**2025年第32周**

**境外学者发表的结核病英文文章摘要**

**（65篇）**

**PubMed Publication date: 2025/8/4 --- 2025/8/10**

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

**1. Nature. 2025 Jul 30. doi: 10.1038/s41586-025-09286-3. Online ahead of print.**

SuFEx-based antitubercular compound irreversibly inhibits Pks13.

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A(2), Engelhart C(3), Kumar P(4)(5), Harbut MB(2), Liu D(2), Tsuda B(2), Qin

B(2), Bare GAL(6), Li G(6), Chi V(2), Gambacurta J(7), Hvizdos J(7), Reagan

M(7), Jones IL(7), Massoudi LM(8), Woolhiser LK(8), Cascioferro A(2), Kundrick

E(2), Singh P(4)(5), Reiley W(7), Ioerger TR(9), Kandula DR(10), McCabe JW(10),

Guo T(11), Alland D(4)(5), Boshoff HI(12), Schnappinger D(3), Robertson GT(8),

Mdluli K(13), Lee KJ(2), Dong J(11), Li S(2), Schultz PG(2)(14), Joseph SB(2),

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Mycobacterium tuberculosis (Mtb) remains the world's deadliest bacterial

pathogen1. There is an urgent medical need to develop new drugs that shorten the

treatment duration to combat widespread multi-drug-resistant and

extensive-drug-resistant Mtb. Here, we present a preclinical covalent compound,

CMX410, that contains an aryl fluorosulfate (SuFEx)2 warhead and uniquely

targets the acyltransferase domain of Pks13, an essential enzyme in cell-wall

biosynthesis. CMX410 is equipotent against drug-sensitive and drug-resistant

strains of Mtb and efficacious in multiple mouse models of infection. Inhibition

by CMX410 is irreversible through a previously undescribed mechanism: CMX410

reacts with the catalytic serine of the AT domain of Pks13, rapidly and

irreversibly disabling the active site by forming a β-lactam. CMX410 is highly

selective for its target and thus demonstrates excellent pharmacological and

safety profiles, including no adverse effects in a 14-day rat toxicity study up

to 1,000 mg kg-1 per day. The distinctive mode of action from current drugs,

high potency across all tested clinical isolates, oral bioavailability,

favourable performance in drug combination testing and superior pharmacological

and safety characteristics make CMX410 a promising first-in-class candidate to

replace outdated cell-wall biosynthesis inhibitors, such as isoniazid and

ethambutol, in tuberculosis regimens.

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DOI: 10.1038/s41586-025-09286-3

PMID: 40739353

**2. Reports (MDPI). 2024 Jul 29;7(3):61. doi: 10.3390/reports7030061.**

Association of SARS-CoV-2 Seropositivity with Persistent Immune Activation in

HIV/Tuberculosis Co-Infected Patients.

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We asked if SARS-CoV-2 seropositivity in HIV/TB co-infected patients plays a

role in precipitating active tuberculosis in HIV-infected individuals and alters

inflammatory status. A prospective study was conducted on HIV/TB co-infected

patients presenting with pulmonary (n = 20) or extrapulmonary (n = 12)

tuberculosis. Abbott SARS-CoV-2 IgG kits assessed the presence of

anti-nucleoprotein antibodies. Inflammatory markers viz. osteopontin, total and

full-length galectin-9, and C-reactive protein were tested at baseline and the

end of antituberculosis treatment. The inflammatory score (INS) was assessed

based on the percentage of reduction in the inflammatory markers' levels at the

end of the treatment. Anti-SARS-CoV-2 antibodies were detected in five male

patients diagnosed with pulmonary (n = 2) and extrapulmonary (n = 3) TB. None of

them reported symptomatic COVID-19. Inflammatory marker levels did not differ

significantly at baseline compared to those in seronegative patients. However,

the INS correlated negatively with SARS-CoV-2 seropositivity (r = -0.386, p =

0.039), indicating persistently raised inflammatory markers in these patients at

the end of the treatment compared to seronegative individuals. Among the four

markers studied, total galectin-9 levels failed to decrease significantly in

these patients (p = 0.030). The majority of HIV/TB co-infected patients enrolled

in our study (84.5%) were SARS-CoV-2-seronegative, indicating that SARS-CoV-2

infection might not have played a role in precipitating TB reactivation.

DOI: 10.3390/reports7030061

PMCID: PMC12225232

PMID: 40729284

**3. J Vis Exp. 2025 Jul 11;(221). doi: 10.3791/67679.**

Separation and Fractionation of Culture Filtrate Proteins (CFPs) from

Mycobacterium tuberculosis.

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Secreted proteins of Mycobacterium tuberculosis (M. tuberculosis) play a crucial

role in tuberculosis pathogenesis, immune modulation, and disease progression.

Understanding their composition and function is essential for identifying novel

biomarkers that can aid in tuberculosis diagnosis, vaccine development, and

therapeutic interventions. This study focuses on the systematic isolation,

fractionation, and characterization of culture filtrate proteins (CFPs) to

enable comprehensive immunological and proteomic analyses. CFPs were obtained

from M. tuberculosis H37Rv cultures grown in chemically defined conditions to

ensure controlled protein expression. The culture supernatant was purified

through filtration and concentrated using a hollow fiber system to retain

proteins above 10 kDa. Fractionation was achieved through liquid-phase

isoelectric focusing, separating proteins based on their isoelectric points into

20 distinct fractions. A further resolution was performed using preparative

sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE), followed

by electroelution, yielding 30 protein fractions. The fractionated proteins

obtained through this approach provide a valuable resource for immunological

profiling and mass spectrometry-based proteomic analyses. By systematically

isolating and characterizing secreted proteins, this study contributes to the

identification of tuberculosis-specific protein biomarkers, which could improve

diagnostic accuracy and advance our understanding of M. tuberculosis

pathogenesis.

DOI: 10.3791/67679

PMID: 40720418 [Indexed for MEDLINE]

**4. Oxf Med Case Reports. 2025 Jul 27;2025(7):omaf122. doi: 10.1093/omcr/omaf122.**

**eCollection 2025 Jul.**

Reactivation of BCG vaccination SCAR after influenza vaccination: a case report.

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The Bacillus Calmette-Guerin (BCG) vaccine, a live attenuated vaccine derived

from Mycobacterium bovis, is widely used for tuberculosis prevention and has

been linked to various immunological responses beyond its intended purpose. A

23-years-old healthy and allergy-free man was vaccinated for the current year's

influenza on his left arm. Two days after inoculation, the patient's BCG scar on

his left arm was erythematous, while the influenza vaccination site (located

3 cm from the BCG scar) remained unchanged. A possible ipsilateral relationship

between the BCG scar and the influenza vaccine site is suggested. BCG

vaccination influences the increase in TNF-α and IL-6 production following

influenza vaccination. In BCG-vaccinated subjects, hemagglutinin-inhibition

antibody responses against the A(H1N1)pdm09 vaccine strain is markedly enhanced,

with a trend toward more-rapid seroconversion. Understanding this BCG and

influenza vaccines interaction is crucial for healthcare providers to

differentiate between benign post-vaccination reactions and those that may

require further clinical evaluation.

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DOI: 10.1093/omcr/omaf122

PMCID: PMC12296394

PMID: 40718526

**5. Front Immunol. 2025 Jul 11;16:1583439. doi: 10.3389/fimmu.2025.1583439.**

**eCollection 2025.**

Comparative transcriptomic analysis of mouse macrophages infected with live

attenuated vaccine strains of Mycobacterium tuberculosis.

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The BCG vaccine has been used against tuberculosis (TB) for over a hundred

years; however, it does not protect adults from pulmonary TB. To develop

alternative vaccines against TB, we generated Mycobacterium tuberculosis H37Rv

(Mtb)-derived vaccine strains by rationally deleting key virulent genes,

resulting in single (SKO; ΔfbpA), double (DKO; ΔfbpA-ΔsapM), triple (TKO-D;

ΔfbpA-ΔsapM-ΔdosR and TKO-Z; ΔfbpA-ΔsapM-Δzmp1), and quadruple (QKO;

ΔfbpA-ΔsapM-Δzmp1-dosR) strains. To understand how macrophages, the host cells

that defend against infection and process antigens for presentation to immune

cells, respond to these vaccine strains, we performed transcriptomic analyses of

mouse bone marrow-derived macrophages (BMDMs) infected with these strains. The

transcriptomic data were compared with similar data obtained from macrophages

infected with Mtb H37Rv and BCG. Our analyses revealed that genes associated

with various immune and cell signaling pathways, such as NF-kappa B signaling,

TNF signaling, cytokine-cytokine receptor interaction, chemokine signaling,

hematopoietic cell lineage, Toll-like receptor signaling, IL-17 signaling, Th1

and Th2 cell differentiation, Th17 cell differentiation, and T cell receptor

signaling were differentially expressed in BMDMs infected with our vaccine

strains. Enhanced expression of cytokines and chemokines, including

proinflammatory cytokines such as TNF-α, IL-6, GM-CSF, and IL-1, which are

essential for the immune response against Mtb infection, was also observed in

BMDMs infected with these strains. In particular, BMDMs infected with all

vaccine strains exhibited a significant upregulation of genes associated with

the IL-17 pathway. These results may indicate that our vaccine strains could

induce a protective immune response against TB.

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Jagannath, Ramos, Gadad and Dhandayuthapani.

DOI: 10.3389/fimmu.2025.1583439

PMCID: PMC12289490

PMID: 40718493 [Indexed for MEDLINE]

**6. Cureus. 2025 Jun 25;17(6):e86711. doi: 10.7759/cureus.86711. eCollection 2025 Jun.**

Active Case Finding (ACF) of Tuberculosis Among School Students: Insights From a

Tribal District in Seoni, Madhya Pradesh, India.

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**BACKGROUND:**  Tuberculosis (TB) remains a major public health concern in India,

particularly among tribal populations who face structural and socioeconomic

barriers to healthcare access. Despite ongoing efforts by the National

Tuberculosis Elimination Program (NTEP), many tribal districts report

persistently high TB burdens. Active case finding (ACF) has demonstrated

effectiveness in improving early TB detection and reducing transmission.

**OBJECTIVE:**  This study aims to assess the effectiveness of a school-based ACF

initiative in identifying symptomatic individuals and potential TB cases within

the tribal communities of Seoni district, Madhya Pradesh.

**MATERIALS AND METHODS:**  A cross-sectional record review was conducted from March

to April 2024 across nine educational institutions in Seoni district. School

students, oriented by NTEP staff, screened their family members using a

12-question format that addresses TB symptoms and risk factors. Data from 2,210

individuals were compiled and analyzed using Jamovi version 2.3.28 (Computer

Software; retrieved from https://www.jamovi.org).

**RESULTS:**  Thirty percent with appetite loss and 26% with >5 kg weight loss

underwent TB testing, with these symptoms showing strong associations with

testing (p < 0.001). Only four individuals were diagnosed with TB. History of TB

in the past one to two years and generalized weakness were significant

predictors of diagnosis. Logistic regression revealed age, symptom count, and TB

history as significant predictors of testing and diagnosis.

**CONCLUSION:**  School-based ACF is a feasible and promising strategy for TB

detection in tribal areas. While the diagnostic yield was low, the model

showed potential for broader implementation and community mobilization. Further

studies are warranted to evaluate the long-term impact and optimize the

implementation.

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DOI: 10.7759/cureus.86711

PMCID: PMC12290735

PMID: 40718303

**7. Sci Rep. 2025 Jul 26;15(1):27298. doi: 10.1038/s41598-025-11768-3.**

Design of a multi-epitope vaccine against drug-resistant mycobacterium

tuberculosis and mycobacterium bovis using reverse vaccinology.

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The global burden of Mycobacterium tuberculosis (M. tuberculosis) and

Mycobacterium bovis (M. bovis), the rise of drug-resistant strains, necessitates

an urgent need for developing more effective vaccines. This study employed an

in-silico approach to design a multi-epitope vaccine targeting the PE\_PGRS16

protein, a conserved virulence factor found across both species, including

drug-resistant strains. PE\_PGRS16 was chosen due to its extracellular

localization, adhesion properties, and virulence characteristics, making it a

promising vaccine target. Epitopes for B-cells, Cytotoxic T Lymphocytes, and

Helper T Lymphocytes were selected based on antigenicity, non-toxicity, and

immune response potential. The vaccine construct demonstrated favorable

properties, including high antigenicity, solubility, and stability, with a low

instability index (-31.31) and binding energy (-44.566) when docked to TLR4,

suggesting its potential for immune activation. Griselimycin was incorporated as

an adjuvant to enhance immunogenicity, as predicted by C-ImmSim simulations.

Population coverage analysis for East Africa revealed high applicability, with

98.35% coverage for Class I epitopes, 100% coverage for Class II epitopes, and

100% combined coverage, with average hit values of 8.4, 12.26, and 20.66,

respectively. These results suggest broad potential for global vaccine

deployment. This study presents a novel multi-epitope vaccine targeting

PE\_PGRS16, with the potential to combat Mycobacterium tuberculosis and

Mycobacterium bovis infections, including drug-resistant forms. Further

experimental validation is necessary to confirm its efficacy and safety.

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DOI: 10.1038/s41598-025-11768-3

PMCID: PMC12297362

PMID: 40715271 [Indexed for MEDLINE]

**8. Diagn Microbiol Infect Dis. 2025 Jul 15;113(3):117010. doi:**

**10.1016/j.diagmicrobio.2025.117010. Online ahead of print.**

Development of thermostabilized "ready-to-use" multiplex PCR assay for the rapid

detection and distinction between Mycobacterium tuberculosis complex members and

non-tuberculous mycobacteria.

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Tuberculosis (TB) is a worldwide health problem with significant morbidity and

mortality. Current diagnosis of mycobacterial infections is largely based on

clinical features, microscopy and culture. However, these methods can be time

consuming, lack sensitivity and specificity. Therefore, rapid detection of both

M. tuberculosis and NTM are highly desirable. Multiplex PCR assay, which is able

to differentiate M. tuberculosis and NTM in clinical samples was developed in

this study. It is based on the detection of both genus (targeting genes encoding

65-kD heat shock protein and dnaJ protein which are highly conserved in

mycobacteria species) and species (targeting IS6110 and B9 genes which are only

present in M. tuberculosis complex). The sensitivity and specificity of the

multiplex PCR assay were 97.7 % and 100 %, respectively. This multiplex PCR

assay has the potential to be used as a rapid diagnostic tool to detect and

differentiate M. tuberculosis and NTM.

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DOI: 10.1016/j.diagmicrobio.2025.117010

PMID: 40714695

**9. STAR Protoc. 2025 Jul 25;6(3):103984. doi: 10.1016/j.xpro.2025.103984. Online ahead of print.**

Protocol for developing a mouse model of post-primary pulmonary tuberculosis

after hematogenous spread in native lungs and lung implants.

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Here, we present a protocol for a mouse model for studying mechanisms of

post-primary pulmonary tuberculosis (PTB) caused by virulent Mycobacterium

tuberculosis (Mtb) using subcutaneous hock infection and lung tissue

implantation. We describe steps for collagen instillation of lungs, lung and

spleen implantation, preparation of Mtb for infection, and hock infection of

mice. We then detail procedures for the perfusion of the lung and collection of

organs, tissue processing, and histopathologic interpretation. For complete

details on the use and execution of this protocol, please refer to Yabaji et

al.1,2.

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DOI: 10.1016/j.xpro.2025.103984

PMCID: PMC12311599

PMID: 40714561

**10. Int J Med Microbiol. 2025 Jul 16;320:151665. doi: 10.1016/j.ijmm.2025.151665.**

**Online ahead of print.**

Drug resistance of Mycobacterium tuberculosis in West Java, Indonesia.

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Tuberculosis (TB) is currently one of the leading causes of infectious disease

deaths globally, and Indonesia ranks 2nd in annual TB cases, below only India.

Accurate TB diagnosis and detection of multidrug-resistant TB (MDR-TB) in

real-world settings are crucial for prompt treatment and surveillance. We

therefore compared multiple methods for TB detection and drug resistance

profiling, including a cartridge-based nucleic acid amplification test (CBNAAT),

line probe assay (LPA), and phenotypic drug susceptibility testing (pDST) with

targeted long-read next generation sequencing (tNGS) and whole genome sequencing

(WGS) on 133 patients in West Java, Indonesia. WGS enabled comprehensive

phylogenetic analyses and insights into TB evolution and drug resistance

patterns, but its low read counts limit practicality for clinical use.

Comparatively, tNGS demonstrated superior sensitivity and specificity,

effectively identifying resistance profiles across multiple first-line and

second-line drugs with rapid turnaround times. Notably, when compared to LPA,

tNGS showed positive percent agreement (PPA) values of 100 % for rifampicin,

isoniazid and ethionamide, and an overall agreement of 94 % across multiple

drugs. In comparison with CBNAAT, the tNGS PPA for rifampicin remained high at

91 %. The results show that long-read tNGS technology offers a robust tool for

enhanced TB treatment and surveillance, ensuring both timely detection and

enabling effective tracing through in-depth genetic analysis. The findings

significantly contribute to the development of strategies for TB control and

management, especially in regions with a high burden of TB cases.

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DOI: 10.1016/j.ijmm.2025.151665

PMID: 40712340

**11. Int J Surg Case Rep. 2025 Jul 15;134:111687. doi: 10.1016/j.ijscr.2025.111687. Online ahead of print.**

A rare coexistence: Isolated prostate tuberculosis and nodular prostatic

hyperplasia: A case report.

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**INTRODUCTION AND IMPORTANCE:** Isolated prostate tuberculosis is exceedingly rare,

accounting for only 2.6 % of genitourinary TB cases. This condition often

presents with mildly elevated PSA levels and imaging findings that may resemble

those of advanced prostate cancer. This case holds significant value due to the

rarity of documented reports worldwide and diagnostic challenges. It provides an

essential perspective for physicians, encouraging them to maintain a heightened

index of suspicion for prostatic tuberculosis in patients presenting with vague

lower urinary tract symptoms and features of anemia, particularly in endemic

regions.

**CASE PRESENTATION:** Our case is a 75-year-old male patient who presented with

non-specific lower urinary tract symptoms and features of anemia.

Histopathologic examination confirmed the diagnosis of primary tuberculosis with

nodular prostatic hyperplasia. Following anti-Tb treatment he showed notable

improvement.

**CLINICAL DISCUSSION:** The spread of infection to the prostate is primarily

hematogenous. Prostatic tuberculosis is usually asymptomatic or subclinical in

the early stage and nonspecific irritating micturition in the late stage. The

mainstay of management for TB prostatitis is medical treatment using multiple

anti-TB drug combinations. Surgical therapy can be considered if patients do not

respond to medical therapy.

**CONCLUSION:** Isolated prostatic tuberculosis is a rare clinical entity in which

it can mimic non-specific prostatitis and prostatic carcinoma by its similar

clinical presentation and digital rectal examination finding. Definitive

diagnosis must be made by histopathological and bacteriologic studies.

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DOI: 10.1016/j.ijscr.2025.111687

PMCID: PMC12309480

PMID: 40712313

**12. Bioorg Med Chem. 2025 Jul 18;129:118323. doi: 10.1016/j.bmc.2025.118323. Online ahead of print.**

Inhibition of cytochrome bd oxidase in Mycobacterium tuberculosis by

benzothiazole amides.

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Cytochrome bd (Cyt-bd) oxidase, a key enzyme in the Mtb respiratory chain, is

particularly crucial for ATP synthesis when the primary cytochrome bc1:aa3

(Cyt-bc1:aa3) complex is compromised. There are several reported inhibitors of

the Cyt-bd oxidase, predominantly featuring quinoline and quinazoline scaffolds.

This study explores benzothiazole amides as potential inhibitors of Cyt-bd

oxidase for their ability to deplete ATP in the presence of the Cyt-bc1:aa3

inhibitor Q203. These compounds demonstrated significant bactericidal activity

against both replicating and non-replicating Mtb strains in this combined

approach. Methylene blue assays confirmed their ability to inhibit oxygen

consumption, validating their Cyt-bd inhibitory mechanism. Moreover,

cytotoxicity studies indicated low toxicity and high selectivity for bacterial

cells over mammalian cells. Molecular docking studies elucidated favourable

binding interactions with the Cyt-bd protein, while in silico ADME profiling

suggested promising pharmacokinetic properties. These results highlight the

potential of benzothiazole amides as promising candidates for anti-TB drug

development, specifically targeting the Cyt-bd oxidase. Future research will

focus on further optimising these compounds and conducting preclinical

evaluations to realize their clinical potential as adjuncts in TB therapy.

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DOI: 10.1016/j.bmc.2025.118323

PMID: 40712235

**13. J Infect Public Health. 2025 Jul 23;18(11):102912. doi:**

**10.1016/j.jiph.2025.102912. Online ahead of print.**

Recurrence of tuberculosis and associated risk factors among Non-HIV patients in

Taiwan: A retrospective cohort study.

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**BACKGROUND/PURPOSE:** Despite effective short-course anti-tuberculosis (TB)

treatments, TB recurrence remains a significant public health issue. This study

aims to investigate the rate of TB recurrence and its associated risk factors in

Taiwan.

**METHODS:** Patients with active TB who completed anti-TB treatment from 2012 to

2019 at Taipei Veterans General Hospital were identified and included in the

analysis. All enrolled cases were followed for up to 6 years to identify TB

recurrence using the CDC registration database in Taiwan. The evolving trends in

annual TB recurrence rates were examined. Independent demographic, clinical, and

microbiological factors associated with TB recurrence were also investigated.

**RESULTS:** A total of 1875 patients with active TB were enrolled in the analysis.

The overall TB recurrence rate was determined to be 2.0 % (434 per 100,000

person-years), with a median follow-up duration of 72 months. A notable decline

in the recurrence rate was observed post-2017. The peak recurrence rate was

observed during the second year following treatment completion. Independent

factors associated with TB recurrence included a body mass index (BMI) <20 kg/m²

(adjusted hazard ratio [aHR]: 4.38, 95 % CI:1.70-11.30, p = 0.002), a history of

previous TB (aHR 4.28, 95 % CI: 1.77-10.35, p = 0.001), and 2-month sputum TB

culture non-conversion (aHR:3.37, 95 % CI: 1.36-8.38, p = 0.009). These

observations were further corroborated through subgroup analyses, encompassing

pulmonary TB and culture-confirmed pulmonary TB.

**CONCLUSIONS:** The TB recurrence rate in Taiwan is low and shows a declining

trend. Independent factors associated with TB recurrence included low BMI,

previous TB, and 2-month sputum TB culture non-conversion.

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DOI: 10.1016/j.jiph.2025.102912

PMID: 40763458

**14. mBio. 2025 Aug 7:e0155925. doi: 10.1128/mbio.01559-25. Online ahead of print.**

Paired single-cell and spatial transcriptional profiling reveals a central

osteopontin macrophage response mediating tuberculous granuloma formation.

Pyle CJ(1)(2), Wang L(1), Beerman RW(1), Jain V(3), Ohman HKE(1)(2), Thompson

BA(1)(2), Abramson KR(3), Ko DC(1), Gregory SG(3), Smith CM(1), Neff JL(4),

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Granulomas are classic manifestations of tuberculosis pathogenesis. They result

from an ensemble of immune responses to Mycobacterium tuberculosis infection,

but the identities, arrangement, cellular interactions, and regulation of the

cells that comprise them have thus far been incompletely understood. To better

understand the composition of granulomas, we conducted spatial and single-cell

RNA sequencing of granulomas in biopsy specimens from patients with

tuberculosis. We found that granulomas consist of concentric transcriptional

laminae surrounding areas of central necrosis. We identified distinct

populations of granuloma-associated stromal cells, fibroblasts, lymphocytes,

mast cells, dendritic cells, neutrophils, and macrophages. Furthermore, gene

expression among these cell populations differed by location within granulomas.

We used inferential analysis to predict dominant granuloma cell-cell

interactions, the activity of major signaling pathways, and transcription factor

activities. Using spatial deconvolution, we mapped a conserved pattern of

cellular organization dominated by macrophages rich in SPP1/osteopontin

expression. Trajectory analysis of macrophage subtypes mapped their

differentiation and supported the importance of SPP1 to granuloma macrophage

polarization. Using the Mycobacterium marinum-zebrafish model, we found that

mycobacterial infection induces spp1 expression in macrophages and that spp1

ablation results in granuloma formation defects and reduced survival in adult

animals. Cumulatively, we have identified a dominant macrophage granuloma

population as well as its central regulatory gene in human samples and confirmed

the importance of spp1 to granuloma biology in vivo.IMPORTANCETuberculosis is

the world's most deadly single-pathogen infection. Its causative bacterium,

Mycobacterium tuberculosis, sickens over 10 million people annually.

Mycobacterial granulomas are the pathological hallmark of the infection and are

critical determinants of disease trajectory. Granulomas form as a physiological

barrier to contain infected macrophages and reduce bacterial dissemination.

However, that barrier also reduces access of antibiotics and mycobactericidal

immune cells to the pathogen, thereby promoting chronic infection and end-organ

damage. This work supplies the field with a map of the conserved features of

human tuberculosis granulomas and provides a valuable resource for future

exploration of critical factors in tuberculosis pathogenesis, exemplified here

by functional findings around the roles of spp1/osteopontin-expressing

macrophages in mycobacterial granulomas.

DOI: 10.1128/mbio.01559-25

PMID: 40772762

**15. Access Microbiol. 2025 Aug 6;7(8):000787.v4. doi: 10.1099/acmi.0.000787.v4.**

**eCollection 2025.**

A hospital-based observational study on HIV-TB co-infection.

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**Background.** Human immunodeficiency virus (HIV) is the major cause of failure to

reach targets of tuberculosis (TB) control in settings with high HIV loads. TB,

on the other hand, enhances the progression of HIV infection to AIDS. This study

was done to understand the epidemiological and clinical profile of HIV-TB

co-infected patients and to study the impact of TB on the recovery of CD4

counts. **Methodology.** An observational study was conducted in which of the

573 patients newly diagnosed with HIV infection and enrolled at the

antiretroviral therapy (ART) centre, King George's Medical University, Lucknow,

between May 2021 and June 2022, 80 patients who also had newly diagnosed TB were

included. These HIV-TB co-infected patients were analysed for demographic

factors. Also, clusters of differentiation 4 (CD4) counts were done at the time

of enrolment on ART and then later, ~6 to 8 months of recieving ART and

anti-tubercular treatment (ATT) initiation. For comparison, of the 493 HIV-only

patients, 50 age- and gender-matched consecutive patients for whom baseline and

follow-up CD4 counts were available were enrolled as controls. The change from

baseline CD4 count was calculated using a paired t-test and Wilcoxon signed rank

test. **Results.** In the present study, among HIV-TB co-infected patients, baseline

CD4 levels were 194.52±162.27, and follow-up CD4 levels were 285.09±170.33. A

statistically significant increment of 90.57±165.60 in mean CD4 levels was

observed (t=4.019; P<0.001). Likewise, in only HIV-positive patients, a

statistically significant increment of 125.26±191.48 (35.75%) cells in mean CD4

levels was observed (t=4.626; P<0.001). The increase in CD4 counts in HIV only

population was significantly higher than that observed in HIV-TB co0infected

patients. **Conclusion.** Though significant rise in CD4 counts was observed in both

HIV-TB co-infected patients and HIV-only patients after 6 to 8 months of

appropriate therapy, the rise was significantly higher among the HIV-only group

as compared to the HIV-TB co-infected group.

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DOI: 10.1099/acmi.0.000787.v4

PMCID: PMC12328067

PMID: 40771827

**16. Biophys J. 2025 Aug 5:S0006-3495(25)00489-8. doi: 10.1016/j.bpj.2025.07.040.**

**Online ahead of print.**

How PGL finds a sweet spot in phospholipid membranes - a combined multiscale MD

and NMR study.

Schahl A(1), Réat V(1), Malaga W(1), Birbes C(1), Czaplicki G(1), Jolibois F(2),

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Glycolipids from pathogenic Mycobacterium tuberculosis (Mtb) play important

roles during the interaction of the pathogen with macrophages, and can shape the

host cell's immune response by modulating its membrane structure and function.

Here we study the phenolic glycolipids (PGLs) present in the envelope of some

hypervirulent strains of Mtb, and their impact on model membranes. By a

combination of molecular modeling and simulations, and solid-state NMR

experiments, we show that PGLs, like the structurally related lipid PDIM, adopt

a conical shape in lipid membranes which destabilizes the lamellar membrane

phase and promotes a transition to a non-lamellar inverted-hexagonal phase.

Unlike PDIM, in our simulations PGLs remain anchored to the phosphate groups of

the lipid bilayer by its sugar-carrying extremity, preventing lipid flip-flop.

These findings shed new light on a potential biophysical role of PGLs, through

modulation of the properties of the host cell's membrane, in addition to the

recognition of its sugar moiety by host cell immune receptors.

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reserved.

DOI: 10.1016/j.bpj.2025.07.040

PMID: 40770879

**17. BMC Public Health. 2025 Aug 6;25(1):2660. doi: 10.1186/s12889-025-24006-2.**

One year on - the long-term impact of COVID-19 pandemic and government

restrictions on the health-seeking behaviour, financial security and mental

health of TB survivors.

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**BACKGROUND:** People with tuberculosis (TB) may face long-term physical and

psycho-social-economic disability related to TB treatment. The Corona Virus

Disease 2019 (COVID-19) pandemic and government restrictions disrupted health

care services. We describe health-seeking behaviour, perceived financial impact,

and the mental health of TB survivors one year after the COVID-19 pandemic. We

further explore factors associated with the perceived impact of COVID-19 and

government restrictions on health-seeking behaviour.

**METHODS:** This is a cross-sectional study nested in an ongoing observational TB

Sequel cohort study. Adults (≥ 18yrs) who had completed treatment for

drug-susceptible pulmonary TB in South Africa, the Gambia, and Mozambique before

the start of the COVID-19 pandemic, completed a COVID-19 questionnaire which

included the WHO tool for Behavioural Insights on COVID-19, the Kessler

Psychological Distress Scale (K10) and Medical Outcomes Short Form Survey

(SF-36) for health-related quality of life. Questionnaires were administered

during scheduled TB Sequel follow-up study visits between 04/2021 and 10/2021.

We used publicly available data on the number of COVID-19 cases and the start

and end date of each wave to define country-specific COVID-19 "in-wave" and

"out-of-wave" phases. We compared psycho-social and economic measures reported

during these phases. In addition, we explored factors associated with poor

health-seeking behaviour (comprised of moderate or serious impact) using

logistic regression.

**RESULTS:** Four hundred eighty seven TB survivors (69% male, median age 33 years

IQR 25-42, median time since TB treatment completion 16 months IQR 13-27)

completed the COVID-19 questionnaire. About a quarter of TB survivors reported

that their financial status (n = 117; 24%) or their health-seeking behaviour for

any health condition (n = 128; 26%) had been seriously impacted by COVID-19 and

the governments' response. A third of patients (30.4%) reported using coping

strategies. Logistic regression indicated that males, living with HIV and being

on antiretroviral treatment (ART), being impacted financially during COVID-19,

and experiencing social changes, were associated with poor health-seeking

behaviour.

**CONCLUSION:** Governments' response to COVID-19 affected TB survivors'

healthcare-seeking behaviour, financial status and mental health. The long-term

adverse effects on health-seeking behaviour are important for TB survivors who

are at increased risk for recurrent disease and long-term disability in the

first two years after treatment completion.

TRIAL REGISTRATION: Clinical trial number: not applicable.

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DOI: 10.1186/s12889-025-24006-2

PMID: 40770626 [Indexed for MEDLINE]

**18. BMC Public Health. 2025 Aug 6;25(1):2659. doi: 10.1186/s12889-025-23866-y.**

Association of smoking with depression among tuberculosis patients: a systematic

review and meta-analysis.

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**BACKGROUND:** The co-occurrence of smoking and depression presents a significant

public health concern, particularly among individuals with tuberculosis (TB).

Smoking delays the recovery from tuberculosis (TB) and it has also been

associated with depression in those who have been diagnosed with the disease.

The review aimed to find out the association between smoking and depression

among TB patients.

**METHODS:** A systematic review and meta-analysis were conducted following PRISMA

guidelines, in PubMed, Scopus, and ScienceDirect databases. Literature searches

were employed using terms related to "tuberculosis", "smoking," and "depression"

across all articles either by title, abstract, or keywords. To evaluate the risk

of bias, the Joanna Briggs Institute Critical Appraisal Checklist (JBI) was

used. For clinical heterogeneity, a meta-analysis was conducted to pool

estimates using RevMan 5.3 and Stata 13.0 software was used for publication bias

assessment.

**RESULTS:** From the 1393 studies identified, eleven studies were eligible for

inclusion in this study. There were nine cross-sectional, and two cohort

studies. Only 5 studies reported effect size calculation suitable for

multivariate analysis. The pooled analysis indicates that smoking TB patients

were associated with a higher odds of depression (OR = 2.56, 95% CI: 1.11-5.92),

though the wide confidence interval and substantial heterogeneity (I² = 71%,

p = 0.003) indicates uncertainty regarding the effect size. Subgroup analysis

based on depression assessment tools revealed a stronger association between

smoking TB patients with depression (OR = 3.36; 95% CI: 1.19-9.50) with high

heterogeneity (I² = 75%). Publication bias, as indicated by Egger's test (bias

coefficient = 0.59, p = 0.874).

**CONCLUSIONS:** Existing evidence suggests a potential association between

depression and smoking among tuberculosis patients, which encourages more

studies to explore whether smoking cessation would contribute to the improvement

of mental health outcomes in this population.

TRIAL REGISTRATION: This review was developed and registered in the

International Prospective Register of Systematic Reviews

(PROSPERO). CRD42024528399 Registered on 06 April 2024.

© 2025. The Author(s).

DOI: 10.1186/s12889-025-23866-y

PMID: 40770616 [Indexed for MEDLINE]

**19. Nat Commun. 2025 Aug 6;16(1):7253. doi: 10.1038/s41467-025-62485-4.**

CUT&Tag reveals unconventional G-quadruplex landscape in Mycobacterium

tuberculosis in response to oxidative stress.

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Mycobacterium tuberculosis (Mtb), the causative agent of tuberculosis, remains a

global health threat due to increasing drug resistance and high mortality rates.

To combat tuberculosis effectively, novel therapeutic targets are urgently

needed. G-quadruplexes (G4s) represent promising candidates for this purpose. In

this study, we successfully apply the cleavage under targets and tagmentation

(CUT&Tag) technique for the first time in bacteria, mapping the G4 landscape in

Mtb under standard and oxidative stress conditions, the latter mimicking the

environment Mtb faces within macrophages. We validate the CUT&Tag protocol using

an antibody against the RNA polymerase β-subunit, confirming its association

with actively transcribed genes. Employing the anti-G4 antibody BG4, we

discovered that Mtb G4s, unlike their eukaryotic counterparts, predominantly

locate within gene coding sequences and consist of two-guanine tract motifs.

Notably, oxidative stress increases G4 formation, correlating with reduced gene

expression. Our findings provide the first evidence of G4 formation in Mtb cells

and suggest their potential role in bacterial survival within macrophages. This

study demonstrates the successful application of CUT&Tag in bacteria and unveils

an unconventional G4 landscape in Mtb, offering new insights into bacterial

stress response mechanisms and potential therapeutic targets.

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DOI: 10.1038/s41467-025-62485-4

PMID: 40770179 [Indexed for MEDLINE]

**20. World J Microbiol Biotechnol. 2025 Aug 7;41(8):300. doi:**

**10.1007/s11274-025-04510-8.**

S292L mutation in Rv1258c efflux pump drives pyrazinamide efflux and a novel

inhibitor designed for co-therapy to improve MDR-TB treatment outcomes.

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DOI: 10.1007/s11274-025-04510-8

PMID: 40770126

**21. Microb Pathog. 2025 Aug 4:107949. doi: 10.1016/j.micpath.2025.107949. Online**

**ahead of print.**

Deciphering Genetic Overlaps Between Pulmonary Tuberculosis and GERD for Drug

Target Discovery: A Structural Bioinformatics Perspective.

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Pulmonary tuberculosis (PTB) and gastroesophageal reflux disease (GERD) are

clinically distinct but may share common molecular mechanisms. This study used

integrative bioinformatics to identify 23 significantly dysregulated genes

common to both conditions. Key regulatory microRNAs (hsa-miR-34a-5p,

hsa-let-7b-5p, hsa-let-7g-5p) and macrophage-associated pathways were

implicated. Interferon alpha/beta signaling emerged as a central shared pathway

between PTB and GERD. Five hub genes (MYL9, OASL, ACTA2, DDX60L, and DDX60) were

identified as common between these two conditions and their expressions were

validated using quantitative real-time PCR. Drug repurposing analysis identified

ribavirin as a promising candidate targeting the hub gene OASL, supported by a

favorable binding affinity (-6.6 kcal/mol) and acceptable ADMET properties.

These findings pave the way for understanding the molecular overlap between PTB

and GERD and for developing targeted therapeutic strategies.

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DOI: 10.1016/j.micpath.2025.107949

PMID: 40769224

**22. Medwave. 2025 Aug 6;25(7):e3088. doi: 10.5867/medwave.2025.07.3088.**

Time from arrival in Chile to tuberculosis diagnosis in migrants treated at

primary care centers in two Metropolitan Region municipalities, Chile.

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

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**INTRODUCTION:** In Chile, the number of migrants affected by tuberculosis has

experienced a significant increase from 7.1% in 2014 to 29.7% in 2023, ranking

as the first group at risk. The objective was to estimate the time to diagnosis

of tuberculosis from arrival in Chile in a series of migrants undergoing

treatment between January 2021 and March 2022.

**METHODS:** We analyzed a cohort of migrants over 18 years of age with a diagnosis

of tuberculosis treated in the communes of Recoleta and Independencia. Those who

agreed to participate and signed the informed consent form were included. Cases

with non-tuberculous mycobacteria and residents outside the Metropolitan Region

were excluded. Sociodemographic, clinical, and arrival dates, as well as

symptoms and diagnoses, were recorded. Proportional hazards models in STATA v.18

were used to analyze times according to independent variables. A p value < 0.05

was considered significant.

**RESULTS:** The median time to diagnosis was 93.5 months, varying by subgroup. The

recent migration subgroup without Chilean documentation had a hazard ratio of

13.1, which indicates that, at any time after arrival, these individuals have a

13-fold increased risk of tuberculosis diagnosis compared to the reference

subgroup (traditional migration with Chilean identity documents). This hazard

ratio is reduced by 2.4 times when these types of migrants have documentation

from Chile (95% confidence interval: 1.2 to 4.5).

**CONCLUSIONS:** There is a wide range of time from arrival in Chile to the

diagnosis of tuberculosis. Factors such as the type of migration and the type of

identity document have an impact on the development of this disease. It is

necessary to expedite the legal administrative process for migrants and

implement timely screening policies, along with follow-up and improved access to

healthcare, to reduce exposure and risk of tuberculosis.

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License.

DOI: 10.5867/medwave.2025.07.3088

PMID: 40768753 [Indexed for MEDLINE]

**23. Chem Biodivers. 2025 Aug 6:e01892. doi: 10.1002/cbdv.202501892. Online ahead of print.**

Antibacterial and Antibiofilm Activity of 8-Hydroxyquinoline Derivatives Against

Mycobacterium and Staphylococcus Species.

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PH(2), Ho KV(2), Lin CH(2), Quave CL(5)(6), Twilley D(1).

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Georgia, USA.

A series of 8-alkoxyquinoline derivatives (QD-1-12) were designed and

synthesized on the basis of analogues of 8-hydroxyquinoline (8-HQ) (HQ 1-4). The

compounds were evaluated for biofilm inhibition against Mycobacterium smegmatis

and Staphylococcus aureus, including antibacterial activity against

Mycobacterium tuberculosis, M. smegmatis and S. aureus. Cytotoxicity was

evaluated against human monocyte (U937) and African green monkey kidney (Vero)

cell lines. The 8-O-prenyl derivative (QD-12) showed a minimum inhibitory

concentration (MIC) of 12.5 µM, indicating an approximate 8-fold increased

selectivity for the biofilm phenotype and an increased inhibitory activity

against methicillin-resistant S. aureus (MRSA) by up to 2-fold.

5,7-Dichloro-8-hydroxy-2-methylquinoline (HQ-2) showed the highest inhibitory

potential with MIC values of 0.1, 1.56, 2.2 and 1.1 µM against M. tuberculosis,

M. smegmatis, methicillin-sensitive S. aureus (MSSA) and MRSA, respectively. The

results indicate the importance of the 8-OH group for antibacterial and

antimycobacterial activity. Cytotoxicity revealed low-to-moderate toxicity of

8-HQ (HQ-1). All the compounds, except HQ-1, were tested for the first time for

their growth and biofilm inhibitory activity against Mycobacterium spp. and S.

aureus.

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DOI: 10.1002/cbdv.202501892

PMID: 40768666

**24. Sci Adv. 2025 Aug 8;11(32):eadx2067. doi: 10.1126/sciadv.adx2067. Epub 2025 Aug 6.**

A streamlined CRISPR-based test for tuberculosis detection directly from sputum.

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Daivaa N(2), Davis JL(3)(4), Vargas DA(5)(6), Banada P(2), Xie YL(2), Myhrvold

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Mycobacterium tuberculosis (Mtb) is a major threat to global health, and there

is an urgent need for affordable, simple tuberculosis (TB) diagnosis in

underresourced areas. Here, we combine recombinase polymerase amplification with

Cas13a and Cas12a detection to create two parallelized one-pot assays that

detect two conserved elements of Mtb (IS6110 and IS1081) and a human DNA

internal control. These assays are compatible with lateral flow and can be

readily lyophilized. Our final assay showed a limit of detection of 69.0 CFU per

milliliter for Mtb H37Rv and 80.5 CFU per milliliter for Mycobacterium bovis BCG

in spiked sputum, with no cross-reactivity to diverse bacterial or fungal

isolates. Clinical tests on 13 blinded sputum samples revealed 100% (six of six)

sensitivity and 100% (seven of seven) specificity compared to culture. SHINE-TB

streamlines TB diagnosis from sample to answer by combining amplification and

detection while being compatible with lateral flow and lyophilization.

DOI: 10.1126/sciadv.adx2067

PMCID: PMC12327463

PMID: 40768573 [Indexed for MEDLINE]

**25. Braz J Microbiol. 2025 Aug 6. doi: 10.1007/s42770-025-01755-1. Online ahead of print.**

Immunoinformatics analysis of the proteins MPT83 and MPT51 to design a possible

chimeric vaccine against Mycobacterium tuberculosis.

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Mycobacterium tuberculosis (Mtb) is the pathogen that causes tuberculosis (TB).

This disease affects one-third of the world's population, mainly in its latent

form. The use of reverse vaccinology and immunoinformatics stands out for the

production of vaccines based on peptides or proteins, since they are more

specific, safe, effective and economical. The present study evaluated the

immunological potential of the proteins MPT83 and MPT51 for vaccine production,

comparing them with MPT64. To do this, the sequences of these proteins from MTB

H37Rv were downloaded and analyzed. The prediction of T and B cell epitopes was

performed, and the adjuvant (50 S L7/L12) was included in the fusion of MPT83

and MPT51 to enhance the immune response. The allergenicity, antigenicity,

solubility and physicochemical properties of the fused protein fragments were

evaluated. Through different programs, a variety of bioinformatics tools were

used to predict, analyze and validate the tertiary structure. The results of the

in silico immunological simulation of the chimeric protein demonstrated that the

best region for use as an epitope is the initial part of MPT83, consisting of

100 amino acid residues, and the final portion of MPT51, consisting of 99 amino

acid residues, with a significant immunological response, excellent antigenicity

(1.02) and no allergenicity. The secondary structure revealed that the majority

of alpha-helices are in the initial part of the proteins, and the chimeric

vaccine has 3 beta strands along its length. Finally, the chimeric vaccine

candidate and MPT64 were efficiently cloned into the bacterial vector and

successfully expressed in Escherichia coli thereby facilitating future in vivo

studies with potentially promising results.

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Microbiologia.

DOI: 10.1007/s42770-025-01755-1

PMID: 40768028

**26. Epidemiol Serv Saude. 2025 Aug 4;34:e20240778. doi:**

**10.1590/S2237-96222025v34e20240778.en. eCollection 2025.**

Temporal trends in incidence and mortality from pulmonary tuberculosis: time

series study, Sul da Bahia, 2010-2023.

[Article in English, Portuguese]

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Divinópolis, MG, Brazil.

**OBJECTIVE:** To analyze the temporal trend of incidence and mortality from

pulmonary tuberculosis in Southern Bahia.

**METHODS:** Time series study of new cases and deaths from pulmonary tuberculosis

conduccted on Costa do Descobrimento and in the Extremo Sul of Bahia. The number

of new cases and deaths from pulmonary tuberculosis was obtained from the

Notifiable Diseases Information System, between 2010 and 2023, and used to

calculate incidence and mortality. Prais-Winsten regression was used to

calculate the annual percentage variation (APV) and 95% confidence interval

(95%CI) and to classify trends.

**RESULTS:** 4,005 new cases and 128 deaths from pulmonary tuberculosis were

registrated during the period of the study. The average incidence was 34.91

cases per 100,000 inhabitants, and mortality was 1.11 deaths per 100,000

inhabitants. Incidence and mortality showed stationary trends. Decreasing

incidence occurred in females (APV -0.01; 95%CI -0.02; -0.01) and in the age

groups of 0-9 years (APV -0.02; 95%CI -0.04; -0.01), 40-59 years (APV -0.01;

95%CI -0.02; -0.01) and 60 years or older (APV -0.01; 95%CI -0.04; -0.01). Costa

do Descobrimento showed a decreasing incidence for females (APV -0.02; 95%CI

-0.03; -0.01) and for the age group of 40-59 years (APV -0.02; 95%CI -0.03;

-0.01). In Extremo Sul, the incidence decreased in the 20-39 age group (APC

-0.01; 95%CI -0.02; -0.01).

**CONCLUSION:** Although temporal trend of incidence and mortality were stationary,

public health strategies are necessary, especially on Costa do Descobrimento,

which maintained the highest rates of pulmonary tuberculosis.

DOI: 10.1590/S2237-96222025v34e20240778.en

PMID: 40767738 [Indexed for MEDLINE]

**27. Curr Med Chem. 2025 Aug 4. doi: 10.2174/0109298673362583250705102313. Online**

**ahead of print.**

Hybrids/Conjugates/Chimera Drugs-Antimicrobial Hybrids: Antibiotics,

Antifungals, Antituberculars, Antimalarials.

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Antimicrobial hybrids are compounds that can inhibit, stop the growth of, or

kill microorganisms, including bacteria, fungi, and parasites. Antibiotics, a

subset of an-timicrobial agents, specifically target bacteria and include

well-established classes such as β-lactams, macrolides, quinolones, and

oxazolidinones. Other antimicrobial hybrids are designed for treating a wide

range of diseases, including fungal infections, leish-maniasis, parasitic

diseases (such as trypanosomiasis and malaria), leprosy, and tuber-culosis. Some

hybrids are designed to treat a variety of diseases. This review highlights

studies primarily published between 2000 and 2023, with a few from 2024,

underscor-ing the dynamic and rapidly evolving nature of antimicrobial hybrid

research.

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epub@benthamscience.net.

DOI: 10.2174/0109298673362583250705102313

PMID: 40765081

**28. BMJ Glob Health. 2025 Aug 5;10(8):e019270. doi: 10.1136/bmjgh-2025-019270.**

Cost-effectiveness of different tuberculosis diagnostic approaches in Nigeria

based on decision analytical modelling.

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YN(9), Dankishiya FS(10), Ibrahim A(11), Garzali IU(5), Galadanci AA(12)(13),

Suleiman AK(14), Olawumi AL(15), Abdullahi UF(11), Mahmud FM(10), Umar

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**BACKGROUND:** Tuberculosis (TB) remains a leading cause of morbidity and mortality

in Nigeria, particularly among people living with HIV (PLWH), who face

significantly higher risks of developing active TB. Conventional diagnostic

methods such as sputum smear microscopy and chest radiography often fail to

detect TB accurately in this population due to smear-negative presentations and

atypical radiographic findings. Recent diagnostic innovations, including the

Xpert MTB/RIF Ultra, TB lipoarabinomannan (TB-LAM) and TB loop-mediated

isothermal amplification (TB-LAMP) tests, offer improved sensitivity and

specificity, but their cost-effectiveness in resource-limited settings remains

unclear.

**METHODS:** In this economic evaluation, we combined a decision tree with

cost-effectiveness analysis to compare three TB diagnostic algorithms tailored

for PLWH in Nigeria: (1) Xpert MTB/RIF Ultra following chest radiography (chest

X-ray; CXR), (2) TB-LAM following CXR and (3) TB-LAMP following CXR. Data on

test accuracy, costs and TB prevalence were obtained from systematic reviews and

meta-analyses, with costs adjusted for inflation and local purchasing power. We

estimated the incremental cost-effectiveness ratios (ICERs) for the three

diagnostic approaches. Sensitivity analyses were conducted to assess the

robustness of results across varying input parameters.

**RESULTS:** TB/LAM was found to be the most cost-effective option at a cost of

US$17 per TB case detected when compared with US$20 and US$22 per TB case

detected for the baseline strategy of Xpert MTB/RIF Ultra and TB-LAMP,

respectively. These ICERs are consistent with willingness-to-pay thresholds set

at three times Nigeria's gross domestic product (GDP) and remained robust over a

wide range of costs and epidemiological parameter inputs.

**CONCLUSION:** Among PLWH in Nigeria, the TB-LAM algorithm represents the most

cost-effective diagnostic strategy. However, the Xpert MTB/RIF Ultra may provide

additional value in settings with sufficient infrastructure and funding. This

study underscores the need for tailored diagnostic approaches that balance

accuracy, scalability and affordability to enhance TB detection and management

in vulnerable populations.

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DOI: 10.1136/bmjgh-2025-019270

PMID: 40763982 [Indexed for MEDLINE]

**29. EBioMedicine. 2025 Aug 4;119:105875. doi: 10.1016/j.ebiom.2025.105875. Online**

**ahead of print.**

Comparative assessment of line probe assays and targeted next-generation

sequencing in drug-resistant tuberculosis diagnosis.

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**BACKGROUND:** Rapid and accurate detection of drug-resistant tuberculosis (DR-TB)

is crucial for ensuring effective treatment, halting transmission and preventing

the amplification of resistance. Comparative evaluations of molecular diagnostic

assays in high-burden settings are essential for informing clinical

decision-making for DR-TB treatment.

**METHODS:** The Seq&Treat clinical study previously evaluated the performance of

two targeted next-generation sequencing (tNGS) workflows, GenoScreen Deeplex

Myc-TB and Oxford Nanopore Technologies Tuberculosis Drug Resistance Test, on

direct sediment samples from persons at risk for DR-TB. Hain Line Probe Assay

(LPAs-MTBDRplus and MTBDRsl) were run as a comparator test using an aliquot of

the same sediment samples. Diagnostic performance of the LPAs and previously

established tNGS performance were compared, including sensitivity and

specificity, for rifampicin, isoniazid, fluoroquinolones (moxifloxacin,

levofloxacin), and amikacin, using a composite reference standard of phenotypic

drug susceptibility testing and whole-genome sequencing.

**FINDINGS:** Among 720 clinical samples tested, MTBDRplus LPA sensitivity for

rifampicin and isoniazid was 92.3% (95% CI 88.9-94.8) and 91.9% (88.4-94.4),

each significantly lower than ≥95% achieved by both tNGS workflows (p < 0.01).

For fluoroquinolones (moxifloxacin and levofloxacin), the MTBDRsl LPA and ONT

had similar sensitivities (94.3% and 92.7%, and 94.8% and 93.9%, respectively),

while GenoScreen outperformed both (97.3% and 96.6%). GenoScreen also

demonstrated the highest sensitivity for amikacin resistance (94.6%) compared to

LPAs (88.7%) and ONT (88.3%). Complete assay failure rates were low for LPAs

(4.9%) and ONT (5.0%) and moderately higher for GenoScreen (8.6%), with

differences in single-target failures across all assays.

**INTERPRETATION:** LPAs demonstrated lower sensitivity and more limited drug

resistance detection compared to tNGS workflows, underscoring the advantages of

tNGS for improving DR-TB diagnostic algorithms. These findings provide critical

evidence to guide updates in DR-TB diagnostic programs.

FUNDING: Support for the Seq&Treat project was provided through funding from

Unitaid (2019-32-FIND MDR).

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DOI: 10.1016/j.ebiom.2025.105875

PMID: 40763426

**30. Sci Rep. 2025 Aug 4;15(1):28335. doi: 10.1038/s41598-025-13227-5.**

Factors associated with unfavourable treatment outcomes among patients with

Multidrug-resistant Tuberculosis receiving outpatients care.

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Enhancing treatment outcomes for drug-resistant tuberculosis is a major global

priority for tuberculosis control programs. India has the highest number of

Multidrug-resistant Tuberculosis cases worldwide, yet no longitudinal studies

have assessed the factors affecting treatment outcomes in public sector

conditions. This study aimed to evaluate factors associated with ineffective

treatment outcomes in patients with Multidrug-resistant Tuberculosis receiving

outpatient care under the National Tuberculosis Elimination Programme in

Puducherry, India, from January 2020 to December 2023. We employed multivariate

regression methods to calculate odds ratios with 95% confidence intervals to

identify factors linked to unsuccessful treatment outcomes. Clinical data from

patients with Multidrug-resistant Tuberculosis revealed an overall treatment

success rate of 60.42%. The findings showed that patients undergoing retreatment

were more likely to experience unsuccessful outcomes. Additionally, co-infection

with HIV, as well as the use of alcohol or tobacco, increased the odds of

treatment failure. Patients with heteroresistant patterns had 2.72 times higher

odds of unsuccessful treatment outcomes compared to those with inferred and

true-resistant patterns. Furthermore, patients living in rural areas typically

experienced worse treatment outcomes than those in urban areas, with higher

rates of loss to follow-up. Patients on longer treatment regimens were also more

likely to be lost to follow-up compared to those on shorter regimens. Notably,

true resistance due to rpoB gene mutations accounted for 65.9% (29 out of 44) of

total deaths, with mutations at codon S450L contributing to 47.7% of these

fatalities, a finding that has not been reported elsewhere. The study

highlighted a strong association between heteroresistance in the rpoB gene and

poor treatment outcomes. These results emphasize the need for detailed

molecular-level studies to improve treatment outcomes by ensuring appropriate

drug selection for MDR/RR Tuberculosis. Additionally, further research is

necessary to determine the impact of heteroresistance on treatment outcomes in

individual patients.

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DOI: 10.1038/s41598-025-13227-5

PMCID: PMC12322265

PMID: 40760140 [Indexed for MEDLINE]

**31. NPJ Antimicrob Resist. 2025 Aug 4;3(1):70. doi: 10.1038/s44259-025-00143-x.**

The Parkinson's drug benztropine possesses histamine receptor 1-dependent

host-directed antimicrobial activity against Mycobacterium tuberculosis.

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JD(1), Langdon G(1), Hancock REW(2), Chen J(3), Av-Gay Y(4).

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Intracellular pathogens such as Mycobacterium tuberculosis (Mtb) evade host

defence mechanisms to infect and survive within host cells. Host-directed

therapy (HDT) offers a promising alternative to antibiotics and may overcome

antimicrobial resistance. Using high-content screening, we identified

benztropine (BZT), an approved Parkinson's disease drug, as a potent inhibitor

of intracellular Mtb. BZT is active in both human and murine macrophages but is

inactive in broth. In an aerosol Mtb mouse infection model, oral administration

of BZT reduced the burden of Mtb in the lungs by up to 70%. BZT was also active

against Salmonella enterica serovar Typhimurium (STm) in an abscess model of

infection, significantly reducing size and bacterial load. Chemical competition

assays, CRISPR knockouts, and siRNA silencing assays revealed that BZT's

activity against Mtb is mediated via macrophage histamine receptor 1 (HRH1). Our

findings establish BZT as a promising repurposed candidate and a lead compound

for developing HRH1-targeting antibacterial HDTs.

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DOI: 10.1038/s44259-025-00143-x

PMCID: PMC12322000

PMID: 40760081

**32. Int J Adolesc Med Health. 2025 Aug 6. doi: 10.1515/ijamh-2025-0064. Online ahead of print.**

Nutritional status of adolescents undergoing tuberculosis treatment in urban

Bangladesh: prevalence and determinants of malnutrition.

Hasib Joarder MA(1), Saha P(2), Chakraborty S(1), Akter K(1), Amir S(3),

Chowdhury MR(1), Dowllah IM(4), Alam UK(1), Jai Maug AK(5), Alam MM(6).

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**OBJECTIVES:** Tuberculosis is a global public health challenge, disproportionately

affecting adolescents in low-and middle-income countries. Malnutrition worsens

immune function, delays recovery and increases the risk of treatment failure in

Tuberculosis patients. The objectives of this study was to assess the

nutritional status of adolescents undergoing TB treatment in urban Bangladesh

and identify the determinants of malnutrition.

**METHODS:** A cross-sectional study was conducted from November 1, 2023, to May 31,

2024, among 339 adolescents receiving Tuberculosis treatment in five hospitals

in Dhaka, Bangladesh. Nutritional status was primarily assessed by

Patient-Generated Subjective Global Assessment (PG-SGA). Anthropometric data

were collected to calculate BMI-for-age and height-for-age z-scores to verify

nutritional status.

**RESULTS:** The prevalence of severe malnutrition was 14.2 % and another 41.6 %

were found moderately malnourished in PG-SGA. The z-scores also showed 14.2 %

had severe malnutrition and 21.2 % had moderate malnutrition. The mean BMI was

17.89, with 59.3 % of participants underweight and 63.7 % experiencing some

degree of stunting. Eating difficulties, particularly appetite loss, were

reported by 45.4 % of adolescents. While 52.8 % received some nutrition-related

information, only 1.8 % received comprehensive nutritional care. Logistic

regression identified significant predictors of malnutrition, including female

gender (AOR=0.51, p=0.01), presence of major comorbidities (AOR=3.67, p=0.01),

eating difficulties (AOR=3.41, p<0.01), Type I Tuberculosis (AOR=2.57, p<0.01),

and less than four meals (AOR=2.69, p=0.01).

**CONCLUSIONS:** Both PG-SGA and anthropometric indicators revealed significant

nutritional deficits. Integrated nutritional support and management of

comorbidities should be prioritized alongside Tuberculosis care to improve

treatment outcomes.

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DOI: 10.1515/ijamh-2025-0064

PMID: 40758943

**33. PLoS Pathog. 2025 Aug 4;21(8):e1013342. doi: 10.1371/journal.ppat.1013342.**

**eCollection 2025 Aug.**

Two-pore channels in MR1-dependent presentation of Mycobacterium tuberculosis

infection.

Karamooz E(1)(2), Kim SJ(2)(3), Peterson JC(1), Tammen AE(3), Soma S(2), Soll

ACR(1), Meermeier EW(4), Khuzwayo S(5), Lewinsohn DM(1)(2)(3).

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MR1 is a ubiquitously expressed MHC-Ib molecule that presents microbial

metabolites to MR1-restricted T cells, but there are differences in the antigen

presentation pathway of an intracellular microbe compared to exogenously

delivered antigen. We have shown the importance of endosomal trafficking

proteins in MR1-dependent presentation of Mycobacterium tuberculosis (Mtb)

infection. Two pore channels (TPCs) are endosomal calcium channels that regulate

endosomal trafficking. Due to their location on endosomes, we hypothesized that

TPCs could be required for MR1-dependent presentation of antigens derived from

the intracellular microbe Mtb. We found that TPC1 is critical for the

presentation of Mtb infection by MR1; inhibition of TPCs had no effect on MR1

presentation of exogenously delivered antigens, HLA-B presentation, or HLA-II

presentation. Finally, we found that the calcium-sensitive trafficking protein

Synaptotagmin 7 was also key in the presentation of Mtb infection by MR1. TPC1

and Synaptotagmin 7 may be part of an endosomal pathway by which MR1 can sample

intracellular mycobacterial infections.

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DOI: 10.1371/journal.ppat.1013342

PMID: 40758737 [Indexed for MEDLINE]

**34. Infect Dis (Lond). 2025 Aug 4:1-10. doi: 10.1080/23744235.2025.2533319. Online ahead of print.**

Extraordinarily high incidence rates of tuberculosis among Greenlanders living

in Denmark, 2006-2022.

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Denmark.

**BACKGROUND:** Many Greenlanders move from Greenland, a tuberculosis (TB)

high-incidence country, to Denmark, a TB low-incidence country. Surprisingly,

according to official statistics, the TB incidence among Greenlanders in Denmark

is much higher than in Greenland.

**OBJECTIVES:** This study investigates factors contributing to the extraordinarily

high TB incidence among Greenlanders residing in Denmark.

**METHODS:** Retrospective, register-based cohort study including all Greenlanders

≥18 years notified with TB in Denmark and Greenland, and Danes ≥18 years with TB in Denmark, 2006-2022. Demographic and microbiological characteristics were

compared across groups using parametric and non-parametric statistical tests.

**RESULTS:** The TB incidence was extraordinarily high among Greenlanders in Denmark

(341/100,000; n = 813), compared to Danes in Denmark (2/100,000; n = 1799) and

Greenlanders in Greenland (149/100,000; n = 1088). Additionally, they were more

often part of a TB cluster (75.6%) compared to Danes in Denmark (53.3%) and

Greenlanders in Greenland (64.0%) and demonstrated very high rates of recurrent

TB (23.9%), with 75.6% of cases being reinfections involving new Mycobacterium

tuberculosis strains.

**CONCLUSION:** TB poses a significant public health challenge for Greenlanders in

Denmark. Their high incidence combined with elevated clustering and reinfection

rates suggest substantial active TB transmission, and their cluster distribution

indicates that many infections are locally acquired rather than reactivations of

infection acquired in Greenland. Greenlanders with TB in Denmark are likely part

of a socially marginalised minority with TB high-risk behaviours similar to

Danes developing TB. These findings highlight the need for targeted TB

prevention and control strategies for Greenlanders residing in Denmark.

DOI: 10.1080/23744235.2025.2533319

PMID: 40758341

**35. Cochrane Database Syst Rev. 2025 Aug 4;8(8):CD012768. doi:**

**10.1002/14651858.CD012768.pub4.**

Low-complexity automated nucleic acid amplification tests for extrapulmonary

tuberculosis and rifampicin resistance in adults and adolescents.

Kohli M(1), Inbaraj LR(2), Salomon A(3), Scandrett K(4), Korobitsyn A(5), Ismail

N(5)(6), Srinivasalu VA(7), Daniel J(8), Steingart KR(9), Takwoingi Y(4).

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Update of

doi: 10.1002/14651858.CD012768.pub3.

**BACKGROUND:** Low-complexity automated nucleic acid amplification tests

(LC-aNAATs) are molecular World Health Organization (WHO)-recommended rapid

diagnostic tests widely used for simultaneous detection of Mycobacterium

tuberculosis complex and rifampicin resistance in sputum. To extend our previous

review on extrapulmonary tuberculosis, we performed this update to inform a WHO

policy update.

**OBJECTIVES:** To estimate the diagnostic accuracy of LC-aNAATs for extrapulmonary

tuberculosis and rifampicin resistance in adults and adolescents with

presumptive extrapulmonary tuberculosis.

**SEARCH METHODS:** We searched the Cochrane Central Register of Controlled Trials,

MEDLINE, Embase, Science Citation Index, Latin American Caribbean Health

Sciences Literature, Scopus, ClinicalTrials.gov, the WHO International Clinical

Trials Registry Platform, the International Standard Randomized Controlled Trial

Number Registry, and ProQuest, up to 11 October 2023, without language

restriction. A WHO public call for data was made between 30th November 2023 and

15th February 2024 to identify unpublished studies.

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

non-respiratory specimens and eight forms of extrapulmonary tuberculosis:

tuberculous meningitis and pleural, lymph node, bone or joint, genitourinary,

peritoneal, pericardial, and disseminated tuberculosis. Reference standards were

culture and a study-defined composite reference standard (tuberculosis

detection); and phenotypic drug susceptibility testing with or without genotypic

drug susceptibility testing (rifampicin resistance detection). Index tests

included Xpert Ultra, Truenat assays, STANDARD M10, and Iron qPCR.

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

and assessed the risk of bias and applicability using the QUADAS-2 tool. For

tuberculosis detection, we performed separate analyses by specimen type and

reference standard using the bivariate model to estimate summary sensitivity and

specificity with 95% confidence intervals (CIs). Based on a pre-defined

condition, based on sample sizes and type of technology for performing

class-based analysis, data for Truenat MTB Plus were not included in the

meta-analyses for LC-aNAATs. Hence, we present results for Xpert Ultra and

Truenat MTB Plus separately. We assessed the certainty of evidence using the

GRADE approach.

**MAIN RESULTS:** We included 37 unique studies where 36 studies evaluated Xpert

Ultra and three studies evaluated Truenat MTB plus. We found no eligible studies

for the other index tests. Overall, the risk of bias was low for patient

selection, index test, and flow and timing domains. For the reference standard,

the risk of bias for included studies was low (75%) or unclear (25%).

Applicability for the patient selection domain was unclear for most studies

because we were unsure of the clinical settings, and the applicability concern

was low for most studies for the reference standard domain. Cerebrospinal fluid

Xpert Ultra (16 studies) Xpert Ultra summary sensitivity and specificity (95%

CI) against a microbiological reference standard were 88.2% (83.7 to 91.6) (287

participants; high-certainty evidence) and 96.0% (86.8 to 98.9) (1397

participants; moderate-certainty evidence). Truenat MTB Plus (2 studies) There

were not enough data to meta-analyze, and we have provided descriptive results

for Truenat MTB Plus. The sensitivities in these two studies ranged from 95% to

100% while the specificities ranged from 55% to 100% against a microbiological

reference standard. The sensitivity was 78.7% (70 to 86) and the specificity was

100% (91 to 100) against a composite reference standard from a single study.

Pleural fluid Xpert Ultra (13 studies) Xpert Ultra summary sensitivity and

specificity against a microbiological reference standard were 74.0% (60.8 to

83.9; 264 participants; low-certainty evidence) and 88.1% (78.8 to 93.6; 777

participants; very low-certainty evidence). Truenat MTB Plus (1 study) The

sensitivity was 100% (2.5 to 100) and specificity was 100% (95.3 to 100) against

a microbiological reference standard. Lymph node aspirate Xpert Ultra (6

studies) Xpert Ultra summary sensitivity and specificity (95% CI) against a

composite reference standard were 71.3% (64.3 to 77.4) (243 participants;

moderate-certainty evidence) and 97.4% (82.3 to 99.7) (218 participants; very

low-certainty evidence). Truenat MTB Plus (1 study) The sensitivity and

specificity were 77.1% (66 to 86) and 100% (88 to 100), respectively, against a

microbiological reference standard. The sensitivity was 100% (81 to 100) and

specificity was 56% (45 to 67) against a composite reference standard.

Rifampicin resistance Xpert Ultra (13 studies) Xpert Ultra summary sensitivity

and specificity were 100.0% (93.4 to 100.0; 54 participants; high-certainty

evidence) and 99.4% (92.1 to 100.0; 392 participants; high-certainty evidence).

**AUTHORS' CONCLUSIONS:** LC-aNAATs are helpful in diagnosing extrapulmonary

tuberculosis. Sensitivity varies across different extrapulmonary specimens,

while for most specimens specificity is high, the tests rarely yielding a

positive result for people without tuberculosis. For tuberculous meningitis,

Xpert Ultra had high sensitivity against culture. Xpert Ultra also had high

sensitivity and specificity for rifampicin resistance. Future research should

acknowledge the concern associated with culture as a reference standard in

paucibacillary specimens and consider ways to address this limitation.

Additionally, there is a critical need for robust evidence on other technologies

within the LC-aNAAT class.

FUNDING: Funded by the WHO Global Tuberculosis Program.

REGISTRATION: This is an update to the published review "Xpert MTB/RIF Ultra and

Xpert MTB/RIF assays for extrapulmonary tuberculosis and rifampicin resistance

in adults" via doi: 10.1002/14651858.CD012768.pub3.

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

DOI: 10.1002/14651858.CD012768.pub4

PMCID: PMC12320217

PMID: 40757508 [Indexed for MEDLINE]

**36. Trop Doct. 2025 Aug 4:494755251362076. doi: 10.1177/00494755251362076. Online**

**ahead of print.**

Atypical presentations of cutaneous tuberculosis: A case series of six patients.

Rawat D(1), Malhotra K(2), Nirwal H(3), Verma P(4), Singh U(5), Suvirya S(6).

Author information:

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Cutaneous tuberculosis (CTB), a rare extrapulmonary manifestation of

Mycobacterium tuberculosis, poses a diagnostic challenge owing to its diverse

clinical presentations and paucibacillary nature. We present six atypical cases

diagnosed between January 2022 and January 2025 at a tertiary care centre in

North India. All patients were HIV-negative, with diagnoses confirmed by

histopathology, cartridge-based nucleic acid amplification test (CB-NAAT),

culture, and imaging studies. Unusual manifestations included scrofuloderma of

the hand overlying wrist joint TB, lupus vulgaris with acquired

lymphangiectasia, tubercular gumma mimicking inoculation TB in an

immunocompetent patient, scrofuloderma secondary to rib osteomyelitis,

coexisting papulonecrotic tuberculid with erythema induratum of Bazin, and lupus

vulgaris resembling bacillary angiomatosis. Standard anti-tubercular treatment

(ATT) resulted in clinical resolution in all cases.

DOI: 10.1177/00494755251362076

PMID: 40755039

**37. Front Immunol. 2025 Jul 23;16:1591026. doi: 10.3389/fimmu.2025.1591026.**

**eCollection 2025.**

Antimycobacterial and immunomodulatory activities of sorafenib in a preclinical

mouse model of TB infection through CD4(+)CD25(low) and CD8(+)CD25(low) effector

T cells.

Rajmani RS(1), Surolia A(1)(2).

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Tuberculosis is a communicable disease caused by Mycobacterium tuberculosis

(Mtb). It is one of the major global public health problems that leads to a high

morbidity and mortality rate. Drug resistance in Mycobacterium tuberculosis

(Mtb) is another significant and persistent public health concern. The

development of effective TB vaccines and treatments requires a better

understanding of the intricate interactions between M. tuberculosis and host

immunity. We previously reported that sorafenib (SRB) reduces bacterial growth

by allosterically inhibiting ornithine acetyltransferase (MtArgJ), an essential

enzyme in the arginine biosynthesis pathway of Mtb. Here, we report on the

antimicrobial activity of sorafenib in preclinical mouse models of tuberculosis.

Sorafenib is a potent drug approved by the Food and Drug Administration (FDA)

for treating several types of cancer. The current study is focused on the

immunomodulation that SRB induces in the host, specifically the immunological

response that is triggered to combat the pathogenicity and survival of the

bacteria.Here, we show that SRB significantly sterilizes the bacterial burden in

chronic infection animal models of tuberculosis by reducing the number of

Mtb-susceptible alveolar macrophages (AMs), and that SRB is more effective when

combined with rifampicin (RIF). In the current study, we documented a new immune

modulatory characteristic of sorafenib that, upon SRB treatment, markedly

increased effector T cells (Teff - CD4+CD25low and CD8+CD25low) activity and

decreased regulatory T cells, the immunosuppressive T cells (Treg- CD4+CD25high

and CD8+CD25high) function. In conclusion, our studies revealed that SRB is

beneficial for both boosting an efficient T cell response and lowering the

tubercular load.

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DOI: 10.3389/fimmu.2025.1591026

PMCID: PMC12325335

PMID: 40771802 [Indexed for MEDLINE]

**38. Trans Am Clin Climatol Assoc. 2025;135:269-280.**

REVOLUTIONIZING TUBERCULOSIS REGIMEN DEVELOPMENT.

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Today's first-line tuberculosis regimen was developed in the 1950s to 1970s,

followed by a long period of stagnation. New drugs have progressed to market

only recently, with long timelines from target discovery to clinical trial

success, alongside costly Phase 3 failures. Currently, the tuberculosis drug

development pipeline is robust, containing multiple new chemical entities from

diverse drug classes, motivating us to optimize this opportunity to advance

compounds effectively and efficiently. In this article, we explore how recent

innovations in data integration and computational methods are revolutionizing

tuberculosis drug development, accelerating development timelines, and

heightening the probability of success. We anticipate that these breakthroughs

will lead to approval of novel drugs in unprecedented time frames, marking a

significant milestone in the fight against this age-old disease. This progress

is timely, as resistance to even recently registered drugs is emerging rapidly.

Our hope is that these strategies will also be of value in other medical fields.

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PMCID: PMC12323450

PMID: 40771631 [Indexed for MEDLINE]

**39. BMJ Nutr Prev Health. 2025 Jun 6;8(1):e001213. doi: 10.1136/bmjnph-2025-001213. eCollection 2025.**

Association of serum vitamin D levels and dietary vitamin D intake with latent

tuberculosis infection and long-term mortality: a population-based cohort study.

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Taiwan.

**BACKGROUND:** Vitamin D plays a crucial role in immune function and respiratory

infections, yet its association with latent tuberculosis infection (LTBI) and

long-term mortality remains unclear. This study investigates the relationship

between serum 25-hydroxyvitamin D levels, dietary vitamin D intake, LTBI risk

and mortality.

**METHOD:** We analysed data from the 2011-2012 cycle of the US National Health and

Nutrition Examination Survey, including 5286 adults (≥18 years) who underwent

tuberculosis (TB) testing. Serum 25-hydroxyvitamin D levels were measured using

high-performance liquid chromatography-tandem mass spectrometry, and dietary

vitamin D intake was assessed via a 24-hour dietary recall. LTBI was defined as

an induration>10 mm on the Tuberculin Skin Test or a positive QuantiFERON-TB

Gold-In-Tube test. Mortality data were obtained through linkage with the

National Death Index, with follow-up until 31 December 2019.

**RESULTS:** Among 5286 participants, 708 (13.4%) had LTBI. Individuals with LTBI

had significantly lower serum 25-hydroxyvitamin D levels than those without

LTBI. A 10 nmol/L increase in serum 25-hydroxyvitamin D was associated with a 5%

lower risk of LTBI (adjusted OR: 0.95, 95% CI: 0.92 to 0.99, p<0.05). Among LTBI

participants, low serum 25-hydroxyvitamin D levels (<50 nmol/L) were

independently associated with a higher risk of all-cause mortality (adjusted HR:

3.45, 95% CI: 1.33 to 8.90, p<0.05). However, dietary vitamin D intake was not

significantly associated with LTBI risk or long-term mortality.

**CONCLUSION:** Vitamin D deficiency was associated with an increased risk of LTBI

and long-term mortality in this population-based study. Although adequate serum

25-hydroxyvitamin D levels were linked to more favourable outcomes, the role of

vitamin D supplementation in individuals with TB infection remains uncertain.

Further research is needed to clarify these associations and guide

evidence-based supplementation strategies for TB prevention and management.

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DOI: 10.1136/bmjnph-2025-001213

PMCID: PMC12322562

PMID: 40771511

**40. JAMA Netw Open. 2025 Aug 1;8(8):e2525207. doi:**

**10.1001/jamanetworkopen.2025.25207.**

Integrating Early Tuberculosis States Into Contact Management in Peru.

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**IMPORTANCE:** Tuberculosis (TB) is now understood to exist on a spectrum from TB

infection to active TB disease. While World Health Organization guidelines

target TB infection and TB disease, they overlook individuals with early TB in

the middle of this spectrum.

**OBJECTIVE:** To evaluate chest radiograph (CR)-guided screening strategies among

household contacts (HHCs) of patients with TB in a high-burden setting.

**DESIGN, SETTING, AND PARTICIPANTS:** This decision analytical model was

constructed from June 1 to November 31, 2024. Community-based care in an

environment with high TB burden and limited resources was used as the setting in

Lima, Peru. Participants included a hypothetical cohort of 1000 HHCs with

positive results of a tuberculin skin test and negative results of a sputum

culture who were cleared of TB disease based on a clinician's evaluation. The

hypothetical cohort was based on the clinical and demographic features of a

cohort studied between September 1, 2009, and August 29, 2012.

**INTERVENTIONS:** Strategy 1 included CR screening to rule out TB disease followed

by TB preventive therapy for all; strategy 2, CR screening with treatment for TB

disease for those with abnormal CR findings and TB preventive therapy for those

without; and strategy 3, observation without pharmacological intervention. We

modeled 6 intervention scenarios by applying strategies 1 and 2 to the entire

HHC population, to HHCs younger than 35 years, and to HHCs younger than 19 years

(Peru's national TB policy).

**MAIN OUTCOMES AND MEASURES:** TB cases averted, serious adverse events (SAEs), and

drug resistance.

**RESULTS:** A simulated cohort of 1000 HHCs with age and clinical status

distributions was based on a previously published cohort of 12 767 TB HHCs in

Lima, Peru. Of these, 7661 (60.0%) were male, 4212 (33.0%) were younger than 15

years, and 444 (3.4%) developed TB during 1 year of follow-up. Strategy 2

applied to all HHCs reduced TB cases by 71% to 81%, outperforming strategy 1

applied to all HHCs, which reduced cases by 49% to 69%. Strategy 2 reduced

acquired isoniazid resistance but increased SAEs. When both strategies were

restricted to HHCs younger than 19 years, strategy 2 reduced TB cases by 42% to

50%. Expanding treatment to older adults further reduced cases but also

increased SAEs (19-22 additional SAEs).

**CONCLUSIONS AND RELEVANCE:** In this model of TB HHC management, CR-guided

identification and treatment of early TB was more effective than universal

isoniazid preventive therapy, especially in children and young adults.

Trade-offs between benefit and harm must be carefully considered in older

adults.

DOI: 10.1001/jamanetworkopen.2025.25207

PMID: 40768149 [Indexed for MEDLINE]

**41. Res Sq [Preprint]. 2025 Jul 31:rs.3.rs-5046392. doi:**

**10.21203/rs.3.rs-5046392/v1.**

Small-world challenges and solutions identified by mid-level managers within a

decentralised healthcare system during a qualitative sub-study of a

tuberculosis-prevention therapy rollout intervention in Uganda: "When a big drum

like the District Health Officer talks".

Johnson-Peretz J, Christian C, Akatukwasa C, Atwine F, Kamya MR, Havlir DV,

Chamie G, Camlin CS, Kakande E.

**Background** Decentralisation policies that devolve certain administrative and

decision-making powers to local levels can pose challenges for public health and

healthcare systems. For a decentralised health system to function optimally,

mid-level systems must rely on tightly clustered, so-called "small-world"

networks to efficiently scale-up national health campaigns and share best

practices. Few studies have qualitatively tackled the mechanisms of small-world

creation and their potential effects on public health promotion during

centralized national campaigns in a decentralised, mid-level healthcare system

tier. **Methods** We performed a thematic analysis using a rigorous and accelerated

data reduction (RADaR) technique on 23 in-depth interviews and six focus group

discussions with mid-level healthcare managers in a cluster-randomised trial

from 2019 to 2021, whose intervention component aimed to increase isoniazid

preventive therapy (IPT) uptake to prevent tuberculosis among people living with

HIV in Uganda. **Results** Training mid-level managers on management and leadership

skills fostered the creation of small-world networks within a decentralised

healthcare context and promoted mid-level manager agency to address several

drawbacks associated with the decentralisation of healthcare systems. Through

improved communication, intervention groups encouraged teamwork within their

districts, building a denser cluster of networks. This in turn fostered small

world ties that paired transparency with a sense of reciprocal accountability

moving in multiple directions, upwards to the Ministry of Health (MoH),

downwards towards local communities, and horizontally towards peers. **Conclusions**

Increased collaboration demonstrably strengthened the clustering of small-world

network ties at a horizontal level to disseminate knowledge of best practices

more quickly and efficiently in promoting the uptake of IPT while ensuring

accountability to peers, the MoH, and local communities, sustaining these levels

after a centralized national campaign ended. Trial registration NCT03315962.

Registered 20 October, 2017.

DOI: 10.21203/rs.3.rs-5046392/v1

PMCID: PMC12324578

PMID: 40766233

**42. Res Sq [Preprint]. 2025 Jul 29:rs.3.rs-7086994. doi:**

**10.21203/rs.3.rs-7086994/v1.**

Multicohort assessment of plasma metabolic signatures of tuberculosis disease in

children.

Nellis MM, Luiz J, Jaganath D, Mousavian Z, Nkereuwem E, Wambi P, Calderon R,

Paradkar M, Castro R, Nerurkar R, Franke MF, Kinikar A, Wobudeya E, Zar HJ,

Segal M, Sigal G, Swaney DL, Cattamanchi A, Ernst JD, Ziegler TR, Kampmann B,

Collins JM.

Current microbiological tests for tuberculosis (TB) disease in children have

suboptimal accuracy and rely on respiratory samples which may be challenging to

obtain. We sought to use high-resolution metabolomics (HRM) to identify

blood-based biomarkers associated with TB disease in children. We analyzed

plasma samples from 438 children 0-14 years being evaluated for TB disease in

India, Peru, Uganda, The Gambia, and South Africa. All children underwent a

standard clinical evaluation and were followed up after 3 months. Children were

classified as Confirmed (n = 104), Unconfirmed (n = 108), or Unlikely TB

(n = 226) as per NIH consensus definitions. We used liquid chromatography/mass

spectrometry for HRM analysis of plasma samples. Differentially regulated

metabolic pathways in children with confirmed versus unlikely TB in at least

three of the five countries included purine, linoleate, arginine and proline,

aspartate and asparagine, and tryptophan metabolism. Controlling for age and

study site, we found creatine, alanine, retinol, citrulline, fumarate, and

tryptophan to be significantly decreased in children with Confirmed TB disease

versus those with Unlikely TB, while cortisol, nicotinamide, and

butyrylcarnitine were increased (FDR-corrected p-value < 0.2). Using logistic

regression, we found this nine-metabolite signature had an area under the

receiver operator characteristic curve (AUC) of 0.72 in the test set of

participants with Confirmed and Unlikely TB and an AUC of 0.49 in the

Unconfirmed TB group. Of the five cohorts examined, the model performed best

among Indian children with Confirmed TB (AUC = 0.84). These results show a

nine-metabolite plasma signature has moderate accuracy for identification of

Confirmed TB disease in children and could potentially be combined with other

non-sputum biomarkers to inform future TB diagnostics.

DOI: 10.21203/rs.3.rs-7086994/v1

PMCID: PMC12324607

PMID: 40766222

**43. Intest Res. 2025 Jul;23(3):231-232. doi: 10.5217/ir.2025.00117. Epub 2025 Jul 29.**

Assessing tuberculosis risk in Crohn's disease patients receiving biologic

therapies: real-world insights from Japan.

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Comment on

Intest Res. 2025 Jul;23(3):309-317. doi: 10.5217/ir.2024.00076.

DOI: 10.5217/ir.2025.00117

PMID: 40764876

**44. J Infect Public Health. 2025 Jul 24;18(11):102913. doi:**

**10.1016/j.jiph.2025.102913. Online ahead of print.**

Characteristics and prognostic factors of TB loss to follow up (LTFU) in

Malaysia - A 5-year retrospective cohort from 2014 to 2018.

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**BACKGROUND:** Tuberculosis (TB) loss to follow-up (LTFU) disrupts treatment,

compromises patient outcomes, and exacerbates public health challenges. This

study evaluates the prevalence, time to LTFU, and prognostic factors of TB LTFU

among adults in Malaysia between 2014 and 2018.

**METHODS:** A retrospective cohort analysis was conducted using national data from

the MyTB database, comprising 97,542 TB patients. Kaplan-Meier analysis

determined the time to LTFU, while Cox proportional hazards analysis identified

significant prognostic factors.

**RESULTS:** The prevalence of TB LTFU decreased from 7.09 % in 2014 to 5.71 % in

2018. The mean time to LTFU was 54.8 days during intensive phase and 162.5

during continuation phase. Significant risk factors for LTFU included age < 65

years, male gender, urban residence, smoking, diabetes, and initiation of

treatment at government facilities. Notably, the absence of Directly Observed

Therapy (DOT) during the continuation phase markedly increased LTFU risk

(adjusted HR 33.18; 95 % CI: 31.02-35.48).

**CONCLUSION:** Despite a declining trend in TB LTFU prevalence, younger age, urban

residence, and lack of DOT during continuation remain key challenges.

Strengthening DOT implementation and targeted interventions for at-risk groups

are crucial for reducing TB LTFU and improving treatment adherence.

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DOI: 10.1016/j.jiph.2025.102913

PMID: 40763456

**45. Front Vet Sci. 2025 Jul 21;12:1620497. doi: 10.3389/fvets.2025.1620497.**

**eCollection 2025.**

Protection and diagnostic interference induced by heat-inactivated,

phage-inactivated and live vaccine prototypes against animal tuberculosis.

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**INTRODUCTION:** Vaccination emerges as a promising cost-effective tool to reduce

the impact and spread of animal tuberculosis, especially in regions where

test-and-slaughter eradication strategy is socioeconomically unfeasible or

unfruitful for different reasons, provided it is safe, efficacious and

compatible with diagnosis.

**METHODS:** In this study, we preliminarily evaluated the diagnostic interference

(using guinea pigs) and the protective efficacy (using mice) of three

heat-inactivated, three phage-inactivated and one live attenuated vaccine

prototypes prepared from M. bovis, M. caprae, and M. microti.

**RESULTS AND DISCUSSION:** Phage-inactivation killed almost all (96.41-99.92%)

bacteria to be included in vaccines and filtering was used to remove the

remaining viable cells. All the assayed vaccines induced skin test reactions in

response to bovine tuberculin, but they were smaller in the phage-inactivated

vaccine groups. All the vaccines were diagnosis-compatible with defined skin

test antigens based on ESAT-6, CFP-10, and Rv3615c. In contrast with the rest of

prototypes, vaccination with heat- and phage-inactivated M. microti did not

prompt the production of detectable anti-MPB70+MPB83 antibodies. Mean bacterial

burden was lower in all vaccinated groups in comparison with the control, being

significantly reduced in the lungs of the heat-inactivated M. microti and M.

caprae and phage-inactivated M. caprae groups. Considering both diagnostic

interference and protection collectively, the heat-inactivated M. microti

vaccine showed the best performance. Further studies to evaluate these vaccines

and to improve phage-driven inactivation are warranted.

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Elguezabal, Serrano-Mestre, Vázquez-Iniesta, Prados-Rosales, Michelet,

Boschiroli, Pérez de Val, Jones, Juste, Garrido and Sevilla.

DOI: 10.3389/fvets.2025.1620497

PMCID: PMC12320537

PMID: 40761839

**46. Front Immunol. 2025 Jul 21;16:1593263. doi: 10.3389/fimmu.2025.1593263.**

**eCollection 2025.**

MetE: a promising protective antigen for tuberculosis vaccine development.

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**INTRODUCTION:** Tuberculosis (TB), caused by Mycobacterium tuberculosis (MTB),

remains a significant global health concern. The existing vaccine, Bacillus

Calmette-Guérin (BCG), provides inconsistent protection, highlighting the

pressing need for a more effective vaccine. We aimed to identify novel MTB

antigens and assess their protective efficacy as TB vaccine candidates.

**METHODS:** Using immunopeptidomics, we identified 64 and 80 unique mycobacterial

antigens derived from BCG and MTB, respectively. We prioritised antigens based

on HLA allele coverage through an immunoinformatics approach.

**RESULTS:** The candidates, hisD, metE, and mmpL12, delivered as DNA vaccines, were

evaluated for efficacy in mice using the ex vivo Mycobacterial Growth Inhibition

Assay (MGIA) and metE was identified as a promising candidate. In vivo murine

MTB challenge experiments confirmed the protective efficacy conferred by metE

when formulated as recombinant protein with AS01™ or AddaS03™ adjuvants,

compared to the naïve group. The immunogenic profiles of metE formulated in the

two different adjuvants differed, with metE-AS01™ inducing antigen-specific

IFN-γ, TNF-α, IL-2, IL-17, IgG1 and IgG2a-c, while metE-AddaS03™ induced TNF-α, IL-2, IL-17, IL-4, IgM, IgG1, IgG2b.

**CONCLUSION:** Our findings highlight metE as a promising protective antigen for

future TB vaccine development.

Copyright © 2025 Almujri, Stylianou, Nicastri, Satti, Korompis, Li, De Voss,

Polo Peralta Alvarez, Tanner, Bettencourt, Ternette and McShane.

DOI: 10.3389/fimmu.2025.1593263

PMCID: PMC12319054

PMID: 40761798 [Indexed for MEDLINE]

**47. AME Case Rep. 2025 Jun 6;9:76. doi: 10.21037/acr-24-211. eCollection 2025.**

A case report of long-segment tuberculous myelitis with concomitant tuberculous

meningitis.

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**BACKGROUND:** Tuberculous myelitis is a form of central nervous system

tuberculosis (TB) that can be associated with intracranial involvement but

rarely presents with extensive longitudinal involvement of more than one

segment. We are reporting a case with tuberculous meningitis and long-segment

myelitis in a previously undiagnosed patient with TB.

**CASE DESCRIPTION:** A 53-year-old hypertensive male, presented with subacute lower

limbs weakness, sensory level below his nipples, and urine retention.

Erythrocyte sedimentation rate (ESR) was above 112 mm/hour. Magnetic resonance

imaging (MRI) spine showed a long segment of hyperintense signal seen on the

T2-weighted image (T2WI) images in the spinal cord extending from C6 to D3

vertebral segments, with heterogeneous post-contrast enhancement. Cerebrospinal

fluid (CSF) analysis showed lymphocytic pleocytosis with high protein and low

glucose, and polymerase chain reaction (PCR) for Mycobacterium tuberculosis

(MBTB) was positive. The patient received intravenous methylprednisolone daily

for 5 days and standard anti-TB medications [rifampicin, isoniazid (INH),

pyrazinamide, and ethambutol] for 12 months. However, repeated CSF analysis 3

months after starting anti-TB medications showed a negative PCR for MBTB, normal

cell count, and glucose with slightly elevated protein. Still, the patient did

not show any clinical improvement.

**CONCLUSIONS:** Long-segment tuberculous myelitis (LSTM) is a rare form of central

nervous system TB that can be accompanied by tuberculous meningitis. It must be

considered a differential diagnosis of neuromyelitis optica spectrum disorder

(NMOSD), especially in endemic areas of TB, as the management approach is

completely different.

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DOI: 10.21037/acr-24-211

PMCID: PMC12319586

PMID: 40761219

**48. Brain Behav. 2025 Aug;15(8):e70665. doi: 10.1002/brb3.70665.**

Improving Treatment Adherence in Youths With Multidrug-Resistant Tuberculosis

With Psychosocial Intervention.

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**INTRODUCTION:** Multidrug-resistant tuberculosis (MDR-TB) deeply impacts the

well-being of adolescents and young adults (AYA), resulting in poor treatment

adherence. Identifying psychosocial challenges and preferred interventions is

essential to enhance treatment adherence and outcomes in this unique group.

**METHODS:** This was a mixed-method study where participants aged between 15 and 24

years, diagnosed with MDR-TB, were recruited for in-depth interviews and a

semi-structured questionnaire.

**RESULTS:** The individual-level psychosocial challenges included mental stress,

suicidal ideation, reluctance to continue medication, perceived and experienced

stigma, and socio-economic burdens. Health system-related challenges encompassed

delayed diagnosis, drug stockouts, and negative experiences with Health Care

Providers (HCPs). Among 75 participants, the median age was 20.5 years, with 57%

(n = 41) females, 85% (n = 62) single, and a median treatment duration of 8

months at the interview. Seventy-two percent (n = 54) of the participants

reported psychological issues such as irritation, loneliness, anxiety, sleep

disorder, suicidal ideation, and stigma. Individual-level interventions were

preferred by 61% (n = 46) of participants, including social media, deep

breathing, and exercise training.

**CONCLUSIONS:** To enhance results in MDR-TB, it is crucial to develop and assess

personalized psychosocial interventions with tailored adjustments to tackle the

psychosocial obstacles encountered by adolescents and young adults with MDR-TB.

© 2025 The Author(s). Brain and Behavior published by Wiley Periodicals LLC.

DOI: 10.1002/brb3.70665

PMCID: PMC12321948

PMID: 40760794 [Indexed for MEDLINE]

**49. J Microbiol Immunol Infect. 2025 Jul 30:S1684-1182(25)00148-3. doi:**

**10.1016/j.jmii.2025.07.013. Online ahead of print.**

Active drug-safety monitoring and management in the treatment of

rifampicin-resistant tuberculosis: a nationwide multicenter prospective study.

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**BACKGROUND:** Active tuberculosis drug-safety monitoring and management (aDSM) is

recommended in the treatment of rifampicin-resistant tuberculosis. We

established comprehensive aDSM and conducted a nationwide multicenter

prospective study in Taiwan.

**METHODS:** We designed a treatment initiation form to capture characteristics of

patients at baseline, a treatment review form to monitor symptoms, blood tests,

QT intervals, and audiometry during treatment, and an adverse event report form

for reporting severe adverse events (grade 3 or more), serious adverse events

and adverse events resulting in discontinuation of anti-tuberculosis drugs.

Severity of adverse events were categorized by using Common Terminology Criteria

for Adverse Events v4.03, and causality was assessed by using the World Health

Organization - Uppsala Monitoring Centre system.

**RESULTS:** Of 333 patients with rifampicin-resistant tuberculosis enrolled from

May 2017 to February 2020, 329 (98.8 %) had adverse events and 196 (58.9 %) had

severe adverse events during treatment. The top three severe adverse events were

metabolism disorders (104, 31.2 %), hearing impairment (102, 30.6 %), and

hepatotoxicity (64, 19.2 %). Of 403 severe adverse events reported, 284 (70.5 %)

were classified as drug-related. The top five drugs associated with severe

adverse events were bedaquiline (27.6 %), clofazimine (26.7 %), kanamycin

(25.1 %), pyrazinamide (22.4 %) and linezolid (22.2 %). Forty-four (13.2 %)

patients were hospitalized and 15 (4.5 %) had prolonged hospitalization due to

adverse events. One death was considered drug-related.

**CONCLUSION:** Severe adverse events in the treatment of rifampicin-resistant

tuberculosis were more frequent than previously reported and needed to be

closely monitored and timely managed by systematic and comprehensive aDSM.

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DOI: 10.1016/j.jmii.2025.07.013

PMID: 40759626

**50. Arq Neuropsiquiatr. 2025 Jul;83(7):1-6. doi: 10.1055/s-0045-1810406. Epub 2025 Aug 4.**

Active tuberculosis and multiple sclerosis: the importance of screening before

treatment.

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Tuberculosis (TB), a chronic infection caused by the Mycobacterium tuberculosis

complex, has an increased risk of reactivation in conditions that affect the

immune system, such as MS, and its treatment with disease-modifying drugs

(DMDs). The present is a retrospective study of 2,036 patients diagnosed with MS

followed at the Department of Neurology and Neurosurgery of Escola Paulista de

Medicina, Universidade Federal de São Paulo, from February 1994 to September

2023. Of that total, 6 were included in this case series, taking different DMDs:

fingolimod (n = 2), interferon beta 1a (n = 2), glatiramer acetate (n = 1) and

cyclophosphamide (n = 1). In our study, two patients experienced worsening

disability during tuberculosis treatment, while three others had increased

disability after completing treatment. We reinforce the importance of screening

all patients eligible for DMD treatment, especially the highly effective modern

ones, and the importance of developing research-based guidelines for screening

infectious diseases among patients with MS.

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DOI: 10.1055/s-0045-1810406

PMCID: PMC12321418

PMID: 40759404 [Indexed for MEDLINE]

**51. Microbiology (Reading). 2025 Aug;171(8):001583. doi: 10.1099/mic.0.001583.**

Engineering the TCA cycle regulator GarA to increase erythromycin production in

Saccharopolyspora erythraea.

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Actinobacteria are important for industrial production of antibiotics, fine

chemicals and food and a source of new compounds for drug discovery. Their

central metabolism is regulated by a conserved protein GarA that is unique to

the Actinobacteria and has been studied in Mycobacterium tuberculosis and

Corynebacterium glutamicum. GarA regulates the TCA cycle and glutamate

metabolism by direct binding to enzymes to modulate their activity on glutamate

and alpha-ketoglutarate. Given the importance of the TCA cycle in the synthesis

of acyl-CoA precursors for antibiotic biosynthesis, and increasing evidence for

the role of nitrogen regulators in control of secondary metabolism, we

hypothesized that engineering GarA could be used to enhance production of

valuable metabolites. His6-tagged GarA was introduced into Saccharopolyspora

erythraea, an overproducer of the polyketide antibiotic erythromycin.

Phosphorylation of GarA was detected at the N-terminal ETTS motif, suggesting

that it is regulated by protein kinases like in M. tuberculosis. GarA expression

was observed at all growth stages, and a truncated form lacking the

phosphorylation site accumulated during late fermentation. Engineered S.

erythraea expressing phosphoablative GarA produced twofold more erythromycin,

both in standard fermentation broth and in minimal medium. To investigate the

mechanism for the increased titre, the engineered strain was characterized for

transcription of erythromycin biosynthetic genes, as well as its ability to

metabolize glutamate and its intracellular and extracellular aa content. The

observed alterations in aa metabolism are consistent with the role of GarA as a

TCA cycle regulator that may influence precursor supply for polyketide

biosynthesis.

DOI: 10.1099/mic.0.001583

PMCID: PMC12321487

PMID: 40758561 [Indexed for MEDLINE]

**52. Reports (MDPI). 2024 Sep 24;7(4):82. doi: 10.3390/reports7040082.**

Tuberculosis-Induced Immune-Mediated Necrotizing Myopathy: A Challenging Case

Scenario in a Non-Endemic Country.

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**Background and Clinical Significance:** Tuberculosis (TB) poses a significant

global health challenge; although low-middle income countries carry the heaviest

burden, its diagnosis and treatment can be challenging in any country. The

clinical picture can be complex and vary from person to person, with autoimmune

complications that can hinder TB diagnosis and treatment. Case Presentation: We

report the case of a 38-year-old man from Bangladesh who had recently arrived in

Italy through the Balkan route. He presented with TB in the cervical lymph nodes

and long-standing chronic myalgias. While a wide range of TB-triggered

autoimmune entities can be found in the literature, this case is the first to

describe immune-mediated necrotizing myopathy (IMNM) triggered by active TB.

**Conclusions:** IMNM has been previously associated only with other infections like

SARS-CoV-2 and Dengue. The successful diagnosis and management of TB-induced

IMNM was achieved through a collaborative, multidisciplinary approach involving

rheumatologists, immunologists, and infectious diseases specialists, showcasing

an innovative treatment strategy and adding new insights into the complexities

of TB and IMNM.

DOI: 10.3390/reports7040082

PMCID: PMC12199865

PMID: 40757675

**53. ACG Case Rep J. 2025 Aug 1;12(8):e01777. doi: 10.14309/crj.0000000000001777.**

**eCollection 2025 Aug.**

Successful Use of Corticosteroids to Accelerate Recovery in Severe

Autoimmune-like Hepatitis From Isoniazid.

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Drug-induced autoimmune-like hepatitis represents a distinct phenotype of

drug-induced liver injury characterized by clinical, biochemical, and/or

histological features resembling autoimmune hepatitis. We present a case of

severe Isoniazid (INH) -induced drug-induced autoimmune-like hepatitis in a

62-year-old man with a dramatic response to corticosteroid therapy after INH

discontinuation alone proved insufficient. Initial laboratory tests showed

markedly elevated transaminases and profound hyperbilirubinemia. Despite INH

discontinuation, his clinical condition did not improve. Liver biopsy revealed

severe acute hepatitis with interface hepatitis, lymphoplasmacytic infiltration,

and multiple foci of lobular confluent necrosis. Prednisone therapy led to rapid

clinical improvement and normalization of liver biochemistries over 3 months.

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American College of Gastroenterology.

DOI: 10.14309/crj.0000000000001777

PMCID: PMC12316346

PMID: 40757080

**54. Urol Case Rep. 2025 Jul 23;62:103136. doi: 10.1016/j.eucr.2025.103136.**

**eCollection 2025 Sep.**

Difficulties in diagnosing genitourinary tuberculosis: A case of delayed

diagnosis resulting in nephrectomy.

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Genitourinary tuberculosis (GUTB) is a rare infectious disease, yet delays in

diagnosis can lead to serious complications. This study presents a case of GUTB

in which diagnosis was delayed due to negative conventional laboratory tests,

ultimately necessitating nephrectomy at an advanced stage. Initially, the

symptoms mimicked a urinary tract infection, which resulted in progressive renal

damage. The diagnostic challenges and treatment approaches are discussed in

light of the current literature through this case.

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DOI: 10.1016/j.eucr.2025.103136

PMCID: PMC12318259

PMID: 40756378

**55. Case Rep Pulmonol. 2025 Jul 27;2025:9939815. doi: 10.1155/crpu/9939815.**

**eCollection 2025.**

Visual Recovery Following Linezolid Cessation in an MDR-TB Patient: Detailed

Case Analysis.

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Multidrug-resistant tuberculosis (MDR-TB) is characterized by resistance to at

least isoniazid and rifampicin. Linezolid is an antibiotic used for

drug-resistant Gram-positive bacteria and is a treatment option for MDR-TB.

However, its use is associated with optic neuropathy, presenting as acute

worsening and bilateral vision loss, typically within 4 months of therapy. A

47-year-old male with MDR-TB relapsed during the sixth month of an

individualized treatment regimen at Dr. Soetomo General Academic Hospital,

Surabaya. The patient presented with weakness and anemia, receiving a regimen

including levofloxacin (750 mg), linezolid (600 mg), clofazimine (100 mg), and

cycloserine (500 mg). In the ninth month, the patient developed visual

disturbances, initially suspected to be caused by an intracranial tumor. Despite

various examinations and treatments, there was no improvement until linezolid

was discontinued. The patient's visual complaints gradually improved following

the cessation of linezolid therapy. This case underscores the potential for

linezolid to cause optic neuropathy during prolonged treatment for MDR-TB.

Detailed ophthalmologic examinations, including optical coherence tomography

(OCT) and magnetic resonance imaging (MRI), confirmed optic neuropathy without

intracranial pathology. Despite high-dose steroid therapy, the patient's vision

improved only after 1 month since discontinuing linezolid. This highlights the

importance of monitoring for ocular toxicity in patients undergoing long-term

linezolid therapy and suggests that timely intervention can prevent permanent

visual impairment. The case demonstrates the reversible nature of

linezolid-induced optic neuropathy upon drug cessation and emphasizes the need

for regular ophthalmologic assessments in patients receiving prolonged linezolid

treatment. This report contributes to the understanding of the adverse effects

of linezolid and underscores the importance of vigilant monitoring and

alternative therapeutic strategies for MDR-TB.

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by John Wiley & Sons Ltd.

DOI: 10.1155/crpu/9939815

PMCID: PMC12318621

PMID: 40756245

**56. J Prev Med Hyg. 2025 May 31;66(1):E67-E74. doi:**

**10.15167/2421-4248/jpmh2025.66.1.3233. eCollection 2025 Mar.**

The burden of Tuberculosis in a province of a low incidence country:

epidemiological differences between Italy-born, regular foreigner and irregular

foreigner TB cases.

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**INTRODUCTION:** Tuberculosis (TB) represent a serious public health issue even in

most developed countries, where TB cases are mostly concentrated in some risk

groups, like immigrants from high-incidence TB countries. Aim of the study was

to describe the occurrence of TB in Siracusa Local Health Authority (Italy) and

to explore its determinants in three different populations: Italy-born, regular

foreigner and irregular foreigner.

**METHODS:** Cases were classified per patient origin and legal ground: Italy-born

(IB); regular foreigners (REF); irregular foreigners (IRF). All the

notifications were evaluated and uploaded to the Notification System of

Infectious Diseases (PREMAL) by the Epidemiology Unit of the Prevention

Department of Siracusa LHA.

**RESULTS:** During the study period, 183 TB cases were detected: 72 (39.3%) were

Italy-born, 26 (14.2%) were regular foreigners and 85 (46.5%) were irregular

foreigners. Overall, foreign-born cases (regularly and irregularly residents)

accounted for 60.7% of all cases. We demonstrated significative differences in

epidemiological, demographic and clinical features among the three different

groups.Furthermore, we registered a decrease in TB notifications of 59.5% among

Italy-born patients, 46.0% among regular foreigners and 95.5% among irregular

foreigners, who, however, remain the population group with the highest incidence

of tuberculosis in Siracusa LHA.

**CONCLUSIONS:** TB control in migrants is considered key to achieving TB

elimination in low TB incidence countries, in accordance with the World Health

Organization (WHO)'s End TB Strategy, that set ambitious targets for 2020-2035,

including 90% reduction in TB incidence and 95% reduction in TB deaths by 2035,

compared with 2015.

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DOI: 10.15167/2421-4248/jpmh2025.66.1.3233

PMCID: PMC12312716

PMID: 40756190 [Indexed for MEDLINE]

**57. J Prev Med Hyg. 2025 May 31;66(1):E145-E152. doi:**

**10.15167/2421-4248/jpmh2025.66.1.3465. eCollection 2025 Mar.**

Historical and Social Considerations upon Tuberculosis.

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The present article offers a concise perspective on tuberculosis (TB) ranging

from antiquity to the present day and highlights the dangerousness of the

disease in the light of its historical manifestations and current antibiotic

resistance. Reflections on the social and economic impact of tuberculosis are

presented together with notes on TB's interplay with malnutrition and the social

stigma linked to this disease in modern times. Different types of evidence from

palaeopathological to artistic ones are offered and the need for a more

comprehensive understanding on the disease's history and evolution is stressed.

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DOI: 10.15167/2421-4248/jpmh2025.66.1.3465

PMCID: PMC12312709

PMID: 40756185 [Indexed for MEDLINE]

**58. Clin Case Rep. 2025 Aug 1;13(8):e70710. doi: 10.1002/ccr3.70710. eCollection**

**2025 Aug.**

Pulmonary Tuberculosis Presenting as Bronchogenic Carcinoma in a Young Ghanaian

Adult: A Case Report and Review of the Literature.

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Tuberculosis is an infectious disease that primarily affects the lungs and can

pose diagnostic challenges to physicians. This case report discusses a

23-year-old male who initially presented with signs suggestive of lung

carcinoma. A pleural biopsy done confirmed a TB-related right pleura necrotizing

granuloma that responded well to anti-TB medications.

© 2025 The Author(s). Clinical Case Reports published by John Wiley & Sons Ltd.

DOI: 10.1002/ccr3.70710

PMCID: PMC12317100

PMID: 40756078

**59. PeerJ. 2025 Jul 29;13:e19736. doi: 10.7717/peerj.19736. eCollection 2025.**

Factors associated with incomplete latent tuberculosis infection preventive

treatment in Sabah, Malaysia.

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**BACKGROUND:** Latent tuberculosis infection (LTBI) is a critical public health

issue in Malaysia, particularly in regions like Sabah, where the incidence of

tuberculosis (TB) remains high. LTBI can progress to active TB if left

untreated, making preventive treatment essential in reducing TB transmission.

However, adherence to LTBI preventive treatment remains a significant challenge,

with incomplete treatment potentially undermining efforts to control TB. This

study aimed to determine the proportion of individuals with LTBI who did not

complete preventive treatment and to identify associated factors.

**METHODS:** A retrospective record review was conducted among individuals with LTBI

registered in the Sabah State Health Department's LTBIS 401A registry. Multiple

logistic regression analyses were applied to determine the factors associated

with incomplete preventive treatment.

**RESULTS:** A total of 895 individuals with LTBI were included in the study. The

proportion of incomplete LTBI preventive treatment was 9.2%. Factors that were

significantly associated with the incomplete preventive treatment were non-HCW

occupation (adj.OR = 4.21, 95 CI [1.25-14.22]), residents of Tawau Division

(adj.OR = 2.00, 95% CI [1.10-3.65]), and individuals with LTBI without contact

to TB patients (adj.OR = 2.79, 95% CI [1.42-5.48]).

**CONCLUSION:** The proportion of incomplete preventive treatment among individuals

with LTBI in Sabah was comparatively lower than many previous studies. Targeted

interventions should be developed to address the specific needs of the groups

with higher odds of having incomplete preventive treatment. It includes tackling

the social determinants of health, like improving healthcare system

accessibility. A prospective study to evaluate these interventions'

effectiveness in improving preventive treatment completion rate is recommended.

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DOI: 10.7717/peerj.19736

PMCID: PMC12315825

PMID: 40755793 [Indexed for MEDLINE]

**60. Cureus. 2025 Jul 3;17(7):e87220. doi: 10.7759/cureus.87220. eCollection 2025**

**Jul.**

An Unfortunate Case of Tuberculous Meningitis in a 25-Year-Old Primigravida in

the Postpartum Period.

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Tuberculosis remains a significant global health concern, with substantial

diagnostic challenges in extrapulmonary tuberculosis, particularly in vulnerable

states like pregnancy and the postpartum period. The postpartum period is

associated with significant immunomodulation that can predispose women to

reactivation or progression of tuberculosis. A healthy 25-year-old woman who

presented to the obstetrics and gynaecology department with premature rupture of

membranes, delivered vaginally while being on conservative management. In

the postpartum period, she developed high-grade fever with chills and headache,

which progressed to altered sensorium and diplopia. The patient

underwent imaging and lumbar puncture after informed consent and was diagnosed

with tubercular meningitis. TB can present with non-specific symptoms.

Recognition of risk factors for TB is crucial for prompt diagnosis and treatment

of this deadly disease.

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DOI: 10.7759/cureus.87220

PMCID: PMC12317423

PMID: 40755577

**61. Patient Prefer Adherence. 2025 Jul 28;19:2213-2226. doi: 10.2147/PPA.S520341.**

**eCollection 2025.**

Emerging Research Trends on Medication Adherence in Tuberculosis Treatment: A

Bibliometric Study of Research Between 2015 and 2024 to Inform Future Research

Trajectory.

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**INTRODUCTION:** Current knowledge regarding tuberculosis (TB) medication adherence

largely stems from scientific publications. However, to date, the volume and

characteristics of studies specifically focused on TB medication adherence in

Southeast Asia have not yet been systematically assessed. This study aims to

conduct a comprehensive bibliometric analysis of research on medication

adherence in TB treatment within this region.

**METHODS:** A bibliometric analysis was conducted using the Scopus database to

identify research articles related to medication adherence in TB treatment in

Southeast Asia, published in English between 2015 and 2024. The analysis

included the number of publication trends, country of origin, citation metrics,

co-authorship networks, keyword co-occurrence, and the most frequently cited

documents.

**RESULTS:** A total of 146 journal articles were retrieved. Indonesia emerged as

the most prolific contributor and demonstrated strong international

collaboration. Keyword co-occurrence analysis revealed four major research

themes: (1) clinical and demographic characteristics, (2) pharmacological

management and disease burden, (3) socio-behavioral factors related to

adherence, and (4) digital health-based treatment evaluation. Burst analysis of

reference and keyword highlighted emerging research trends, particularly in

"primary-community based care" and "digital health interventions", indicating

potential trajectories for future research in TB medication adherence.

**CONCLUSION:** This study provided an overview of the evolving research landscape

on TB medication adherence in Southeast Asia. These findings highlight the

growing emphasis on primary-community based care and digital health

interventions, pointing toward shaping future research and practice.

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DOI: 10.2147/PPA.S520341

PMCID: PMC12316179

PMID: 40755529

**62. Commun Biol. 2025 Aug 7;8(1):1175. doi: 10.1038/s42003-025-08593-9.**

Structural Insights into the Protein Mannosyltransferase from Mycobacterium

tuberculosis reveal a WW-Domain-Like Protein Motif in Bacteria.

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We have previously demonstrated that protein-O-mannosylation (POM), a widespread

post-translational glycosyl modification of proteins, is a key virulence factor

of Mycobacterium tuberculosis (Mtb), the world's deadliest infectious agent.

Here, we report a detailed analysis of the structure-function relationship of

MtPMT, the enzyme that catalyzes POM in Mtb. Using mutagenesis and in cellulo

monitoring of POM activity, we demonstrate that, despite notable structural

differences, MtPMT shares functional homologies with yeasts' PMTs in the

mechanism of the sugar transfer from lipidic donors. Furthermore, we provide

evidence that the selectivity for proline-rich target glycosylation sites that

differentiates MtPMT from its eukaryotic homologues, relies on a WW-like domain,

which preferentially interacts with proline-rich acceptor substrate analogues.

This first identification of a functional WW-like domain in a prokaryotic

protein raises questions about its potential evolutionary linkage with

eukaryotic WW modules and provides new insights into PMT's acceptor-substrate

recognition mechanism paving the way for the development selective inhibitors of

MtPMT with potential therapeutic application against tuberculosis.

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DOI: 10.1038/s42003-025-08593-9

PMID: 40775265 [Indexed for MEDLINE]

**63. Planta Med. 2025 Aug 7. doi: 10.1055/a-2660-2042. Online ahead of print.**

Antimycobacterial Activities of Cryptolepis sanguinolenta, Lantana camara,

Zanthoxylum leprieurii Modeled as a Function of Their Fingerprints for Active

Compounds Identification.

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There is a pressing need to discover novel anti-tuberculosis agents to combat

emerging drug-resistant strains. Cryptolepis sanguinolenta, Lantana camara, and

Zanthoxylum leprieurii have been identified as potential sources of

anti-tuberculosis (TB) drug candidates. Previous studies have examined the

metabolites and metabolic pathways in mycobacterial strains affected by

methanolic extracts of these plants, but the specific active compounds

responsible for the antimycobacterial activity, the effect on affected

metabolites and metabolic pathways of mycobacterial cell cultures, remain

unclear. Untargeted metabolic fingerprinting may help identify the active

compounds. The objective of this study was to model the antimycobacterial

activity of methanolic extracts of C. sanguinolenta, L. camara, and Z.

leprieurii as a function of their UHPLC-MS fingerprints and determine whether

specific peaks (compounds) in the fingerprints contributed significantly to the

activity. In this study, fingerprints of 18 methanolic extracts from C.

sanguinolenta roots, L. camara leaves, and Z. leprieurii stem barks were

obtained with ultra-high-performance liquid chromatography-mass spectrometry

(UHPLC-MS). The minimal inhibitory concentrations (MICs) of these extracts

against a pan-sensitive M. tuberculosis strain were determined using a

resazurin-based microdilution assay. Fingerprints were processed and analyzed

using regions of interest-multivariate curve resolution (ROIMCR). Partial least

squares (PLS) regression was employed to model the MICs. Potential active

compounds, including cryptolepine (from C. sanguinolenta), verbascoside (from

L. camara), and isofagaridine (from Z. leprieurii), were identified as

antimycobacterial compounds. These compounds likely influence mycobacterial

metabolic processes, including cell wall synthesis, protein production,

nucleotide metabolism, and energy generation. Further investigations are

required to validate our findings.

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DOI: 10.1055/a-2660-2042

PMID: 40774310

**64. J Infect Public Health. 2025 Jul 24;18(11):102902. doi:**

**10.1016/j.jiph.2025.102902. Online ahead of print.**

Effects of intense exercise on innate bacterial killing in close contacts of

patients with TB/MDR-TB.

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**BACKGROUND:** Close contacts of patients with multidrug-resistant tuberculosis

(MDR-TB) face a high infection risk due to limited chemoprophylaxis. Exercise is

known to enhance the lung defense mechanisms. This study evaluated whether

intense exercise can boost innate bacterial immunity in close contact by

improving the in vitro killing of intracellular Mycobacterium tuberculosis.

**METHODS:** Twelve males (20-40 years) from a tuberculosis clinic were randomly

assigned to exercise or no-exercise groups. The exercise group performed

high-intensity cycling at 70-80 % of heart rate reserve (HRR) for 30-60 min,

three days/week for 12 weeks. The no-exercise group engaged in self-directed

exercise. Blood monocytes were isolated before and after the program and

differentiated into inflammatory M1 and anti-inflammatory M2 macrophages. We

infected the isolated monocytes and M1 and M2 macrophages with the

mCherry-expressing laboratory reference M. tuberculosis strain H37Rv and a local

strain of MDR-TB with a multiplicity of infection (MOI) is 10 for 0 and 72 h,

and mycobacterial survival was determined via high content imaging.

**RESULTS:** Mycobacterial survival percentages were normalized to the 0-h infection

control. In the exercise group, H37Rv survival was significantly decreased in

monocytes, M1, and M2 macrophages compared to that in the no-exercise group.

However, the local MDR strain reduced the survival of M1 macrophages but not

that of monocytes or M2 macrophages. Additionally, cytokine secretion after

H37Rv infection in monocytes showed a significant reduction in IL-1β levels,

whereas no significant changes were observed in M1 and M2 macrophages.

**CONCLUSION:** Intense exercise may enhance mycobacterial killing in individuals

exposed to TB, particularly inflammatory M1 macrophages. Promoting intense

exercise among close contacts of patients with TB may be beneficial.

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DOI: 10.1016/j.jiph.2025.102902

PMID: 40773852

**65. Microb Pathog. 2025 Aug 5:107966. doi: 10.1016/j.micpath.2025.107966. Online**

**ahead of print.**

Mycobacterium tuberculosis PE5 stimulates anti-inflammatory cytokine production

via innate immune Toll-Like Receptor 4 signaling.

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Mycobacterium tuberculosis possesses an intricate system of virulence factors

that aid in providing resilience to the pathogen within the milieu of the host.

M.tb expresses unique proteins, PE/PPE, that are conserved and play a crucial

role in pathogenesis. A conserved member of the PE family Rv0285 (PE5) of

Mycobacterium tuberculosis (M.tb) has been earlier characterized as an essential

and secretory protein that is a critical regulator of host immune response. We

have shown that the PE5 protein consists of lysosomal targeting sequences and is

stable at low pH, thereby allowing the protein to be localized to the lysosome.

In-silico studies suggest that PE5 interacts with TLR4. This was validated using

the TLRs knockout macrophage cell lines. PE5 increases the anti-inflammatory

cytokine via the TLR4 receptor. Recombinant M. smegmatis expressing M.tb-PE5

protein survives within the macrophage as compared to control M. smegmatis,

suggesting its role in providing resilience to survive within the macrophage.

FDA drugs were screened for that interaction with the PE5 protein. Interaction

of Nystatin and Conivaptan hydrochloride with PE5 results in stable binding and

provides proof of concept about the possibility of repurposing these molecules

as an anti-tubercular drug.

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DOI: 10.1016/j.micpath.2025.107966

PMID: 40774564