently occurs in individuals with

strong immune systems who have experienced a hypersensitivity reaction to an

extracutaneous source of Mycobacterium tuberculosis (MTB), it can be challenging

to diagnose. This case series emphasizes the diverse clinical manifestations of

CTB, highlighting the urgent need for prompt diagnosis and effective treatment.

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DOI: 10.7759/cureus.86906

PMCID: PMC12302438

PMID: 40726898

**90. Arch Pharm (Weinheim). 2025 Jul;358(7):e70065. doi: 10.1002/ardp.70065.**

Promising Antimycobacterial Agents: Salicylidenehydrazines.

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Tuberculosis (TB) remains a major global health challenge, underscoring the

urgent need for new therapeutic options. In this study, a series of

salicylidenehydrazine derivatives were synthesized and characterized using

spectroscopic techniques. Their antimycobacterial activity was assessed against

Mycobacterium tuberculosis H37Rv. Among the 35 synthesized compounds, nine

demonstrated significant inhibitory activity, with MIC values ranging from 0.78

to 50 μM. These active molecules were further evaluated against clinical

isoniazid-resistant (bearing inhA promoter and/or katG mutations) and

multidrug-resistant (MDR) M. tuberculosis strains. A particularly potent

compound derived from 2-bromo-4-nitrosalicylaldehyde exhibited an MIC of 0.78 μM against H37Rv and demonstrated low MIC values of 6.25, 1.56, and 1.56 μM against the inhA + , katG + , and MDR strains, respectively. Molecular docking studies were also conducted to investigate the interaction of active compounds with the target enzyme InhA. Overall, the results indicate that salicylidenehydrazine derivatives represent promising lead structures for the development of new anti-TB agents effective against both drug-sensitive and drug-resistant M. tuberculosis strains.

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DOI: 10.1002/ardp.70065

PMID: 40726231 [Indexed for MEDLINE]

**91. J Clin Med. 2025 Jul 15;14(14):4990. doi: 10.3390/jcm14144990.**

Prevalence and Risk Factors of Latent Tuberculosis Infection Detected by IGRA in

Patients with Immune-Mediated Inflammatory Diseases Before and During Biologic

DMARD Therapy (TITAN Study).

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**Background/Objectives:** Patients with immune-mediated inflammatory diseases

(IMIDs) treated with disease-modifying antirheumatic drugs (DMARDs) are at

increased risk of latent tuberculosis infection (LTBI) reactivation, influenced

by DMARD type. This study aimed to determine LTBI prevalence using

interferon-gamma release assays (IGRAs) and identify associated risk factors in

IMID patients in a middle-high TB burden setting in Mexico. **Methods:** A

cross-sectional study was conducted from July 2024 to April 2025 at an IMID

clinic. Patients aged ≥18 years, either receiving DMARDs or prior to initiating

treatment, were included. LTBI was diagnosed using the QuantiFERON-TB Gold Plus

assay. Bivariate analysis was performed using the chi-square test, and

multivariate analysis was conducted. **Results**: LTBI prevalence was 34.2% (95% CI

29.1-39.7%) according to QFT-Plus and 35.6% (95% CI 29.7-42.0%) according to

TSTs (n = 230). Prior TB exposure was the strongest risk factor (aOR 4.20, 95%

CI 1.74-10.12, p = 0.001), while rheumatoid arthritis was associated with a

lower LTBI likelihood (aOR 0.31, 95% CI 0.16-0.59, p < 0.001). **Conclusions:** A

high prevalence of LTBI was observed in patients with IMIDs treated with DMARDs.

Prior tuberculosis exposure was strongly associated with LTBI. These findings

highlight the importance of LTBI screening in this population to prevent

reactivation.

DOI: 10.3390/jcm14144990

PMCID: PMC12295402

PMID: 40725683

**92. Int J Mol Sci. 2025 Jul 8;26(14):6573. doi: 10.3390/ijms26146573.**

In Experimental Tuberculosis Infection, the Bacteriostatic Function of

Macrophages Is Activated by Th1 CD4(+) T-Effectors in a Nitrite-Independent

Manner.

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The pivotal component in the protection against TB is the tissue macrophages

(Mф). These cells have been demonstrated to play a crucial role in the

elimination of pathogens and mycobacterial killing. Elucidation of the molecular

and phenotypic events that determine the outcome of infection in Mф is

fundamental to understanding the key features of these cells that are so

important in fighting infection. Mф activation is driven by cytokines and other

inflammatory mediators secreted by T lymphocytes. The interaction between

Mycobacterium tuberculosis (Mtb) and host Мф has been the subject of extensive

in vitro research. This dynamic interplay represents a pivotal step in the

progression of mycobacterial infection because pulmonary macrophages constitute

the primary line of defense against the pathogen, thereby serving as the initial

immune cells to which Mtb must adapt to establish a replicative foothold within

the host. Our studies have demonstrated that highly differentiated Th1 effectors

with the CD27low phenotype exhibit superior efficacy in activating both

peritoneal (Mф: T cell ratio ranging from 125:1 to 625:1) and pulmonary

macrophages (Mф: T cell ratio = 5:1) compared to cells with the CD27high

phenotype. Furthermore, our findings indicate that this activation mechanism is

not contingent upon the production of reactive nitrogen species. To effectively

activate the bacteriostatic function of macrophages, CD27high T lymphocytes must

differentiate into effectors with the CD27low phenotype.

DOI: 10.3390/ijms26146573

PMCID: PMC12295194

PMID: 40724823 [Indexed for MEDLINE]

**93. Life (Basel). 2025 Jul 4;15(7):1068. doi: 10.3390/life15071068.**

Severe ARDS Complicated by Active Pulmonary Tuberculosis and Recurrent

Nosocomial Infections: Therapeutic Challenges and Clinical Outcomes.

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**Background:** Acute respiratory distress syndrome (ARDS) secondary to tuberculosis

(TB) is rare and associated with high mortality. Management is further

complicated by comorbidities and ICU-related complications. **Methods:** We report a

43-year-old woman with post-polio sequelae and uncontrolled diabetes who

developed ARDS due to pulmonary TB, complicated by recurrent nosocomial

infections and gastrointestinal bleeding. Early bronchoscopy and GeneXpert

MTB/RIF PCR were performed on ICU Day 2, enabling anti-TB therapy initiation by

ICU Day 3. The patient received lung-protective ventilation, prone positioning,

tailored antibiotics, and multidisciplinary care. **Results:** The patient's

clinical course was complicated by two episodes of ventilator-associated

pneumonia and gastrointestinal bleeding, but with individualized management, she

achieved ventilator weaning and functional recovery. **Conclusions:** Early TB

recognition in ARDS is crucial. Multidisciplinary ICU management, including

prudent steroid use, improves outcomes.

DOI: 10.3390/life15071068

PMCID: PMC12299266

PMID: 40724570

**94. Int J Environ Res Public Health. 2025 Jul 21;22(7):1154. doi:**

**10.3390/ijerph22071154.**

Sociodemographic and Clinical Predictors of Tuberculosis and Unsuccessful

Treatment Outcomes in Davao City, Philippines: A Retrospective Cohort Study.

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**BACKGROUND/OBJECTIVES:** Tuberculosis (TB) remains a major public health challenge

in Davao City, Philippines, with persistent issues in both disease burden and

treatment outcomes. Understanding the risk factors for TB and its unsuccessful

treatment is essential for guiding effective interventions. This study aimed to

evaluate the association of sociodemographic and clinical factors with TB

occurrence and to identify predictors of unsuccessful TB treatment outcomes

among patients in Davao City.

**METHODS**: A retrospective cohort study was conducted using data from 521 patients

diagnosed with drug-susceptible TB at Davao Chest Center between January 2021

and May 2024. The sociodemographic and clinical profiles of the patients were

described using descriptive statistics. Chi-square tests were used to assess the

associations between sociodemographic and clinical variables with TB risk and

treatment outcomes.

**RESULTS:** The patient cohort was predominantly aged 31-50 years (n = 201,

38.58%), male (n = 284, 54.51%), and married (n = 285, 54.70%), with most

residing in Districts I and II (n = 98, 38% each), and had no previous TB

treatment (n = 344, 66.03%). Among the 456 patients assessed for comorbidities,

56.14% (n = 256) had at least one comorbidity. Evaluation of the risk factors

for TB occurrence among the study population revealed that comorbidity status

was not significantly associated with an increased risk of TB diagnosis (p =

0.682). However, among patients diagnosed with TB, the presence of comorbidities

was significantly associated with unsuccessful treatment outcomes (p = 0.003).

**CONCLUSIONS:** Although sociodemographic factors did not significantly influence

TB risk or treatment outcomes, the presence of comorbidities was a significant

predictor of unsuccessful TB treatment. These findings highlight the importance

of integrating comorbidity management with TB care to improve treatment success

in high-burden urban settings.

DOI: 10.3390/ijerph22071154

PMCID: PMC12295419

PMID: 40724219 [Indexed for MEDLINE]

**95. Antibiotics (Basel). 2025 Jul 21;14(7):732. doi: 10.3390/antibiotics14070732.**

Genotypic and Phenotypic Methods in the Detection of MDR-TB and Evolution to

XDR-TB.

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**Background:** Accurate and rapid diagnosis of drug-resistant tuberculosis is

essential for initiating appropriate treatment and preventing the transmission

of these strains. This study compares phenotypic and genotypic methods of drug

susceptibility testing for Mycobacterium tuberculosis (M. tuberculosis).

**Methods:** Resistance to first-line drugs, as well as resistance to second-line

drugs (fluoroquinolones and aminoglycosides), was assessed using the

Löwenstein-Jensen medium phenotypic method and the GenoType MTBDRplus genotypic

method and analyzed. **Results:** The phenotypic resistance rate was 84.85% for INH

(n = 56), 46.97% for RIF (n = 31), 48.48% for STR (n = 32), and 30.30% for EMB

(n = 20). Of the MDR-TB isolates (n = 29), 41.37% were resistant to

fluoroquinolones (n = 12) and 31.03% were resistant to both fluoroquinolones and

injectable aminoglycosides, being classified as XDR-TB (n = 9). In addition,

22.73% of the MDR-TB isolates were resistant to all four first-line drugs (n =

15). The overall concordance between the line probe assay method and phenotypic

testing was 94.74% for RIF and 95.16% for INH. Discordances were identified in

three cases for RIF and two cases for INH, where isolates were reported as

susceptible by GenoType MTBDRplus, but phenotypically resistant. **Conclusions:**

Genotypic testing using GenoType MTBDRplus provides rapid and accurate results,

but some cases of phenotypic resistance are not detected by this method. The

results highlight the importance of using combined phenotypic and genotypic

methods for accurate diagnosis of MDR-TB, as well as the need to integrate

genomic sequencing to improve diagnostic accuracy.

DOI: 10.3390/antibiotics14070732

PMCID: PMC12292002

PMID: 40724033

**96. Antibiotics (Basel). 2025 Jul 20;14(7):728. doi: 10.3390/antibiotics14070728.**

Liposome-Encapsulated Antibiotics for the Therapy of Mycobacterial Infections.

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About a quarter of the world's population is infected with Mycobacterium

tuberculosis. Growing antibiotic resistance by this microorganism is a major

problem in the therapy of the disease. M. avium-M. intracellulare that emerged

as a major opportunistic infection of HIV/AIDS continues to afflict

immunocompromised individuals. We describe the use of liposome-encapsulated

antibiotics in the experimental and clinical therapy of mycobacterial

infections, as well as recent experimental liposomal vaccines against

tuberculosis. Liposome-mediated intravenous or inhalational delivery of

antibiotics enhances the antibacterial effects of the drugs, particularly for

infections of resident macrophages, where the liposomes are passively targeted.

Despite experimental successes of liposomal antibiotics in the treatment of

mycobacterial and other bacterial infections, applications of this method to the

clinic have been lagging. This review underscores the significance of liposomes

in the treatment of mycobacterial infections, encompassing their synthesis

methods, limitations, and both preclinical and clinical studies, providing

guidance for the development of future therapeutic approaches and innovative

antimicrobial strategies.

DOI: 10.3390/antibiotics14070728

PMCID: PMC12291690

PMID: 40724029

**97. Antibiotics (Basel). 2025 Jul 2;14(7):673. doi: 10.3390/antibiotics14070673.**

Multidrug-Resistant Tuberculosis in Central Asia and Predominant Beijing

Lineage, Challenges in Diagnosis, Treatment Barriers, and Infection Control

Strategies: An Integrative Review.

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**Background:** Multidrug-resistant tuberculosis (MDR-TB) remains a significant

public health threat in Central Asia, where rising resistance to first-line

anti-TB drugs challenges control efforts. As of 2024, the World Health

Organization (WHO) reports that over 2.5% of new TB cases and 18% of previously

treated cases are resistant to first-line TB drugs worldwide. **Objectives:** This

integrative review synthesizes current evidence on MDR-TB in Kazakhstan,

Kyrgyzstan, Tajikistan, Turkmenistan, and Uzbekistan, with a focus on infection

control, diagnostic advancements, and evolving treatment strategies. **Methods**: A

comprehensive literature search was conducted across five electronic databases:

PubMed, Scopus, Web of Science, Embase, World Health Organization (WHO) Global

Tuberculosis Database, and ClinicalTrials.gov. A total of 29 articles from

Central Asian countries met the inclusion criteria. **Results**: Four main themes

were identified: "genetic variability and resistance patterns of MDR-TB

strains"; "barriers to effective treatment"; "diagnostic tools", and "infection

control strategies". **Conclusions**: This review underscores the importance of

comprehensive, multifactorial approaches in addressing drug-resistant TB in the

region. The implementation of early diagnosis and all-oral treatment regimens

has improved adherence in recent studies.

DOI: 10.3390/antibiotics14070673

PMCID: PMC12291989

PMID: 40723976

**98. Antibiotics (Basel). 2025 Jun 30;14(7):664. doi: 10.3390/antibiotics14070664.**

Determinants of Tuberculosis Treatment Outcomes in Patients with TB/HIV

Co-Infection During Tuberculosis Treatment at Selected Level One Hospitals in

Lusaka, Zambia.

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**Background/Objectives:** Tuberculosis (TB) and HIV co-infection pose significant

challenges in resource-limited settings, contributing to multi-drug-resistant TB

when treatment fails. This study aimed to identify determinants of TB treatment

outcomes among HIV/TB co-infected patients in Lusaka, Zambia. **Methods:** A

retrospective cohort study was conducted at Chilenje, Chipata, and Chawama level

one hospitals, using systematic sampling to select 586 patient files. Data were

analyzed with SPSS version 23, employing descriptive statistics, chi-square

tests, and hierarchical logistic regression. **Results:** Among the study population

(n = 586), consisting predominantly of working-age adults (25-44 years: 61.6%)

and males (56.5%), treatment success was 81.3%, with a 12.5% mortality rate

across treatment phases. Baseline smear-negative TB, viral load (100,000-199,999

copies/mL), diabetes without hypertension, and negative smear at follow-up

independently predicted treatment outcomes. Higher treatment failure odds were

linked to smear-negative TB, high viral load, and hypertension-diabetes

comorbidity, while CD4 count and HIV treatment status showed no independent

effects. **Conclusions**: These findings underscore the influence of viral load, TB

type, comorbidities, and sputum conversion on treatment success, emphasizing the

need for targeted monitoring and integrated care, particularly in the

continuation phase, to enhance outcomes in this vulnerable population.

DOI: 10.3390/antibiotics14070664

PMCID: PMC12291881

PMID: 40723967

**99. Biomolecules. 2025 Jul 17;15(7):1036. doi: 10.3390/biom15071036.**

The Intricate Process of Calcification in Granuloma Formation and the

Complications Following M. tuberculosis Infection.

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Mycobacterium tuberculosis-an acid-fast staining bacterium-is a serious global

health challenge that can have both short-term and long-term complications.

Although the immune response helps trap the infection, it can also cause

necrosis and calcification, leading to lung tissue damage. Calcification is a

known outcome of chronic granuloma evolution in TB. Multiple pathways contribute

to fibrosis and calcification; some examples are IL-1β, TGF-β, and TNF-α.

Current antifibrotic drugs, such as nintedanib and pirfenidone, are effective

but may increase the risk of latent tuberculosis reactivation in certain

patients. Experimental therapies such as artemisinin derivatives have shown

promise in preclinical TB fibrosis models, while cell-based therapies like bone

marrow-derived mononuclear cells are also under early investigation for dual

antifibrotic and immunomodulatory effects. This literature review will explore

recent studies on the pathogenesis of M. tuberculosis, the mechanisms underlying

calcification in granuloma formation, and subsequent complications of the

disease process.

DOI: 10.3390/biom15071036

PMCID: PMC12292817

PMID: 40723907 [Indexed for MEDLINE]

**100. Biomedicines. 2025 Jul 14;13(7):1721. doi: 10.3390/biomedicines13071721.**

Clinical and Evolutive Features of Tuberculous Meningitis in an Immunosuppressed

Adolescent During the COVID 19 Pandemic.

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**Background/Objectives:** Tuberculous meningitis is the most severe form of

tuberculosis in children, with a high mortality and morbidity rate if it is not

diagnosed and treated in a timely manner. The aim of this study is to highlight

the challenges associated with establishing a diagnosis of tuberculous

meningitis in a child with immunosuppression, given the presence of nonspecific

clinical manifestations. **Methods:** We present the case of a 15-year-old

adolescent with systemic lupus erythematosus, on immunosuppressive therapy, who

is diagnosed with tuberculous meningoencephalitis presenting the clinical,

diagnostic and imaging characteristics, as well as the diagnostic traps and

limitations associated with this condition. Antituberculosis therapy was started

empirically, because there was no improvement in the clinical status with

conventional antibiotic therapy; the diagnosis was established 7 days after the

start of the antituberculosis treatment, with the help of an acid-fast bacilli

culture from the cerebrospinal fluid. **Results:** The course of the tuberculous

meningoencephalitis was slowly favorable, despite the superimposed COVID-19

infection. Delay in administering immunosuppressive therapy led to the onset of

renal and joint manifestations. **Conclusions:** Tuberculous meningitis is a highly

lethal, often underdiagnosed disease with nonspecific clinical and imaging

manifestations, which can have a favorable outcome if the diagnosis is

established early on and treatment is started promptly.

DOI: 10.3390/biomedicines13071721

PMCID: PMC12292272

PMID: 40722791

**101. Diagnostics (Basel). 2025 Jul 14;15(14):1776. doi: 10.3390/diagnostics15141776.**

Diagnostic Accuracy of AdvanSure(TM) and PowerChek(TM) Real-Time PCR Assays for

the Detection of Mycobacterium tuberculosis and Nontuberculous Mycobacteria.

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**Background:** Accurate differentiation between Mycobacterium tuberculosis (MTB)

and nontuberculous mycobacteria (NTM) is essential for proper diagnosis and

treatment. This study compares the diagnostic performance of two commercial

real-time PCR kits, AdvanSureTM TB/NTM and Kogene PowerChekTM MTB/NTM, for

detecting MTB, NTM, and negative (no growth, NG) clinical specimens. **Methods**: A

total of 390 clinical residual specimens were collected from patients between

December 2022 and June 2023. The samples, including sputum, bronchoalveolar

lavage, tracheal aspirate and body fluid, were initially tested with MGIT

culture and then analyzed using both PCR kits. Sensitivity, specificity,

positive predictive value (PPV), negative predictive value (NPV), and overall

accuracy were evaluated. Discrepant results between the two PCR assays were

further investigated using sequencing to identify the detected mycobacterial

species, and final diagnoses were verified by culture results and review of

electronic medical records. **Results:** Of the 390 specimens, both AdvanSureTM and

PowerChekTM real-time PCR assays demonstrated 100% sensitivity for both MTB and

NTM detection. For MTB detection, AdvanSureTM demonstrated a specificity of

100%, with a PPV, NPV, and overall accuracy all reaching 100%. In comparison,

PowerChekTM showed a specificity of 98.62%, a PPV of 96.15%, an NPV of 100%, and

an overall accuracy of 98.97%. For NTM detection, both AdvanSureTM and

PowerChekTM exhibited identical performance metrics. The specificity was 99.58%

for both assays, with a PPV of 99.34%, NPV of 100%, and an overall accuracy of

99.74%. Five discrepant results were finally confirmed as four NTM detection

cases and one negative case by culture and clinical diagnosis which showed four

cases of PowerChekTM MTB+NTM detection and one case of NTM detection,

respectively. **Conclusions:** The PowerChekTM MTB/NTM real-time PCR kit

demonstrated excellent diagnostic performance for the detection of MTB and NTM,

with high sensitivity, specificity, and accuracy. Minor discrepancies,

particularly in detecting MTB+NTM mixed infections, highlight the importance of

complementary sequencing analysis for resolving uncertain results. These

findings support the clinical utility of both PCR assays as reliable tools for

rapid diagnosis of mycobacterial infections. PowerChekTM showed occasional false

positives, suggesting that optimizing the assay's cutoff threshold or

amplification parameters could enhance its specificity and reduce false-positive

results in clinically ambiguous cases.

DOI: 10.3390/diagnostics15141776

PMCID: PMC12293586

PMID: 40722525

**102. Nurs Clin North Am. 2025 Sep;60(3):491-506. doi: 10.1016/j.cnur.2024.10.004.**

**Epub 2024 Nov 5.**

Overview of the Epidemiology, Diagnosis, and Clinical Care Considerations for

People Living with and at Risk for Tuberculosis in the United States.

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Tuberculosis (TB) remains an ongoing threat. TB requires exposure to

Mycobacterium tuberculosis, but disease development is driven by exposure,

infectiousness, susceptibility, and environment. TB elimination requires

increased awareness about TB prevention and treatment strategies. The centers of

TB excellence complement current guidelines from the Center for Disease Control

and Prevention, the National TB Coalition of America, and the Infectious Disease

Society of America to support nurses and providers. Enhanced contact

investigation, prevention, and treatment will aid in the pathway to a TB-free

North America. To address disparities in TB, nurses in practice, research, and

policy settings must address individual, interpersonal, and organizational

barriers to care and ongoing treatment adherence.

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DOI: 10.1016/j.cnur.2024.10.004

PMID: 40716809 [Indexed for MEDLINE]