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**境外学者发表的结核病英文文章摘要**

**（104篇）**

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**1. Lancet Infect Dis. 2025 Sep 4:S1473-3099(25)00436-0. doi:**

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A 3-month clofazimine-rifapentine-containing regimen for drug-susceptible

tuberculosis versus standard of care (Clo-Fast): a randomised, open-label, phase

2c clinical trial.

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**BACKGROUND:** Based on results from preclinical and clinical studies, a five-drug

combination of isoniazid, rifapentine, pyrazinamide, ethambutol, and clofazimine

was identified with treatment shortening potential for drug-susceptible

tuberculosis; the Clo-Fast trial aimed to determine the efficacy and safety of

this regimen. We compared 3 months of isoniazid, rifapentine, pyrazinamide,

ethambutol, and clofazimine, administered with a clofazimine loading dose, to

the standard 6 month regimen of isoniazid, rifampicin, pyrazinamide, and

ethambutol in drug-susceptible tuberculosis.

**METHODS:** Clo-Fast was a phase 2c open-label trial recruiting participants at six

sites in five countries. Participants aged 18 years or older with pulmonary

tuberculosis who were sputum smear positive for acid-fast bacilli or molecular

tuberculosis assay positive (with Mycobacterium tuberculosis with sensitivity to

rifampicin and isoniazid) were eligible for enrolment. Individuals with HIV

infection with a CD4+ cell count ≥100 cells per mm3 could participate.

Participants were randomly assigned in a 2:1 ratio (group 1: group 2) or a 2:1:1

ratio (group 1: group 2: group 3), depending on consent to participate in the

intensive pharmacokinetic visits required in group 3, using a central web-based

system with permuted blocks. The group 1 regimen included 8 weeks of

rifapentine-isoniazid-pyrazinamide-ethambutol-clofazimine, with a 2-week 300 mg

clofazimine loading dose, followed by 5 weeks of rifapentine-isoniazid-pyrazinamide-clofazimine (13 weeks total). The group 2 control regimen included 8 weeks of isoniazid-rifampicin-pyrazinamide-ethambutol followed by 18 weeks of rifampicin-isoniazid. Group 3 was identical to group 1 over the first 4 weeks of treatment, except that the regimen was administered without a clofazimine loading dose (100 mg daily); after 4 weeks of group 3 treatment, participants transitioned to local standard of care to complete treatment. Group 3 was designed to assess the effect of a 2-week loading dose on clofazimine pharmacokinetics. Randomisation was stratified by HIV status and advanced disease on chest radiograph. The primary efficacy endpoint was time to sputum culture-negative status by 12 weeks. The primary safety endpoint was the proportion of participants experiencing any grade 3 or worse adverse event over 65 weeks. The key secondary endpoint was unfavourable clinical or bacteriological outcomes by week 65. The efficacy analysis population contained participants assigned to groups 1 and 2 who were not late exclusions (no positive culture at screening, entry, or week 1, or if rifampicin resistance or isoniazid resistance was detected at screening or entry); the safety analysis

population contained all randomly assigned participants who took at least one

dose of treatment. The trial was registered with ClinicalTrials.gov ID:

NCT04311502.

**FINDINGS:** 104 participants were randomly assigned to group 1 (n=58), group 2

(n=31), and group 3 (n=15). 82 (79%) were male and 74 (71%) had radiographically

advanced disease; 30 (29%) were people with HIV. The trial was stopped early for

lack of clinical efficacy. For the primary efficacy outcome, 49 (89%) of 55

group 1 participants and 28 (90%) of 31 group 2 participants had stable sputum

culture conversion by week 12 (adjusted hazard ratio 1·21 [90% CI 0·82-1·79];

p=0·2089). Adverse events grade 3 or worse occurred in 26 (45%) of 58 group 1

participants and five (16%) of 31 group 2 participants (difference 30%, 90% CI

14-45; p=0·002). The cumulative probability of a week 65 unfavourable outcome

was 52% (95% CI 37-69) in group 1 versus 27% (14-50) in group 2 (p=0·049).

**INTERPRETATION:** Although the trial was stopped early, we found that a 3-month

regimen containing clofazimine and rifapentine had 12-week culture conversion

rates that did not differ statistically from the standard of care. The regimen

was associated with an unacceptably high proportion of participants with

unfavourable composite clinical outcomes and grade 3 or worse adverse events.

**FUNDING:** US National Institutes of Health Advancing Clinical Therapeutics

Globally for HIV/AIDS and Other Infections (ACTG) and the National Institute of

Allergy and Infectious Diseases.

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**2. Lancet Infect Dis. 2025 Sep 4:S1473-3099(25)00479-7. doi:**

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Shaping opportunities for future clinical trials in tuberculosis.

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DOI: 10.1016/S1473-3099(25)00479-7

PMID: 40915310

**3. Ther Innov Regul Sci. 2025 Sep 6. doi: 10.1007/s43441-025-00865-0. Online ahead of print.**

The Use of Unmanned Aerial Vehicles (UAV) on Delivering Biological Samples for

COVID-19 and Tuberculosis Diagnosis: A Scoping Review.

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**PURPOSE:** To identify and review scientific evidence from experimental studies

utilizing unmanned aerial vehicles (UAVs) to transport samples for the diagnosis

of COVID-19 and tuberculosis (TB). This exploratory study aims to support the

future development of UAVs for transporting biological samples within the

Brazilian Unified Health System (SUS).

**METHODS:** This scoping review defined its eligibility criteria using the PECO

acronym, focusing on: Population: biological samples for diagnosing COVID-19 or

TB; Exposure: UAV transportation; Comparator: land transportation; Outcomes:

Cost, effectiveness, methods for sample preservation, flight parameters (time,

altitude, speed, distance), and quality of transported samples. Eligible studies

were identified through searches in Medline via PubMed, Scopus, Embase, and Web

of Science. Grey literature was explored via Google Scholar.

**RESULTS:** Of the 2,052 articles initially found, 797 were duplicates, 1,247 were

screened by title and abstract and excluded, eight were retrieved (and fully

read) of which five met the eligibility criteria and were included in the

review. These studies provided diverse evidence regarding cost, operational

performance, safety, and sample integrity.

**CONCLUSION:** The reviewed studies demonstrate promising applications of UAVs in

healthcare logistics. However, regulatory and legal frameworks require

adaptation to ensure operational safety. Further experimental studies are

necessary, particularly involving beyond visual line of sight (BVLOS)

operations, to evaluate scalability and potential cost reductions.

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**4. BMJ Case Rep. 2025 Sep 5;18(9):e265263. doi: 10.1136/bcr-2025-265263.**

Tuberculous constrictive pericarditis: challenges and surgical management.

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Constrictive pericarditis is a condition in which inflammation of the

pericardium results in the loss of pericardial elasticity, leading to restricted

ventricular filling. This case reports a male in his 50s who presented with

symptoms of bilateral pedal oedema and dyspnoea. Examination revealed a raised

jugular venous pulse, abdominal dullness and crepitations in both lungs.

Echocardiography and cardiac computed tomography revealed the characteristic

features of chronic constrictive pericarditis, including septal involvement,

calcific deposits and right-sided heart failure. The patient was also diagnosed

with chronic liver cirrhosis. The patient underwent a surgical pericardiectomy.

Histopathological examination of the pericardial tissue confirmed a tuberculous

aetiology. The patient was postoperatively managed for heart failure and

antitubercular medication and was subsequently discharged. The patient was

readmitted with symptoms of right-sided heart failure and eventually died. This

case highlights that constrictive pericarditis with myocardial involvement has

poor outcomes after intervention, emphasising the need for early diagnosis.

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**5. Int J Biol Macromol. 2025 Sep 3:147338. doi: 10.1016/j.ijbiomac.2025.147338.**

**Online ahead of print.**

Inhibition of Mycobacterium tuberculosis UvrB by small molecules: Potent NER

disruption and structural insights into dimer conformation.

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The nucleotide excision repair (NER) pathway in Mycobacterium tuberculosis (Mtb)

is important for DNA damage repair and bacterial survival under stress, yet

specific inhibitors targeting its components remain scarce. Here, we targeted

the UvrB protein, a central component of the Mtb UvrABC NER pathway, and

identified novel small molecule inhibitors against its nucleotide binding domain

(NBD). Using in silico structure-based screening involving the Maybridge library

(~54,000 compounds), Molecular dynamics (MD) simulations, and Biolayer

interferometry (BLI), we identified four potent inhibitors: SPB08143, RJC04069,

NRB00936, and DP00786 with IC50 values of 9.8 μM, 3.7 μM, 36.5 μM, and 37.68 μM, respectively, for disrupting the UvrB-DNA complex. Binding kinetics revealed a high affinity for SPB08143 (KD = 0.31 μM), which is better than UvrB's affinity

for its DNA substrate (KD = 1.4 μM). Survival assays in Mycobacterium smegmatis

demonstrated significant bactericidal activity, with SPB08143, RJC04069, and

NRB00936 killing 85.3 %, 80.6 %, and 90 % of UV-treated cells, respectively,

indicating effective NER inhibition. Small-angle X-ray scattering (SAXS) and

Size exclusion chromatography (SEC) further revealed that apo Mtb UvrB adopts an

open, extended dimeric conformation (Rg = 6.65 nm, Dmax = 17.4 nm), potentially

facilitating DNA recognition. These inhibitors represent the first reported

compounds targeting Mtb UvrB, and offer a novel strategy to inhibit Mtb DNA

repair. Moreover, our findings provide structural and functional insights into

UvrB inhibition by these compounds, with potential for development against

drug-resistant Mtb strains.

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**6. PLoS Pathog. 2025 Sep 5;21(9):e1013474. doi: 10.1371/journal.ppat.1013474.**

**Online ahead of print.**

Genome-wide phenotypic insights into mycobacterial virulence using Drosophila

melanogaster.

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Drosophila melanogaster (Drosophila) is one of the most extensively studied

animal models we have, with a broad, advanced, and organized research community.

Yet, Drosophila has barely been exploited to understand the underlying

mechanisms of mycobacterial infections, which cause some of the deadliest

infectious diseases humans are currently battling. Here, we identified

mycobacterial genes required for the pathogen's growth during Drosophila

infection. Using Mycobacterium marinum (Mmar) to model mycobacterial pathogens,

we first validated that an established mycobacterial virulence factor, EccB1 of

the ESX-1 Type VII secretion system, is required for Mmar growth within the

flies. Subsequently, we identified Mmar virulence genes in Drosophila in a

high-throughput genome-wide phenotypic manner using transposon insertion

sequencing. Of the 181 identified virulence genes, the vast majority (91%) had

orthologs in the tuberculosis-causing M. tuberculosis (Mtb), suggesting that the

encoded virulence mechanisms may be conserved across Mmar and Mtb species. By

studying one of the identified genes in more depth, the putative ATP-binding

protein ABC transporter encoded by mmar\_1660, we found that both the Mmar gene

and its Mtb ortholog (rv3041c) were required for virulence in human macrophages

as well. We pinpointed the probable virulence mechanism of the genes to their

requirements for growth during iron limitation, a condition met by mycobacteria

during host infection. Together, our results bring forward Drosophila as a

promising host model to study and identify mycobacterial virulence factors,

providing insights that may transfer to Mtb human infection.

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**7. PLoS One. 2025 Sep 5;20(9):e0329668. doi: 10.1371/journal.pone.0329668.**

**eCollection 2025.**

Machine learning for predicting the diagnosis of tuberculous versus malignant

pleural effusion: External validation and accuracy in two different settings.

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**OBJECTIVE:** To perform an external validation of a previously reported machine

learning (ML) approach for predicting the diagnosis of pleural tuberculosis.

**PATIENTS AND METHODS:** We defined two cohorts: a Training group, comprising 273

out of 1,220 effusions from our prospective study (2013-2022); and a Testing

group, from a retrospective analysis of 360 effusions from 832 consecutive

patients in Bajo Deba health district (1996-2012). All the effusions included

were exudative and lymphocytic. In Training and Testing groups respectively, 49

and 104 cases were tuberculous, 143 and 92 were malignant, and 81 and 164 were

diagnosed with "other diseases"; pre-test probabilities of pleural tuberculosis

were 4% and 12.7%. Variables included were: age, pH, adenosine deaminase,

glucose, protein, and lactate dehydrogenase levels, and white cell counts (total

and differential) in pleural fluid. We used two ML classifiers: binary

(tuberculous and non-tuberculous), and three-class (tuberculous, malignant, and

others); and compared them with Bayesian analysis.

**RESULTS:** The best binary classifier yielded a sensitivity of 88%, specificity of

98%, and accuracy of 95%. The best three-class classifier achieved the same

accuracy and correctly classified 83% (77/92) of malignant cases. The ML models

yielded higher positive predictive values than Bayesian analysis based on

ADA > 40 U/l and lymphocyte percentage ≥ 50% (92%).

**CONCLUSIONS: T**his external validation confirms the good performance of the

previously reported ML approach for predicting the diagnosis of pleural

tuberculosis based on exudative and lymphocytic pleural effusions, and for

discriminating the cases most likely to be malignant. Additionally, ML was more

accurate than the Bayesian approach in our study.

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**8. PLOS Glob Public Health. 2025 Sep 5;5(9):e0004539. doi:**

**10.1371/journal.pgph.0004539. eCollection 2025.**

Appropriateness, barriers, and facilitators of multi-month dispensing of

tuberculosis drugs in rural eastern Uganda: A qualitative study to inform a

non-inferiority randomized trial.

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Multi-month dispensing of tuberculosis (TB) drugs is an innovative strategy that

may reduce frequent clinic visits and travel costs among people with TB (PWTB)

in rural areas. To inform a planned trial, we explored the appropriateness,

barriers, and facilitators to multi-month dispensing among PWTB and healthcare

providers in rural eastern Uganda. We used qualitative methods situated within

the Consolidated Framework for Implementation Research to explore two refill

schedules for multi-month dispensing of TB drugs-a four- or five-visit refill

schedule. In December 2024, we collected data through interviews with PWTB,

their treatment supporters, and healthcare providers at the regional, district,

and health facility levels. Data were analyzed using thematic analysis. All

participants (n = 39; 22 healthcare providers, 12 PWTB, and five treatment

supporters) expressed willingness to adopt multi-month dispensing, with a

four-visit schedule as the preferred option. Healthcare providers preferred the

five-visit schedule for individuals with complex health conditions: severe

illness, clinical instability, or bacteriologically confirmed pulmonary TB.

Multi-month dispensing was perceived to benefit healthcare providers by reducing

workload, improving patient flow, and enhancing patient management. Perceived

benefits to PWTB included reduced clinic visits and travel costs, time savings,

improved treatment adherence, reduced wait times and TB-related stigma, and

increased satisfaction with care. Facilitators included integration with

existing treatment models, person-centeredness, community and family support,

reliable drug supply, clear operational guidelines, healthcare provider training

and readiness, enhanced monitoring and evaluation, clinic accessibility,

readiness to utilize multi-month dispensing, and leadership support. Barriers

included undefined eligibility criteria, uncertain effects of multi-month

dispensing, differing refill schedules for PWTB and HIV, treatment non-adherence

due to forgetfulness and medication sharing, and patient disengagement due to

insufficient follow-up. Multi-month dispensing is perceived to benefit PWTB and

healthcare providers. Further studies to measure the impact on treatment

outcomes should leverage facilitators and address barriers to adoption and

effectiveness.

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PMCID: PMC12412997

PMID: 40911557

**9. Clin Infect Dis. 2025 Sep 5:ciaf491. doi: 10.1093/cid/ciaf491. Online ahead of print.**

Prevention of Tuberculosis in Patients Treated With Biological Therapies: Twenty

Years' Experience in a Specialised Tuberculosis Clinic in a Low-prevalence

Country.

Pérez-Recio S(1), Grijota-Camino MD(2), Guardiola J(3)(4), Juanola X(5), Notario

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Santin M(10)(4)(11); Prevention of Tuberculosis Associated with Biologic

Therapies Study Group.

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**BACKGROUND:** This study builds on previous evidence to assess the risk of

tuberculosis (TB) in patients treated with biologic therapies (BioT), the role

of the interferon-γ-release assay (IGRA) QuantiFERON-TB (QFT) Gold as a

stand-alone screening test, and whether periodic re-testing is warranted for

patients with a negative pre-BioT screening.

**METHODS:** A total of 1,368 patients starting BioT were screened for TB infection

using four screening strategies over four consecutive periods: (1) two-step

tuberculin skin test (TST); (2) two-step TST plus QFT Gold In-Tube; (3)

single-step TST plus QFT Gold In-Tube; and (4) QFT Gold In-Tube (or QFT Gold

Plus) alone. All patients with TB infection were offered preventive therapy.

**RESULTS:** TB infection was diagnosed in 327 (23.9%) patients (40.8%, 39.5%,

25.3%, and 14.8% in the first, second, third and fourth periods, respectively; P

= .000). The adjusted odds ratios (ORs) with respect to the first period were

0.89 (95%CI, 0.55-1.44), 0.49 (95%CI, 0.33-0.73), and 0.23 (95%CI, 0.15-0.36)

for the second, third and fourth periods, respectively. During follow-up, 11

patients (0.8%) developed TB. The probability of remaining TB-free after 11

years of BioT exposure was 99.1%, with no significant differences between

screening periods (P = .372). All TB cases in patients with negative baseline

screening occurred within the first year of BioT exposure, which would make

systematic re-screening pointless.

**CONCLUSIONS:** Although BioT-associated TB can be significantly reduced, it is not

completely preventable. Neither dual testing nor periodic systematic

re-screening for TB infection is warranted after a negative pre-BioT test.

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PMID: 40911528

**10. Glob Health Action. 2025 Dec;18(1):2547150. doi: 10.1080/16549716.2025.2547150. Epub 2025 Sep 5.**

A discourse analysis of social inequities, gender, and stigma in tuberculosis

policies of seven countries from Africa, Asia, Europe and South America.

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**BACKGROUND:** Interventions tackling the social aspects of tuberculosis (TB) are

widely suggested, yet we miss insights into how policies incorporate these. The

language and framing of policies to address TB can lend important insights into

how these social drivers are perceived, problematized, and responded to.

**OBJECTIVE:** To understand how discourses in current TB policies frame social

dimensions of TB, especially concepts of social inequity, gender, and stigma.

**METHODS:** We conducted a comparative critical discourse analysis of twenty-one

publicly available TB-related policies from Belarus, Brazil, Indonesia,

Mozambique, Netherlands, Portugal, and Romania, countries with diverse

epidemiological, geographical and sociopolitical contexts. Documents were

sourced from public websites from May - September 2024. The Bacchi approach was

used to analyze policy framings of social inequities, gender, and stigma.

**RESULT:** While policies from Brazil and Indonesia showed greater attention to

social inequities, gender, and stigma, and were more explicitly reflective of an

equity-oriented and people-centered approach, overall, a dominant biomedical

perspective was observed that individualizes responsibility for cure. This tends

to disregard issues of social inequity, obscures gender relationships and the

multiple dimensions of stigma. At the same time, allocation of individual as

well as structural responsibility for TB risk and outcomes co-existed.

**CONCLUSIONS:** Explicit and implicit discourses about TB within health-related

policies can influence the nature of attention given to the social dimensions of

TB and can shape corresponding responses to the disease. We recommend a

participative policy process that includes a broader set of actors to ensure

documents are responsive to social realities.

Plain Language Summary: Main findings: The discourses used within tuberculosis

policy documents have the potential to shift the focus of issues between

different stakeholders or reduce the urgency to address a problem.Added

knowledge: This study comparatively analyzed policy documents from seven

different countries and uncovered a dominant biomedical perspective which might

overshadow the complexity of the biopsychosocial needs of persons affected by

tuberculosis.Global health impact for policy and action: Policymakers and

various stakeholders should be mindful of how documents frame tuberculosis,

affected communities, and care efforts.

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PMID: 40910864 [Indexed for MEDLINE]

**11. Elife. 2025 Sep 5;13:RP97870. doi: 10.7554/eLife.97870.**

The Mycobacterium tuberculosis complex pangenome is small and shaped by

sub-lineage-specific regions of difference.

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Update of

 doi: 10.1101/2024.03.12.584580.

 doi: 10.7554/eLife.97870.1.

 doi: 10.7554/eLife.97870.2.

 doi: 10.7554/eLife.97870.3.

The Mycobacterium tuberculosis complex (MTBC) is a group of bacteria causing

tuberculosis (TB) in humans and animals. Understanding MTBC genetic diversity is

crucial for insights into its adaptation and traits related to survival,

virulence, and antibiotic resistance. While it is known that within-MTBC

diversity is characterised by large deletions found only in certain lineages

(regions of difference [RDs]), a comprehensive pangenomic analysis incorporating

both coding and non-coding regions remains unexplored. We utilised a curated

dataset representing various MTBC genomes, including under-represented lineages,

to quantify the full diversity of the MTBC pangenome. The MTBC was found to have

a small, closed pangenome with distinct genomic features and RDs both between

lineages (as previously known) and between sub-lineages. The accessory genome

was identified to be a product of genome reduction, showing both divergent and

convergent deletions. This variation has implications for traits like virulence,

drug resistance, and metabolism. The study provides a comprehensive

understanding of the MTBC pangenome, highlighting the importance of genome

reduction in its evolution, and underlines the significance of genomic

variations in determining the pathogenic traits of different MTBC lineages.

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**12. IJU Case Rep. 2025 Jun 24;8(5):454-457. doi: 10.1002/iju5.70063. eCollection**

**2025 Sep.**

A Case of Advanced Urothelial Carcinoma Requiring Treatment Following a Positive

Interferon-Gamma Release Assay Prior to Avelumab Administration.

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**INTRODUCTION:** The association between the risk of latent tuberculosis infection

(LTBI) reactivation and immune checkpoint inhibitor (ICI) administration has

been reported.

**CASE PRESENTATION:** A man in his seventies underwent robot-assisted laparoscopic

radical cystectomy with ileal conduit diversion for muscle-invasive bladder

cancer. Three years postoperatively, CT revealed metastases to the para-aortic

lymph nodes and rectum. Four cycles of gemcitabine and carboplatin were

administered, with CT showing a partial response (PR). Avelumab maintenance

therapy was initiated following radiotherapy for the rectal metastasis. Prior to

avelumab administration, LTBI was diagnosed based on a positive interferon-gamma

release assay (IGRA). Isoniazid was administered concurrently with avelumab for

6 months. No active tuberculosis developed, and PR was maintained.

**CONCLUSION:** IGRA screening is advisable prior to ICI initiation. Prompt and

appropriate management is warranted in patients with LTBI.

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Ltd on behalf of Japanese Urological Association.

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PMID: 40909323

**13. Trans R Soc Trop Med Hyg. 2025 Sep 5:traf089. doi: 10.1093/trstmh/traf089.**

**Online ahead of print.**

Using digital annual household survey data to prioritize high-risk villages for

tuberculosis active case-finding.

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**BACKGROUND:** Tuberculosis (TB) active case-finding (ACF) among high-risk

populations is recommended to detect the missing people with TB. In Rajasthan,

India, a state with a high TB prevalence:notification ratio, leveraging digital

annual health survey data could enhance ACF by targeting villages with a high

burden of TB risk factors.

**METHODS:** We conducted an ecological study across 19 districts of Rajasthan using

data from the digital annual health survey. High-risk villages were identified

based on three factors: multidimensional poverty index (MDPI), high proportion

(>60%) of socially marginalized populations and geographic access (distance to

primary health centre >7 km).

**RESULTS:** The survey covered 24.6 million individuals across 20 803 villages.

Thirty-five percent of individuals belonged to socially marginalized

populations. At the household level, 39% used solid fuels, indicating potential

exposure to indoor air pollution. Nine percent of villages had high poverty

(MDPI >0.21) and 25% had a high proportion (>60%) of socially marginalized

populations. Approximately 34% of villages had at least one of the three

high-risk factors.

**CONCLUSIONS**: This study demonstrates the potential of existing digital annual

survey data for targeted ACF. Further research is being planned to assess the

yield of ACF in identified high-risk villages and to advocate for similar

data-driven interventions in other settings.

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**14. BMJ Open. 2025 Sep 4;15(9):e098851. doi: 10.1136/bmjopen-2025-098851.**

Economic evaluation of integrating nutritional support intervention in India's

National Tuberculosis Elimination Programme: implications for low-income and

middle-income countries.

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**OBJECTIVES:** This study aimed to evaluate the cost-effectiveness of integrating

nutritional support into India's National Tuberculosis Elimination Programme

(NTEP) using the MUKTI initiative.

**DESIGN:** Economic evaluation.

**SETTING:** Primary data on the cost of delivering healthcare services,

out-of-pocket expenditure and health-related quality of life among patients with

tuberculosis (TB) were collected from Dhar district of Madhya Pradesh, India.

**INTERVENTION:** Integration of nutritional support (MUKTI initiative) into the

NTEP of India.

**CONTROL:** Routine standard of care in the NTEP of India.

**PRIMARY OUTCOME MEASURE:** Incremental cost per quality-adjusted life year (QALY)

gained.

**METHODS:** A mathematical model, combining a Markov model and a compartmental

susceptible-infected-recovered model, was used to simulate outcomes for patients

with pulmonary TB under NTEP and MUKTI protocols. Primary data collected from

2615 patients with TB, supplemented with estimates from published literature,

were used to model progression of disease, treatment outcomes and community

transmission dynamics over a 2-year time horizon. Health-related quality of life

was assessed using the EuroQol 5-Dimension 5-Level scale. Costs to the health

system and out-of-pocket expenditures were included. A multivariable

probabilistic sensitivity analysis was undertaken to estimate the effect of

joint parameter uncertainty. A scenario analysis explored outcomes without

considering community transmission. Results are presented based on health-system

and abridged societal perspectives.

**RESULTS:** Over 2 years, patients in the NTEP plus MUKTI programme had higher life

years (1.693 vs 1.622) and QALYs (1.357 vs 1.294) than those in NTEP alone, with

increased health system costs (₹11 538 vs ₹6807 (US$139 vs US$82)). Incremental

cost per life year gained and QALY gained were ₹67 164 (US$809) and ₹76 306

(US$919), respectively. At the per capita gross domestic product threshold of

₹161 500 (US$1946) for India, the MUKTI programme had a 99.9% probability of

being cost-effective but exceeded the threshold when excluding community

transmission.

**CONCLUSION:** The findings highlight the potential benefits of a cost-effective,

holistic approach that addresses socio-economic determinants such as nutrition.

Reduction in community transmission is the driver of cost-effectiveness of

nutritional interventions in patients with TB.

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**15. J Mol Biol. 2025 Sep 2:169416. doi: 10.1016/j.jmb.2025.169416. Online ahead of print.**

Molecular insights into the structure, function, and stability of the DNA

polymerase processivity factor from Mycobacterium tuberculosis.

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Emergence of drug resistance in Mycobacterium tuberculosis (Mtb) calls for newer

drugs and drug targets. Essential proteins such as DNA polymerase (DNAP)

processivity factor, also called sliding clamp (DnaN), are indispensable for

bacterial survival, and are excellent drug targets. Here, we constructed a

dnaN-conditional knockout in Mycobacterium smegmatis (MsmΔdnaN) and were able to

successfully complement it with Mtb DnaN (DnaNMtb). To explore its

structure-function-stability relationship, we generated Ala-substituted mutants

of the DnaNMtb subunit-subunit interface, and identified R115, F116, and E319 as

crucial for MsmΔdnaN survival in our complementation assay. We used biophysical,

biochemical, and in silico molecular dynamics simulation methods to decipher the

importance of these residues. We show that mutants exist as dimers, with lesser

stability than wildtype. Except F116A, the mutants are largely folded with their

CD profiles similar to wildtype. We also assembled and purified Mtb Clamp Loader

Complex and used it to assess DNAP processivity function of DnaNMtb. Our in

vitro DNA synthesis data show that PolAMtb does not interact with DnaNMtb,

whereas E. coli Pol-I Klenow fragment shows enhanced DNA synthesis in presence

of DnaNMtb, which was abolished by Griselimycin, an antibiotic that inhibits

clamp-DNAP interaction. Interestingly, DnaNMtb mutants that did not complement

loss of DnaN in MsmΔdnaN also did not support enhanced DNA synthesis by Klenow,

corroborating our in vivo observation. We suggest that the Mtb clamp

subunit-subunit interface is crucial for maintaining

structure-function-stability, and thus can be used for the targeted development

of small molecule inhibitors and peptidomimetics as potent drugs against

tuberculosis.

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**16. Am J Trop Med Hyg. 2025 Sep 4:tpmd240808. doi: 10.4269/ajtmh.24-0808. Online**

**ahead of print.**

Acute Respiratory Distress Syndrome Secondary to Miliary Tuberculosis.

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**17. Int J Surg Case Rep. 2025 Sep 2;135:111886. doi: 10.1016/j.ijscr.2025.111886.**

**Online ahead of print.**

Tuberculous septic pseudoaneurysm of the right subclavian artery: A rare case

report.

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**INTRODUCTION:** Pseudoaneurysm of the right subclavian artery is very rare, and

its most serious complication is rupture, which is unpredictable and fatal.

Among the infectious causes, tuberculous pseudoaneurysms represent an

exceptionally rare but significant subset, arising from the direct invasion of

the arterial wall by Mycobacterium tuberculosis.

**CASE REPORT:** We present the case of a 60-year-old hypertensive male diagnosed

with a right subclavian artery septic pseudoaneurysm, which is rare but serious,

often resulting from an infection that weakens the arterial wall. Although

bacterial infections are the most common etiologies, mycobacterial infections,

such as those caused by Mycobacterium tuberculosis, should also be considered in

regions with a high prevalence of tuberculosis or in patients with risk factors

for this infection. The patient was successfully treated through a cervicotomy

and challenging dissection of major neck vessels. A bypass graft between the

distal right subclavian artery and the right carotid artery was performed,

restoring vascular flow. Postoperative outcomes were favorable, with full

recovery at one week and three months follow-up.

**DISCUSSION:** This case underscores the importance of timely diagnosis and

surgical intervention in managing septic pseudoaneurysms, including those of

tuberculous origin, to avoid life-threatening complications such as rupture or

systemic sepsis. Comprehensive management should include appropriate

antimicrobial therapy tailored to the underlying infectious agent to ensure

long-term recovery and graft patency.

**CONCLUSION:** Early diagnosis is crucial to prevent the potentially

life-threatening complications of a right subclavian artery pseudoaneurysm;

therefore, this condition should be considered in patients with a history of

trauma or infection presenting with a pulsatile supraclavicular mass or

unexplained upper limb symptoms.

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**18. Vaccine. 2025 Sep 3;64:127679. doi: 10.1016/j.vaccine.2025.127679. Online ahead of print.**

Screen first, vaccinate later: Enhancing tuberculosis vaccination safety through

newborn immunodeficiency screening.

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Kranj, Slovenia.

Tuberculosis (TB) remains a global health challenge, with around 10 million new

cases reported annually and multidrug-resistant strains complicating control

efforts. Although incidence has declined in many high-income regions, neonatal

populations remain vulnerable, underscoring the continued role of Bacillus

Calmette-Guérin (BCG) vaccination. BCG vaccination provides strong protection

against severe forms of TB in infancy, though its efficacy against pulmonary

disease in adolescents and adults is modest. However, the BCG vaccine carries a

risk of disseminated infection in immunocompromised newborns, emphasizing the

importance of integrating immunodeficiency screening into vaccination

strategies. Slovenia introduced universal newborn screening for inborn errors of

immunity (IEI) in 2024 and, in 2025, revised its neonatal BCG vaccination

protocol to incorporate screening results before vaccination. Under this

approach, blood sampling occurs at ≥48 h, results are available by days 5-7, and BCG is administered between 7 and 14 days of life. This model balances timely TB protection with safety for at-risk infants. The Slovenian experience exemplifies a precision vaccination strategy that integrates real-time immunogenetic data with targeted BCG administration. This approach aligns with World Health Organization goals to modernize TB prevention while awaiting next-generation vaccines and may serve as a guide for other low-incidence countries.

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**19. ACS Appl Mater Interfaces. 2025 Sep 4. doi: 10.1021/acsami.5c13207. Online ahead of print.**

Strategic Modulation of Isoniazid Solubility through Cocrystal Formation for

Long-Acting Microneedle Therapy of Tuberculosis.

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Tuberculosis (TB), caused by Mycobacterium tuberculosis, remains a global health

emergency, particularly in low- and middle-income countries. Despite effective

pharmacotherapy, prolonged treatment, poor adherence, and drug resistance

continue to hinder eradication. Isoniazid (ISZ), a first-line antitubercular

drug, is effective but limited by high aqueous solubility and short half-life,

necessitating daily administration and causing plasma fluctuations. Considering

these limitations, strategies to modulate ISZ solubility without altering

pharmacodynamics are therefore of therapeutic interest. In this study, we report

the design, synthesis, and characterization of a cocrystal of ISZ with salicylic

acid (SA), a GRAS-status coformer with low solubility. Cocrystallization was

employed to reduce ISZ solubility, enhancing its potential for sustained

release. The ISZ-SA cocrystal was confirmed as a distinct crystalline phase by

FTIR, DSC, and PXRD, and subsequently incorporated into dissolving microneedle

array patches (MAPs) fabricated from biocompatible polymers via aqueous casting.

These MAPs dissolve after skin insertion, releasing their load into the dermal

microenvironment. FTIR confirmed the cocrystal's structural integrity within the

polymeric matrix, with no dissociation observed during formulation. In vitro

release studies showed that ISZ-SA exhibited a slower, more sustained release

compared to pure ISZ. Ex vivo dermatokinetic studies revealed significantly

greater deposition of ISZ in epidermis (89%, 171.1 μg) and dermis (90%, 468.3

μg) with the cocrystal versus pure drug (36%, 210.0 μg). Enhanced dermal

retention suggests localization within skin layers, acting as a depot for

gradual systemic absorption. In contrast, pure ISZ permeated faster but

deposited less, underscoring the cocrystal's sustained delivery advantage. This

work is among the first demonstrations of pharmaceutical cocrystals integrated

into dissolving MAPs for transdermal delivery. Cocrystal engineering combined

with MAPs may overcome inherent limitations of hydrophilic drugs like ISZ,

enabling long-acting formulations that reduce dosing frequency, improve

adherence, and enhance TB treatment outcomes, with potential application to

other high-solubility drugs.

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**20. J Med Chem. 2025 Sep 4. doi: 10.1021/acs.jmedchem.5c01412. Online ahead of**

**print.**

A Novel Peptide Antibiotic Targeting Gram-Negative Infections Designed from

Mycobacterium tuberculosis Adenylate Kinase.

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We explored the lipopolysaccharide-binding properties of adenylate kinase from

Mycobacterium tuberculosis (MtAdk) to facilitate the design of novel peptide

antibiotics. Notably, we de novo designed 11-mer peptides derived from the

AMP-binding domain (Lys44 to Asp54) of MtAdk. Among 71 designed peptides,

DD-S067 was the most effective, especially against carbapenem-resistant

Acinetobacter baumannii (CRAB), with minimal development of drug resistance.

DD-S067 exhibited multiple antibacterial mechanisms, including disrupting both

the outer and inner bacterial membranes, and inducing reactive oxygen species

that trigger lipid peroxidation. Transcriptome analysis revealed that DD-S067

disrupted key cellular pathways in CRAB by inhibiting the electron transport

chain and triggering oxidative stress responses, ultimately suppressing CRAB

virulence mechanisms. Furthermore, DD-S067 exhibited significant protective

effects in a CRAB-induced septic shock mouse model, highlighting its potential

as a novel peptide antibiotic for treating Gram-negative infections. These

findings pave the way for innovative strategies in developing protein-based

antibiotics.

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PMID: 40906914

**21. PLoS Pathog. 2025 Sep 4;21(9):e1013476. doi: 10.1371/journal.ppat.1013476.**

**Online ahead of print.**

Mycobacterium tuberculosis impairs protective cytokine production via

transcription factor MafB manipulation.

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Y(3), Mukai T(3), Hamada M(5), Takahashi S(5), Tanaka T(6), Kaisho T(7)(8),

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Although an increased expression of the transcription factor v-maf avian

musculoaponeurotic fibrosarcoma oncogene homolog B (MAFB) has been reported in

patients with active tuberculosis (TB), its potential role in Mycobacterium

tuberculosis infection remains unknown. Herein, we report that MafB in

macrophages is a regulator of the pro-inflammatory cytokines, TNF-α and

IL-12p40, which are crucial for host defense against M. tuberculosis infection.

Cell-based luciferase assays showed that MafB inhibited TNF-α and IL-12p40

transcriptional activity in a dose-dependent manner. At the molecular level,

MafB interacted with IFN regulatory factor (IRF)-5 and PU.1 and inhibited IRF-5-

and PU.1-mediated transactivation, via the basic-leucine zipper domain. Analysis

using gene-deficient macrophages demonstrated that the suppressed

pro-inflammatory cytokine production during M. tuberculosis infection depends on

MafB expression. Finally, in vivo studies indicated that M.

tuberculosis-mediated increase of MafB expression was responsible for the

exacerbation of M. tuberculosis infection. Thus, our results provide a

functional view of MafB as a cytokine regulator as well as novel insights into

host factors involved in TB susceptibility.

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DOI: 10.1371/journal.ppat.1013476

PMID: 40906796

**22. Am J Health Promot. 2025 Sep 4:8901171251376650. doi: 10.1177/08901171251376650. Online ahead of print.**

Risk Perceptions Regarding Tuberculosis Among Hispanic Adults - United States,

2020-2022.

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**Purpose** Risk perception for tuberculosis (TB) and previous receipt of a TB test

and/or vaccine were assessed to inform TB prevention efforts.**Design** Cross-sectional.SettingThe 2020, 2021, and 2022 Estilos survey data.**Subjects** 2837 U.S. Hispanic adults (≥18 years).**Measures** Self-reported receipt of a TB test and/or vaccine, perceived risk for TB, and demographic characteristics.AnalysisWeighted proportions and 95% Confidence Intervals (CIs) were calculated. Associations between demographic characteristics and TB questions were assessed using chi-square tests. Multinomial logistic regression was used to examine perceived risk for TB among those who received a TB test and/or vaccine vs those who did not.ResultsOverall, 7.2% (95%CI [4.8, 10.5]) of U.S. Hispanic adults reported receiving a TB test but not a vaccine, 15.3% (95%CI [12.5, 18.7]) reported receiving a vaccine but not a test, and 28.3% (95%CI [24.7, 32.2]) reported receiving both a TB test and TB vaccine. Respondents who reported previous receipt of a TB test, with or without previous receipt of a TB vaccine, had a significantly higher odds of feeling any risk for TB than those without previous receipt of a TB test or vaccine (aOR = 2.79, 95% CI = 1.19-6.52 for those tested but not vaccinated; aOR = 1.89, 95% CI = 1.11-3.20 for those both tested and vaccinated).**Conclusion** Findings can help inform education and interventions to raise awareness and encourage TB testing for those at risk for TB.

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PMID: 40906515

**23. Infection. 2025 Sep 4. doi: 10.1007/s15010-025-02632-7. Online ahead of print.**

Genetic and clinical risk factors for anti-tuberculosis drug-induced liver

injury: insights from a prospective cohort study in central Ethiopia.

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**PURPOSE:** Drug-induced liver injury (DILI) is a relevant adverse event of

tuberculosis treatment (TBT) especially in sub-Saharan Africa, but data remains

limited. Genetic hepatic transport proteins polymorphisms (HTPP) are potential

contributors. This study aimed to assess frequency and timing of DILI, identify

risk factors, and explore the association of HTPP with DILI risk in Ethiopian

TBT-patients.

**METHODS:** In this prospective study, 424 confirmed tuberculosis patients in

Ethiopian were recruited before initiation of TBT. Liver function tests were

conducted during the first 8 weeks of treatment. Baseline evaluations included

sociodemographic-, lifestyle- and clinical data including testing for viral

co-infections, and HTPP as well as liver stiffness measurement by transient

elastography (TE). Multivariable logistic regression, Cox proportional hazards

models, and Fine and Gray competing risks analyses were employed for statistical

analysis.

**RESULTS:** Cumulative DILI incidence was 16.0% with 4.2% classified as severe

occurring most commonly within the first two weeks. Urban residence (OR 2.00,

95% CI 1.03-3.84; HR 1.80, 95% CI 1.00-3.22) was associated with increased DILI

risk. In the competing risks model, urban residence (sHR 6.26, p = 0.010) and

pathologic TE (sHR 5.23, p = 0.005) predicted severe DILI. The investigated

HTPPs were not significantly associated with DILI.

**CONCLUSION:** DILI is a common early complication of TBT in Ethiopian patients.

Assessment of sociodemographic factors and TE before TBT may help identify

high-risk individuals and offers a pragmatic approach for DILI management in

resource-limited settings.

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PMID: 40906064

**24. FEBS J. 2025 Sep 3. doi: 10.1111/febs.70251. Online ahead of print.**

The genomic SELEX-based method identifies 350 SigA-specific promoters in

Mycobacterium tuberculosis.

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The gene regulation in Mycobacterium tuberculosis by different sigma factors,

including the principal sigma factor, sigmaA (SigA), is poorly understood. Here,

we have developed a modified genomic systematic evolution of ligands by

exponential enrichment (SELEX)-Seq approach that identifies 350 new SigA-binding

sites in M. tuberculosis. SigA-binding ability and promoter activity of

representative DNA sequences were confirmed by electrophoretic mobility shift

assay (EMSA) and reporter assay, respectively. Among these DNA sequences, 38 are

located in the intergenic region, indicating these regions as possible SigA

promoters of the surrounding genes. The remaining 312 DNA sequences are located

within the intragenic region, suggesting a previously unknown role of these

binding sites, including SigA-dependent regulatory roles. We reveal that the

intragenic SigA-binding sites are responsible for synthesizing 62 transcripts

and 14 noncoding RNAs from the existing database. We have further identified 88

new proteins, different from annotated open reading frames (ORFs) in the genome

sequences, downstream of the intragenic SigA-binding sites. Out of 350

SigA-binding sites, (a) 156 sequences contain -10 elements (T[C][N][N]N[T]) with

a certain degree of degeneracy, including 38 having an additional extended -10

TG sequence, (b) 66 DNA sequences contain both -35 (T[G/T][G/T][C/T][N][C]) and

-10 elements with a spacer of 5-25 bp, and (c) intriguingly, 128 SigA-binding

sites contain only 35-like elements. Thus, our study reveals that the promoter

architecture of M. tuberculosis significantly differs from the generalized

concept of bacterial promoters and opens a new avenue to study gene regulation

in M. tuberculosis.

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PMID: 40903908

**25. BMJ Open Respir Res. 2025 Sep 3;12(1):e002802. doi: 10.1136/bmjresp-2024-002802.**

Health system-related barriers and facilitators to tuberculosis preventive

treatment: a qualitative case study comparing implementation in the Republic of

Moldova and Georgia.

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**INTRODUCTION:** Despite WHO's recommendations and the 2023-2030 Tuberculosis (TB)

action plan, uptake of TB preventive treatment (TPT) remains suboptimal. In this

paper, we use two countries of the WHO Europe Region, the Republic of Moldova

and Georgia, that are at different stages of implementation of TB prevention

policies, as a case study to examine health system barriers and facilitators to

TPT scale-up.

**METHODS:** In this case study, we used methods of qualitative research-interviews

with three stakeholder groups: health service providers and National TB

Programme staff; civil society organisations and international partners or

donors. The data were collected via videoconference, transcribed, then coded and

analysed using NVivo V.14. Thematic analysis was conducted.

**RESULTS:** Facilitators for TPT delivery in both settings include an established

TB clinical network, well-functioning communication systems and an uninterrupted

supply of TPT medicines.In both settings, healthcare providers generally exhibit

positive attitudes towards treating TB infection; however, some remain sceptical

and cautious, particularly regarding prescribing TPT without confirmation of TB

infection, a challenge compounded by limited access to testing for TB infection.

Evidence of TB infection is also important for patients' decisions on initiation

and adherence to treatment. Other barriers to effective service delivery of TPT

include shortages and high workload of primary healthcare personnel, ambiguity

in the role of family doctors in the management of TPT and low prioritisation of

TPT during regular monitoring visits.

**CONCLUSIONS**: The case study identified similar challenges in the rollout of TPT

across both settings, highlighting common barriers hindering effective

implementation. For optimal TPT rollout, enhancing provider confidence,

improving access to testing for TB infection and strengthening integration with

primary healthcare with refined roles of family doctors are essential. Both

settings would also benefit from improved monitoring and evaluation systems and

prioritisation of TB prevention in monitoring.

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**26. Ther Drug Monit. 2025 Sep 2. doi: 10.1097/FTD.0000000000001378. Online ahead of print.**

Pharmacogenetics of First-Line Antitubercular Drugs: An Update.

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Turin, Amedeo di Savoia Hospital, Turin, Italy.

**BACKGROUND:** Tuberculosis (TB) treatment relies on a prolonged first-line

antibiotic regimen, including isoniazid, rifampicin (RF), ethambutol (EMB), and

pyrazinamide.Pharmacogenetics plays a crucial role in optimizing TB treatment by

addressing individual variability in drug metabolism and responses. Genetic

polymorphisms can significantly affect pharmacokinetics and therapeutic

outcomes. The aim of this review was to explore the role of pharmacogenetics in

first-line antibiotics used to treat TB.

**METHODS:** We reviewed the literature using PubMed, Scopus, Web of Science, and

the Cochrane Library, focusing on articles published in the last 10 years (from

December 2014 to December 2024) on the pharmacogenetics of first-line anti-TB

drugs. Only English-language studies involving human subjects were included,

prioritizing those investigating genetic variants that affect drug

bioavailability.

**RESULTS:** In this study, 33 manuscripts were included.N-acetyltransferase 2

Single-nucleotide polymorphisms were associated with different isoniazid

acetylation rates, which affect toxicity and efficacy. Genetic variations in

CYP2E1, GSTM1, and MnSOD also contribute to hepatotoxicity.For RF, variants in

SLCO1B1, ABCB1, PXR, CAR, CES1, and CES2 genes were related to variability in

drug absorption, metabolism, and clearance, highlighting the need for

personalized dosing strategies. Notably, SLCO1B1 rs4149056 polymorphism is

associated with decreased OATP1B1 RF transport activity, potentially leading to

increased plasma exposure, whereas other polymorphisms modulate drug exposure

and clearance rates. In addition, sex, body weight, and genotype influenced RF

pharmacokinetics, suggesting the need for tailored dosing recommendations based

on patient characteristics.Similarly, variability in EMB pharmacokinetics is

associated with CYP1A2 2159, which is related to a 50% reduction in

bioavailability, necessitating dose adjustments in patients coinfected with TB

and HIV. Some variants of ABCB1, OATP1B1, PXR, VDR, CYP24A1, and CYP27B1 may

further modulate the plasma and intracellular concentrations of EMB, thereby

influencing drug efficacy.

**CONCLUSIONS:** This review highlights the importance of integrating

pharmacogenetic insights into clinical practice to enhance the efficacy of TB

treatment, minimize toxicity, and prevent drug resistance. Despite promising

evidence, further research and clinical validation are required to implement

pharmacogenetics in routine TB management. Future advancements in therapeutic

drug monitoring and omics technologies will pave the way for precision medicine

in TB therapy.

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**27. J Pharmacol Toxicol Methods. 2025 Sep 1:108393. doi:**

**10.1016/j.vascn.2025.108393. Online ahead of print.**

PolyCheck: A hybrid model for predicting polypharmacy-induced adverse drug

reactions in tuberculosis treatment using heterogenous drug-target-ADR networks.

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Kabul, Afghanistan.

Polypharmacy during tuberculosis (TB) treatment, particularly in patients with

comorbidities such as diabetes mellitus (DM), significantly increases the risk

of adverse drug reactions (ADRs) due to complex drug-drug interactions (DDIs).

Existing computational methods primarily focus on pairwise drug interactions,

often failing to capture the multifactorial nature of ADRs in polypharmacy

contexts. To address this gap, we developed PolyCheck, a hybrid predictive model

that integrates network-based and rule-based methods to identify potential ADRs

arising from multi-drug regimens. We constructed a heterogeneous Drug-Target-ADR

interaction network comprising first-line anti-TB and antidiabetic drugs, their

targets, and associated ADRs. The Random Walk with Restart (RWR) algorithm was

employed to rank ADR nodes, and a rule-based layer further refined predictions

by incorporating the biological relevance of Drug-Target-ADR associations.

Evaluation using cross-validation and case-based testing demonstrated strong

predictive performance, with accuracy, precision, recall, F1-score, and AUPRC

values of 0.70, 0.74, 0.92, 0.81, and 0.74, respectively. PolyCheck offers a

scalable and interpretable approach for predicting ADRs in complex treatment

regimens and can support safer, individualized TB therapy in patients with

comorbid conditions.

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**28. PLoS One. 2025 Sep 3;20(9):e0327243. doi: 10.1371/journal.pone.0327243.**

**eCollection 2025.**

Activation and proliferation profiles of M.tuberculosis specific dual functional

CD4+T cells from smear negative pulmonary TB patients.

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San Francisco, California, United States of America.

**BACKGROUND:** Tuberculosis is a major public health challenge in the

resource-limited endemic setting of sub-Saharan Africa. The diagnostic challenge

becomes worse for smear-negative TB cases. Even if efforts for non-sputum-based

TB diagnostic and prognostic biomarkers, there was limited data on blood-based

immunological biomarkers among smear-negative PTB patients.Therefore, we

assessed the phenotypic profile (HLA-DR, CD-38, Ki-67) of M. tuberculosis

specific CD4 + T cells expressing dual IFN-γ and TNF-α cytokines from smear

negative PTB patients in Addis Ababa, Ethiopia.

**METHODOLOGY:** An institutional-based longitudinal cohort study was conducted in

Addis Abeba, Ethiopia, on new smear-negative PTB who were adult and HIV-negative

in comparison with multiple comparator groups. A total of 149 (confirmed

patients with non-TB respiratory disease -33, smear-negative TB-29,

smear-positive TB-34, apparently healthy - 53) study participants was enrolled.

The expression level of activation (HLA-DR, CD-38) and proliferation (Ki-67)

markers from dual IFN-γ and TNF-α cytokines expressing PPD specific CD4 + T

cells were assessed after surface and intracellular cytokine staining. To

confirm the presence of M. tuberculosis, MGIT/LJ culture, PCR, and smear

microscopy were performed.

**RESULT:** The overall level of HLA-DR and CD-38 expression in smear-negative and

positive pulmonary TB patients were substantially higher than that of confirmed

non-TB respiratory illness, apparently healthy QFT positive and negative study

participants (p-value = 0.0127, p-value < 0.0001, p-value = 0.0043, p-value

<0.0001, respectively) before commencing anti TB treatment. Also, among the

smear-negative and positive pulmonary TB cohort, the expression of CD-38,

HLA-DR, and HLA-DR + CD-38 + expression was reduced in the second month and

six-month cohort compared with baseline data (p-value= < 0.0001,

p-value = 0.00365, p -value = 0.0001, respectively).

**CONCLUSION:** In this study, we found the diagnostic and prognostic potential of

activation markers, particularly CD-38, in smear-negative PTB patients from dual

M. tuberculosis-specific IFN-γ + TNF-α+ cytokine producing CD4 + T cells in both the presumed ex vivo and antigen-specific stimulation assays.

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PMID: 40901996 [Indexed for MEDLINE]

**29. Proc Natl Acad Sci U S A. 2025 Sep 9;122(36):e2509997122. doi:**

**10.1073/pnas.2509997122. Epub 2025 Sep 3.**

Loss of the ESX-5 secretion locus in Mycobacterium tuberculosis reshapes the

mycomembrane and enhances ESX-1 substrate secretion.

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The ESX-5 secretion system, uniquely found in slow-growing mycobacteria, is

predicted to secrete over 150 proteins across the inner membrane of

Mycobacterium tuberculosis (M.tb). Although many of these substrates are

believed to promote M.tb virulence, most remain poorly characterized. Here, we

use a complete locus deletion strain of ESX-5 in M.tb to examine the molecular

changes caused by a broad loss in ESX-5 secretory substrates. We confirmed the

selective loss of PE/PPE proteins secreted by ESX-5 into both the culture

filtrate (CF) and outer mycomembrane (OMM) fractions of the M.tb ∆esx5 mutant.

In examining other ESX systems, we found that ESX-1 substrate levels were

increased in both the CF and OMM fractions of the ∆esx5 mutant. Conversely, the

ESX-3 locus was transcriptionally repressed upon ESX-5 deletion. We noted that

the ∆esx5 mutant had altered morphology in the form of wrinkled distortions of

the bacterial surface. Likewise, we identified increased susceptibility of the

∆esx5 mutant to a variety of large (molecular weight >550 g/mol) antimicrobial

compounds, suggesting that an intact ESX-5 system is required for M.tb to

exclude such molecules. Our findings suggest that removing the ESX-5 system from

M.tb fundamentally alters the properties of the mycobacterial OMM and impacts

the expression and secretion activity of other ESX systems.

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PMID: 40901885 [Indexed for MEDLINE]

**30. PLoS One. 2025 Sep 3;20(9):e0329670. doi: 10.1371/journal.pone.0329670.**

**eCollection 2025.**

Lung and abdominal ultrasound accuracy for tuberculosis: An Indian prospective

cohort study.

Weber SF(1)(2)(3), Wolf R(1)(3), Manten K(3)(4), Thangakunam B(5), Isaac B(5),

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**BACKGROUND:** Tuberculosis (TB) diagnosis remains a challenge, particularly in

low-resource settings. Point-of-care ultrasound (POCUS) has shown promise, but

most studies focus on HIV-infected populations. In the case of TB, data on lung

ultrasound (LUS) are sparse. Therefore, this study evaluates the diagnostic

accuracy of lung and abdominal ultrasound for TB diagnosis in an Indian tertiary

care hospital.

**METHODS:** We prospectively enrolled adults with presumed TB and performed

comprehensive ultrasound assessments. Accuracy of individual and combined

sonographic findings was evaluated against a robust reference standard

(mycobacterial culture and PCR). Comparators were C-reactive protein at a

cut-off of 5mg/l and chest x-ray (CXR). A multivariable model incorporating

clinical and ultrasound findings was explored using generalized mixed models and

a random forest approach. (Trial registry DRKS00026636).

**FINDINGS:** Among 541 participants, 102 (19%) were diagnosed with TB and 1% were

HIV-positive. The "Focused Assessment with Sonography for HIV-associated TB"

(FASH) demonstrated moderate sensitivity (51%) and specificity (70%).

Consolidations <1 cm on LUS showed high sensitivity (93%) but low specificity

(16%) and were also seen in non-TB lung infections and other conditions like

bronchial asthma and COPD. Accuracy of larger (≥1 cm) consolidations (72%

sensitive, 55% specific) on LUS was comparable with CXR suggesting possible TB

(81% sensitive, 58% specific). Predictive modeling suggests moderate diagnostic

performance (AUC = 0.79).

**INTERPRETATION:** In our study, POCUS did not meet WHO targets for a stand-alone

facility-based screening test. Nevertheless, diagnostic accuracy for some

findings is comparable to CXR and could be integrated into diagnostic algorithms

to improve TB screening where CXR cannot reach. Future research should explore

artificial intelligence to enhance TB-POCUS accuracy and accessibility, as was

previously reported for CXR.

**RESEARCH IN CONTEXT:** Prior to this study, lung ultrasound (LUS) for TB had been

assessed in only a few studies, limited by uncertain sonographic

characterization of TB-related findings, lack of consistent terminology, and

small numbers of participants with confirmed non-TB diagnoses to determine

specificity for TB. Studies evaluating Focused assessment with sonography for

HIV-associated tuberculosis (FASH) almost exclusively included HIV-infected

individuals and demonstrated moderate sensitivity and specificity. However,

varying study designs and reference standards limit broader generalization of

their findings. Our prospective study from a TB-endemic setting (India)

recruited 541 predominantly HIV-negative participants with presumed TB. This is

the largest cohort to date assessing LUS, FASH, and additional ultrasound

findings for TB diagnosis. Our study demonstrates that no single ultrasound

finding alone, or even in combination, reaches the accuracy targets of the

target product profile for a facility-based screening test (triage) proposed by

WHO. FASH accuracy in our study aligned with previously reported data in

HIV-negative participants but was less specific in HIV-positive participants.

The accuracy of additional ultrasound items of LUS and FASH was comparable to

chest x-ray (CXR). In summary, this study demonstrates accuracy of ultrasound

for TB diagnosis, backed by a robust study design and using a comprehensive

reference standard and CXR comparator for LUS. Modelling suggests that an

algorithmic approach combining ultrasound and clinical findings may be of

highest value to inform risk of TB and guide further testing to confirm the

diagnosis of TB. Other use cases of POCUS, which may aid clinical decision

making in the assessment of disease severity, sampling strategy, and monitoring,

should be evaluated by future studies. These should also focus on the accuracy

of POCUS in people living with HIV and children, as well as evaluate POCUS more

broadly as part of a diagnostic algorithm and by using artificial intelligence

to improve the yield of TB-POCUS.

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**31. RSC Adv. 2025 Sep 1;15(38):31360-31401. doi: 10.1039/d5ra03759j. eCollection**

**2025 Aug 29.**

Advancements in the design and development of pyrazoline-based antimycobacterial

agents: an update and future perspectives.

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Pyrazoline scaffolds have attracted significant interest in medicinal chemistry

due to their broad spectrum of pharmacological activities. Pyrazole-based drugs

are either already approved or are currently undergoing clinical trials across a

range of therapeutic areas. Pyrazolines (Δ2-pyrazolines or 2-pyrazoline or

4,5-dihydropyrazoles) evolved as cyclic analogues of thioacetazone and were

explored for enhanced antitubercular activity over the past five decades. The

scope of this review focused on how extensively the chemical space around

pyrazolines has been explored in relation to their antitubercular activity,

rather than presenting a general structure-activity relationship (SAR) account.

In this exercise, we covered key molecular modifications, including rationale

substitutions and conjugations, aimed at enhancing the potency in general.

Additionally, information pertaining to in vitro/in silico target interaction

and ADMET studies are also covered. A dedicated section is included to showcase

target-oriented strategies (InhA, cytochrome P450 14α-sterol demethylase, and

enzymes involved in the mycobactin biosynthesis pathway), recent patents,

suggested schemes for reported pyrazolines, and an overview of research

methodologies and evaluation models. We believe that this review will enable

medicinal chemists to map unexplored chemical space in identifying critical

research gaps. This is essential for the rational design and development of

potent antitubercular agents against tuberculosis (TB), drug-resistant

tuberculosis (DR-TB), and other non-tubercular mycobacterial diseases (NTMD).

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**32. RSC Adv. 2025 Sep 1;15(38):31272-31288. doi: 10.1039/d5ra03641k. eCollection**

**2025 Aug 29.**

Isoniazid-rhodanine molecular hybrids: design, synthesis, antimycobacterial

activity and computational validation.

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A novel series of isoniazid-rhodanine (INH-Rh) molecular hybrids (9a-t) was

prepared and structurally characterized using different spectroscopic

techniques, including FTIR, NMR (1H, 13C, HMBC, and HSQC), and HRMS. All the

hybrids (9a-t), including their precursors (3a-t and 8a-t), were assessed for

their in vitro anti-tubercular activity, alongside the standard anti-tubercular

drug, INH. Among them, 9d (MIC = 1.56 μg ml-1), 9j (MIC = 12.50 μg ml-1), and 9n (MIC = 12.50 μg ml-1) displayed the most potent activity against M. tuberculosis (Mtb), with 9d emerging as the most active. However, limited efficacy was observed for seven selected compounds (3h, 3i, 9d, 9j, 9l, 9n, and 9p) against

INH-resistant Mtb strains harboring mutations in KatG. Moreover, the Mtb strain

overexpressing the enoyl acyl carrier protein reductase (InhA) exhibited

significant resistance to 9d, 9j, and 9n, suggesting InhA as their likely

target. Molecular docking studies revealed that the binding modes and key

intermolecular interactions of the selected compounds closely resembled those of

INH, a known inhibitor of InhA. ADME/T analysis indicated favorable

pharmacokinetic and safety profiles for the synthesized compounds, while DFT

calculations provided further insights into their global reactivity

characteristics.

This journal is © The Royal Society of Chemistry.

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PMCID: PMC12400508

PMID: 40901448

**33. Ann Med Surg (Lond). 2025 Jul 28;87(9):6135-6138. doi:**

**10.1097/MS9.0000000000003647. eCollection 2025 Sep.**

Undifferentiated inflammatory arthritis in a tuberculosis-positive patient: a

diagnostic and therapeutic challenge - a case report.

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**BACKGROUND:** In clinical practice, some cases gently challenge our assumptions,

reminding us that not everything is what it seems. This is the story of a young

woman receiving treatment for tuberculosis who began showing signs that pointed

beyond infection alone. It underlines how autoimmunity can surface in the

shadows of another illness, demanding careful attention and an open mind.

**CASE PRESENTATION:** A 27-year-old woman receiving treatment for pulmonary

tuberculosis presented to us with worsening joint pain, swelling, facial rash,

and muscle weakness. She had trouble with basic movements like climbing stairs

and noticed rashes over her face and knuckles. On examination, she had a malar

rash and Gottron's papules, with noticeably weakness in her upper and lower

limbs. Her lab results showed elevated ESR and a positive PM-Scl antibody;

meanwhile, other autoimmune markers were negative. Her imaging revealed

tenosynovitis and microvascular changes on capillaroscopy. She was then

diagnosed with undifferentiated inflammatory arthritis, within the myositis

spectrum - and was started on steroids and DMARDs while continuing her TB

therapy.

**DISCUSSION:** This case highlights the challenges of diagnosing autoimmune disease

in a patient already being treated for TB. In endemic areas, it is easy to blame

new symptoms on infection alone, but her evolving clinical picture urged us to

dig deeper. It reinforces the need for careful clinical judgment and teamwork

when managing overlapping infectious and autoimmune conditions.

**CONCLUSION:** For patients like her, timely recognition of autoimmune features -

especially in the context of chronic infections - can change outcomes. Her

journey highlights not only the complexity of medicine but also the value of

listening closely, thinking broadly, and responding with a multidisciplinary

approach.

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**34. J Clin Microbiol. 2025 Sep 3:e0064325. doi: 10.1128/jcm.00643-25. Online ahead of print.**

Diagnostics and new treatment regimens for TB: can the Xpert MTB/XDR assay fill

the gap for fluoroquinolone testing?

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Rapid diagnosis of resistance-conferring mutations to antibiotics used for the

treatment of tuberculosis (TB) is critical for patient care and public health

control efforts. Prior guidelines included the use of fluoroquinolones (FQs) for

the treatment of drug-resistant TB, including multidrug-resistant TB,

pre-extensively drug-resistant TB, and extensively drug-resistant TB. More

recently, a short-course regimen for antibiotic-susceptible TB was introduced,

which includes the use of a FQ, a drug class that diagnostic algorithms in the

United States (US) typically do not test for if all first-line agents are

susceptible. However, FQ mono-resistance has been documented by previous

studies, and for this reason, we tested 319 archived Mycobacterium tuberculosis

complex (MTBC) strains spanning a 14-year period of time using the Xpert MTB/XDR

assay. Resistance to FQs was detected in 4.4% (14/319) of the isolates tested,

with mutations predominating in the gyrA region (13/14; 92.9%). A single isolate

(1/14; 7.1%) was found to have a gyrB mutation. A broth microdilution assay

demonstrated the minimum inhibitory concentrations for resistant strains that

ranged from 0.5 µg/mL to 8.0 µg/mL. Importantly, three strains were FQ

mono-resistant and would have been completely missed by standard testing

algorithms. Although currently unavailable in the US, the GeneXpert XDR assay

has the potential to fill the significant diagnostic gap in susceptibility

testing of MTBC resistance to FQs and support the use of the currently

recommended short-course regimen.IMPORTANCE This study provides insight into the

need for additional rapid testing for the detection of drug resistance

(specifically to fluoroquinolones) in tuberculosis (TB) cases in the United

States (US). The current regimens for TB treatment rely on knowing resistance

patterns to optimize treatment, and missed resistance could have a negative

impact on the health of the patient, as well as contribute to increased

drug-resistance mutations in new TB cases. There are currently limited platforms

for expanded rapid drug resistance testing for TB cases in the US, and this

study looks at past TB cases that had drug resistance missed by routine testing.

DOI: 10.1128/jcm.00643-25

PMID: 40899881

**35. J Bacteriol. 2025 Sep 3:e0023625. doi: 10.1128/jb.00236-25. Online ahead of**

**print.**

A trans-translation inhibitor that targets ribosomal protein bL12 kills

Mycobacterium tuberculosis.

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New antibiotics with novel mechanisms of action are needed to treat infections

by multidrug-resistant strains of Mycobacterium tuberculosis. Here, we show that

KKL-1005, an anti-tubercular triazole-based molecule, binds to ribosomal protein

bL12 and specifically inhibits the trans-translation ribosome rescue pathway, a

process essential for the survival of M. tuberculosis. Our data demonstrate that

KKL-1005 binds to the N-terminal domain of bL12, both in vitro and in bacterial

cells, and specifically inhibits trans-translation and not normal translation.

These results suggest that tmRNA-SmpB interacts with bL12 differently from tRNA

and raise the possibility of developing antibiotics targeting

bL12**.IMPORTANCE** Tuberculosis continues to be a leading cause of death worldwide,

and antibiotics that target new pathways are urgently needed. trans-Translation

is a ribosome rescue pathway required for the survival of Mycobacterium

tuberculosis. We identified a small molecule, KKL-1005, that specifically

inhibits trans-translation without affecting translation from a library of

compounds that prevent the growth of M. tuberculosis. KKL-1005 targets bacterial

ribosomal protein bL12, which is essential for the recruitment and activation of

GTPase translation factors. The specificity of KKL-1005 for trans-translation

indicates that bL12 interacts differently with the translation machinery during

trans-translation than during canonical translation. KKL-1005 is bactericidal

against M. tuberculosis, suggesting that inhibiting trans-translation by

targeting bL12 is a new strategy for developing antibiotics against

drug-resistant infections.

DOI: 10.1128/jb.00236-25

PMID: 40899852

**36. Clin Infect Dis. 2025 Sep 3:ciaf475. doi: 10.1093/cid/ciaf475. Online ahead of print.**

Body Mass Index and Incident Tuberculosis in Close Tuberculosis Contacts.

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**BACKGROUND:** Approximately 95% of people infected with M. tuberculosis do not

progress to tuberculosis (TB) disease. Identifying key determinants of TB

progression could focus prevention efforts.

**METHODS:** Contacts of pulmonary TB patients were enrolled in a prospective

multi-center cohort study (RePORT-Brazil) from 2015-2019 and followed for 24

months. Empirical review and LASSO regression, using baseline clinical and

laboratory information, were used as dimension reduction techniques to determine

factors for inclusion in prediction models. Models were created for: 1) all

contacts, 2) contacts IGRA-positive at baseline, and 3) IGRA-positive contacts

who did not receive TB preventive therapy (TPT; <30 days isoniazid). Internal

validation was performed using bootstrapping.

**RESULTS:** Among 1846 contacts of 619 TB index patients, 25 (1.4%) progressed to

TB. No TPT was a risk factor for progression to TB among all contacts

[mixed-effects adjusted hazard ratio (aHR)=16.55, 95% confidence interval (CI):

2.22-124.45]. Internal validation with all contacts yielded an area under the

ROC curve of 0.80 [95%CI: 0.72-0.86]. Body mass index (BMI) was inversely

associated with increased risk of progressing to active TB among IGRA-positive

contacts who did not receive TPT (aHR=0.89, 95%CI: 0.80-0.99). IGRA-positive

contacts with BMI <25 kg/m2 had a 4.14-fold (95%CI: 1.17-14.67) higher risk of

progression to TB than IGRA-positive contacts with BMI ≥25 kg/m2: 8.4% vs. 2.1%,

respectively.

**CONCLUSIONS:** BMI <25 kg/m2, a readily available biomarker, identified

IGRA-positive close TB contacts at high risk of progressing to TB disease.

Prioritizing this high-risk group for TB preventive therapy could improve TB

prevention efforts.

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Infectious Diseases Society of America.

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PMID: 40898999

**37. BMC Nurs. 2025 Sep 2;24(1):1160. doi: 10.1186/s12912-025-03796-1.**

Technology-integrated nursing interventions to improve adherence to tuberculosis

medication: a scoping review.

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**BACKGROUND:** Despite global efforts, adherence to tuberculosis (TB) treatment

remains suboptimal. Nurses play a crucial role in supporting treatment adherence

through direct care and the integration of digital health tools. Nursing

interventions utilizing technology have great potential to enhance medication

adherence by providing education, reminders, and remote monitoring tailored to

patient needs.

**OBJECTIVE:** To explore nursing interventions involving technology that improve

medication adherence among TB patients.

**METHODS:** This scoping review followed the Arksey and O'Malley framework.

Literature was systematically searched through Scopus, PubMed, and Web of

Science using keywords such as "nursing intervention," "tuberculosis," and

"medication adherence." Inclusion criteria encompassed studies published within

the last ten years, involving people with TB, and describing

technology-integrated nursing interventions aimed at improving treatment

adherence. A total of 12 studies were included and thematically analyzed using a

descriptive qualitative approach with NVivo software.

**RESULTS:** Five main themes were identified: (1) The effectiveness of digital

technology in improving medication adherence, (2) Limitations in access to

healthcare services and the role of technology as a solution, (3) Video

technology for directly observed therapy (VDOT), (4) Interactive reminder system

(Two-Way SMS), and (5) Patient motivation in adhering to TB treatment through

digital technology. Nurses were central to assessing patients' needs, training

them to use digital tools, and maintaining adherence through follow-up and

education.

**CONCLUSION:** Nursing interventions that incorporate digital technology, such as

SMS reminders, VDOT, and mobile health applications are effective in supporting

medication adherence among TB patients. These tools empower nurses to extend

care beyond the clinical setting, particularly in underserved areas.

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PMID: 40898157

**38. BMJ Open. 2025 Sep 2;15(9):e095878. doi: 10.1136/bmjopen-2024-095878.**

Improving tuberculosis treatment adherence: a qualitative study of patients'

perspectives from a pragmatic trial of the tuberculosis treatment support tools

intervention.

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Seattle, Washington, USA.

**OBJECTIVE:** To explore patient perspectives on using a digital adherence

technology (DAT) for tuberculosis (TB) treatment, specifically, the TB Treatment

Support Tools (TB-TST) intervention, which integrates a mobile app designed to

enhance patient-centred support, monitoring and communication, alongside a drug

metabolite test.

**DESIGN:** Qualitative study conducted as part of a pragmatic randomised controlled

trial.

**SETTING AND PARTICIPANTS:** Four public reference hospitals in Argentina. All

patients in the intervention group were invited to participate; 33 patients in

the intervention group and five treatment supporters were included.

**DATA COLLECTION AND ANALYSIS:** semistructured interviews were conducted. The

normalisation process theory guided analysis to understand factors that enable

or hinder the intervention's integration into routine practice for TB treatment

medication adherence.

**RESULTS:** Patients identified medication reminders, educational messages and

direct communication with treatment supporters (TSs) as the most helpful

components of the intervention. Many reported using the app to ask TSs questions

they felt uncomfortable raising with physicians in person. Initially, many

patients did not fully understand the purpose and use of the metabolite test.

Over time, their understanding of the app improved, though some continued to

misinterpret the test results. Motivation to adhere to TB treatment was

primarily driven by a desire to protect family members and resume normal daily

activities. Reported barriers to app use included time constraints due to work,

technical issues, limited internet connectivity and the burden of medication

side effects. While the intervention was generally perceived as supportive and

user-friendly, patients suggested improvements such as faster response times

from TSs, expanded availability and better technical reliability and internet

access.

**CONCLUSION:** These findings highlight the importance of tailoring digital

adherence interventions to meet the diverse needs of patients and reinforce the

pivotal role of the TS as a trusted and accessible source of guidance throughout

TB treatment.

TRIAL REGISTERATION NUMBER: NCT04221789;

https://clinicaltrials.gov/ct2/show/NCT04221789.

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PMID: 40897502 [Indexed for MEDLINE]

**39. Open Forum Infect Dis. 2025 Aug 20;12(9):ofaf474. doi: 10.1093/ofid/ofaf474.**

**eCollection 2025 Sep.**

Performance of Tongue Swabs for Tuberculosis Diagnosis in Hospitalized Children

Under 5 Years of Age.

Lala SG(1), Ealand C(2), Dangor Z(1)(3), Hlongwane K(4), Milovanovic M(4)(5),

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University, Baltimore, Maryland, USA.

**BACKGROUND:** Tuberculosis (TB) diagnosis remains difficult in children under 5

years of age (under-5s), who have high TB morbidity and mortality rates. In a

high-burden TB setting, we investigated the diagnostic characteristics of Xpert

MTB/RIF Ultra testing of tongue swabs (TS-XU) collected from under-5s.

**METHODS:** In a masked, prospective, observational study, tongue swabs were

collected from enrolled hospitalized under-5s deemed high risk for TB disease

who were categorized into 1 of the following: confirmed, unconfirmed, or

unlikely TB.

**RESULTS:** Of 201 enrolled under-5s, 11 (5.5%) had confirmed TB, 53 (26.4%)

unconfirmed TB, and 137 (68.2%) unlikely TB. TS-XU testing reported "Mtb

detected" in 116 (57.7%) of 201 under-5s: positive results were "trace" (90/116,

77.6%), "very low" (21/116, 18.1%), and "low" or "medium" (4/116 [3.4%] and

1/116 [0.8%], respectively). There were no "high" TS-XU results. When trace

results were presumed negative, TS-XU sensitivity was 17.2% (95% CI, 7.9%-26.4%)

and specificity 89.1% (95% CI, 83.8%-94.3%), and TS-XU detected Mtb in 15

(10.9%) of 137 children with unlikely TB. Our data showed that TS-XU, in

addition to routine TB testing, increased TB detection rates by 19.2%.

**CONCLUSIONS:** Despite the difficulty of interpreting trace-positive results,

TS-XU testing increased TB detection rates in hospitalized under-5s with

presumptive TB.

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Infectious Diseases Society of America.

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**40. Health Sci Rep. 2025 Aug 27;8(9):e71192. doi: 10.1002/hsr2.71192. eCollection**

**2025 Sep.**

Unraveling the Drivers of Tuberculosis: A Retrospective Panel Data Study Across

70 Developing Countries.

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**BACKGROUND AND AIMS:** Tuberculosis (TB) remains a major global cause of death,

particularly in developing countries. This study aims to identify key risk

factors contributing to high TB incidence in these nations, analyze regional

variations, and assess how risk factors differ across continents.

**METHODS:** We conducted a retrospective analysis using data from 70 developing

countries spanning 2000 to 2020, sourced from the World Bank Open Data.

Variables included TB incidence, HIV prevalence, smoking rates, literacy rates,

undernourishment, and population density. A random-effects model was employed to

examine the associations between these factors and TB incidence.

**RESULTS:** HIV prevalence (coefficient = 37.53, 95% CI: 34.28-40.79), smoking

(3.51, 2.99-4.02), undernourishment (1.56, 1.02-2.10), and population density

(0.16, 0.07-0.24) showed significant positive associations with TB incidence.

Literacy rate was negatively associated with TB incidence (-0.11, -0.54 to

0.33), though not significantly. These findings highlight the strong influence

of socio-demographic and health-related factors on TB burden.

**CONCLUSION:** TB continues to pose a serious health challenge in developing

countries. HIV control, reduction of undernourishment and smoking, and managing

population density are critical to reducing TB incidence. Regional differences

underscore the need for tailored prevention strategies.

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PMCID: PMC12391018

PMID: 40895246

**41. Clin Case Rep. 2025 Aug 29;13(9):e70834. doi: 10.1002/ccr3.70834. eCollection**

**2025 Sep.**

Stroke Mimicry: Unmasking a Brainstem Tuberculoma in a Young Patient.

Palanisamy NN(1), Sivasubramanian D(2), Senthilkumar V(1), Aravind S(1), Sanil

S(3), Balasubramanian K(4).

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Intracranial tuberculomas are rare brain lesions caused by the spread of

Mycobacterium tuberculosis from distant sites, typically the lungs. They can

mimic strokes, especially in young, immunocompetent individuals without typical

tuberculosis symptoms. Early diagnosis and antitubercular therapy are crucial

for recovery, particularly in regions where tuberculosis is endemic.

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PMCID: PMC12396934

PMID: 40893397

**42. Proc Natl Acad Sci U S A. 2025 Sep 9;122(36):e2421336122. doi:**

**10.1073/pnas.2421336122. Epub 2025 Sep 2.**

Metabolic rewiring of isoniazid sensitivity in Mycobacterium tuberculosis.

Wang ER(1)(2), Cho K(3)(4)(5), Harrison GA(1)(2), Smelyansky SR(6)(7), Soni

V(8), Smirnov A(1)(2), McKee SR(1)(2), Ghabrial GS(1)(2), Flentie KN(1)(2),

Beatty W(1), Ofori-Anyinam B(9)(10), Sarkar S(11), Hurtaux T(1), Loza L(1),

Almqvist F(11)(12), Doering TL(1), Yang JH(9)(10), Kiessling LL(6)(7)(13), Rhee

KY(8), Patti GJ(3)(4)(5), Stallings CL(1)(2).

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Isoniazid (INH) inhibits mycolic acid synthesis in Mycobacterium tuberculosis

(Mtb) and is a cornerstone of treatment regimens against this deadly pathogen.

However, over 10% of Mtb infections are INH-resistant. The compound C10 can

sensitize clinically relevant INH-resistant mutants to killing by INH. Thus,

understanding the mechanism of action for C10 could aid in designing new

strategies for circumventing drug resistance. We find that C10 treatment

reroutes carbon flux toward valine, drawing carbon away from gluconeogenesis and

the TCA cycle. As a result, C10 decreases cell envelope capsule thickness and

blocks an accumulation of peptidoglycan precursors that occurs in response to

INH treatment in an INH-resistant Mtb katG mutant. In this altered metabolic

state induced by C10, INH treatment of the INH-resistant Mtb katG mutant

inhibits peptidoglycan synthesis, precipitating collapse of cell envelope

integrity. Pyruvate supplementation relieves the C10-induced requirement for

carbon flux toward valine, enhancing carbon assimilation into cell envelope

precursors and restoring resistance to INH. In addition, we identify the

formation of isoniazid-pyruvate in INH-treated katGW328L Mtb, where pyruvate

sequesters INH, lowering the concentration of INH available to inhibit Mtb.

Together, our findings reveal a bactericidal activity for INH in Mtb that can

function in INH-resistant mutants independently of INH-mediated inhibition of

mycolic acid synthesis. This activity for INH can be elicited by shifting carbon

flux toward valine and away from cell envelope precursor synthesis, highlighting

a metabolic vulnerability that can be exploited to kill INH-resistant Mtb.

DOI: 10.1073/pnas.2421336122

PMID: 40892921 [Indexed for MEDLINE]

**43. PLOS Digit Health. 2025 Sep 2;4(9):e0000988. doi: 10.1371/journal.pdig.0000988. eCollection 2025 Sep.**

Opportunistic use of artificial intelligence with X-ray imaging for diagnosis of

HIV status in tuberculosis patients in Uganda and Tanzania.

Cherezov D(1), Dam T(1), Najjingo I(2), Mbabazi M(2), Kisembo H(3), Kirenga

B(2), Soka G(4), Ngadaya E(4), Mfinanga S(4), Madabhushi A(1)(5).

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DOI: 10.1371/journal.pdig.0000988

PMCID: PMC12404497

PMID: 40892846

**44. Lung India. 2025 Sep 1;42(5):438-442. doi: 10.4103/lungindia.lungindia\_653\_24.**

**Epub 2025 Sep 2.**

Tissue sample taken by transbronchial biopsy in the diagnosis of tuberculosis;

benefits-risks.

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**OBJECTIVES:** Tuberculosis (TB) poses a serious health risk in Turkey and globally

and is often difficult to diagnose. It may be sometimes necessary to obtain

bronchoalveolar lavage (BAL) and, in some cases, biopsy samples via bronchoscopy

to acquire an adequate sample. Our aim is to assess the contribution of

transbronchial lung biopsy (TBLB) alongside BAL in diagnosing TB. In addition,

we will evaluate the risk of pneumothorax associated with TBLB and determine the

overall risk-benefit ratio.

**METHODS:** Flexible fiberoptic bronchoscopy (FFB) reports performed for suspected

TB between March 2011 and July 2018 were retrospectively reviewed. Patients who

had both BAL and tissue samples taken via TBLB were included in the study. Of

the 606 patients included, age, sex, the lung area where the biopsy was taken,

BAL and biopsy AFB and culture results, and complications such as pneumothorax

and chest tube application were recorded.

**RESULTS:** A total of 606 patients were included in the study. Of these, 391

patients were male (64.5%) and 215 were female (35.5%). A total of 37 (6.1%)

patients had a positive culture for TB. Nineteen (59.4%) patients were positive

on both BAL and tissue culture, while 5 patients were only positive on tissue

culture. Pneumothorax developed in 34 patients (5.6%), 28 of whom required a

chest tube.

**CONCLUSION:** Using various modalities such as BAL and TBLB together for

diagnosing pulmonary TB can be advantageous when appropriate, particularly given

the absence of significant complications during the procedure. Our findings

indicate that incorporating TBLB alongside BAL impacted the diagnosis of

pulmonary TB.

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DOI: 10.4103/lungindia.lungindia\_653\_24

PMID: 40892816

**45. Lung India. 2025 Sep 1;42(5):414-420. doi: 10.4103/lungindia.lungindia\_602\_24.**

**Epub 2025 Sep 2.**

Yield of systematic screening for tuberculosis among patients with obstructive

airway disease using inhalational corticosteroids.

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Education and Research (JIPMER), Puducherry, India.

**INTRODUCTION:** The increased risk of tuberculosis associated with inhalation

corticosteroids has been demonstrated in various studies. However, the specific

risk factors for developing tuberculosis in this context are less studied. So,

this study was planned.

**METHODS:** This cross-sectional study was carried out in the Department of

Pulmonary Medicine of a tertiary care centre in Puducherry, India. Those

patients who were on inhalational corticosteroid for more than 1 year and having

presumptive TB symptom were included in the study. Sputum smears, chest

radiography, and CBNAAT were done in all cases of presumptive tb cases, and

bronchoscopies and BAL where necessary were used to diagnose patients. The

patient was diagnosed with tuberculosis diagnosis upon microbiologic

confirmation.

**RESULTS:** 1550 patients had symptoms of presumptive tuberculosis and were thus

included in the study. The mean age of our study population was 50.97 ± 19.25.

Male gender, use of higher doses of steroids, coronary artery disease, smoking,

and alcohol use were the risk factors for the development of tuberculosis. On

multivariate regression analysis, diabetes (OR: 6.4, 95% CI: 2.275-18.121, P

value: 0.001) and higher doses of steroid use (OR: 7, 95% CI: 2.485-20.026, P

value: 0.001) were identified as independent risk factors for the development of

tuberculosis among patients using inhalational corticosteroids. The number

indeed to screen was 262.

**CONCLUSION:** Patients who were on higher doses of inhalational corticosteroids

and diabetic patients should be advised to undergo targeted screening and

testing for tuberculosis. In order to get one case tuberculosis patient, we have

to screen 262 cases of OAD patients.

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DOI: 10.4103/lungindia.lungindia\_602\_24

PMID: 40892813

**46. PLoS One. 2025 Sep 2;20(9):e0331035. doi: 10.1371/journal.pone.0331035.**

**eCollection 2025.**

Burden of tuberculosis in Eastern Africa region from 1990-2021: A systematic

analysis for the Global Burden of Disease 2021 Study.

Yismaw L(1)(2), Zewotir T(3), Muluneh EK(2), Getnet F(4)(5), Getinet K(6)(7),

Getahun HA(2)(8), Zewale TA(2), Tariku MK(1)(2), Asrat A(2), Andualem M(9),

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**BACKGROUND:** Tuberculosis (TB), despite being a preventable and curable disease,

remains a leading infectious cause of death. In Eastern Africa, TB poses a

significant public health challenge. This study examined TB incidence,

prevalence, mortality, and disability-adjusted life years (DALYs) from 1990 to

2021. This study aims to provide evidence for policy and healthcare stakeholders

in Eastern Africa.

**METHOD:** This analysis is part of the Global Burden of Disease (GBD) Study 2021

to estimate TB incidence, prevalence, TB-specific mortality, and DALYs. The GBD

study applies several analytical tools and uses data from national health

surveys, vital registration systems, WHO reports, and hospital records. The

results were presented by age group, sex, location, and year, accounting for 95%

uncertainty intervals.

**RESULT:** A significant decline was observed in TB burden across East African

countries between 1990 and 2021. The age standardized TB incidence rate dropped

by 53% (95% UI: 50.7%, 55.1%), from 518.8 per 100,000 in 1990-244 in 2021, while

TB prevalence dropped by 29.1% (95% UI: 26.3%, 31.7%), from 38,577.6-27,366.1

per 100,000. TB-related deaths fell by 64.6% (95% UI: 55.0%, 71.4%), and TB

related DALYs declined by 68.2% (95% UI: 60.3%, 73.6%). Despite these

improvements, men consistently experienced higher TB incidence, prevalence,

mortality, and DALYs compared to women. Ethiopia showed the highest reductions

in terms of TB-related mortality and DALYs compared to countries in the region,

with annual reduction rates of 6.0% and 6.6%, respectively. Conversely, Somalia

had the highest TB burden in 2021 in terms of incidence, mortality, and DALYs.

Mauritius and Seychelles maintained the lowest TB burden, attributed to strong

health systems and socio-economic conditions.

**CONCLUSION:** A significant decline was observed in TB burden across eastern

African countries between 1990 and 2021. However, TB rates remain significantly

higher than global and African averages. Therefore, continued investment in

health systems and tailored interventions is essential to alleviate the disease

burdens, specifically in high-prevalence areas.

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DOI: 10.1371/journal.pone.0331035

PMCID: PMC12404479

PMID: 40892766 [Indexed for MEDLINE]

**47. Antimicrob Agents Chemother. 2025 Sep 2:e0010125. doi: 10.1128/aac.00101-25.**

**Online ahead of print.**

Evaluation of cycloserine dose regimens in an Indian cohort with

multidrug-resistant tuberculosis: a population pharmacokinetic analysis.

Resendiz-Galvan JE(#)(1), Arora PR(#)(2), Lokhande RV(2), Udwadia ZF(2),

Rodrigues C(2), Gupta A(3)(4)(5), Tornheim JA(#)(3)(4)(5), Denti P(#)(1),

Ashavaid TF(#)(2); The MDR-TB MUKT and Indo-South Africa Study Teams; MDR-TB

MUKT and Indo-South Africa Study Teams.

Collaborators: Pinto L, Mullerpattan JB, Sunavala A, Pater JM, Naik PR, Dherai

AJ, Pandya H, Surve U, Choi W, Vania C, Martinson NA, Nabeemeeah F, Wiesner L,

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Cycloserine is recommended for inclusion in regimens for multidrug-resistant

tuberculosis (MDR-TB). Its efficacy is time dependent and relies on the

concentration remaining above the minimum inhibitory concentration (MIC);

however, there is a concentration-dependent risk of neurotoxicity. Limited

pharmacokinetic (PK) data are available in individuals of Indian origin, despite

the high burden of MDR-TB in India. We enrolled adults and adolescents receiving

cycloserine for MDR-TB at a tertiary hospital in Mumbai, India, in a prospective

cohort. Total daily doses ranged from 500 to 750 mg, and participants underwent

serial PK sampling on multiple visits starting 1 month after treatment

initiation. PK data were analyzed using non-linear mixed-effect modeling. A

total of 180 participants (117 females) were enrolled, with a median age of 27

years (interquartile range [IQR] 21-35), weight of 56.0 kg (IQR 46.0-65.9), and

fat-free mass of 38.6 kg (IQR 32.3-47.1). Cycloserine PK was best described by a

one-compartment model with first-order elimination and transit compartment

absorption. Allometric scaling by fat-free mass provided the best adjusment for

body size. Serum creatinine improved the model fit and allowed separate

estimation of renal and non-renal clearances, whose typical values were 0.589

and 0.901 L/h, respectively. Simulations showed median exposure of 308 mg·h/L

after 250 mg twice daily (BID), which is lower than reported in literature.

Monte Carlo simulations suggested that doses of 500 or 750 mg BID are required

to reach efficacy targets of ≥30% and ≥64% time within dose interval above MIC.

The reasons behind the low exposure identified in this Indian population require

further investigation.

DOI: 10.1128/aac.00101-25

PMID: 40891988

**48. FEMS Microbiol Rev. 2025 Sep 2:fuaf040. doi: 10.1093/femsre/fuaf040. Online**

**ahead of print.**

Exploring the multilayered response of TB bacterium Mycobacterial tuberculosis

to lysosomal injury.

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Mtb subverts host immune surveillance by damaging phagolysosomal membranes,

exploiting them as replication niches. In response, host cells initiate a

coordinated LDR, integrating membrane repair, selective autophagy, and de novo

biogenesis. This review delineates a systems-level model of lysosomal quality

control governed by three critical regulatory axes: LGALS3/8/9, TRIM E3

ubiquitin ligases, and the AMPK-TFEB signaling pathway. LGALSs detect exposed

glycans on ruptured membranes, triggering ESCRT-mediated repair and recruiting

ARs. TRIM proteins mediate context-specific ubiquitination, enhancing cargo

selection and facilitating transcriptional reprogramming via TFEB.

Simultaneously, AMPK-TFEB signaling links metabolic stress to lysosomal

regeneration, reinforcing immune defense and cellular adaptation. We highlight

emerging mechanisms, including ATG8ylation, CASM, Ca2 + leakage, and SG

formation, that refine this multilayered response. Mtb virulence factors

selectively disrupt these pathways, revealing their relevance to pathogen

persistence. Beyond infection, this triadic network maintains lysosomal

integrity in neurodegeneration, inflammation, and lysosomal storage disorders.

Understanding its modular design reveals novel therapeutic targets and HDTs for

combatting drug-resistant TB. This review integrates recent advances into a

coherent framework that redefines lysosomal function as a dynamic,

immune-regulatory hub essential for cellular resilience under infectious and

metabolic stress.

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DOI: 10.1093/femsre/fuaf040

PMID: 40891899

**49. Monaldi Arch Chest Dis. 2025 Sep 1. doi: 10.4081/monaldi.2025.3258. Online ahead of print.**

Interferon-γ release assay.

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Traditionally, tuberculosis (TB) has been viewed as having two distinct

manifestations, known as TB infection (TBI) and TB disease. The spectrum,

however, has recently been expanded to include the elimination of TBI with the

help of innate and/or adaptive immunity, TBI, incipient and subclinical TB

disease, and TB disease. Epidemiologically speaking, identifying individuals

with TBI is critical since diagnosis and treatment of TBI are essential in

controlling the TB burden. It is important to identify high-risk individuals

with TBI who are more likely to progress to active TB disease. There are two

diagnostic methods for identifying TBI. These include the conventional

tuberculin skin test (TST) and interferon-γ release assay (IGRA). However, these

methods are not the 'gold standard.' Furthermore, all of these methods are

indirect, relying on the host's adaptive immune response to Mycobacterium

tuberculosis-derived protein antigens. This review will describe the various

tests for TBI, such as TST, IGRAs, newer skin and blood tests, methods for

performing IGRAs, interpretation strategies, and limitations.

DOI: 10.4081/monaldi.2025.3258

PMID: 40891796

**50. Monaldi Arch Chest Dis. 2025 Sep 1. doi: 10.4081/monaldi.2025.3126. Online ahead of print.**

Fetal-maternal complications due to pregnancy-acquired tuberculosis: a narrative

review of the literature.

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Tuberculosis (TB) during pregnancy can cause certain deleterious effects to both

the mother and the fetus, leading to significant morbidity and mortality. The

risk of TB rises significantly during pregnancy due to dampening of the immune

response in females and certain factors yet to be studied. Since pregnant

females are ruled out of clinical trials due to their pregnancy status, not much

clinical data is available on how to combat TB in them or about the clinical

safety and efficacy of certain drugs. Hence, not only is it important to make

pregnant females vital study participants of clinical trials, but also to

enhance their knowledge regarding the disease so that they may timely access

quality care. It is also important to facilitate these TB-positive pregnant

females through the introduction of gender-sensitive policies that are more

exclusive and allow access to quality TB control programs that provide timely

care, nutritional support, and quality and supportive management.

DOI: 10.4081/monaldi.2025.3126

PMID: 40891795

**51. Future Med Chem. 2025 Sep 2:1-14. doi: 10.1080/17568919.2025.2552642. Online**

**ahead of print.**

Structural insights into Arylidenehydrazinyl Benzenesulfonamides as potent

mycobacterial carbonic anhydrase inhibitors.

Kumar P(1), Singampalli A(1), Bandela R(1), Bellapukonda SM(1), Maddipatla S(1),

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of Florence, Sesto Fiorentino (Florence), Italy.

**AIMS:** To design, synthesize, and assess novel sulfonamide hydrazone derivatives

as selective inhibitors of Mycobacterium tuberculosis carbonic anhydrase.

**MATERIALS AND METHODS:** Two series of 4-(arylidenehydrazinyl)benzenesulfonamides

(5a-r) and N-arylidene-4-methylbenzenesulfonohydrazides (6a-h) were synthesized

and evaluated against recombinant MtCA isoforms 1 and 3, and human carbonic

anhydrase isoforms I and II by enzyme inhibition assays. Molecular docking and

molecular dynamics simulations assessed the binding stability and coordination

with the active-site zinc ion. Anti-mycobacterial activity was determined by

minimum inhibitory concentrations (MICs) against M. tuberculosis. Time-kill

kinetics and cytotoxicity assays evaluated the bactericidal potential and

selectivity of the compound toward mammalian cells.

**RESULTS:** The compounds showed potent inhibition of MtCA 3 and hCA II, with

moderate activity against MtCA 1 and hCA I. Notably, compounds 3e and 3f

exhibited Ki values of 0.0931 µM and 0.0984 µM, respectively, surpassing

acetazolamide (Ki = 0.104 µM). Docking and simulations confirmed stable zinc

coordination. MIC values ranged from 4 to 128 µg/mL. Time-kill and cytotoxicity

studies confirmed rapid bactericidal activity and low mammalian toxicity.

**CONCLUSION:** These sulfonamide hydrazone derivatives demonstrate potent,

selective MtCA inhibition, robust antimycobacterial efficacy, and favorable

safety profiles, representing promising scaffolds for novel tuberculosis

therapies with a novel mode of action.

DOI: 10.1080/17568919.2025.2552642

PMID: 40891745

**52. HLA. 2025 Sep;106(3):e70384. doi: 10.1111/tan.70384.**

Host Genetic Factors and Clinical Comorbidities Associated With Tuberculosis

Risk.

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HLA influence the immune response, shaping genetic susceptibility or resistance

to tuberculosis (TB). This study aimed to investigate the associations of host

genetics and comorbidities with TB infection in Taiwanese populations. This

retrospective case-control study utilised data from the Taiwan Precision

Medicine Initiative. TB cases and non-TB controls were compared using

genome-wide association studies (GWAS), HLA allele typing, and genotype data.

Multivariate logistic regression identified independent predictors of TB and

interactions between risk factors. A total of 390 TB cases and 3,909 controls

were analysed. Risk factors for TB included bronchiectasis (OR = 2.76; 95% CI

1.54-4.44; p < 0.001), diabetes mellitus (OR = 1.30; 95% CI 1.00-1.68;

p = 0.050), malignancy (OR = 1.46; 95% CI 1.15-1.85; p = 0.002), smoking

(OR = 1.42; 95% CI 1.08-1.88; p = 0.012), and steroid use (OR = 1.66; 95% CI

1.29-2.13; p < 0.001). HLA-DRB1\*16:02 was associated with a higher frequency in

the TB group (OR = 1.47; 95% CI 1.04-2.09; p = 0.030). Interaction analysis

showed HLA-DRB1\*16:02 increased TB risk in non-smokers (OR = 1.58; 95% CI

1.02-2.46; p = 0.042), but not in smokers. HLA-DRB1\*16:02 was associated with a

higher risk for TB. While carriers of HLA-DRB1\*16:02 did not exhibit an

increased risk of TB among smokers, we demonstrated a heightened risk among

non-smokers.

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**53. Trop Med Health. 2025 Sep 2;53(1):122. doi: 10.1186/s41182-025-00805-6.**

Progress and challenges in tuberculosis preventive treatment in the Western

Pacific Region: a situational analysis of seven high tuberculosis burden

countries.

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**BACKGROUND:** Tuberculosis preventive treatment (TPT) can avert progression from

infection to disease, yet scale-up across the World Health Organization Western

Pacific Region is patchy. To guide acceleration, we assessed progress,

challenges and responses in seven high-burden countries-Cambodia, China, Lao

People's Democratic Republic (PDR), Mongolia, Papua New Guinea, the Philippines

and Viet Nam-drawing on 2015-2023 programme data, structured questionnaires,

follow-up interviews and a regional validation workshop.

**MAIN BODY:** Six of the seven countries have issued national TPT guidelines and

five now offer shorter rifapentine- or rifampicin-based regimens. The number of

people started on TPT rose sharply in most settings, driven by household

contacts aged ≥ 5 years in Cambodia, Mongolia and the Philippines and by people

living with HIV in Lao PDR and Papua New Guinea. However, coverage of children

under five and other high-risk groups remains low. Cascade analysis revealed

major attrition between screening and TPT initiation. Key obstacles, viewed

through a socio-ecological lens, include: individual complacency, fear of

adverse events and limited provider confidence; stigma and consent barriers in

migrant households; intermittent staff training, medicine stock-outs and weak

digital tools; long journeys to health facilities; and policy-practice gaps such

as the absence of child-friendly formulations and non-notification of

tuberculosis infection. Countries and partners endorsed a tiered package

combining patient-centred counselling, mobile reminders, shorter paediatric

regimens, stigma-reduction campaigns and remote e-consent. Health systems will

reinforce staff training, digital supply-chain and adherence tools, while

decentralised one-stop outreach and community health-workers extend coverage. A

multisector task force will fast-track paediatric fixed-dose registration, make

infection notifiable and absorb preventive treatment costs into national budgets

and insurance schemes.

**CONCLUSIONS:** The introduction of shorter regimens and rising enrolment confirm

that rapid gains are achievable, yet wide disparities persist across age groups,

risk categories and care-cascade stages. Implementing the agreed client,

community, institutional and policy interventions-backed by integrated

governance and sustainable domestic funding-can convert TPT from a promising

guideline into a routine, life-saving component of primary health care

throughout the Western Pacific Region.

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**54. BMC Infect Dis. 2025 Sep 1;25(1):1087. doi: 10.1186/s12879-025-11449-6.**

Long-term impact of national tuberculosis program interventions on incidence and

disparities by age and geography.

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**BACKGROUND:** Evaluations of the national tuberculosis control programs (NTPs)

frequently lacked insights into the uneven long-term impacts on distinct age

groups and geographic regions.

**METHODS:** We analyzed tuberculosis cases notified from 1990 to 2019 in Changhua,

Taiwan. A Bayesian hierarchical change-point model was developed to estimate the

NTP’s effects on different age groups and townships and project the long-term

tuberculosis incidence trend to 2035.

**RESULTS:** A total of 23,149 tuberculosis cases were identified. Tuberculosis

incidence peaked at 106.6 per 100,000 in 2002, then declined steadily. Annual

reductions estimated after the establishment of the laboratory network, directly

observed therapy implementation, and post-2015 projections were 3.3%, 4.5%, and

5.7%, respectively. Tuberculosis incidence fell by 44.8% from its peak to 2016,

with our model projecting a further reduction of 69.0% by 2035. The predicted

overall incidence (per 100,000) is 15.7 in 2035, with age-specific rates and

corresponding projected reductions expected to be 1.6 (68.1%), 3.6 (75.1%), 12.3

(76.6%), and 113.1 (65.4%) for ages 0 to 29, 30 to 49, 50 to 69, and over

70 years old, respectively. Older adults constituted over two-thirds of cases,

showing intractable reduction. Geographical disparities persisted, with higher

incidences noted in remote rural townships.

**CONCLUSIONS:** The NTP has significantly decreased tuberculosis incidence in

Changhua; however, additional efforts will likely be required to reach the END

TB targets by 2035. Future programs must expand preventive treatments for latent

tuberculosis infection and consistently address barriers within the TB care

cascade, with a specific focus on the elderly and residents of underserved

areas.

SUPPLEMENTARY INFORMATION: The online version contains supplementary material

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PMID: 40890655

**55. Sci Rep. 2025 Sep 2;15(1):32270. doi: 10.1038/s41598-025-17959-2.**

Development and validation of a risk prediction model for pulmonary tuberculosis

in presumptive tuberculosis patients in Tigray, northern Ethiopia.

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The incidence of tuberculosis (TB) has increased in Tigray, Ethiopia due to war

and a crippled healthcare system. Although early detection and treatment are

critical for TB control, over 30% of TB cases are missed using current

diagnostic techniques. Thus, we developed and validated a risk prediction model

for pulmonary TB in presumptive cases. In this multicenter cross-sectional

study, we consecutively enrolled 907 respondents from primary healthcare

facilities in Tigray, northern Ethiopia. We used least absolute shrinkage and

selection operator regression to identify variables for the model. Risk scores

were generated from the coefficients of multivariable logistic regression. We

evaluated the model performance using the area under the curve and calibration

plots, and clinical utility using decision curves. Among all respondents, 155

(17%) had GeneXpert-confirmed pulmonary TB. At an optimal cutoff value of 8.5,

the model demonstrated a discrimination accuracy of 0.82 (95% CI: 0.78-0.85), a

sensitivity of 82.6%, and a specificity of 68.9%. The model had a calibration

slope of 0.98 and an intercept of 0.001. The model exhibits acceptable

discrimination and calibration performance. Thus, it can be used for screening

patients for pulmonary TB in primary healthcare settings where accurate

diagnostic resources are limited.

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**56. Sci Rep. 2025 Sep 1;15(1):32127. doi: 10.1038/s41598-025-18112-9.**

Association of CD14 rs2569190 and rs2569191 polymorphisms with tuberculosis

susceptibility in the Kurdish population of Iran.

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Tuberculosis (TB), caused by Mycobacterium tuberculosis (Mtb), remains a leading

cause of infectious disease mortality globally. Host genetic factors,

particularly those involved in innate immunity like Cluster of Differentiation

14 (CD14), may influence susceptibility to TB. This study investigated the

association of two CD14 promoter polymorphisms, rs2569190 (C-159 T) and

rs2569191 (A-1145G), with TB susceptibility in the Kurdish population of Iran. A

prospective case-control study was conducted, enrolling 303 newly diagnosed TB

patients (280 drug-sensitive, 23 MDR-TB) and 288 age- and sex-matched healthy

Kurdish controls from Ilam, Iran. Genotyping for rs2569190 and rs2569191 was

performed using PCR-RFLP. The TT genotype of rs2569190 and the GG genotype of

rs2569191 were significantly more frequent in both drug-sensitive and MDR-TB

patient groups compared to controls (P < 0.05). Under the codominant model, the

TT genotype of rs2569190 (OR = 1.68, 95% CI 1.15-2.45) and the GG genotype of

rs2569191 (OR = 1.55, 95% CI 1.06-2.26) were associated with increased TB

susceptibility. Haplotype analysis revealed a higher prevalence of the CG

haplotype in TB patients and an association of the TG haplotype with increased

TB risk. In conclusions, this study suggests that the CD14 promoter

polymorphisms rs2569190 and rs2569191 are associated with increased

susceptibility to tuberculosis in the Kurdish population of Iran. These findings

highlight the potential role of CD14 genetic variations in TB pathogenesis and

warrant further investigation in other populations and functional studies to

elucidate the underlying mechanisms.

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**57. BMJ Open Respir Res. 2025 Sep 1;12(1):e003292. doi: 10.1136/bmjresp-2025-003292.**

Trends and determinants of unfavourable outcomes in paediatric tuberculosis:

insights from a 20-year cohort in Cameroon.

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

mortality in resource-limited settings. Despite progress in TB care,

unfavourable treatment outcome persists, highlighting the need to identify

determinants and address gaps in paediatric TB management. This study aimed to

assess treatment outcomes and identify determinants of unfavourable outcomes in

children treated for TB at a referral centre in Cameroon.

**METHODS:** This retrospective cohort study included children aged <15 years

diagnosed with TB and followed at the Jamot Hospital of Yaoundé from 2001 to

2020. Treatment outcome was classified as favourable (cured or treatment

completed) or unfavourable (death, treatment failure or loss to follow-up).

Sociodemographic and clinical data were recorded. A Poisson regression model was

applied to evaluate temporal trends in the annual incidence of unfavourable

outcomes. Logistic regression was used to identify determinants of unfavourable

outcome.

**RESULTS:** Of the 881 children included, 52.1% were female and 40.7% were ≤5

years. HIV status was unknown for 36.9% and positive for 10.1% of children.

Extrapulmonary TB was found in 34.5% of children. The cumulative incidence of

unfavourable outcome was 24.5% (95% CI 21.7% to 27.5%). Loss to follow-up

(19.8%) was the most frequent unfavourable outcome, followed by death (4.5%) and

treatment failure (0.2%). A decreasing trend in the annual proportion of

unfavourable outcomes was observed. Determinants of unfavourable outcome

included: residence out of Yaoundé (adjusted OR (aOR) 12.51; 95% CI 1.10 to

5.58; p=0.02), unknown HIV status (aOR 2.10; 95% CI 1.47 to 3.00; p<0.001) and

retreatment status (aOR 7.25; 95% CI 1.98 to 29.45; p=0.003).

**CONCLUSIONS:** Despite encouraging improvements over time, unfavourable outcomes

remain high in paediatric TB. Strengthening HIV testing, follow-up systems and

access to care for children in rural areas is essential to sustain and

accelerate progress in TB treatment success.

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**58. J Neurosurg Case Lessons. 2025 Sep 1;10(9):CASE25349. doi: 10.3171/CASE25349.**

**Print 2025 Sep 1.**

Surgical management of biventricular hydrocephalus caused by

tuberculosis-induced bilateral obstruction of the foramen of Monro: illustrative

case.

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**BACKGROUND:** Occlusion of the foramen of Monro is an exceedingly rare condition

in adults and can lead to obstructive hydrocephalus. The authors present the

first reported case of biventricular hydrocephalus caused by

tuberculosis-induced bilateral obstruction of the foramen of Monro. They also

discuss the technical nuances and surgical challenges associated with this

condition.

**OBSERVATIONS:** A 47-year-old female presented with a 3-month history of

short-term memory disturbances, ultimately leading to loss of consciousness.

Neuroimaging revealed symmetrical biventricular hydrocephalus accompanied by

periventricular interstitial edema. A lumbar puncture indicated

lymphocytic-dominant pleocytosis and reduced glucose levels. During the

endoscopic approach, significant stenosis of the foramen of Monro was noticed

and monroplasty and septostomy were performed. Pathological examination revealed

granulomatous inflammation. At the 1-year follow-up, the patient demonstrated

significant clinical and radiological improvement, with resolution of symptoms

and hydrocephalus.

**LESSONS:** Tuberculosis-induced bilateral idiopathic occlusion of the foramen of

Monro is an extremely uncommon cause of hydrocephalus. Neuroendoscopy allows for

visualization, biopsy, and direct treatment of the obstruction simultaneously.

While conservative management may be adequate for asymptomatic cases,

neuroendoscopic procedures such as septostomy or foraminoplasty provide a

minimally invasive option for restoring CSF flow, avoiding unnecessary shunt

insertion in symptomatic cases. https://thejns.org/doi/10.3171/CASE25349.

DOI: 10.3171/CASE25349

PMCID: PMC12400846

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**59. Eur Spine J. 2025 Sep 1. doi: 10.1007/s00586-025-09315-9. Online ahead of print.**

Diagnostic and therapeutic outcomes in spinal tuberculosis: a retrospective

study integrating GeneXpert MTB/RIF, histopathology, and clinical management

strategies.

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**PURPOSE:** Spinal tuberculosis (STB) remains prevalent in developing nations and

significantly contributes to morbidity, often resulting in kyphotic deformity

and neurological deficits. In this study, we correlate the diagnostic,

therapeutic and prognostic factors according to the current standard of

management of STB.

**METHODS:** This retrospective study evaluated diagnostic and prognostic factors in

77 patients with STB treated surgically (37.7%) or non-surgically (62.3%)

between 2018 and 2023. Diagnostic tools included GeneXpert MTB/RIF(GXMTB/RIF)- a

rapid molecular test for detecting Mycobacterium tuberculosis and rifampicin

resistance- and histopathological confirmation via biopsy. Clinical outcomes

were assessed using Visual Analogue Scale, Oswestry Disability Index,

inflammatory markers (ESR, CRP), kyphotic deformity correction, and neurological

improvement.

**RESULTS:** GeneXpert MTB/RIF detected Mycobacterium tuberculosis in 94.8% of

cases, with 5.2% showing rifampicin resistance. Histopathology revealed

granulomatous infiltration in 96.1% of biopsies, underscoring the importance of

combining diagnostic methods. Both groups showed significant improvement over 12

months, with surgical patients exhibiting higher baseline kyphosis angles

(47.41° vs. 19.27°, p < 0.001) and greater post-treatment correction (14.14° vs. 2.71°, p = 0.04). Neurological status, evaluated via ASIA Impairment Scale

improved post-treatment, with 93.5% achieving normal neurology. Deformity

presence strongly correlated with surgical intervention (51.9% vs. 8%,

p < 0.001).

**CONCLUSION:** The study highlights the efficacy of anti-tubercular therapy (ATT)

and the role of surgery in severe deformity or neurological compromise. Notably,

rare discrepancies between GXMTB/RIF and histopathology (5.2% GXMTB/RIF -

negative but histopathology- positive) emphasize the need for clinical judgment

alongside laboratory findings. Surgical intervention is pivotal for deformity

correction and neurological recovery, while ATT remains the cornerstone.

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**60. Lancet Infect Dis. 2025 Sep;25(9):947. doi: 10.1016/S1473-3099(25)00485-2.**

New advances for drug-resistant tuberculosis.

The Lancet Infectious Diseases.

DOI: 10.1016/S1473-3099(25)00485-2

PMID: 40846442

**61. Lancet Glob Health. 2025 Sep;13(9):e1490-e1491. doi:**

**10.1016/S2214-109X(25)00305-5.**

The high cost of donor withdrawal: implications for tuberculosis progress.

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PMID: 40845869

**62. Carbohydr Res. 2025 Aug 30;558:109652. doi: 10.1016/j.carres.2025.109652. Online ahead of print.**

Synthesis and inhibition studies of substrate analogues for MshC (cysteine

ligase) enzyme in Mycobacterium tuberculosis.

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Mycothiol cysteine ligase (MshC) from Mycobacterium tuberculosis (TB) plays a

vital role in the biosynthesis of mycothiol (MSH) and can serve as a potential

target for designing novel anti-mycobacterial compounds. Herein we report the

synthesis of MshC substrate GlcN-Ins and substrate-based analogues as potential

inhibitors for MshC. We obtained IC50 values in the micromolar range for our

substrate analogues; comparable to other reported inhibitors. Our strategy

exploits the synthesis of substrate analogues through the modification of the

C-2 position of GlcN-Ins.

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**63. J Mol Graph Model. 2025 Aug 28;142:109158. doi: 10.1016/j.jmgm.2025.109158.**

**Online ahead of print.**

Identification of potential alternatives for isoniazid: An in silico molecular

dynamics study.

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Tuberculosis (TB) remains a major global health concern that affects millions

and results in several casualties and these numbers are further increased

because of the drug-resistant strains of Mycobacterium tuberculosis (M. tb).

Current treatments, such as Isoniazid (INH), while effective, are increasingly

compromised by resistance and associated side effects, emphasizing the urgent

need for new therapeutic options. This study focuses on identifying novel

inhibitors for the Enoyl-Acyl Carrier Protein Reductase (InhA), a crucial enzyme

in mycobacterium cell wall biosynthesis. Using a combination of ligand-based and

structure-based virtual screening, we screened a library of FDA-approved drugs

to find potential alternatives to INH. Several promising compounds with superior

binding affinities to the INH-NAD adduct were identified. These compounds

underwent further refinement and analysis through molecular dynamics

simulations, where their stability, binding interactions, and free energy

profiles were thoroughly evaluated. Our simulations revealed that Bictegravir

and Vibegron demonstrated strong electrostatic interactions and favourable

binding energies, making them a potential candidate for TB treatment. This

computational approach provides a foundation for discovering safer and more

effective therapies against both drug-sensitive and drug-resistant TB strains.

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**64. Front Public Health. 2025 Aug 20;13:1642015. doi: 10.3389/fpubh.2025.1642015.**

**eCollection 2025.**

Epidemiology of tuberculosis in Minas Gerais, Brazil, between 2013 and 2023 and

the impact of the COVID-19 pandemic.

do Bem Braga RC(1), Meurer IR(2), D'Carmo Sodré MM(3), de Carvalho LD(4), Marin

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**BACKGROUND:** Tuberculosis (TB), a disease caused by bacteria of the Mycobacterium

tuberculosis complex (MTC), is one of the oldest diseases in human history, and

despite several global efforts to reduce case numbers, it remains one of the

main causes of death worldwide due infectious agents. This study aimed to

analyze the epidemiological trends of tuberculosis in Minas Gerais, Brazil, from

2013 to 2023, with emphasis on the impact of the COVID-19 pandemic on case

notification.

**METHODS:** Based on epidemiological data obtained from the DATASUS platform,

spanning the period from 2013 to 2023, the number of cases, the distribution of

confirmed cases by sex, race, education, age group, HIV co-infection and

presence of comorbidities such as diabetes, and risk factors like smoking and

alcoholism were evaluated. Additionally, the municipalities with the highest

number of confirmed cases were identified.

**RESULTS:** The research revealed a steady annual rise in TB cases, having the

highest number of cases in 2023, with 12.55% of all reported cases. Men between

25 and 54 years of age, with a lower educational level, were the most affected

by the disease. Regarding race, the majority of the reported cases were

attributed to Brown-skinned people. The co-infection rate involving TB and HIV

increased proportionally to the reported cases of TB statewide. Regarding

comorbidities and risk factors, diabetes, smoking, and alcoholism composed a

large part of the tuberculosis caseload, with alcoholism and smoking being

especially related to the male population.

**CONCLUSION:** The results reinforced the gravity of tuberculosis as a public

health challenge, while highlighting the impact of the COVID-19 pandemic on

underreporting and the subsequent increase in reported cases of drug resistance

involving tuberculosis.

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Silvério and Garcia.

DOI: 10.3389/fpubh.2025.1642015

PMCID: PMC12405410

PMID: 40910054 [Indexed for MEDLINE]

**65. medRxiv [Preprint]. 2025 Aug 26:2025.08.21.25334178. doi:**

**10.1101/2025.08.21.25334178.**

Urine metabolomic biomarkers linked to C-reactive protein-interleukin-6 axis in

persons living with HIV and tuberculosis.

Doltrario AB, Lee MH, Broll S, Dupnik K, Rouzier V, Severe P, Dorvil N, Pape JW,

Koenig SP, Fitzgerald DW, Rhee KY.

Diagnosing pulmonary tuberculosis (PTB) remains challenging, particularly in

people living with HIV (PLWH) who have a high rate of false-negative tests using

expectorated sputum. Urine, a non-invasive sample, offers a valuable source of

metabolites reflecting systemic changes in disease. This study utilized liquid

chromatography-mass spectrometry to investigate urinary biomarkers previously

identified in other cohorts, using a well-characterized population of people

newly-diagnosed with HIV who screened positive for TB symptoms in

Port-au-Prince, Haiti. In this study, we identified a urinary metabolomic

signature associated with PTB in PLWH, confirming significant elevations of

ureidopropionic acid, 3-hydroxykynurenine, and m/z 115.0498. Untargeted

metabolomic analysis revealed a putative isoform of hydroxytryptophan and

kynurenic acid as additional PTB-associated metabolites. Four of these five

metabolites were also significantly elevated in serum when clinically and

microbiologically combined PTB groups were analyzed. Serum metabolite levels

correlated positively with elevated blood C-reactive protein (CRP) and IL-6, key

inflammatory markers associated with PTB pathology. Moreover, the diagnostic

performance of urinary metabolites in participants with CD4+T count below 200

cells/mm³ was not different from that of CRP. Urine metabolomic profiling may

complement a patient-centered approach, providing a non-invasive means for TB

biomarker discovery and investigating the immunometabolic processes underlying

TB in PLWH.

DOI: 10.1101/2025.08.21.25334178

PMCID: PMC12407615

PMID: 40909855

**66. bioRxiv [Preprint]. 2025 Aug 25:2025.08.25.672169. doi:**

**10.1101/2025.08.25.672169.**

Direct visualization of bacterial transcripts in the infected lung illuminates

spatiotemporal environmental adaptation of Mycobacterium tuberculosis.

Lawrence AE, Tan S.

Spatiotemporal environmental variation results in marked heterogeneity in

bacterial infection progression and disease outcome, with vital consequences for

treatment success. For the globally important pathogen Mycobacterium

tuberculosis (Mtb), while the pronounced intra-host spatial heterogeneity in

lesion immune cell composition and phenotype has been well-described, the highly

complex Mtb cell envelope has presented a particular challenge for the required

equivalent insight into bacterial heterogeneity. Here, we develop hybridization

chain reaction- fluorescence in situ hybridization (HCR-FISH)-based methodology

for Mtb mRNA visualization in the context of intact lung and lesion

architecture. In combination with a Mtb transcriptional/translational activity

reporter, we reveal spatiotemporal differences in gene expression relating to

Mtb lipid metabolism, response to key environmental signals, and the ESX-1 type

VII secretion system. Our results establish a framework for in situ analysis of

Mtb mRNA, opening the path to elucidating critical bacterial drivers that

underlie the marked heterogeneity in Mtb-host interactions.

DOI: 10.1101/2025.08.25.672169

PMCID: PMC12407809

PMID: 40909630

**67. bioRxiv [Preprint]. 2025 Aug 31:2025.08.27.672444. doi:**

**10.1101/2025.08.27.672444.**

Interstitial macrophages prevent tuberculosis relapse by restricting

Mycobacterium tuberculosis immune evasion.

Vinette V, Castro A, Kim H, Trujillo C, Xie M, Gengenbacher M, Ioerger TR, Ehrt

S.

Alveolar macrophages (AMs) are the first immune cells to encounter Mycobacterium

tuberculosis (Mtb) in the lungs, but they frequently fail to eliminate this

causative agent of tuberculosis (TB), allowing Mtb to persist or replicate.

Interstitial macrophages (IMs) are recruited to restrict Mtb growth and limit

immune evasion. While IMs have been implicated in the control of acute Mtb

infection, their role during latent tuberculosis infection (LTBI) has not yet

been explored. We hypothesized that IMs contribute to maintaining latency and

that their depletion during LTBI would promote Mtb reactivation, leading to TB

relapse and disease. To test this, we utilized our previously established mouse

model of paucibacillary Mtb infection that mimics aspects of LTBI in humans to

selectively deplete IMs during the latent phase. IM depletion led to TB relapse

in 26% of mice compared to 2% in control mice. The transitory depletion of this

macrophage subset transiently affected both pulmonary macrophage and neutrophil

populations. Mice that relapsed exhibited an increased proportion of

pro-inflammatory IMs and elevated concentrations of G-CSF, GM-CSF, IL3, IL-12,

IL-13, IL-17A and KC in the lung. These findings indicate that IMs play a

critical role in controlling latent Mtb and preventing TB relapse.

DOI: 10.1101/2025.08.27.672444

PMCID: PMC12407821

PMID: 40909595

**68. Cureus. 2025 Aug 4;17(8):e89312. doi: 10.7759/cureus.89312. eCollection 2025**

**Aug.**

Unveiling the Uncommon Ventriculitis in Tubercular Meningitis.

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Tubercular (TB) meningitis is one of the manifestations of central nervous

system tuberculosis, a form of extrapulmonary tuberculosis. Despite the high

incidence of TB meningitis in developing countries, there are hardly any reports

of associated ventriculitis, making it one of the rare complications.

Ventriculitis complicating TB meningitis is devastating not only to the

immunocompromised but also to the immunocompetent population. The diagnosis of

TB meningitis is indeed challenging, owing to the clinical similarities with

other types of meningitis and laboratory techniques that are rather insensitive

and slow. Thus, this under-recognized complication can impact the morbidity and

mortality of the people affected by it, making it imperative for it to be

diagnosed and managed early. We present a case of a 52-year-old man with no

known comorbidities, who presented with fever, chills, headache, vomiting, and

altered mental status for four days, and showed a Glasgow Coma Scale (GCS) score

of 8 (E2V2M4), stiffness of the neck, sluggishly reactive pupils, and

tachycardia on arrival. The pathological findings, including CSF analysis, MRI,

and cartridge-based nucleic acid amplification test (CBNAAT), diagnosed the case

as TB ventriculitis with meningitis. The patient was mechanically ventilated and

then treated with anti-TB treatment and steroids. The case thus illustrates a

rare and challenging presentation of TB meningitis that can present with a

variety of neurological sequelae and complications, including ventriculitis, as

in this case, which can have devastating consequences if left untreated. It can

result in persistent neurological sequelae, hydrocephalus, and prolonged

hospital stay. Hence, our case highlights the need for a timely diagnosis and

treatment that can help improve the prognosis, thereby reducing morbidity and

mortality.

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DOI: 10.7759/cureus.89312

PMCID: PMC12405796

PMID: 40909082

**69. Cureus. 2025 Aug 4;17(8):e89361. doi: 10.7759/cureus.89361. eCollection 2025**

**Aug.**

Unmasking Tuberculosis: A Case of Pericardial Effusion in a Young Adult With

Recurrent Pneumonia.

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This case presents a 25-year-old Indian male with no significant past medical

history presenting to the emergency department (ED) due to two weeks of

productive cough with pleuritic chest pain. The patient presented one week

earlier to the ED; however, he left against medical advice and was given a 5-day

course of Azithromycin 250 mg that minimally improved his symptoms. He returned

to the ED shortly after completing the antibiotics and was admitted for further

evaluation. He was diagnosed with multifocal pneumonia and started on

intravenous antibiotics, then discharged two days later on oral outpatient

therapy. One month later, the patient returned to the ED with similar symptoms

of worsening productive cough and pleuritic chest pain. CT chest findings

revealed a left-sided pleural effusion and large pericardial effusion, which

later prompted microbiological testing that confirmed a Mycobacterium

tuberculosis infection. A pericardial window was indicated due to tamponade

physiology. Although the patient did not present with classic constitutional

symptoms of tuberculosis, this case shows the importance of keeping TB high in

the differential list among those with recurrent pneumonia and unexplained

pleural and pericardial effusions, especially in patients with recent

immigration or insidious risk factors, despite how rare pathologies such as

pericardial TB can be. Early correct diagnosis and appropriate diagnostic

workup, including imaging and microbiological studies, should be ordered to

prevent delay in treatment and reduce morbidity.

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DOI: 10.7759/cureus.89361

PMCID: PMC12407569

PMID: 40909081

**70. Biomark Med. 2025 Aug;19(16):769-782. doi: 10.1080/17520363.2025.2548196. Epub 2025 Sep 4.**

Electro-impedimetric detection of human anti-mycolate antibody biomarkers of TB

before, during, and after treatment.

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(4)Department of Medical Microbiology, Faculty of Health Sciences, University of

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**AIM:** This study assessed electro-impedimetric detection (EIS-MARTI) of

anti-mycolate antibodies (AMAb) in TB patients before, during, and after

treatment, compared to sputum culture (MGIT) as the gold standard.

**METHODS:** A prospective pilot study enrolled 15 confirmed TB patients and

73 healthy controls at a Pretoria hospital (2016-2017). A prospective monitoring

study followed 25 confirmed TB patients over 6 months of treatment at a Pretoria

clinic (2019-2020) to evaluate biomarker behavior. Outcomes were analyzed using

descriptive statistics, wherein diagnostic accuracy and predictive values were

assessed by ROC curve analysis.

**RESULTS:** EIS-MARTI detected 14/15 true TB-positive cases independent of HIV

co-infection and 68/73 true TB-negatives in the pilot study. In the monitoring

study, EIS-MARTI correlated with culture in 7/8 cases at treatment end, but not

during the first 2 months.

**CONCLUSION:** AMAbs arise independently of HIV co-infection in active TB, recede

during treatment, and are rapidly detected by a hand-held EIS-MARTI device.

While suitability for treatment monitoring remains uncertain, EIS-MARTI shows

promise for rapid, accurate TB diagnosis and confirming cure.

Plain Language Summary: The purpose of this work was to investigate

anti-mycolate antibodies as a suitable biomarker for diagnosing tuberculosis,

monitoring treatment, and screening people at risk for TB.

DOI: 10.1080/17520363.2025.2548196

PMID: 40904229 [Indexed for MEDLINE]

**71. Tuberculosis (Edinb). 2025 Aug 28;155:102680. doi: 10.1016/j.tube.2025.102680.**

**Online ahead of print.**

ESAT-6 of Mycobacterium tuberculosis downregulates cofilin1, leads to

filamentous actin enrichment and reduces the phagosome acidification in infected

macrophages, which are partially reversed by a single methionine mutation.

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Mycobacterium tuberculosis (M. tuberculosis) persists within macrophages by

evading phagosome maturation. In this study, we considered the role of actin

dynamics in this process. Macrophages infected with virulent M. tuberculosis

showed high F-actin/G-actin ratio, accompanied by reduced expression of the

actin-depolymerizing protein cofilin1 and increased levels of its inactive

phosphorylated form. Overexpression of a constitutively active cofilin1 variant

reduced F-actin accumulation and enhanced phagosome acidification. Similar

effects were observed with sorafenib, a PI3K-dependent activator of cofilin1,

which decreased F-actin levels and promoted phagosome acidification in infected

macrophages. Ectopic expression of the mycobacterial virulence factor ESAT-6 in

macrophages led to cofilin1 downregulation. ESAT-6 also increased F-actin,

altered cell morphology and impaired phagosome acidification in infections with

avirulent M. tuberculosis strain. As cofilin1 is positively regulated by

reactive oxygen species (ROS), we examined the role of methionine in

ESAT-6-mediated ROS suppression. Mutation of methionine 93 in ESAT-6 increased

intracellular ROS, enhanced phagosome acidification, and decreased F-actin

levels. These findings reveal that M. tuberculosis impairs phagosome

acidification by modulating host actin dynamics at least partially through

ESAT-6-mediated suppression of cofilin1 and ROS. Enhancing cofilin1 activity may

represent a potential therapeutic strategy to restore phagosome function and

improve bacterial clearance, more specifically during the initial establishment

of infection.

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DOI: 10.1016/j.tube.2025.102680

PMID: 40902220

**72. Nucleic Acids Res. 2025 Aug 27;53(16):gkaf842. doi: 10.1093/nar/gkaf842.**

Mycobacterial MutT1-mediated dephosphorylation of the sensor histidine kinases

reveals a new link in the regulation of the two-component signaling.

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Bacterial pathogens such as Mycobacterium tuberculosis majorly rely on

two-component signaling (TCS) systems to sense and generate adaptive responses

to the dynamic and stressful host environment. TCS comprises a sensor histidine

kinase (SHK) that perceives the environmental signal and a response regulator

(RR) that modulates the target gene expression. TCS occurs via a phosphotransfer

event from SHK to RR. However, the mechanisms that regulate phosphotransfer

events are not well understood. We explored the role of MutT1, originally

characterized to hydrolyze oxidized GTP (8-oxo-GTP) and dGTP (8-oxo-dGTP), in

TCS regulation. Unlike other MutT proteins, mycobacterial MutT1 comprises two

domains (N-terminal domain, NTD; and C-terminal domain, CTD). Structurally,

MutT1 NTD is like MutT proteins in other organisms. However, the MutT1 CTD is

similar to Escherichia coli SixA, a histidine phosphatase with an Arg-His-Gly

(RHG) motif. We show that MutT1 CTD dephosphorylates many SHKs and impacts

expression of their target genes, highlighting the role of MutT1 in regulating

TCS. These novel findings are of special significance because they provide us

with an extrinsic phosphatase mechanism to reset TCS signaling. The study

reveals an intricate interplay between an enzyme that sanitizes the cellular

nucleotide pool and bacterial signaling pathways, offering insights into the

adaptation mechanisms.

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DOI: 10.1093/nar/gkaf842

PMCID: PMC12407098

PMID: 40902001 [Indexed for MEDLINE]

**73. J Adv Pharm Technol Res. 2025 Jul-Sep;16(3):133-138. doi:**

**10.4103/JAPTR.JAPTR\_376\_24. Epub 2025 Aug 9.**

In vitro release and in vivo study of quercetin-loaded alginate-kappa

carrageenan pulmospheres.

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Some antituberculosis drugs were reported to have adverse effects. The study

investigates the use of quercetin pulmospheres as an alternative to traditional

antituberculosis drugs. Formulated with alginate and kappa carrageenan as F1,

F2, and F3 (1:1, 1:2, and 1:3), the pulmospheres were observed for the release

and deposition in rat lungs. Results show a sustained release of 50.47%

±0.43%-58.37% ±0.57% in 10 h above minimum inhibitory concentration (MIC)

against Mycobacterium tuberculosis and provided Higuchi kinetics model.

Pulmospheres delivered quercetin to the lungs and showed a deposition with high

concentrations. The slowest rate was occurred in pulmospheres with polymer ratio

of 1:2. Formula F2 showed the most optimal results with the lowest rhodamine B

concentration of 11.934 ± 2.751-12.364 ± 0.070 µg/g and 6.987 ± 1.931-8.685 ±

2.672 µg/g for left and right lung, respectively, which produced same MIC

compare to F1 and F3. The study suggests further evaluation of effective doses

for antituberculosis.

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PMCID: PMC12401518

PMID: 40901444

**74. Cureus. 2025 Aug 1;17(8):e89235. doi: 10.7759/cureus.89235. eCollection 2025**

**Aug.**

A Rare Case of Tuberculous Osteomyelitis in a Toddler: Diagnostic Clues and

Management Approach.

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Tuberculous osteomyelitis of the proximal tibia is an extremely rare condition

in pediatric patients, often presenting as chronic pain, swelling, and

nonspecific symptoms that mimic pyogenic osteomyelitis or bone tumors. We report

the case of a three-year-old boy who presented with localized swelling and pain

in the right proximal tibia for the past 1.5 months. A plain radiograph revealed

lytic lesions with marrow involvement, and a biopsy confirmed granulomatous

inflammation with caseous necrosis. The patient was diagnosed with tuberculous

osteomyelitis and was started on standard anti-tubercular therapy. Significant

clinical and radiological improvement was noted on six-monthly follow-up. This

case highlights the importance of maintaining a high index of suspicion for

skeletal tuberculosis in endemic regions, even in atypical presentations. Early

diagnosis and treatment are critical to prevent complications such as growth

disturbances, deformities, and joint involvement, ensuring positive outcomes in

pediatric patients.

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PMCID: PMC12399915

PMID: 40901214

**75. Math Biosci Eng. 2025 Jul 28;22(9):2506-2525. doi: 10.3934/mbe.2025092.**

On macrophage response to primary Mycobacterium tuberculosis in humans.

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Tuberculosis stands as the leading cause of death worldwide, driven by infection

from a single bacterial agent, and has been recognized as a global public health

concern by the World Health Organization. Recent studies highlight that the

innate immune response has a central role in controlling the initial spread of

Mycobacterium tuberculosis (Mtb) within the host, and triggers adaptive immune

response. We developed and analyzed a model examining the interactions among

macrophages, innate cells, and Mtb to determine whether the infection is

controlled by the innate immune response or whether a specific adaptive response

is triggered. Findings suggest that if an individual infected by Mtb has an

adequate immunological state to prevent bacteria from infecting the macrophage

population (that is, if the external bacteria engulfed by macrophages are

eliminated by them, or if their capacity to replicate inside them is limited),

then the innate immune response will effectively control the primary infection.

DOI: 10.3934/mbe.2025092

PMID: 40899168 [Indexed for MEDLINE]

**76. Dev Comp Immunol. 2025 Aug 31;170:105451. doi: 10.1016/j.dci.2025.105451. Online ahead of print.**

PCV-2 vaccination modifies the cytokine serum profile in wild boar (Sus scrofa)

coinfected with tuberculosis and PCV-2.

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Animal tuberculosis (TB) and porcine circovirus 2 (PCV-2) coinfections have been

associated to the development of severe patterns of tuberculous lesions. These

coinfections are frequently observed in wild boar, considered the main wild

reservoir of TB in Spain. The vaccination of wild boar with a single dose of

PCV-2 vaccine has been associated with less severity of lesions. However, the

underlying immune mechanisms affecting these animals remain scarcely known. The

aim of this study was to determine whether PCV-2 vaccination alters cytokine

concentrations in the serum of wild boars naturally coinfected with TB and

PCV-2. Serum samples were collected from hunted wild boar in game estates where

part of the population had been previously vaccinated against PCV-2. Serum

cytokine concentrations were measured using the MILLIPLEX MAP multiplex assay,

and the results were analysed using Principal Component Analysis (PCA). The

results suggest significant differences in the concentrations of IL-1β, IL-2,

IL-10, IL-12, and IL-18 cytokines between PCV-2-vaccinated and non-vaccinated

animals, with lower levels observed in the vaccinated group. IL-1β, IL-2, IL-12

and IL-18 are pro-inflammatory cytokines involved in Th1 response. Exacerbated

inflammatory responses can result in more severe lesional patterns. Therefore,

the reduced levels of these cytokines observed in PCV-2-vaccinated animals could

be associated with the presence of less severe tuberculous lesional patterns.

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DOI: 10.1016/j.dci.2025.105451

PMID: 40897268

**77. Gates Open Res. 2025 Aug 27;9:65. doi: 10.12688/gatesopenres.16360.1.**

**eCollection 2025.**

Driving innovation from discovery to access: Meeting report of the 7 (th) Global

Forum on TB Vaccines (8-10 October 2024, Rio de Janeiro, Brazil).

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Update of

 doi: 10.12688/verixiv.1073.1.

We urgently need novel, effective, and accessible vaccines to end tuberculosis

(TB) as a public health crisis. The 7th Global Forum on TB Vaccines was convened

from 8-10 October 2024 in Rio de Janeiro, Brazil. Under the theme of "Driving

innovation from discovery to access," the program covered the breadth of TB

vaccine research and development (R&D) through implementation, while

underscoring the need for greater innovation and investments to advance

development and ensure rapid, affordable, and equitable access. Participants

shared the latest research on: approaches to diversify the TB vaccine pipeline,

candidates advancing through late-stage trials toward licensure, and efforts to

ensure new TB vaccines reach the populations that most need them. The forum

provided a platform to learn from diverse experts across the field, including

researchers, industry, funders, civil society, and affected communities.

Participants examined cross-cutting enablers throughout, including opportunities

to establish novel partnership and financing models, enhance open science,

optimize R&D practices, and strengthen leadership and engagement with community

members and high burden countries alike. In this report, we synthesize key

themes and findings from the meeting, highlighting progress and priorities in

the TB vaccine field.

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PMCID: PMC12391588

PMID: 40896556 [Indexed for MEDLINE]

**78. IDCases. 2025 Aug 13;41:e02345. doi: 10.1016/j.idcr.2025.e02345. eCollection**

**2025.**

Esophageal tuberculosis presenting as progressive dysphagia in a 30-year-old

female from rural Gondar, Ethiopia.

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Esophageal tuberculosis (TB) is an exceptionally rare manifestation of

extra-pulmonary TB, often presenting diagnostic challenges due to its

nonspecific symptoms and similarity to malignancies. We report the case of a

30-year-old female from rural Gondar, Ethiopia, who presented with progressive

dysphagia and significant weight loss. Diagnosis was confirmed through

endoscopic biopsy, revealing tuberculous esophageal ulcer. Our case underscores

the importance of considering TB in the differential diagnosis of esophageal

ulcers, particularly in TB-endemic regions. In addition, we compare this case

with the existing literature, which highlights the varied clinical presentations

and diagnostic challenges of esophageal TB.

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**79. Case Rep Infect Dis. 2025 Aug 21;2025:5416948. doi: 10.1155/crdi/5416948.**

**eCollection 2025.**

Paradoxical Reactions of Central Nervous System Tuberculosis: Report of Three

Immunocompetent Cases.

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**Introduction:** Paradoxical reactions during tuberculosis (TBC) therapy are

characterized by clinical or radiological worsening of preexisting tuberculous

lesions or the appearance of new manifestations following appropriate TBC

treatment. Identifying this phenomenon is crucial, since it can be mistaken with

treatment failure or relapse. Although widely described in HIV patients

following immune reconstitution inflammatory syndrome, the literature on

HIV-negative patients is scarce. **Case Series**: We present three cases of

immunocompetent patients with central nervous system tuberculosis (CNS-TBC) who

developed paradoxical reactions following appropriate TBC therapy. These

included diverse clinical and radiological manifestations, such as persistent

headaches, apparition or progression of tuberculomas, cerebral infarcts, and

dorsal myelitis. Paradoxical reactions occurred within an average of 2.5 months

from the start of anti-TBC treatment. **Conclusion**: Our findings underscore the

importance of closely monitoring patients following anti-TBC treatment to

identify potential complications rapidly. Paradoxical reactions due to

exaggerated immune response to Mycobacterium tuberculosis complex antigens

should be considered in a thorough differential diagnosis including other CNS

infections, granulomatous or neoplastic disorders, treatment failure, or

treatment-related toxicities. Ensuring adequate adherence to anti-TBC treatment

and immunosuppressants is essential in such cases.

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**80. Data Brief. 2025 Aug 20;62:111983. doi: 10.1016/j.dib.2025.111983. eCollection 2025 Oct.**

Comprehensive genomic insights into Mixta calida isolated from the faecal sample

of a tuberculosis patient in India.

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Mixta calida, formerly known as Pantoea calida, is a motile Gram-negative,

facultatively anaerobic bacterium with coccoid rod morphology. Although

previously considered non-pathogenic, emerging case studies indicate its

potential role in causing serious infections, including bacteraemia, meningitis,

sepsis, and implant-associated infections. This study presents the first

whole-genome sequence of M. calida of Indian origin, isolated from the stool

sample of a tuberculosis patient undergoing treatment. Sequencing was performed

using the Illumina NextSeq 2000 and Oxford Nanopore PromethION platforms. The

genomic data provides valuable insights into the antimicrobial resistance traits

and mobile genetic elements of the bacterium, contributing to a deeper

understanding of its pathogenic potential.

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**81. Cureus. 2025 Jul 31;17(7):e89186. doi: 10.7759/cureus.89186. eCollection 2025**

**Jul**.

Rasmussen Aneurysm and Fungal Co-infection in a Healthy Young Adult With

Tuberculosis.

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A 24-year-old British Indian male experienced a severe and complex course of

cavitating pneumonia caused by a rare co-infection with Staphylococcus

aureus, Mycobacterium tuberculosis, and a non-albicans Candida species. He

initially presented with symptoms of community-acquired pneumonia and was

treated with antibiotics and subsequently discharged. Four days later, he

re-presented with hemoptysis, hypoxia, and sepsis, requiring intensive care

admission. Imaging revealed extensive cavitating lesions in the right lower

lobe, empyema, pneumothorax, and a Rasmussen aneurysm. Management included 24 h

in the intensive care unit, multiple chest drains, embolization of the aneurysm,

and a three-month course of combined antibiotic, antifungal, and antituberculous

therapy. Comprehensive immunological workup, including HIV testing, was

negative, confirming the patient's immunocompetent status. This case highlights

the extreme rarity of such a multifaceted pulmonary co-infection in a young,

otherwise healthy individual, and underscores the importance of early

identification and aggressive management of concurrent infections and rare but

life-threatening complications such as Rasmussen aneurysm and invasive fungal

co-infection.

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PMID: 40896035

**82. Cureus. 2025 Jul 30;17(7):e89072. doi: 10.7759/cureus.89072. eCollection 2025**

**Jul.**

An Uncommon Presentation of a Common Disease: Hoarseness of Voice in a Young

Patient With Tuberculosis.

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Pulmonary and extrapulmonary tuberculosis impose a major load of chronic disease

burden. Lymph node and pleural tuberculosis are the most common types of

extrapulmonary tuberculosis. Isolated hoarseness of voice is a rare presenting

feature of lymph node tuberculosis. We present the case of a young girl who

presented to us with the complaint of hoarseness of voice for two months. A

contrast-enhanced CT of the neck and chest revealed bilateral cervical and

mediastinal lymphadenopathy encroaching on the aortopulmonary window. A

70-degree rigid endoscopy revealed left vocal cord paralysis. A cervical lymph

node excision biopsy showed necrotizing granulomatous inflammation and

Langhan-type giant cells. The diagnosis was confirmed by culture on

Löwenstein-Jensen medium and drug susceptibility testing, which identified

Mycobacterium tuberculosis sensitive to all first-line antitubercular drugs. She

was put on weight-based antitubercular therapy, after which her voice showed

improvement, and she gained four kilograms. We present this case to highlight

the importance of being familiar with uncommon presentations of common diseases,

particularly in areas of high disease endemicity, to allow for timely diagnosis

and treatment.

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PMCID: PMC12399184

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**83. J Clin Tuberc Other Mycobact Dis. 2025 Aug 10;41:100556. doi:**

**10.1016/j.jctube.2025.100556. eCollection 2025 Dec.**

Symptomatic (STB) and Asymptomatic (ATB) tuberculosis in Italy: Results from a

multicenter retrospective study.

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L(3), Zimmerhofer F(4), Pipitò L(4), De Iaco G(1), Bruno G(5), Fasano M(6),

Pontarelli A(7), Botta A(7), Iacovazzi T(6), Lattanzio R(1), Papagni R(1), De

Vita E(1), Zolezzi A(8), Panico G(9), Libertone R(8), Monari C(3), Brindicci

G(1), Santoro CR(1), Musto A(10), Ronga L(1), Niglio M(11), Ieva F(9), De

Gregorio F(11), Ciminelli F(11), Alessio L(3), Curatolo C(3), Gualano G(8),

Minniti S(10), Buccoliero GB(5), Santantonio T(11), Lo Caputo S(11), Carbonara

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**OBJECTIVE:** Asymptomatic tuberculosis (ATB) represents a significant proportion

of tuberculosis (TB) cases. This study aimed to compare ATB and symptomatic TB

(STB) cases in terms of demographic and clinical characteristics, adverse

events, hospital length of stay, and treatment outcomes.

**METHODS:** This multicenter retrospective study included 510 microbiologically

confirmed pulmonary TB patients across ten Italian hospitals between 2018 and

2023. STB cases presented with at least one symptom such as cough, fever, chest

pain, hemoptysis, dyspnea, night sweats or weight loss. ATB cases presented with

no symptoms. The endpoints included adverse events, length of hospital stay, and

incompleteness of the treatment.

**RESULTS:** ATB accounted for 36.4 % of cases (184/510). STB was significantly

associated with diabetes (p = 0.03), hepatitis B/C infections (p < 0.0001), and history of TB (p = 0.01). Adjusting for clinically relevant confounders, STB was associated with higher occurrence of adverse events (odds ratio 2.04, 95 % confidence interval 1.31 to 3.23; p = 0.002), more severe adverse events (odds ratio 8.07, 95 % confidence interval 2.58 to 33.34; p = 0.001) and a 24 % increase in length of hospital stay (95 % confidence interval 7 % to 47 %; p = 0.005), but was not associated with incomplete treatment (odds ratio 0.79, 95 % confidence interval 0.47 to 1.32; p = 0.37).

**CONCLUSIONS:** STB is associated with a higher burden of adverse events. ATB poses

challenges for TB elimination due to its asymptomatic nature.

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**10.1016/j.jctube.2025.100558. eCollection 2025 Dec.**

Long-term occupational risk of latent tuberculosis infection in Hamburg,

Germany: Findings from a 13-year prospective observational study.

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**BACKGROUND:** Only limited population-based data are available on the risk of

latent tuberculosis infection (LTBI) in health care workers (HCWs).

OBJECTIVE: To assess the long-term effects of protective measures of HCWs on

LTBI risk in Hamburg, Germany.

**METHODS:** Close contacts of smear-positive and smear-negative, but

culture-confirmed, pulmonary TB index cases were prospectively enrolled from

June 2005 to December 2017 and tested with the QuantiFERON TB (QFT) test

approximately eight weeks after last exposure. Sociodemographic and clinical

data were collected by trained healthcare personnel using a standardized

questionnaire.Contacts with known previous positive TST or IGRA results were

excluded.

**RESULTS:** After exclusion of prevalent TB cases and contact persons who had been

tested positive in other settings, valid results were available for 937 index

cases and 6980 close contacts (average per case 7.45; standard deviation

(SD) ± 9.99; range 1-83). Of the contacts, 3459 (49.6 %) were males and 3520

(50.4 %) females. 771 contacts (11.05 %) belonged to 11 HCW subgroups, most of

them (475, or 62.8 %) hospital or geriatric nurses. Foreign-born HCW did not

differ significantly from non-HCW regarding origin from high-incidence

countries.By adjusting for confounders, logistic regression analysis confirmed

household contact as strongest predictor for acquiring LTBI (OR 3.8, p < 0.001),

followed by foreign-born status (OR 2.2, p < 0.001) and male gender (OR 1.28,

p < 0.001). Contact with a smear-positive index case only slightly increased the risk of IGRA positivity, by 16 % (OR 1.16, p = 0.024). For each additional year of age, higher odds were found at 1.86 % (OR 1.019, p < 0.001] and for each additional hour of contact at approximately 0.11 % (OR 1.011, p < 0.001). BCG vaccination had no significant effect on IGRA test results (OR 0.95,

p = 0.41).Employment in healthcare overall was associated with a 26 % lower risk of IGRA positivity compared to non-HCWs (OR 0.74, p = 0.013); however, in a second adjusted model focusing on specific HCW subgroups, this risk reduction

was statistically significant only for hospital and geriatric nurses, with no

significant difference observed in other HCW subgroups.

**CONCLUSION:** Working in a health-care facility overall was associated with a

lower LTBI risk compared to other risk factors. These findings suggest that

protective measures might be particularly effective in hospital and geriatric

nursing, while no risk reduction was evident for other HCW subgroups. Continued

targeted protective measures remain important in high-risk care environments and

support the relevance of recommendations issued (and last updated 2023) by the

German Central Committee against Tuberculosis (DZK).

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**85. J Clin Tuberc Other Mycobact Dis. 2025 Aug 19;41:100559. doi:**

**10.1016/j.jctube.2025.100559. eCollection 2025 Dec.**

Distribution of nontuberculous Mycobacteria among presumptive drug resistance

tuberculosis patients from a ministry of health drug resistance surveillance

program, in western Kenya.

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Tuberculosis Program, Nairobi, Kenya.

**INTRODUCTION:** Nontuberculous Mycobacteria (NTM) species are emerging pathogens

causing Pulmonary diseases with no definitive treatment. Molecular techniques

enable characterization and drug resistance profiling, this study sought to

determine NTM prevalence, circulating species, and distribution factors among

presumptive multidrug-resistant tuberculosis (MDR-TB) patients in western Kenya.

**METHOD:** Sputum samples were collected between March through October 2022, and

transported for testing at Kenya Medical Research Institute (KEMRI) TB

laboratory, in Kisumu. The standard NALC-NaOH MGIT culture technique, smear,

HAIN AS/CM and NTM drug resistance were carried out.

**RESULTS:** Of the 155 specimens analyzed, 106 (68.4 %) were males, 41 (26.5 %) HIV positive, and participants of ages 36-45 years, the majority. An overall NTM

prevalence of 99 (63.9 %), of whom 63 (63 %) among males reported. In addition,

11 NTM species identified, with M. intracellulare (44, 44 %).

**CONCLUSIONS: H**igh prevalence of NTM species was observed among middle-aged males

and HIV negative participants, Kisumu led in distribution (29 %) and among HIV

positive. The NTM prevalence among smear negative vs smear positive, was

significant a p < 0.001, hence adequate TB/HIV integration and management, use

of molecular techniques, and accurate identification is critical.

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**86. bioRxiv [Preprint]. 2025 Aug 23:2025.08.23.671944. doi:**

**10.1101/2025.08.23.671944.**

Conserved Heterochromatin-like Structures with Local Regulators Mediate the Iron

Stress Response in Mycobacteria.

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Recent studies have demonstrated the importance of dynamic heterochromatin-like

regions in bacterial gene regulation, particularly for adaptation to changing

environments. Here, we have measured the dynamic regulatory protein-DNA

landscape of the tuberculosis vaccine strain, M. bovis BCG Pasteur, under the

pathogenically-relevant condition of iron starvation. Our results capture for

the first time the overall protein occupancy landscape of the genome of M. bovis

BCG, identifying extended protein occupancy domains likely composed of diverse

sets of nucleoid-associated proteins and transcription factors. Importantly, we

find chromatin-directed regulation of stress-responsive genes like siderophores.

Furthermore, through comparison with the free-living M. smegmatis, we identified

a specific class of extended protein occupancy domains that are associated with

conserved genomic regions across the two organisms, whereas regions with low

protein occupancy often lack conservation. Our findings thus comprehensively

reveal the contributions of both local regulators and chromatin structure to

gene regulation and evolution in mycobacteria.

DOI: 10.1101/2025.08.23.671944

PMCID: PMC12393510

PMID: 40894633

**87. bioRxiv [Preprint]. 2025 Aug 21:2025.08.21.671522. doi:**

**10.1101/2025.08.21.671522.**

Essential Role of MHC II in the Antitubercular Efficacy of Pyrazinamide.

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Antibacterial drug mechanisms have traditionally been examined through a

drug-pathogen lens, often overlooking the host's role in shaping drug activity.

However, growing evidence suggests that the host environment is crucial for

antibacterial efficacy. Pyrazinamide (PZA), a key component of modern

tuberculosis therapy, exemplifies this complexity-exhibiting potent in vivo

activity despite its inability to reduce Mycobacterium tuberculosis viability in

standard in vitro culture. Here, using macrophage and murine infection models,

we identify a critical role for host cell-mediated immunity in PZA's

antitubercular action. Through the use of MHC II knockout mice, we demonstrate

that CD4 T cell help is essential for PZA efficacy. Notably, while IFN-γ is

required for PZA-mediated clearance of M. tuberculosis at extrapulmonary sites,

bacterial reduction in the lungs occurs independently of IFN-γ signaling.

Additionally, we show that PZA leverages cell-mediated immunity in part through

activation of the oxidative burst. Our findings underscore the need to

incorporate host factors into antibacterial drug evaluation and highlight

potential avenues for host-directed therapies and adjunctive antibiotics in

first- and second-line tuberculosis treatment.

DOI: 10.1101/2025.08.21.671522

PMCID: PMC12393548

PMID: 40894627

**88. Int J Genomics. 2025 Aug 23;2025:6664418. doi: 10.1155/ijog/6664418. eCollection 2025.**

Impact of Genetic Polymorphisms on the Efficacy and Safety of Isoniazid in Saudi

Tuberculosis Patients.

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University, Jeddah, Saudi Arabia.

**Introduction:** Responses to antitubercular drugs like isoniazid (INH) are

influenced by genetic polymorphisms in metabolizing enzymes and transporters.

Objectives: This study is aimed at analyzing genetic polymorphisms of NAT2,

CYP2E1, and GSTM1 genes in Saudi TB patients, monitoring INH drug levels, and

exploring correlations between these genetic variations, drug levels,

hepatotoxicity incidence, and clinical outcomes. **Method:** This prospective cohort

design was conducted at King Abdul-Aziz University Hospital in Jeddah, Saudi

Arabia. It followed 50 TB patients undergoing first-line anti-TB treatment for 6

months. Genotyping and INH serum concentration measurements were conducted.

**Results:** The mean INH plasma drug levels measured in 30 patients were 2.86 ±

2.80. The presence or absence of the GSTM1 does not statistically affect the

plasma INH level between the TB patients with no significant association between

GSTM1 and clinical response, while high plasma concentration of INH was

significantly associated with improved clinical response. The present study

demonstrated no NAT2 and CYP2E1 gene variations in Saudi TB patients but has

identified a GSTM1 variant in 68% of patients. The presence or absence of the

GSTM1 gene variant appears to not affect INH drug level or clinical outcomes.

**Conclusion:** Clinicians should consider individualized TB treatment based on

genetic and demographic factors.

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**89. medRxiv [Preprint]. 2025 Aug 24:2025.08.20.25334077. doi:**

**10.1101/2025.08.20.25334077.**

Effect of smoking on drug-resistant tuberculosis treatment outcomes and

exploring potential pathways: A multicountry cohort study.

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C(6), Padayachee S(7), Flores EH(8), Oyewusi L(9), Khan PY(10)(11), Huerga

H(12), Bastard M(12), Rich ML(4)(5), Tefera GB(13), Rashitov M(14), Kirakosyan

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People who smoke are at increased risk of unfavorable tuberculosis (TB)

treatment outcomes compared with those who do not, but the pathways explaining

this effect are unclear. We estimated the effect of smoking on a successful

end-of-treatment outcome for multidrug-resistant and rifampicin-resistant

(MDR/RR) TB and examined if intervening on loss to follow-up mitigates this

effect. The endTB Observational Study was a prospective cohort of people with

MDR/RR-TB who were treated with longer regimens containing bedaquiline and/or

delamanid. We used marginal standardization to examine the effect of smoking (≥1 cigarette daily at enrollment) on treatment success (cured/completed). To

simulate intervening on lost to follow-up, we censored participants and applied

inverse probability of censoring weights. Among 1786 participants in 12

countries, 539 (30.2%) reported smoking. At the end of treatment, 73.5% of

people who smoked and 80.3% of people who did not smoke had treatment success

(risk difference in percentage points: -6.8, 95% CI: -11.1, -2.6). After

adjusting for baseline confounders including demographics, social history, and

comorbidities, the risk difference was similar (-5.2 percentage points) but 95%

CIs were less precise (-14.1, 3.2). In a pseudopopulation without loss to

follow-up, the risk difference was reduced (-1.9 percentage points; 95% CI:

-10.2, 5.1). People who smoked had less frequent MDR/RR-TB treatment success

compared with those who did not smoke. A simulated intervention on loss to

follow-up reduced this difference, suggesting that pathways related to retention

in care were a driver of this effect.

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PMID: 40894162

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**10.21203/rs.3.rs-7196158/v1.**

Exploring facilitators and barriers to early TB case finding at private

community pharmacies in Kampala, Uganda using the Consolidated Framework for

Implementation Research (CFIR).

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**BACKGROUND:** Tuberculosis (TB) remains one of the leading global infectious

diseases killer, with Uganda among the countries bearing the highest TB/HIV

burden. The World Health Organization's (WHO) ambitious End TB strategy by 2030

emphasizes the strong involvement of private healthcare providers in TB efforts.

In line with this, Uganda has adopted the WHO's public-private mix (PPM) model.

This study explored the facilitators and barriers to engaging private community

pharmacies in the early detection of TB cases in Kampala, Uganda.

**DESIGN/METHODS:** We conducted a qualitative study at five private community

pharmacies in Kampala. We used in-depth interviews with healthcare providers

(HCPs) dispensing medications at private community pharmacies, pharmacy clients,

and key informant interviews with pharmacy owners/managers. Data was analyzed

using an inductive thematic approach, identifying themes as barriers or

facilitators to engaging private community pharmacies in TB case finding. These

themes were then mapped to the Consolidated Framework for Implementation

Research (CFIR) domains and constructs.

**RESULTS:** Facilitators of TB screening at private community pharmacies include:

pharmacy staff's willingness to be trained and collaborate with healthcare

professionals to screen for TB. Healthcare providers acknowledge TB as a serious

public health threat and view community pharmacies as valuable partners in early

detection and prevention. Leveraging existing community awareness and targeted

communication campaigns can further enhance patient engagement in TB screening

services.The barriers identified include limited space and the high facility

expansion costs, inadequate access to TB screening tools and equipment, and

persistent stigma and public misconceptions about TB that may deter patients

from seeking screening. Pharmacy staff also face knowledge gaps, resource

constraints, and potential revenue losses from referring patients to hospitals.

**CONCLUSIONS:** These findings provide a basis for designing contextually

appropriate interventions targeting factors that are likely to promote the

engagement of private community pharmacies in Uganda in early TB case findings.

Future studies should assess the impact of addressing identified barriers.

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**eCollection 2025 Aug 27.**

Carbamate Prodrugs Restrict In Vivo Metabolism and Improve the Pharmacokinetics

of Isoniazid.

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Isoniazid (INH), an important first-line drug in tuberculosis (TB) treatment,

faces significant challenges primarily due to hepatotoxicity and peripheral

neuropathy as major side effects. These adverse effects often lead to poor

patient compliance and treatment dropouts. The INH's in vivo metabolism is

responsible for these adverse effects. INH's reactive terminal -NH2 group is

involved in its undesired in vivo metabolic transformations. To address this, we

designed and synthesized carbamate-based prodrugs of INH by masking the -NH2

group to reduce its metabolic activity. Herein, we report our efforts to develop

such prodrugs and their impact on in vivo metabolism and the pharmacokinetic

profile of free INH. The ex vivo stability, bioconversion, and in vivo

pharmacokinetic profile with detailed metabolite analysis of these prodrugs were

determined in mice. The lead prodrug 1d demonstrated enhanced systemic exposure

of free INH (1.5-fold, AUC ≈ 3948 ng·h/mL), reduced formation of undesired

metabolites, and prolonged half-life (1.3-fold, t 1/2 ≈ 0.88 h) compared to

naive INH. This prodrug approach represents a promising strategy for safer and

more effective TB therapy, with the potential for less frequent dosing and

improved patient compliance.

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**92. New Microbes New Infect. 2025 Aug 21;67:101623. doi: 10.1016/j.nmni.2025.101623. eCollection 2025 Oct.**

Anti-TB treatment outcomes in TB meningitis: A systematic review and

meta-analysis.

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**INTRODUCTION:** Tuberculous meningitis (TBM) remains a leading cause of mortality

and neurological disability in both children and adults. This systematic review

and meta-analysis aim to assess the treatment outcomes of anti-tuberculosis

drugs in TBM patients, focusing on mortality and neurological disability.

**METHODS:** We conducted a comprehensive literature search on PubMed/MEDLINE,

EMBASE, and Cochrane CENTRAL databases to identify articles reporting treatment

outcomes in TBM up to December 15, 2024. Studies included in the analysis

reported treatment outcomes for TBM patients. Pooled analyses were performed

using random-effects model to assess mortality rates, neurological disability,

and loss to follow-up.

**RESULTS:** A total of 10 studies involving 2005 patients were included in the

analysis. The pooled all-cause mortality rate across studies was 27.7 % (95 %

CI: 22.6-33.4 %, I 2 : 76 %), with higher mortality observed in HIV-positive

individuals (40.3 %) compared to HIV-negative patients (17.1 %). The pooled rate of loss to follow-up was 6.6 % (95 % CI: 4.7-9.1 %). Subgroup analysis revealed that the mortality rate increased from 18.9 % at 3 months to 29.1 % at 6 months. The frequency of neurological disability was higher among studies using the Modified Rankin Scale (41.7 %) compared to the Barthel Index (14.1 %).

**CONCLUSIONS:** This study highlights the high mortality and significant

neurological disability in TBM patients, particularly in HIV-positive

individuals. Our findings emphasize the need for standardized outcome reporting

and the incorporation of new therapeutic strategies, and improved diagnostic

tools, to enhance clinical outcomes. Future research should focus on addressing

these areas to optimize treatment protocols and reduce the burden of TBM.

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**93. OpenNano. 2025 May;23:100240. doi: 10.1016/j.onano.2025.100240. Epub 2025 Feb 25.**

Microbicidal mechanisms for light-activated molecular nanomachines in

Mycobacterium smegmatis: A model for pathogenic bacteria.

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There is a global health crisis of antimicrobial resistance, responsible for

over a million deaths annually. Mycobacterial infections are a major contributor

to this crisis, causing more deaths than any other single infectious agent.

Notably, the rise of multidrug-resistant (MDR), extensively drug-resistant

(XDR), and totally drug-resistant (TDR) strains of Mycobacterium tuberculosis

has led to higher mortality rates and challenge all existing antibiotic

regimens. Light-activated molecular nanomachines (MNMs) represent a promising

class of broad-spectrum antimicrobial agents that could help counter this rise

in antimicrobial resistance. Addressing a key knowledge gap, this study explores

the mechanisms of action for MNMs in Mycobacterium smegmatis, a surrogate model

for pathogenic mycobacteria. We show that fast-rotor MNMs significantly reduce

bacterial viability, achieving up to 97 % reduction in M. smegmatis with 30

minutes of light activation when compared to non-activated MNM 1 (p < 0.0001, t

= 24.55), as determined by an unpaired t-test. Using fluorescence and confocal

microscopy, we also show the colocalization of MNM 1 with M. smegmatis as part

of their mechanism of action. The ability to translate these observations to

pathogenic mycobacteria was demonstrated by the ability of MNM 1 to kill 93.5 %

of M. tuberculosis with 5 minutes of light activation when compared to

non-activated MNM 1 (p < 0.0001, t = 19.24). These findings suggest that MNMs

have the potential to be innovative and sustainable antimicrobial agents for the

treatment of pathogenic mycobacterial infections.

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**94. Cell Surf. 2025 Aug 12;14:100150. doi: 10.1016/j.tcsw.2025.100150. eCollection 2025 Dec.**

Innate immune recognition of Mycobacterium tuberculosis: receptor engagement and

inflammatory outcomes at the site of infection.

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M. tuberculosis is a notorious global pathogen responsible for over a million

fatalities annually. It has been estimated that one-third of the world's

population is latently infected with M. tuberculosis; however, only ∼10 million

individuals develop an active disease annually. The innate immune defence system

is the first to encounter the bacilli and initiates a cascade of events to

protect the host from developing tuberculosis. Innate immune cells such as

pulmonary epithelial cells, alveolar macrophages, and dendritic cells express

Toll-like Receptors (TLRs), C-type Lectin Receptors (CLRs), NOD-like Receptors

(NLRs), Scavenger Receptors, Surfactant Proteins, RIG-I-like Receptors (RLRs),

Complement Receptors, and Fc Receptors upon exposure to M. tuberculosis

Pathogen-Associated Molecular Patterns (PAMPs). The interaction between host

Pathogen Recognition Receptors (PRRs) and M. tuberculosis PAMPs results in the

activation of several signalling pathways that initiate an inflammatory response

through the production of cytokines and chemokines at the site of infection.

This Surface Feature manuscript provides an up-to-date report on the expression

of host PRRs in pulmonary epithelial cells, alveolar macrophages and dendritic

cells and their interactions with M. tuberculosis PAMPs to initiate an

inflammatory response at the site of infection. Furthermore, this manuscript

sheds light on the role of this inflammatory response as a "double-edged sword"

in the fight against M. tuberculosis infection. Understanding these interactions

provides a directive for host-directed therapies to modulate the innate immune

response.

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Patterns of Liver Injury and Adaptation in Patients With Abdominal Tuberculosis

on Antituberculosis Treatment: A Prospective Cohort Study.

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**BACKGROUND:** Extra-pulmonary tuberculosis is associated with a higher risk of

drug-induced liver injury (DILI) with antituberculosis treatment (ATT).

Nevertheless, hepatic dysfunctions in some patients can also regress to

normalization due to hepatic adaptation (HA). Prospective data specifically

addressing these issues in patients with abdominal tuberculosis (ATB) is

lacking. This study was aimed to evaluate the patterns of hepatic injury, HA,

and their predictors in patients with ATB receiving ATT.

**METHODS:** This was a prospective cohort study involving 140 patients with ATB and

normal baseline liver function tests (LFTs). Patients received standard

four-drug ATT, and LFTs were serially monitored. Predictive factors were

evaluated using multivariable logistic regression.

**RESULTS:** LFT abnormalities occurred in 71 patients (50.7%). Of these, 20 (14.2%)

met DILI criteria at first abnormality. Among the remaining 51, 18 (35.3%)

progressed to DILI, while 33 (64.7%) showed spontaneous resolution, consistent

with HA. Overall, 27.1% patients developed DILI, and 46.4% of LFT abnormalities

resolved due to HA. The majority (89%) of DILI occurred within the first 8 weeks

of treatment, and median time for HA was 21 days. Low serum albumin and vitamin

D independently predicted DILI progression. Full reintroduction of ATT was

successful in 65.8% of cases. Pyrazinamide was most commonly associated with

reintroduction failure. None of DILI cases progressed to acute liver failure.

**CONCLUSION:** LFT abnormalities is common in ATB patients receiving ATT; however,

nearly half experience spontaneous resolution due to HA. Hypoalbuminemia and

vitamin D deficiency independently predicted progression to DILI, highlighting

the need for vigilant LFT monitoring.

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training, and similar technologies.

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In Silico Screening and Molecular Dynamics Simulations of Small Molecules

Targeting Peptidyl tRNA Hydrolase for Drug-Resistant Tuberculosis.

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The translation machinery of bacteria plays a crucial role in their survival,

making it an attractive target for the development of antibiotics. The

translation process may be halted due to various factors, leading to ribosome

stalling and the release of lethal peptidyl-tRNA. Peptidyl tRNA hydrolase (PtH)

cleaves the ester bond between the peptide and the tRNA in peptidyl-tRNA to

rescue the cell. Therefore, targeting this enzyme holds significant potential

for combating drug-resistant bacteria, as it represents a novel target and plays

an indispensable role in bacterial survival. In this study, we virtually

screened three different databases: DrugBank, Maybridge, and ZINC natural

products to identify potential inhibitors of PtH from Mycobacterium

tuberculosis. We evaluated the stability of the PtH-inhibitor complexes obtained

from screening through Molecular Dynamics (MD) simulations. Furthermore, we

estimated their binding energy and performed per-residue decomposition to

understand the contributions of individual amino acids. We also assessed the top

ten potential inhibitors for their ADMET properties and drug-likeness. Although

experimental validation is currently pending, this study represents a

significant step toward the development of potent and specific inhibitors of

PtH.

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**97. Eur J Gastroenterol Hepatol. 2025 Oct 1;37(10):1186. doi:**

**10.1097/MEG.0000000000003035. Epub 2025 Aug 27.**

The role of chest X-ray in latent tuberculosis infection screening for

inflammatory bowel disease patients in low-incidence countries: in response to

Gatt et al. (Eur J Gastroenterol Hepatol 2025;37:728-732).

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Comparative analysis of tuberculosis management in Indigenous North Canada and

Alaska, USA from 1950s to 2019.

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School of Public Health, University of Toronto, Toronto, Ontario, Canada.

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**BACKGROUND:** Both Alaska and Indigenous North Canada share similarities in

geographic location, population, and a history of colonization. While both

regions have seen a significant decline in tuberculosis (TB) prevalence over the

last century, Nunavut, Canada, has reported a troubling resurgence of TB cases

since the early 2000s.

**OBJECTIVE:** To identify analogies and highlight dissimilarities between the two

regions using a comparative health systems approach within the historical and

sociopolitical contexts. We also aim to provide governments with insights on

employing best practices and adopting effective policies for improved TB

management to achieve the WHO END-TB target by 2035.

**METHOD**: This study applied a modified version of the WHO Health Systems Building

Blocks Framework to assess TB programs in both regions through a contextual

lens. A scoping review inspired review of academic literature, government

reports, and open-source documents (1950-2019) informed the analysis.

**RESULTS:** In Indigenous Northern Canada, TB control is hindered by limited

healthcare investment, reliance on evacuation policies, and workforce shortages.

Social determinants, such as overcrowded housing and food insecurity, exacerbate

the issue. In contrast, Alaska's early infrastructure development led to the

establishment of local healthcare services, workforce training, and

community-based programs, resulting in more effective TB management.

**CONCLUSION:** The underdeveloped economy, inadequate primary healthcare, weak

community health services, dependence on medical travel, and persistent social

determinants hinder TB control in Nunavut. The comparison of TB responses in

Alaska and Indigenous Northern Canada highlights the necessity for

well-resourced local and regional healthcare that actively involves the

community.

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Evaluation of the Roche cobas MTB and MTB-RIF/INH for detecting Mycobacterium

tuberculosis complex and resistance to isoniazid and rifampicin: A prospective,

multicenter diagnostic accuracy study.

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**OBJECTIVES:** To evaluate the diagnostic performance of Roche cobas MTB and

MTB-RIF/INH assays for detecting Mycobacterium tuberculosis complex (MTBC) and

resistance to isoniazid (INH) and rifampicin (RIF).

**METHODS:** This multicenter study was conducted in Taiwan between September 2023

and June 2024. Clinical specimens were collected from adult patients with

presumptive tuberculosis (TB). All samples underwent acid-fast staining,

culture, Xpert MTB/RIF Ultra assay, and cobas MTB assays. The MTB-RIF/INH assay

was conducted as a reflex test for specimens that tested positive with the cobas

MTB assay. Thirty-seven MTBC control strains from the Taiwan Centers for Disease

Control (TCDC) were also analyzed to assess drug resistance detection. Whole

genome sequencing was used to resolve discrepancies with phenotypic drug

susceptibility testing (pDST).

**RESULTS:** A total of 425 clinical samples from 378 adult patients were analyzed.

Among 392 respiratory samples, 53 were culture-positive for MTBC. cobas MTB

showed 98.1% sensitivity (95% confidence interval [CI], 89.9%-100%) and 95.9%

specificity (95% CI, 93.2%-97.7%) for MTBC detection. Drug resistance detection

was evaluated using 37 TCDC stains. For RIF resistance, the cobas MTB-RIF/INH

assay correctly identified all 11 phenotypically resistant strains. Among the 26

phenotypically susceptible strains, 25 were correctly identified, with one

false-positive result (overall accuracy: 97.3%). For INH resistance (0.2 μg/mL),

the assay identified 16 resistant and 19 susceptible strains, with two

false-negatives (accuracy: 94.6%).

**CONCLUSION:** Roche cobas MTB and MTB-RIF/INH assays demonstrated high accuracy

for detecting MTBC and drug resistance, supporting their use as reliable

diagnostic tools in clinical practice.

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Chemotherapy. All rights reserved.

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**Online ahead of print.**

Diagnostic accuracy and clinical value of polymerase chain reaction tests for

Mycobacterium tuberculosis in peritoneal dialysis effluent: A 20-year

single-centre retrospective study.

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Mycobacterium tuberculosis (MTB)-related peritonitis is a rare but serious

complication in patients receiving maintenance peritoneal dialysis (PD). Early

diagnosis is difficult due to the low sensitivity and delayed results of

conventional microscopy and culture methods. MTB polymerase chain reaction (PCR)

testing in PD effluent is recommended as a diagnostic adjunct, but real-world

data remain limited. We conducted a 20-year single-centre retrospective study in

a tuberculosis-endemic region to evaluate the diagnostic accuracy and clinical

utility of MTB-PCR in PD effluent. Among 372 tests, MTB-PCR demonstrated

sensitivity 50%, specificity 100%, negative-predictive value 94.6% and

positive-predictive value 100%, using diagnoses based on a composite of clinical

and laboratory criteria as the reference standard. Sensitivity showed a

numerical trend of improvement from 33.3% with earlier assays to 50-85.7% with

newer assays. Of 72 patients with culture-confirmed MTB-PD peritonitis, 13

(18.1%) were diagnosed via MTB-PCR. Compared to those diagnosed by non-PCR

methods, MTB-PCR-diagnosed patients had shorter time to anti-tuberculosis

treatment initiation (median 8 vs. 22 days, p ≤ 0.001) and shorter hospital stay

from presentation to treatment (median 8 vs. 17 days, p = 0.008). They also had

a numerically lower rate of PD catheter removal prior to treatment initiation

[0/13 (0%) vs. 9/53 patients (17.0%), p = 0.186]. Rates of permanent transfer to

haemodialysis and all-cause mortality at 1 year were similar among the two

groups. These findings suggest a role for early MTB-PCR testing in suspected

MTB-PD peritonitis. Further studies are needed to confirm the findings and

optimize diagnostic strategies.

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**eCollection 2025.**

Developing and validating anti-ADA2 single-chain antibodies coupled to alkaline

phosphatase for diagnosing pleural tuberculosis.

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**INTRODUCTION:** Adenosine deaminases ADA1 and ADA2 reduce adenosine

concentrations, which regulate cellular immune responses to activation signals.

It has been shown that ADA2 activity increases in the pleural fluid of patients

with tuberculosis (TB).

**METHODS:** We engineered recombinant scFv-AP antibodies using phage display

technology to select high-affinity binders against ADA2. These were incorporated

into a sandwich ELISA, allowing for the precise measurement of ADA2 levels in

pleural fluid.

**RESULTS:** The assay was tested on pleural samples from 41 patients with TB and 47

with non-TB effusions, including those with malignancies and parapneumonic

effusions. Results showed that ADA2 concentrations were significantly higher in

patients with TB than in other groups, and the ADA2-based assay exhibited

improved diagnostic specificity (91%) compared with total ADA testing (76%). A

cutoff of 300 ng/mL for ADA2 yielded a sensitivity of 98% and a negative

likelihood ratio of 0.03, effectively ruling out TB when the result was

negative.

**DISCUSSION:** The new ADA2 assay offers a simple, reliable, and more specific

alternative for diagnosing pleural TB, with potential applications in other

ADA2-related disorders.

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The dual burden of tuberculosis and diabetes mellitus: an epidemiological

correlation.

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This study examined the association between diabetes mellitus and tuberculosis

(TB) in a cohort of 200TB-positive patients, stratified by gender, age,

treatment regimen, and comorbidities, including diabetes, acute gastroenteritis,

and hypertension, compared to TB patients without additional complications.

Clinical parameters-Random Blood Sugar (RBS), C-reactive protein (CRP), and

Erythrocyte Sedimentation Rate (ESR)-were assessed at baseline and after four

months of anti-TB therapy. The results showed no significant changes in mean RBS

or CRP levels post-treatment, but a notable reduction in mean ESR was observed.

Age and gender had minimal impact on therapeutic outcomes for RBS, CRP, or ESR,

though females exhibited higher ESR values than males. Treatment regimens,

whether Myrin P Forte alone or combined with streptomycin, did not significantly

alter clinical parameters. However, CRP levels improved in TB patients with

comorbidities, such as diabetes, hypertension, or gastroenteritis. A significant

prevalence of diabetes (21.42%) was found among TB patients, with higher rates

in females and those over 50 years. These findings highlight a notable

association between diabetes and TB. However, the minimal effect of anti-TB

therapy on clinical parameters suggests that ESR and CRP may not be reliable

prognostic markers for TB. The study underscores the need for further

large-scale case-control studies and molecular research to better understand the

relationship between diabetes and TB, particularly given the high prevalence of

diabetes among TB patients.

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**ahead of print.**

Mannosylated chitosan-decorated PLGA nanoparticles for targeted pulmonary

delivery of Isoniazid: A promising approach in the treatment of Tuberculosis.

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Tuberculosis (TB), caused by Mycobacterium tuberculosis (M. tb), represents a

significant challenge to global health. The management of the disease requires

an extended course of antibiotic therapy, spanning a duration of 6 to 9 months.

The complexity and duration of these regimens frequently lead to significant

adverse effects, gastrointestinal issues, and the development of drug

resistance. To address these challenges, the nanoparticulate based inhalable

drug delivery system was designed as such by synthesizing mannosylated chitosan

decorated PLGA nanoparticles loaded with isoniazid (MC-PLGA-INH-PNPs) for

targeted pulmonary delivery. Hence, nanoparticle based drug delivery system

offers the potential to target and deliver the loaded drug directly into the

M.tb infected cells. The prepared and optimized nano-formulation had a particle

size of 154.9 ± 21 nm, zeta potential -23.2 ± 0.52 mV and entrapment efficiency

of 79.8% ± 0.45. Additionally, the MC-PLGA-INH-PNPs exhibited a sustained drug

release profile at physiological pH 7.4 for a period of 24 hr. An in vivo study

of the MC-PLGA-INH-PNPs was performed on a mouse model utilizing

lipopolysaccharide as an inducer. The data obtained from the in vivo studies

showed substantial improvements in lung tissues architecture and reduced

inflammation. The group of animals treated with the MC-PLGA-INH-PNPs showed

significant improvement in restoration of the disease when compared to pure drug

treated group. These findings further indicate that these inhalable

MC-PLGA-INH-PNPs hold a promising strategy for the treatment of tuberculosis and

considerably improves pulmonary drug delivery to the target site. However,

detailed investigations and testing of this nano-formulation on other relevant

animal models will be essential to successfully translate this concept from

laboratory to clinical practice.

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PMID: 40887733

**104. Contemp Clin Trials. 2025 Sep 5:108075. doi: 10.1016/j.cct.2025.108075. Online ahead of print.**

Phase 2C clinical trial of novel short-course regimens for the treatment of

pulmonary tuberculosis: TBTC study 38/CRUSH-TB design.

Kurbatova EV(1), Dooley KE(2), Carr W(3), Stout JE(4), Nuermberger EL(5),

Phillips PPJ(6), Scott NA(3), Upton CM(7), Ignatius E(5), Haas M(8), Walter

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**INTRODUCTION:** Preclinical and clinical study data show that combining

bedaquiline (B or BDQ), moxifloxacin (M), and pyrazinamide (Z), known as BMZ,

has potent antimicrobial activity that might shorten treatment duration for

drug-susceptible pulmonary tuberculosis.

**METHODS/DESIGN:** We describe the design of Tuberculosis Trials Consortium (TBTC)

Study 38/CRUSH-TB (NCT05766267), an open-label multicenter international

randomized controlled phase 2C trial that compares two four-month regimens, BMZ

plus rifabutin (Rb) (2BMZRb/2BMRb) or BMZ plus delamanid (D or DLM)

(2BMZD/2BMD), with standard 6-months isoniazid, rifampin, pyrazinamide, and

ethambutol (HRZE). All drugs are administered seven days per week, under direct

observation, at least five days per week. A total of 288 participants, aged

≥12 years, newly diagnosed with sputum smear-positive or Xpert MTB/RIF

(Ultra)-positive drug-susceptible pulmonary tuberculosis, will be randomized

1:1:1 to receive BMZRb, BMZD, or HRZE. Participants are followed until 78 weeks

post-randomization, or until the last enrolled participant completes 52 weeks

post-randomization, whichever comes first. The primary endpoint is time to

sputum culture negative in liquid media. Secondary endpoints include sustained

cure, safety, and additional mycobacteriology and pharmacokinetic and

pharmacodynamic outcomes. This trial has an adaptive design, wherein new arms

can be added.

**DISCUSSION:** This trial tests the hypothesis whether four-month BMZ-based

regimens with Rb or D can shorten time to culture negativity while being safe

and tolerable for participants. The study design is adaptive, allowing for

additional study arms as new drugs become available. Findings from this trial

might have important implications for clinically managing drug-susceptible

pulmonary tuberculosis at individual and programmatic levels. Trial registration

IND Number: 158058. IND Sponsor: U.S. Centers for Disease Control and

Prevention.

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