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**境外学者发表的结核病英文文章摘要**

**（115篇）**

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

**1. Front Microbiol. 2025 Sep 1;16:1633110. doi: 10.3389/fmicb.2025.1633110.**

**eCollection 2025.**

First report of tuberculosis in a cat from Italy caused by Mycobacterium

africanum, lineage 6: genomic characterization and phylogenetic analysis.

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**INTRODUCTION:** Tuberculosis in humans is mainly caused by two closely related

bacteria within the Mycobacterium tuberculosis complex (MTBC), which are

Mycobacterium tuberculosis and Mycobacterium africanum. M. tuberculosis is

widely spread, while M. africanum is more ecologically restricted to Africa.

**METHODS AND RESULTS:** In 2023, we examined a skin biopsy from a 3-year-old female

domestic cat with multifocal nodular cutaneous lesions and respiratory problems.

The animal was an indoor cat kept in Rome, reportedly taken in as a stray kitten

from a village in southern Italy (Central Calabria Region). Skin histology with

Ziehl-Neelsen staining was consistent with suspected mycobacteriosis. Bacterial

cultures for Mycobacterium spp. yielded an isolate, identified by polymerase

chain reaction (PCR) as a Mycobacterium tuberculosis complex (MTBC).

Whole-genome sequencing and bioinformatics further identified the isolate as M.

africanum lineage 6, and phylogeny with 634 other MTBC genomes placed it within

a West African cluster (mainly from Gambia) of the L6.1.2 sublineage. Resistome

analysis indicated the presence of resistance genes intrinsic in M. tuberculosis

and point mutations not associated with resistance. The cat died roughly 1 year

later, most probably from systemic tuberculosis, but the owner did not request a

necropsy.

**DISCUSSION:** This represents the first reported case of M. africanum infection in

a carnivore and in a companion animal. The case history reports a stray kitten

collected in an area of southern Italy, near the first migrant reception centers

and croplands where workers coming from West Africa are often employed,

consistent with our phylogenetic evidence.

Copyright © 2025 Alba, Caprioli, Cocumelli, Eleni, Galietta, Giacomi, Sorbara,

Stravino, Feltrin, Amoruso, Ianzano, Ceccaroni, Frega, Carfora, Franco and

Battisti.

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**2. Front Immunol. 2025 Sep 1;16:1625748. doi: 10.3389/fimmu.2025.1625748.**

**eCollection 2025.**

Tuberculosis in patients with systemic lupus erythematosus.

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Tuberculosis (TB) is an infectious disease caused by Mycobacterium tuberculosis

(M. tb), with approximately 10 million new cases reported worldwide annually.

Patients with immunocompromised states or those receiving immunosuppressive

therapy for autoimmune diseases are at higher risk of M. tb infection or

reactivation. The chronic autoimmune disease, systemic lupus erythematosus

(SLE), is associated with a higher risk of M. tb infection and TB disease during

conventional treatment with corticosteroids and immunosuppressants. However,

whether risk of TB is influenced by the immune disturbances associated with

active SLE when patients are not receiving immunosuppressant treatment remains

unclear. In this review, we describe the pathogenesis of TB and SLE and consider

how autoimmune responses in SLE could influence TB risk.

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**3. Interdiscip Perspect Infect Dis. 2025 Sep 8;2025:2583917. doi:**

**10.1155/ipid/2583917. eCollection 2025.**

Role of Iron Indices in Anemia in Patients With Pulmonary Tuberculosis.

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Iron indices are pivotal in tuberculosis (TB) owing to their influence on

pathogens and immune reactions. Iron indices substantially affect TB

progression, resulting in inflammation and anemia. Tuberculosis can induce iron

deficiency or excess that may result in compromised immunological function. This

study examined the iron index hemoglobin (Hb), serum iron, ferritin, total iron

binding capacity (TIBC), unsaturated iron binding capacity (UIBC), and

transferrin saturation (TSAT) in PTB patients. Between January 2016 and December

2018, the Port Sudan Tuberculosis Diagnostic Center studied a cohort of 100

adult patients definitively diagnosed with PTB. Additionally, 100 healthy

individuals of similar age and sex were chosen as controls for comparative

analysis. Among the 100 PTB patients studied, 90% (90/100) had anemia, with an

odds ratio of 0.923 (95% CI 0.82-1.04). Anemia of chronic disease (ACD) was the

most prevalent type (37%, 31/90). The patients showed diminished levels of HB,

serum iron, TIBC, and TSAT compared to the controls, except for ferritin levels.

UIBC was higher in patients than in controls, but this difference was not

statistically significant. The research concludes that iron metabolism is

modified during tuberculosis infection. Consequently, anemia in PTB patients is

primarily attributed to ACD rather than iron shortage. The indices of serum

iron, TIBC, and UIBC were ineffective in distinguishing between the forms of

anemia in PTB patients, as their levels fluctuated in response to the infection.

Ferritin served as superior metric for distinguishing between anemia of chronic

disease and iron deficiency anemia.

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**4. Am J Respir Crit Care Med. 2025 Sep 23. doi: 10.1164/rccm.202411-2340OC. Online ahead of print.**

The Effectiveness of Isoniazid Preventive Treatment among Contacts of

Multidrug-Resistant Tuberculosis: A Systematic Review and Individual-Participant

Meta-Analysis.

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Grandjean L(15), Hannoun D(16), Hesseling A(17), Horsburgh CR(1), Huang LM(18),

Liu Q(10), Mazahir R(19), Lee CH(20), Lee LN(21)(22), Bennet R(23), Nejat S(24),

Gupta A(25)(26), Das M(27), Murray M(28), Huang CC(29)(30), Del Corral H(31),

Benjumea-Bedoya D(31), Shen Y(32), Becerra M(30)(29), Chang V(33), Krishnan

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**RATIONALE:** Recent empirical research suggests isoniazid may lead to a risk

reduction of incident tuberculosis among close tuberculosis contacts of

multi-drug resistant (MDR) tuberculosis.

**OBJECTIVES:** To evaluate the association between isoniazid tuberculosis

preventive treatment (TPT), compared to no treatment, upon incident tuberculosis

in household contacts of MDR tuberculosis cases using a large global consortium

of tuberculosis contact tracing studies.

**METHODS:** We conducted a systematic review and individual-participant

meta-analysis among observational studies of household contact tracing studies.

Participants were included if they were exposed to someone with MDR-tuberculosis

and were given either 6 months of isoniazid TPT or no TPT. Our primary outcome

was incident tuberculosis in contacts exposed to tuberculosis. We derived

adjusted hazard ratios (aHRs) using mixed-effects, multivariable survival

regression models with study-level random effects. The effectiveness of

isoniazid TPT against incident tuberculosis was estimated through propensity

score matching. We stratified our results by contact age, background

tuberculosis burden, and Mycobacterium tuberculosis infection status.

**MEASUREMENTS AND MAIN RESULTS:** We included participant-level data from 6,668

contacts exposed to multidrug-resistant tuberculosis from 17 countries. The

effectiveness of isoniazid TPT against incident tuberculosis in contacts of

multidrug-resistant tuberculosis was 57% (aHR, 0.43; 95% CI, 0.26-0.71) and did

not appreciably change with adjustment for additional potential confounders. The

reduction in incident tuberculosis was marginally greater among child (<20 years

old) contacts (0.51; 95% CI, 0.28-0.92) compared to adult contacts (0.69; 95%

CI, 0.22-2.20). The reduction in incidence was 73% (0.27; 95% CI, 0.11-0.70) in

the first year of follow-up; effectiveness dropped to 60% (0.40; 95% CI,

0.15-1.06) from 12-23 months of follow-up and was non-significant after two

years (28% effectiveness; 0.72; 95% CI, 0.33-1.54).

**CONCLUSIONS:** Among over 6,500 contacts of MDR-tuberculosis, isoniazid TPT was

highly effective in preventing incident tuberculosis. The reduction was greatest

in high-burden countries and waned after 2 years of follow-up.

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PMID: 40986702

**5. Med Clin (Barc). 2025 Sep 27;165(6):107196. doi: 10.1016/j.medcli.2025.107196.**

**Online ahead of print.**

Cerebral air embolism secondary to spontaneous rupture of pulmonary bullae in

the context of pulmonary tuberculosis.

[Article in English, Spanish]

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**6. Vet J. 2025 Sep 25:106453. doi: 10.1016/j.tvjl.2025.106453. Online ahead of**

**print.**

Haptoglobin response in serum and pleural fluid of tuberculin reactor cattle

assessed by culture and gross pathology.

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Haptoglobin (Hp) serum concentration is a highly sensitive, non-specific

indicator of inflammation. In the present study, following the example of

studies conducted on humans, we analysed whether haptoglobin concentrations in

pleural fluids and sera in tuberculin-reactor cattle could be an additional

biomarker of Mycobacterium bovis infection. The clinical material (serum, n=60,

pleural fluid, n=80) was collected from 140 dairy cattle (Bos taurus) shortly

before culling at slaughter. During postmortem examination, organs were assessed

for tuberculosis-like lesions and tissue samples were collected from all animals

post-mortem for Mycobacterium tuberculosis complex (MTBC) culture. The

relationship of Hp serum concentrations in cattle with and without tuberculous

and the results of MTBC culture were analysed. Serum samples showed a positive

correlation between the Hp concentrations and MTBC culture. However, this

phenomenon was not confirmed in pleural fluids. Thus, Hp concentrations in

cattle serum can be a useful complementary tuberculosis diagnostic tool in

cattle.

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**7. Comput Biol Med. 2025 Sep 26;198(Pt A):111144. doi:**

**10.1016/j.compbiomed.2025.111144. Online ahead of print.**

Immunoinformatics-driven construction of a next-generation epitope-based vaccine

from conserved hypothetical proteins of M. tuberculosis for enhanced TB control.

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Mycobacterium tuberculosis (Mtb) has afflicted humanity for centuries. BCG is

the only vaccine available for TB, but it shows limited protective efficacy in

adults. Therefore, there is an urgent need to develop universal vaccines for

controlling TB worldwide. In this study, four conserved mycobacterial

hypothetical proteins (HPs) were analyzed for their immunological, structural,

and functional properties using various computational tools. The IFN-γ-inducing

MHC class I and II binding peptides of the four conserved HP antigens were

predicted by the IFNepitope 2.0 server. After detailed in silico validations,

the most immunogenic, non-toxic, non-allergenic B-cell, CTL and HTL epitopes

with broad population coverage and conservancy were selected for developing a

new epitope-based vaccine (IDE) construct. Furthermore, the final vaccine

construct was verified for its antigenicity, toxicity, allergenicity and

solubility properties. Molecular docking and MD simulations analyses showed

conformational stability and high binding affinity of the designed vaccine with

TLR4, MHC-I, and MHC-II immune receptors. In silico immune simulation revealed

the production of high levels of IgG, T-helper, T-cytotoxic cells, IFN-γ and

interleukins against the final vaccine construct. Thus, the IDE vaccine could be

a potent next-generation epitope-based vaccine candidate to stimulate both

humoral and cellular responses against Mtb. However, further animal studies are

needed to validate the immunogenicity and biological efficacy of the proposed

vaccine construct.

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PMID: 41014678

**8. BMC Infect Dis. 2025 Sep 26;25(1):1158. doi: 10.1186/s12879-025-11532-y.**

TB/HIV co-infection in homelessness and factors associated with loss to

follow-up of tuberculosis treatment: a retrospective cohort.

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**INTRODUCTION:** In Brazil, the homeless population is 56 times more likely to

become ill with tuberculosis than the general population, plus co-infection with

HIV, which further increases this risk, including unfavorable outcomes. São

Paulo is a major urban center in the Global South with a large population of

people experiencing homelessness, particularly those coinfected with HIV, which

poses challenges to clinical care and municipal management. Although it

represents a significant public health issue, it remains underexplored in

scientific literature. Therefore, this study aims to identify factors associated

with loss to follow-up in tuberculosis treatment among homeless co-infected with

HIV in São Paulo, Brazil, between 2015 and 2023.

**METHOD:** This is a retrospective cohort of TB/HIV co-infection cases in the

homeless population of the municipality of São Paulo, Brazil between 2015 and

2023. The data was obtained from the Information System for Diseases and

Notification. Descriptive analysis was carried out to characterize the clinical

and sociodemographic profile of notified cases and binary logistic regression to

identify associated factors.

**RESULTS:** The results showed a reduction in the percentage of cures and an

increase in the loss to follow-up of tuberculosis treatment in the homeless

population. Loss to follow-up was associated with the absence of Directly

Observed Treatment (ORa = 13.47; 95%CI = 6.17-29.42), positive Sputum smear

result at diagnosis (ORa = 3.44; 95%CI = 1.53-7.71) and re-entry after loss to

follow-up (ORa = 2.10; 95%CI = 1.12-3.96). The progressive performance of

control sputum smear microscopies was considered a protective factor

(ORa = 0.52; 95%CI = 0.44-0.61).

**CONCLUSION:** The factors associated with the loss of tuberculosis follow-up among

the homeless population living with HIV were: type of entry, diagnostic and

control bacilloscopy and the use of Directly Observed Treatment, which are

mainly derived from health care and the link with the user. Thus, strengthening

services and specific supervision strategies, such as the Street Clinic, is

essential for controlling TB/HIV co-infection in this population.

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**9. BMC Infect Dis. 2025 Sep 26;25(1):1164. doi: 10.1186/s12879-025-11545-7.**

Gaps in HIV testing among people with presumptive TB in Mozambique: a 3-year

retrospective cohort study.

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**BACKGROUND:** HIV testing among people with presumptive tuberculosis (PP-TB)

represents a critical entry point for HIV diagnosis and care, especially in

high-burden settings like Mozambique. However, systematic testing in this

population remains suboptimal. This study assessed gaps in HIV testing across

the TB care cascade.

**METHODS:** We conducted a retrospective cohort study using programmatic data from

clients screened for TB through community-based TB interventions in four high TB

burden provinces from 2021 to 2023. Data was extracted from the registry books

and triangulated with an electronic reporting system used by the national TB

program. Descriptive analysis was conducted to identify drop-offs in HIV testing

among PP-TB, particularly at three key stages: community screening,

facility-based TB evaluation, and among confirmed TB clients.

**RESULTS:** Among the 4,607,257 clients screened, 52% were female, and 62% were

aged 15 years and older. Of those screened, 9% (415,654) were identified as

PP-TB from whom 85% (351,255) were referred to health facilities, 97% (341,049)

successfully completed referrals, and 96% (326,664) were further evaluated for

TB. Of those evaluated, 24% (77,584) were diagnosed with TB and 85% were

notified and initiated anti-TB treatment. Three levels of gaps in HIV testing

were identified: (i) HIV testing omission, no evidence of concurrent HIV testing

was documented at community level – community TB lay staff not allowed to

perform HIV testing; (ii) HIV testing gap among TB-negative clients, 76% were

not tested for HIV, despite their presumptive TB status; (iii) HIV testing

deficiency among confirmed TB clients, 14% of these confirmed TB remained with

unknown HIV status. Combining these sequential testing failures, the estimated

overall gap in HIV testing among PP-TB reached 84%.

**CONCLUSION:** HIV testing integration into TB care cascade remains limited in

Mozambique, with substantial missed opportunities at the community level, among

TB-negative clients, and even among confirmed TB clients. Strengthening HIV

testing as a systematic component of TB screening, especially in outreach

context, could enhance early diagnosis, linkage to care, and co-infection

management. These findings call for urgent policy and operational adjustments to

close the gaps in HIV testing, particularly within the community-based TB

services.

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PMCID: PMC12465715

PMID: 41013366

**10. BMC Med Imaging. 2025 Sep 26;25(1):379. doi: 10.1186/s12880-025-01901-z.**

Enhanced CoAtNet based hybrid deep learning architecture for automated

tuberculosis detection in human chest X-rays.

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Tuberculosis (TB) is a serious infectious disease that remains a global health

challenge. While chest X-rays (CXRs) are widely used for TB detection, manual

interpretation can be subjective and time-consuming. Automated classification of

CXRs into TB and non-TB cases can significantly support healthcare professionals

in timely and accurate diagnosis. This paper introduces a hybrid deep learning

approach for classifying CXR images. The solution is based on the CoAtNet

framework, which combines the strengths of Convolutional Neural Networks (CNNs)

and Vision Transformers (ViTs). The model is pre-trained on the large-scale

ImageNet dataset to ensure robust generalization across diverse images. The

evaluation is conducted on the IN-CXR tuberculosis dataset from ICMR-NIRT, which

contains a comprehensive collection of CXR images of both normal and abnormal

categories. The hybrid model achieves a binary classification accuracy of 86.39%

and an ROC-AUC score of 93.79%, outperforming tested baseline models that rely

exclusively on either CNNs or ViTs when trained on this dataset. Furthermore,

the integration of Local Interpretable Model-agnostic Explanations (LIME)

enhances the interpretability of the model's predictions. This combination of

reliable performance and transparent, interpretable results strengthens the

model's role in AI-driven medical imaging research. Code will be made available

upon request.

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PMID: 41013295 [Indexed for MEDLINE]

**11. BMJ Open Respir Res. 2025 Sep 26;12(1):e002663. doi:**

**10.1136/bmjresp-2024-002663.**

'And the stick to fight TB is TPT': nurse-identified barriers and facilitators

of tuberculosis preventive therapy implementation in rural South Africa.

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**BACKGROUND:** A decade after South Africa adopted tuberculosis preventive therapy

(TPT), uptake remains sub-optimal.

**METHODS:** Senior nurses at primary care clinics participated in semistructured

individual interviews. Transcripts were thematically analysed to assess

knowledge and attitudes towards TPT in rural South Africa.

**RESULTS:** Among 22 senior nurses, 86% were female, with the median age of 39

years, and mean of 13.3 years' experience. Participants identified key

individual-level barriers among nurses, interpersonal barriers that nurses

observed among their patients and organisational barriers. While the nurses'

belief in TPT efficacy was strong, their perceived barriers to TPT

implementation included inflexible clinical guidelines, insufficient training

and time to counsel patients, pill burden, patients' perceived HIV stigma and

patients' alcohol use. Nurses believed implementation could be facilitated with

task-shifting and integrating TPT into the antiretroviral (ART) infrastructure

in primary care clinics and into chronic medication dispensing programmes.

Shorter TPT regimens (eg, 12 weeks weekly INH/rifapentine: 3HP) were considered

advantageous.

**CONCLUSIONS:** Nurses identified multiple barriers to TPT implementation,

including insufficient training and time to counsel patients, pill burden, HIV

stigma and alcohol use. Nurses suggested task-shifting, TPT/ART integration and

rollout of 3HP as potential facilitators of TPT implementation in rural South

Africa. Nurses' perspectives are essential to informing TPT implementation

efforts in resource-limited settings.

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DOI: 10.1136/bmjresp-2024-002663

PMID: 41005953 [Indexed for MEDLINE]

**12. J Immunol. 2025 Sep 26:vkaf252. doi: 10.1093/jimmun/vkaf252. Online ahead of**

**print.**

NR4A nuclear receptor expression in human macrophages mediates apoptosis and

controls Mycobacterium tuberculosis growth.

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Tuberculosis (TB), a significant global health issue, needs novel therapeutic

approaches to reduce its burden. Studying host-pathogen interactions provides

new targets for host-directed therapeutics (HDTs). Nuclear receptors (NRs) are

important master regulators of cellular function and bona fide drug targets.

Herein, we identify high basal expression of the NR4A NR family in human

alveolar macrophages and determine that all 3 members (NR4A1, NR4A2, and NR4A3)

are upregulated in response to Mycobacterium tuberculosis (M.tb) infection. NR4A

expression was also increased in our recently developed human alveolar

macrophage-like (AML) cell model compared to monocyte-derived macrophages. We

investigated the role of the NR4As in apoptosis given its importance in

controlling M.tb growth. NR4A small interfering RNA knockdown in AML cells prior

to their treatment with apoptosis-inducing compounds resulted in reduced

caspase-3/7 activity, indicating reduced apoptosis. Additionally, knockdown

prior to M.tb infection resulted in reduced apoptosis of AML cells and increased

M.tb growth. Treatment of AML cells with NR4A ligands significantly reduced M.tb

growth while treatment with an NR4A antagonist significantly increased it. In

conclusion, we identify the expression, location, and apoptotic activity of NR4A

NRs in human macrophages and their potential as new TB HDT therapeutic targets.

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PMID: 41005755

**13. Lancet Microbe. 2025 Sep 23:101247. doi: 10.1016/j.lanmic.2025.101247. Online**

**ahead of print.**

Tuberculosis and the perils of historical amnesia.

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DOI: 10.1016/j.lanmic.2025.101247

PMID: 41005333

**14. PLoS One. 2025 Sep 26;20(9):e0333362. doi: 10.1371/journal.pone.0333362.**

**eCollection 2025.**

Association between cardiometabolic risk factors and multidrug-resistant

tuberculosis: A case-control study.

Poudel S(1)(2), Wagle L(3), Aryal TP(4), Adhikari B(2), Pokharel S(1), Adhikari

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**BACKGROUND:** Multidrug-resistant tuberculosis (MDR-TB) continues to be a major

public health concern, especially in high-burden countries like Nepal. While

individual risk factors are known, the cumulative impact of cardiometabolic

factors on MDR-TB is not well understood.

**METHODS:** A health-facility-based, age- and sex-matched 1:2 case-control study

was conducted at MDR-TB treatment centers in Gandaki Province, Nepal. MDR-TB

patients (cases) and drug-sensitive tuberculosis (DS-TB) patients (controls)

were enrolled. Cases were defined as adults (≥18 years) with confirmed MDR-TB;

controls were adults with sputum-positive DS-TB. Data on sociodemographics,

cardiometabolic risk factors (alcohol, tobacco, abnormal body mass index,

hypertension, diabetes), TB literacy, and treatment history were collected using

a structured, pretested questionnaire by trained medical officers. Data were

analyzed using Stata v13.0. Binary logistic regression was used to assess

associations between risk factors and MDR-TB. Ethical approval was obtained from

the Nepal Health Research Council and written informed consent was obtained from

all participants.

**RESULTS:** A total of 183 participants (61 cases, 122 controls) were included.

Mean age of participants was 42.5 years (SD = 18.5); 73.8% were male. Most

participants were from urban areas (74.9%), and 66.7% were unemployed.

Cardiometabolic risk factors were present in 79.2% of participants. Alcohol and

tobacco use were reported by 59.6% and 45.9%, respectively; 9.8% had diabetes

and 7.1% had hypertension. Known TB contact and prior TB history were reported

by 26.8% and 31.1% respectively. In multivariate analysis, unemployment (AOR:

5.24, 95% CI: 1.33-20.64), and known TB contact (AOR: 8.89, 95% CI: 2.46-32.15)

were significantly associated with MDR-TB. Cardiometabolic risk factors were not

significantly associated.

**CONCLUSION:** Known TB contact and unemployment were significantly associated with

MDR-TB, while the cumulative effect of cardiometabolic risk factors showed no

significant impact, indicating that interventions should prioritize established

TB-related risk factors.

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PMCID: PMC12469359

PMID: 41004454 [Indexed for MEDLINE]

**15. Clin Infect Dis. 2025 Sep 26:ciaf526. doi: 10.1093/cid/ciaf526. Online ahead of print.**

Reducing Household Tuberculosis Transmission: A Pilot Cluster-Randomized

Controlled Trial.

Ruiz-Tagle C(1), Seguel R(1), Villarroel L(2), Bernales M(3), Vargas-García

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Comment in

Clin Infect Dis. 2025 Sep 27:ciaf528. doi: 10.1093/cid/ciaf528.

**BACKGROUND:** The duration of infectiousness following pulmonary tuberculosis

treatment initiation remains uncertain. We aimed to assess whether a bundled

intervention designed to decrease respiratory exposure was feasible and would

reduce new tuberculosis infections in household contacts (HHCs).

**METHODS:** We conducted a pilot cluster-randomized controlled trial with a hybrid

type 1 effectiveness-implementation design in Santiago, Chile. Random allocation

was performed, and two healthcare districts were assigned to the intervention

(n=180 HHCs) and one to standard of care (n=149 HHCs). Eligible participants

were newly diagnosed pulmonary tuberculosis patients and their HHCs. The

intervention included education, mask use, household ventilation, and nightly

separation of tuberculosis patients, for two weeks. Intervention adherence was

evaluated weekly. Effectiveness was assessed at the individual level with

QuantiFERON®-TB Gold Plus (QFT) test conversions in HHCs at 12-week follow-up.

**RESULTS:** Between October 2021 and December 2023, 384 HHCs and 157 tuberculosis

patients were enrolled. Overall, 56.3% of contacts were women, with mean age of

34.6 years and a baseline QFT positivity of 32.3%. A total of 216 contacts had

negative QFT result at baseline, with 179 (82.9%) completing follow-up. QFT

conversions occurred in 11 (12.8%) and 10 (10.8%) HHCs from the intervention and

control arms, respectively (incidence risk ratio 1.10, 95% CI 0.71-1.71,

p=0.849). Good adherence to the respiratory bundle was reported by 53% of

participants on day 7 and 54% on day 14.

**CONCLUSIONS:** Isolation and restrictive measures after tuberculosis treatment

initiation resulted challenging, and did not reduce tuberculosis infections in

HHCs, suggesting limited benefit for transmission control.

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PMID: 41003685

**16. QJM. 2025 Sep 26:hcaf223. doi: 10.1093/qjmed/hcaf223. Online ahead of print.**

Placental tuberculosis secondary to tuberculous peritonitis.

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DOI: 10.1093/qjmed/hcaf223

PMID: 41002274

**17. Mol Microbiol. 2025 Sep 26. doi: 10.1111/mmi.70025. Online ahead of print.**

Panduratin A Induces Autophagy Through AMPK Activation Independent of mTOR

Inhibition and Restricts Mycobacterium tuberculosis in Host Macrophages.

Lamtha T(1), Davies-Bolorunduro OF(1)(2)(3), Phlaetita S(1), Kaofai C(1),

Kanjanasirirat P(4), Khumpanied T(5), Chabang N(6), Munyoo B(5), Tuchinda P(5),

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Tuberculosis (TB), caused by Mycobacterium tuberculosis (Mtb), remains a major

global health burden, especially with the increasing prevalence of

drug-resistant strains. There is an urgent need for new therapeutics that act

via alternative mechanisms. Autophagy, a vital cell-autonomous defense process,

allows macrophages to degrade intracellular pathogens such as Mtb and has gained

attention as a potential target for host-directed therapy. In this study, we

conducted a high-content imaging screen of herb-derived compounds to identify

autophagy inducers in RAW264.7 macrophages. Panduratin A (NPA), a natural

compound from Boesenbergia rotunda, was found to potently induce autophagy. NPA

promoted autophagic vacuole formation in a dose-dependent fashion at low

micromolar levels. Its autophagy-inducing effect was validated using RFP-GFP-LC3

dual fluorescence assays and immunoblotting in the presence of bafilomycin A1.

Further mechanistic analysis revealed that NPA activates autophagy through AMPK

activation, independent of mTOR inhibition. Importantly, NPA significantly

promoted intracellular Mtb clearance and increased colocalization of Mtb with

autophagosomes and lysosomes, in a manner dependent on Beclin-1. These findings

highlight NPA as a potent enhancer of macrophage antimicrobial responses via

autophagy, supporting its potential as a candidate for host-directed adjunctive

therapy against TB.

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DOI: 10.1111/mmi.70025

PMID: 41001742

**18. ANZ J Surg. 2025 Sep 26. doi: 10.1111/ans.70327. Online ahead of print.**

Non-Tuberculous Laryngeal Granulomas: Systematic Review and Case Series.

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**BACKGROUND:** Submucosal laryngeal lesions may pose diagnostic uncertainty and

mimic tumours. Although mycobacterium tuberculosis is the leading cause,

non-tuberculous granulomas arise from multiple aetiologies. This paper presents

a systematic review and case series to elucidate a diagnostic process.

**METHODS:** Systematic review of MeSH terms pertaining to 'granuloma' and 'larynx'

was conducted. Inclusion criteria were granulomatous disease on histological

examination, located in the larynx, of any non-malignant aetiology. Exclusion

criteria were disease located outside the larynx, of a non-autoimmune or

non-infectious aetiology. Risk of bias was assessed with JBI case series and

ROBIN-I tools. Case series data were obtained from a retrospective review of

medical records.

**RESULTS:** Of 2621 studies, nine papers with 30 patients were included. Infectious

causes include leishmaniasis, histoplasmosis, laryngoscleroma, cryptococcosis,

sporotrichosis and botryomycosis. Our case series proposes sarcoidosis as an

autoimmune cause. Repeat biopsies are indicated when non-diagnostic, and

autoimmune testing is non-specific. Four patients in our case series had

non-diagnostic biopsies through microlaryngoscopy, requiring open biopsies to

exclude malignancy.

**CONCLUSION:** Autoimmune and infectious causes of laryngeal granulomas require a

high index of suspicion to guide management. International collaboration may aid

the creation of a diagnostic pathway for laryngeal biopsies for granulomatous

disease.

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DOI: 10.1111/ans.70327

PMID: 41001724

**19. Epidemiol Infect. 2025 Sep 26:1-8. doi: 10.1017/S0950268825100605. Online ahead of print.**

The potential yield of geographically targeted tuberculosis contact

investigation in urban Uganda.

Robsky K, Nalutaaya A, Kitonsa PJ, Mukiibi J, Isooba D, Nakasolya O, Kendall EA,

Zelner J, Ross JM, Katamba A, Dowdy D.

DOI: 10.1017/S0950268825100605

PMID: 40999688

**20. BMC Infect Dis. 2025 Sep 25;25(1):1125. doi: 10.1186/s12879-025-11547-5.**

Treatment outcomes for drug-resistant tuberculosis: a retrospective longitudinal

study.

Akhmedullin R(1), Algazyeva G(2), Rakisheva А(3), Mussabekova G(4), Zhakhina

G(5), Tursynbayeva A(4), Gaipov A(5), Adenov M(2), Erimbetov K(2), Ismailov

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**BACKGROUND:** This study examined the treatment outcomes of multidrug-resistant

tuberculosis (MDR-TB) in Kazakhstan, where its burden is notably high.

**METHODS:** The authors conducted a retrospective longitudinal study using the

National Tuberculosis Registry, this study analyzed treatment outcomes in MDR-TB

patients from 2018 to 2021, and included adult patients (≥ 18 years) who

completed a specific treatment. Outcomes were categorized into successful and

unsuccessful treatments. Bivariate and multivariate Poisson regression models

with modified errors were employed to obtain crude and adjusted risk ratios

(aRR).

**RESULTS:** The study cohort comprised 12,698 cases, of which 10, 306 (81.16%)

completed treatment with a successful outcome, while 2,392 (18.84%) had

unsuccessful outcomes. Male sex (aRR 1.35, 95% CI 1.24-1.45), urban residency

(aRR 1.16, 95% 1.07-1.24), having both extrapulmonary and pulmonary tuberculosis

(aRR 1.49, 95% 1.04-2.15), XDR-TB (aRR 1.31, 95% 1.08-1.59), excessive alcohol

consumption (aRR 1.43, 95% 1.28-1.59), HIV-positive status (aRR 2.24, 95%

2.01-2.47), and drug abuse (aRR 1.37, 95% 1.10-1.71) significantly elevated the

risk of the unsuccessful treatment.

**CONCLUSION:** Our findings underscore the need for focused strategies to reduce

the MDR-TB burden, particularly among adults, male sex, relapsed cases, and

XDR-TB. Despite the encouraging findings observed, further studies are necessary

to update our estimates.

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PMID: 40999320 [Indexed for MEDLINE]

**21. Braz J Microbiol. 2025 Sep 25. doi: 10.1007/s42770-025-01779-7. Online ahead of print.**

Comparison of qPCR methods for the diagnosis of bovine tuberculosis from

granulomas collected at slaughterhouses.

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To improve the direct diagnosis of bovine tuberculosis (bTB) in lesions from

carcasses condemned at slaughterhouses - the primary method for identifying

infected farms within the Surveillance System - two qPCR assays were evaluated

against the gold standard: culture and identification of Mycobacterium bovis. A

total of 167 lesion samples were collected by inspection services in Mato Grosso

and Santa Catarina. Samples were homogenized and analyzed using culture and qPCR

targeting the IS1081 sequence (for the M. tuberculosis complex) and the RD4

region (specific to M. bovis). Both qPCR assays demonstrated acceptable

sensitivity and specificity, confirming the diagnostic value of these targets.

The IS1081 qPCR showed a sensitivity of 0.80 [95% CI: 0.69-0.89] and specificity

of 0.79 [95% CI: 0.70-0.87]. The RD4 qPCR yielded a sensitivity of 0.74 [95% CI:

0.61-0.84] and specificity of 0.84 [95% CI: 0.76-0.91]. Agreement between the

two qPCR assays was high (K = 0.89 [95% CI: 0.82-0.96]). When using the parallel

results of culture and IS1081 qPCR as gold standard, the RD4 assay achieved a

sensitivity of 0.74 [95% CI: 0.64-0.83] and specificity of 1.00 [95% CI:

0.96-1.00]. In conclusion, both assays produced comparable results. The RD4

qPCR, due to its specificity for M. bovis, shows promise as a replacement for

classical bacteriology and conventional PCR in bTB surveillance, offering

operational advantages.

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Microbiologia.

DOI: 10.1007/s42770-025-01779-7

PMID: 40999281

**22. World J Microbiol Biotechnol. 2025 Sep 26;41(10):339. doi:**

**10.1007/s11274-025-04557-7.**

Field-oriented assessment of bovine tuberculosis in Tunisian cattle: IDR,

PCR(Mpb70) and serological test prediction based on AI approaches.

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Bovine tuberculosis (bTB), caused by Mycobacterium bovis (M. bovis), remains a

major zoonotic and economically burdensome disease worldwide. In Tunisia, where

bTB has remained present for many years, Efforts to eliminate the disease have

been slowed down by limited diagnostic tools and a lack of resources. The

tuberculin Intra Dermal Reaction test (IDR), also known as Tuberculin Skin Test

(TST), is still the main tool for surveillance, but its low sensitivity and

specificity show the need for better diagnostic methods. This study evaluated

the diagnostic performance of IDR, PCRMpb70 and three serological rapid tests:

Quickvet Ab® (Ac1, detecting antibodies against a recombinant M.bovis antigen),

Vetdiagnostix Ab® (Ac2, detecting antibodies against a recombinant MPB70/MPB83

fusion protein), and Vetdiagnostix Ag® (Monoclonal antibodies against Bovine

IFN-γ detecting a native M. bovis antigen complex) in Tunisian cattle (n = 32).

Based on AI, Bayesian Latent Class Model (BLCM) analysis, PCRMpb70 was

identified as the most reliable reference standard due to its high sensitivity

(Se) and perfect specificity (Sp) when assessed alongside other tests. Using

PCRMpb70 as a proxy gold standard, supervised machine learning via the Random

Forest algorithm was employed to assess the predictive performance of the

individual and combined diagnostic tests. As a main result, a high bTB

prevalence (46.37%) was confirmed in the tested animals, although prevalence

estimates varied considerably depending on the diagnostic test used

(average ± 9.76). The combinations IDR2/Ac2, IDR2/Ag, and IDR2/Ac2/Ag pair a

second IntraDermal test (IDR2) with antibody tests for Ac2, Ag, or both, proved

to be the most informative and complementary alternatives to PCR. These

approaches provide practical and effective diagnostic options for field settings

where access to molecular testing is limited or unavailable.

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DOI: 10.1007/s11274-025-04557-7

PMID: 40999101 [Indexed for MEDLINE]

**23. Trop Med Int Health. 2025 Sep 25. doi: 10.1111/tmi.70041. Online ahead of print.**

All-Oral Shorter Treatment Regimens for Multidrug- and Rifampicin-Resistant

Tuberculosis: Evaluating Their Effectiveness, Safety, and Impact on the Quality

of Life of Patients in Lao PDR.

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**BACKGROUND:** Drug-resistant tuberculosis remains a major public health challenge

in Lao PDR, with low second-line treatment uptake and suboptimal outcomes. To

improve effectiveness, safety, and tolerability, a shorter all-oral regimen for

multidrug- and rifampicin-resistant tuberculosis (MDR/RR-TB) was introduced

under the TDR Short, all-Oral Regimens for Rifampicin-resistant Tuberculosis

(ShORRT) initiative.

**METHODS:** A retrospective and prospective comparative cohort study was conducted

across five drug-resistant tuberculosis treatment centres from January 2020 to

December 2023. Two programmatic cohorts were analysed during partially

overlapping calendar periods: a standard injectable-containing regimen cohort

and an all-oral regimen cohort. Outcomes were assessed at the end of treatment

and 12 months post-treatment. Safety was evaluated through adverse events,

including serious adverse events and adverse events of special interest.

Health-related quality of life was measured using EQ-5D-5L and EQ-VAS tools.

**RESULTS:** Among 126 participants, 65 received the all-oral regimen and 61 the

standard regimen. Treatment success was higher in the all-oral group (90.8% vs.

80.3%), with lower mortality (7.5% vs. 16.4%) and fewer serious adverse events

(12.3% vs. 19.7%). Anaemia was more common in the all-oral group (46.2%), while

hepatotoxicity and QTcF prolongation were more frequent in the standard group.

Both groups showed improvements in health-related quality of life, but greater

recovery in mobility, daily activities, and anxiety reduction was observed in

the all-oral group. Between group differences did not reach statistical

significance. No cases of tuberculosis recurrence were reported at 12-month

follow-up in either group.

**CONCLUSION:** In this programmatic setting, the all-oral, bedaquiline and

linezolid-based regimen demonstrated high effectiveness and acceptable safety.

Non-significant trends favoured the all-oral regimen for treatment success,

mortality, and quality of life, consistent with but not definitive for improved

outcomes. These findings support the transition to all-oral regimens as the

preferred approach for drug-resistant tuberculosis care, while acknowledging the

observational design and limited power.

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**print.**

Label-Free Electrochemical-Based Biosensor for Gene-phosphatidylinositol

mannosides Detection in Urine for the Determination of Multidrug-resistant

Tuberculosis.

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INDIA.

Tuberculosis (TB) is a significant public health issue, and the existing

diagnostic tests have shortcomings that cause delays in initiating treatment. In

this study, we designed a Gene-pimB-based biosensor for the determination of TB

and tested it using an electrochemical technique. The Gene-pimB has been

reported to be upregulated in mannose-capped lipoarabinomannan (manLAM) in

Multidrug-resistant tuberculosis (MDR-TB). Due to its link with drug resistance,

Gene-pimB holds promise as a biomarker for identifying MDR-TB strains. In this

work, the biosensor is fabricated using Graphite-Zinc Oxide nanofibers

(GPH-ZnO-NFs), which are generated using electrospinning and deposited on glassy

carbon electrodes (GCE). The GPH-ZnO functionalized electrode were further

functionalized with MSA/EDC/NHS protocol to provide efficient immobilization

which enable the effective binding of pimB-sequences to the nanofibers on the

electrodes. In addition, the Gene-pimB hybridization on biosensors immobilized

with Gene-pimB probe sequences was quantified using Cyclic Voltammetry (CV),

Differential Pulse Voltammetry (DPV), and Electrochemical Impedance Spectrometry

(EIS) techniques. The experimental tests revealed that the Limit of Detection

(LoD) for CV is 0.1482pM/mL, for DPV it is 0.196 pM/mL, and for EIS it is 0.302

pM/mL. Our findings suggest that Gene-pimB may prove to be a useful technique in

the creation of novel tests for TB prognosis. The efficacy of the developed

biosensor was confirmed by a hybridization sensing assay including targeted

short oligonucleotide sequences (probe) and Gene-pimB (Target) isolated from the

urine sample. To assess its potential for clinical detection, urine samples were

artificially spiked with the gene to simulate conditions encountered in clinical

diagnostics. This approach allows for evaluating the feasibility of detecting

Gene-pimB in a non-invasive manner, which could aid in the early identification

of drug-resistant TB cases and improve diagnostic strategies for effective

disease management.

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training, and similar technologies, are reserved.

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**25. Infection. 2025 Sep 25. doi: 10.1007/s15010-025-02645-2. Online ahead of print.**

Post-tuberculosis lung disease: a guide for clinicians.

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Post-tuberculosis lung disease (PTLD) is an increasingly recognized condition

that significantly affects survivors' quality of life, creating disability and

incrementing the risk of mortality. PTLD includes a spectrum of structural and

functional lung impairments such as obstructive, restrictive, and mixed

patterns, bronchiectasis, and pulmonary fibrosis that persist beyond

microbiological cure. Global prevalence data highlight a heavy burden of PTLD,

especially in high-incidence regions, driven by late diagnosis and suboptimal

treatment. Functional and radiological evaluation remains critical for timely

diagnosis, with spirometry and imaging revealing lasting abnormalities in a

large proportion of TB survivors. Multidisciplinary care is essential and

includes bronchodilator therapy, infections/complications management and

prevention, pulmonary rehabilitation, and, in selected cases, surgical

intervention. Despite increasing recognition, standardized diagnostic and

therapeutic pathways for PTLD are still lacking, and data on optimal follow-up,

rehabilitation strategies, and preventive measures remain limited. Prospective

studies, better stratification tools, and patient education initiatives are

urgently needed to reduce PTLD morbidity and mortality. This narrative review

synthesizes current evidence on PTLD epidemiology, clinical evaluation and

management while offering practical suggestions for clinicians taking care of

people with TB and addressing research needs.

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**26. J Correct Health Care. 2025 Sep 25. doi: 10.1177/10783458251380507. Online ahead of print.**

Patterns and Treatment Timelines of Tuberculosis in Males From Ecuador's Largest

Prison.

Romero-Sandoval N(1)(2), Torres M(3), Solis VH(3), Orellana F(3), Castells

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The analysis of tuberculosis (TB) registers in prisons provides insights into TB

transmission and highlights conditions that increase susceptibility. This study

aims to characterize TB patient surveillance in Ecuador's largest male

penitentiary over the course of 3 years. Using national TB administrative

records from January 1, 2017, to December 31, 2019, we calculated five

operational indicators. In addition, the number of clinical consultations

(register entries) per patient over the 3 years was calculated. The linkage

process involved merging data from the administrative files to create a new

dataset using encrypted tokens as the linking variables. Data merging yielded

6,560 records and enabled analysis of 645 symptomatic patients, 427 with

confirmed TB. Of these, 82.9% had two to six records, and 88.9% maintained the

same diagnosis. Among those with diagnostic changes, 38.5% converted from

Ziehl-Neelsen negative to positive after 6 months. The median time to diagnosis

was 0 days (range 0-12); and to treatment, 13 days (range 0-652). Treatment

outcomes were available for 353 of 427 patients (82.7%), with a success rate of

only 65.2% and a fatality rate of 0.8%. These results highlight surveillance

challenges and the need for improving TB prevention and control in prisons.

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PMID: 40996080

**27. Clin Infect Dis. 2025 Sep 25:ciaf536. doi: 10.1093/cid/ciaf536. Online ahead of print.**

Reassessing Adherence Trajectories in Multidrug-Resistant Tuberculosis: Recovery

Advantage and Hidden Biases.

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DOI: 10.1093/cid/ciaf536

PMID: 40995655

**28. BMC Public Health. 2025 Sep 24;25(1):3073. doi: 10.1186/s12889-025-24333-4.**

Perceptions of tuberculosis and home-based infection screening among families

and providers in Madagascar: a qualitative study.

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**BACKGROUND:** Madagascar is a country with a high tuberculosis (TB) burden, and

the incidence of the disease has remained unchanged since 2013. TB detection

largely relies on passive strategies, with little attention given to TB

infections (TBIs), which are silent reservoirs that fuel future active TB cases.

**METHOD:** This qualitative study investigated how Malagasy communities perceive TB

and an innovative approach for TBI screening and care. This approach was

developed through the APRECIT operational research project in partnership with

the National Tuberculosis Control Program (NTP). Semi-structured in-depth

interviews were conducted between March and May 2023 with a sample of

stakeholders and health workers (26 HWs) at the national, regional and community

levels and focus groups with household contacts (46 HHCs) of TB patients.

**RESULTS:** The fight against TB remains challenging in Madagascar. Community

knowledge of TB is limited, and the disease is perceived as shameful.

Individuals with TB and their families face stigmatization within their own

family and the community. At the provider level, HWs reported challenges in

promptly detecting and treating TB people with TB due to structural constraints

within the health system and barriers at the household (HH) level. The

introduction of home-based screening for TBI was perceived as a way to interrupt

disease progression and help reduce stigma. For HWs, this strategy helps to

limit TB transmission. However, HWs expressed concerns about giving treatment to

asymptomatic people and the replicability of the strategy at the national level.

**CONCLUSION:** Improving communication about TB and implementing a home-based

screening strategy for HHCs to identify individuals at high risk of TB

progression have the potential to improve TB control in Madagascar.

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**Online ahead of print.**

Protecting households on exposure to newly diagnosed index multidrug-resistant

tuberculosis patients: Study protocol for the PHOENIx phase 3 clinical trial.

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**INTRODUCTION:** Data to guide tuberculosis (TB) preventive treatment (TPT) of

close contacts of people with multidrug-resistant tuberculosis (MDR-TB) are

limited. While levofloxacin-based TPT has been shown safe and efficacious,

alternatives are needed for those exposed to fluoroquinolone-resistant

Mycobacterium tuberculosis (M. tb). The PHOENIx trial evaluates whether using a

novel nitroimidazole, delamanid, in high-risk household contacts (HHCs) of

patients with MDR-TB reduces their risk of developing active TB.

**METHODS/DESIGN:** PHOENIx is a phase 3, open-label, multicenter clinical trial

with a cluster-randomized superiority design (households form the clusters). The

study objectives are to compare efficacy and safety of 26 weeks of delamanid

versus isoniazid for preventing confirmed or probable TB during 96 weeks of

follow-up among HHCs of adults with pulmonary MDR-TB. HHCs are defined as young

children <5 years, people living with HIV or non-HIV immunosuppression, or

people with evidence of M. tb infection. The study was originally designed to

enroll 3452 HHCs to provide 90 % power to detect a 50 % reduction in the

cumulative proportion of HHCs developing confirmed or probable TB during

96 weeks of follow-up from 5 % in the isoniazid arm to 2.5 % in the delamanid

arm. The design included a sample size re-evaluation to address uncertainty in

study design assumptions.

**DISCUSSION:** Preventing MDR-TB is a global priority. Alternatives to

levofloxacin-based TPT are needed since fluoroquinolone resistance is growing.

PHOENIx, a phase 3 trial evaluating delamanid, is poised to inform WHO

guidelines.

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**30. Clin Infect Dis. 2025 Sep 24:ciaf527. doi: 10.1093/cid/ciaf527. Online ahead of print.**

Xpert MTB/RIF® cycle threshold as a marker of TB disease severity; Implications

for TB treatment stratification.

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**INTRODUCTION:** Recent trials have demonstrated that shortened four-month

treatment durations are effective for the majority of people with tuberculosis

(TB). However, there is a population of TB patients who require longer treatment

durations. Prospectively identifying those who require shorter versus longer

treatment durations would support evaluation and implementation of optimized

regimens.

**METHODS:** We analysed data from the RIFASHORT TB treatment-shortening

non-inferiority trial to define a TB phenotype classification. The RIFASHORT

trial primary outcome was reanalysed using the protocol-defined non-inferiority

criterion of eight percentage points, stratifying by those classified as having

limited or extensive disease.

**RESULTS:** Xpert MTB/RIF® semiquantitative bacterial burden in combination with TB

disease involvement grading on chest X-ray achieved the strongest

differentiation between relapse and non-relapse. The extensive disease TB

phenotype (high semiquantitative bacterial burden and extensive TB disease on

X-ray) accounted for one quarter of the RIFASHORT trial population and more than

half of all post-treatment TB relapses (13/23). For the limited TB disease

phenotype (a semiquantitative bacterial burden other than high or no extensive

TB disease on X-ray), the experimental 4-month 1200mg rifampicin-containing

regimen met the protocol-defined non-inferiority criterion in both

modified-intention-to-treat (adjusted risk difference: -1.3% (95% confidence

interval: -6.7% to 4.0%)) and per protocol analyses (1.7% (95% CI: -3.8% to

7.1%)).

**CONCLUSION:** The TB phenotype classification derived here successfully identified

three-quarters of RIFASHORT trial participants for whom a four-month 1200mg

rifampicin regimen was non-inferior to the six-month standard of care. A

definitive phase III randomised trial of disease-stratified rifampicin-based TB

treatment is justified.

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Infectious Diseases Society of America.

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**eCollection 2025.**

Acceptability of Digital Adherence Technologies to support people with

drug-susceptible TB in South Africa.

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**BACKGROUND:** Tuberculosis (TB) remains a challenge in South Africa, with an

estimated 280,000 new cases reported in 2022. Digital Adherence Technologies

(DATs) may be important tools to improve adherence to TB treatment. However,

there is limited knowledge about facilitators and barriers to implementing these

technologies in South Africa.

**METHODS:** This qualitative study was embedded within the Adherence Support

Coalition to End TB cluster-randomised trial which implemented the two

technologies: a smart pillbox and/or a cell phone-based strategy similar to

99DOTS (labels), plus differentiated care, to support people with drug-sensitive

TB (PWTB). In-depth interviews were conducted with purposively sampled

participants comprising PWTB, Healthcare Workers (HCWs) and stakeholders.

Inductive thematic analysis was used for data analysis, while the Unified Theory

of Acceptance and Use of Technology (UTAUT) framework served as the overarching

framework to synthesize and summarise the findings.

**FINDINGS:** Sixty-eight interviews were conducted: 35 with PWTB and 33 with HCWs

and stakeholders. Facilitating factors for the pillbox were alarm reminder,

storage, ease of use, not requiring a phone, social support, and portability.

Barriers to the pillbox were that some found the box unportable and others

experienced box malfunctioning. Facilitating factors for the labels were ease of

use among the young, daily confirmation messages, social support, privacy, and

portability. Barriers to implementing these DATs were older age, illiteracy,

forgetting to send the SMS, lacking understanding, no cell phone access, power

cuts, and unresolvable technical glitches. While differentiated care improved

the client-provider relationship, some PWTB felt home visits were stigmatising.

HCWs and stakeholders expressed willingness to scale up DATs because they

improved their working conditions, and it was advantageous for the PWTB.

**CONCLUSIONS:** Smart pillbox and labels had features which favoured their

acceptability and there were also DAT specific barriers. DATs may improve

person-centredness in TB care. Future guidelines should consider acceptability,

differing situations, and allowing flexibility to possibly increase uptake and

utilisation of DATs.

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**10.1371/journal.pgph.0005246. eCollection 2025.**

Is household contact investigation a missing link for tuberculosis care in

Chhattisgarh, India?-Operational research using programmatic data.

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Household contact (HHC) investigation helps in early identification of people

with tuberculosis (TB) and initiation of TB preventive treatment (TPT) among

those at high risk of developing TB. This cross-sectional study uses National TB

Elimination Program data of all people notified with bacteriologically confirmed

pulmonary TB and their HHCs from October to December 2023, from Chhattisgarh, a

central Indian state, to assess coverage of HHC investigation, proportions

identified with TB and put on TPT (all age groups and age < 5 years).

Sociodemographic, clinical, and health system-related factors were used to

identify predictors of HHC investigation not done, as determined through

modified Poisson regression. Of the 4,221 people notified with TB, an HHC

investigation was conducted for 3,177 (75%) cases. Among a total of 11670

contacts screened, TB was diagnosed in 0.9%(n = 109) for all age groups and

0.7%(n = 9) for children<5 years. TPT was initiated in 66% (n = 7740) for all

age groups and 73% (n = 903) for children<5 years. Women (adjusted prevalence

risk aPR 1.10; 95%CI:1.01-1.19), those notified from non-tribal districts (aPR

1.14; 95%CI:1.01-1.29), current facility being tertiary care (aPR 1.50;

95%CI:1.12-2.00) and private (aPR 1.42; 95%CI:1.08-1.86) facility, diagnosed

with test other than sputum microscopy (aPR NAAT 3.19; 95%CI:2.39-4.28; LPA 8.88

95%CI:6.15-12.82; culture 9.69; 95%CI:5.99-15.68) and for whom diabetes (aPR

1.40; 95%CI:1.16-1.70) and HIV screening (aPR 1.55, 95% CI:1.17-2.05) was

missing predicted higher risk of HHC investigation not done. The study

highlights the need to improve HHC investigation, as well as the low yield of TB

and TPT initiation. Predictors of HHC investigation not done suggest a need to

decentralize it to the primary level and improve data-based program monitoring.

A statewide capacity-building initiative for improving the investigation of HHC

is the way forward.

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unrestricted use, distribution, and reproduction in any medium, provided the

original author and source are credited.

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PMID: 40991581

**33. Med Microbiol Immunol. 2025 Sep 24;214(1):45. doi: 10.1007/s00430-025-00853-z.**

Diagnostic performance of circulating microRNA signatures for differentiating

tuberculosis disease from tuberculosis infection.

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As regulators of innate and adaptive immunity, microRNAs (miRNAs) could aid in

the discrimination between tuberculosis disease (TB) and (latent) TB infection

(TBI). We analysed 754 circulating miRNAs in participants diagnosed with TB and

TBI using TaqMan™ Advanced miRNA Human A and B cards. MiRNAs were normalized

exogenously and endogenously via geometric means of selected reference miRNAs.

Expression analysis was used to identify miRNAs that were significantly

differentially expressed between individuals with TB and those with TBI. We

utilised recursive feature elimination with a Random Forest model to identify

the miRNAs most effective at discriminating TB from TBI and subsequently

validated the miRNA in another group. 95 persons diagnosed with TB or TBI was

divided into a discovery group (n = 36) and a validation group (n = 59). In the

discovery group, we identified 495 distinct miRNAs in 36 persons with TB or TBI

and by recursive feature elimination identified hsa-miR-148a-3p, hsa-miR-204-5p

and hsa-miR-584-5p and created a three-miRNA-diagnostic model. In the validation

group, the three-miRNA-diagnostic model had poorer performance. Expression

analysis revealed 13 significantly differentially expressed miRNAs, including

hsa-miR-148a-3p and hsa-miR-204-5p. Subsequent analysis in a validation group

consisting of 59 persons revealed that six of the 14 miRNAs, including

hsa-miR-148a-3p, exhibited the same pattern, albeit without statistical

significance. Three circulating miRNAs showed potential for differentiating TB

from TBI in the discovery cohort, but these differences were less pronounced in

the validation cohort.

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**Sep 24.**

Human CD4+ T cells recognize Mycobacterium tuberculosis-infected macrophages

amid broader responses.

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CD4+ T cell-mediated control of tuberculosis (TB) requires recognition of

macrophages infected with Mycobacterium tuberculosis (Mtb). Yet, not all

Mtb-specific T cells recognize infected macrophages. Using infected

monocyte-derived macrophages and autologous memory CD4+ T cells from individuals

with stable latent Mtb infection (LTBI), we quantify the frequency of activated

T cells. T cell antigen receptor (TCR) sequencing revealed >70% of unique and

>90% of total Mtb-specific TCR clonotypes in LTBI are linked to recognition of

infected macrophages, while a subset required exogenous antigen exposure,

suggesting incomplete recognition. Clonotypes specific for multiple Mtb

antigens, and other pathogens, were identified. Remarkably, antigen screening

revealed all TCRs to be specific for type VII secretion system (T7SS)

substrates. Mtb-specific clonotypes expressed signature effector functions

dominated by IFNγ, TNF, IL-2, and GM-CSF or chemokine production and signaling.

We propose that TB vaccines, which elicit T cells specific for T7SS substrates,

recognize infected macrophages, and express canonical effector functions, will

offer protection against TB.

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PMID: 40990918 [Indexed for MEDLINE]

**35. Curr Opin Infect Dis. 2025 Sep 25. doi: 10.1097/QCO.0000000000001156. Online**

**ahead of print.**

New drugs for the management of tuberculosis.

Cross GB(1)(2)(3)(4).

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**PURPOSE OF REVIEW:** This review summarizes recent and emerging advances in

tuberculosis (TB) treatment, focusing on new therapeutics, repurposed agents,

and shortened treatment regimens. It aims to contextualize key developments

within the evolving TB treatment landscape and assess their potential to

transform clinical management of both drug-susceptible and drug-resistant

disease.

**RECENT FINDINGS:** Evidence from landmark trials, including Nix-TB, ZeNix,

TB-PRACTECAL, STREAM, Study 31/A5349, SHINE, TRUNCATE-TB, endTB and BEAT-TB has

supported the use of licensed, repurposed, and novel agents as new treatment

strategies. These studies have demonstrated the feasibility of

treatment-shortening regimens for drug-susceptible TB and improved outcomes for

multidrug-resistant TB. Progress has expanded the therapeutic armamentarium,

with promising regimens incorporating new agents, higher-dose rifamycins, and

safer, all-oral combinations.

**SUMMARY:** These advances have direct implications for clinical practice, offering

shorter, safer, and more effective treatment options. Adoption of these new

regimens into treatment guidelines will allow us to reduce treatment burden,

improve adherence, and lower the risk of adverse effects. Continued optimization

of drug combinations, dosing strategies, and safety profiles will be essential

to achieving durable, scalable treatment options. Future research should

prioritize regimen simplification, host-directed therapies, and tools for

predicting and monitoring treatment response to support personalized, globally

accessible TB care.

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DOI: 10.1097/QCO.0000000000001156

PMID: 40990707

**36. Rev Soc Bras Med Trop. 2025 Sep 22;58:e04342024. doi:**

**10.1590/0037-8682-0434-2024. eCollection 2025.**

Prediction of latent tuberculosis infection in Venezuelan immigrants:

construction and validation of a surveillance model.

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de Janeiro, RJ, Brasil.

**BACKGROUND:** Latent tuberculosis infection (LTBI) is a significant concern among

migrant populations, particularly Venezuelans, due to its adverse health and

social conditions. This study aimed to construct and validate a predictive model

of LTBI among Venezuelan migrants.

**METHODS:** This cross-sectional study utilized data from the project "TB and

migrants in BRICS countries: The case of Brazil", carried out in Boa Vista,

Roraima, in 2020. The final sample included 427 participants. For the analysis,

22 variables were selected, and simple and multiple logistic regression analyses

were applied. General measures (Nagalkerke's R2 and Brier's score),

discriminative capacity (accuracy, receiver operating characteristic curve, and

area under the curve [AUC]), and calibration measures (Hosmer-Lemeshow test and

calibration graph) were used to evaluate the model. The model was internally

validated using bootstrapping. Finally, a nomogram and a clinical decision curve

were constructed.

**RESULTS:** Six LTBI predictors (marital status, social benefit, documentation

status, smoking status, presence of comorbidities, and fever) were included in

the final model. The predictive model demonstrated moderate discriminatory

capacity (AUC: 0.676), good calibration, and was also validated with an AUC of

0.678. Additionally, a clinical decision analysis revealed that the use of the

model offers superior benefits compared with traditional treatment strategies.

**CONCLUSIONS:** The predictive model and nomogram proved to be useful tools for

LTBI screening in migrants, potentially guiding border health surveillance

actions in this population.

DOI: 10.1590/0037-8682-0434-2024

PMCID: PMC12455750

PMID: 40990698 [Indexed for MEDLINE]

**37. Rev Soc Bras Med Trop. 2025 Sep 22;58:e01842025. doi:**

**10.1590/0037-8682-0184-2025. eCollection 2025.**

Comprehensive analysis of mutations associated with rifampicin- and

isoniazid-resistant tuberculosis in a high-burden setting.

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**BACKGROUND:** In this study, we aimed to describe the mutations associated with

first-line drug resistance in Mycobacterium tuberculosis complex (MTBC) isolates

from São Paulo, Brazil, between 2019 and 2021.

**METHODS:** Mutations in the coding regions of rpoB and katG genes and in the

promoter region of the inhA gene in MTBC clinical isolates were detected using

the GenoType MTBDRplus assay (LPA). All mutations inferred by LPA were

sequenced.

**RESULTS:** Of the 13,489 MTBC isolates with valid LPA results, 657 (4.9%) harbored

mutations. The overall prevalence rates of rifampicin-resistant (RIF-R)

tuberculosis (TB), isoniazid-resistant (INH-R) TB, and multidrug-resistant (MDR)

TB were 1.5, 2.0, and 1.2%, respectively. A significant proportion of RIF-R

isolates presented inferred rpoB mutations (89.1%), most of which were the

borderline H445N mutation. The inhA promoter C-15T mutation was predominant

among the INH-R isolates (52.8%). Most MDR isolates presented rpoB S450L + katG

S315T1 mutations. Gene sequencing identified mutations not included in the

catalogue of mutations published by the World Health Organization. Phenotypic

drug susceptibility testing on isolates with inferred rpoB mutations revealed

that the 0.5 µg/mL critical concentration of RIF failed to detect most

borderline mutations when using the BACTEC MGIT 960 system.

**CONCLUSIONS:** These findings emphasize the need for continuous surveillance and

the integration of molecular and phenotypic methods to ensure an accurate

detection and management of drug-resistant TB in high-burden settings.

DOI: 10.1590/0037-8682-0184-2025

PMCID: PMC12455751

PMID: 40990696 [Indexed for MEDLINE]

**38. Clin Infect Dis. 2025 Sep 24:ciaf490. doi: 10.1093/cid/ciaf490. Online ahead of print.**

The Role of Youths in Within-Household Tuberculosis Transmission: A Household

Contact Cohort Study.

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T.H. Chan School of Public Health, Boston, Massachusetts, USA.

**BACKGROUND:** Youth aged 15-24 years are significantly impacted by tuberculosis

globally. Their expanding social networks heighten exposure risks, potentially

amplifying tuberculosis transmission, but their role in within-household

transmission remains poorly understood.

**METHODS:** A household contact cohort study in Lima, Peru (2009-2012) enrolled

individuals (>15 years) with incident tuberculosis (index patients) and their

household contacts (HHCs), following them for 12 months. We evaluated whether

the age of index patients and HHCs modified the risk of tuberculosis infection

among HHCs. Study outcomes included: (1) prevalent tuberculosis infection among

child contacts (<15 years) at enrollment and (2) incident tuberculosis infection

among HHCs. Whole-genome sequencing of Mycobacterium tuberculosis (Mtb) isolates

from index-HHC pairs assessed whether index patient age modified the likelihood

of within-household transmission, defined as ≤12 single-nucleotide polymorphism

differences.

**RESULTS:** Child contacts of youth index patients had a lower risk of prevalent

tuberculosis infection than those with adult index patients (aRR = 0.77; 95% CI:

.67-.87). Among index-secondary patient pairs, 62% (26/42) of pairs with a youth

index patient were genetically linked, compared to 72% (48/67) of pairs with an

adult index patient (P = .3). Child and youth contacts had lower incident

tuberculosis infection risk at 12-month follow-up compared to adult contacts

(child vs adult: HR = 0.33; 95% CI: .28-.38; youth vs adult: HR = 0.61; 95% CI:

.52-.71).

**CONCLUSIONS:** Youth play a limited role in household tuberculosis transmission.

Compared to adults, youth transmitted less TB as index patients and were less

likely to be infected as HHCs. Research should explore youth social interactions

and community-based transmission to inform targeted prevention strategies.

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Infectious Diseases Society of America.

DOI: 10.1093/cid/ciaf490

PMID: 40990486

**39. Pediatr Infect Dis J. 2025 Sep 24. doi: 10.1097/INF.0000000000004998. Online**

**ahead of print.**

Diagnostic Performance of Host-based Gene Expression Diagnostics in Children

With Extrapulmonary Tuberculosis: A Systematic Review.

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**BACKGROUND:** Diagnosing extrapulmonary tuberculosis (EPTB) in children is

challenging due to nonspecific presentations and poor diagnostic yield from

conventional microbiologic tests. Host gene expression signatures offer a

non-sputum-based diagnostic alternative. This systematic review evaluates their

diagnostic performance in pediatric EPTB.

**METHODS:** We systematically reviewed host-based gene expression diagnostics for

pediatric EPTB. PubMed, Embase and Cochrane Library (January 1965-May 2025) were

searched for studies in children (0-18 years) with EPTB. Exclusions were

adult-only studies, mixed data on pulmonary TB and EPTB without disaggregation,

pulmonary TB-only studies, reviews and abstracts. Two reviewers screened data,

resolving disagreements by discussion.

**RESULTS:** Of 830 records, 2 studies met the inclusion criteria: Pan et al. (2017)

and Olbrich et al. (2024), both in low and middle-income countries, enrolling a

total of 891 children under 15 years. Olbrich et al.'s 3-gene MTB-HR prototype

showed 59.8% sensitivity against a strict culture-confirmed reference standard

and 50.0% in isolated EPTB with a low risk of bias. Using a microbiologic,

clinical and radiologic composite standard, Pan et al.'s miRNA-29a assay

achieved 67.2% sensitivity, 88.5% specificity in peripheral blood mononuclear

cells; 81.1% sensitivity, 90.0% specificity in cerebrospinal fluid; 84.4%

sensitivity, 95.4% specificity in combined peripheral blood mononuclear

cell/cerebrospinal fluid with a high risk of bias.

**CONCLUSIONS**: Evidence for host gene expression diagnostics in pediatric EPTB is

limited by few studies, small sample sizes, bias and lack of disaggregated data,

with accuracy falling short of the World Health Organization targets.

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PMID: 40990470

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**10.1021/acs.jnatprod.5c00904. Online ahead of print.**

Discovery of Isonitrile Lipopeptide Chalkophores from Pathogenic Mycobacteria.

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The virulence-associated isonitrile lipopeptide (INLP) biosynthetic gene cluster

is conserved across Mycobacterium tuberculosis and many nontuberculous

mycobacteria (NTM) pathogens, yet the corresponding mycobacterial metabolites

have not been fully characterized, and their biological functions are still

debated. Here, we report a precursor neutral loss chromatography based mass

spectrometry strategy that enables the targeted discovery of INLPs from

Mycobacterium fortuitum, a fast-growing NTM pathogen. By monitoring a

characteristic neutral loss of 27.1 Da corresponding to hydrogen cyanide, we

identified a family of INLPs directly from bacterial culture extracts.

Structural elucidation of a representative compound using NMR and

high-resolution MS revealed a distinctive terminal methylated carboxyl group,

contrasting with previously reported INLPs bearing linear alcohol, acetal, or

cyclic motifs. Bioinformatic analysis and in vitro enzymatic assays identified a

methyltransferase encoded within the INLP BGC responsible for methyl ester

formation. Furthermore, metal-binding assays demonstrated selective chelation of

Cu(I) and Cu(II) by the isolated INLP, but no detectable interaction with

Zn(II), suggesting a role in copper homeostasis. These findings represent the

first full structural characterization of an INLP from pathogenic mycobacteria,

expand our understanding of the enzymes involved in INLP modification, and

unequivocally support the copper-binding activity of INLPs from these pathogens.

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PMCID: PMC12462896

PMID: 40987611

**41. BMJ Glob Health. 2025 Sep 22;10(9):e019137. doi: 10.1136/bmjgh-2025-019137.**

Should neighbours of tuberculosis (TB) cases be prioritised for active case

finding in high TB-burden settings? A prospective molecular epidemiological

study.

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**INTRODUCTION:** In high tuberculosis (TB)-burden countries, considerable

transmission of Mycobacterium tuberculosis (M. tb) likely occurs outside of

households. We aimed to estimate the TB prevalence and incidence in households

and neighbourhoods around known TB cases and to understand transmission

patterns.

**METHODS:** Household and neighbourhood contacts of pulmonary TB index cases from

contiguous areas in Bandung, Indonesia, were screened and followed up for 12

months. Sputum samples underwent smear microscopy, M. tb culture, Xpert MTB/RIF,

DNA isolation and whole-genome sequencing (WGS). Pairwise single-nucleotide

polymorphism (SNP) distance ≤12 defined transmission for pairs with known

epidemiological links, or SNP≤3 for pairs without epidemiological link. An

SNP=12 cut-off was used to characterise transmission clusters.

**RESULTS:** From 213 index cases, 514 household and 4141 neighbourhood contacts

underwent TB screening: 19 household (3.70%, 95% CI 2.24 to 5.71) and 45

neighbourhood (1.09%, 95% CI 0.79 to 1.45) contacts were identified with TB, of

whom 18 (3.50%, 95% CI 2.20 to 5.48) and 38 (0.92%, 95% CI 0.65 to 1.13)

respectively, were bacteriologically confirmed. During follow-up, 11 household

and 13 neighbourhood contacts were identified with TB (incidence per 100 000

person-years: 2286 (95% CI 1286 to 4148) and 350 (95% CI 190 to 563)), of whom 6

and 8, respectively, were bacteriologically confirmed (incidence per 100 000

person-years: 1247 (95% CI 560 to 2776) and 201 (95% CI 101 to 402)). A total of

223 patient M. tb isolates underwent WGS. Of 15 intra-household pairs, 8 (53.3%)

were transmission pairs. Of 24 neighbour to index case pairs, 1 (4.2%) was a

transmission pair. 11 of 19 transmission pairs shared no epidemiological link.

We identified 25 M. tb genetic clusters from 205 mono-TB isolates overall.

**CONCLUSION:** Neighbours have lower prevalence and incidence of TB than household

contacts, but twice as many cases. Very few received M. tb from their index

case, suggesting uncontrolled community-wide transmission. Whole population

active case finding may be necessary in high TB-burden settings.

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**42. Am J Respir Crit Care Med. 2025 Sep 23. doi: 10.1164/rccm.202507-1710RL. Online ahead of print.**

IgE, Matrix Metalloproteinases, and Tuberculosis: Immunologic Consequences of

Helminth Co-Infection.

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C(4), Díaz-Soria F(5), Elson WH(6), Kirwan DE(1), Gilman RH(7), Friedland JS(1).

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DOI: 10.1164/rccm.202507-1710RL

PMID: 40986726

**43. Pathog Glob Health. 2025 Sep 23:1-11. doi: 10.1080/20477724.2025.2555926. Online ahead of print.**

Redefinition of transmission clusters by accessing to additional diversity in

Mycobacterium tuberculosis through long-read sequencing.

Buenestado-Serrano S(1)(2), Vallejo-Godoy S(3), Escabias Machuca F(4), Barroso

P(5), Martínez-Lirola M(6), Cabezas T(6), Muñoz P(1)(7)(8), Pérez-Lago L(1),

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Whole-genome sequencing, supported on short-read-sequencing, has revolutionized

the precision to track Mycobacterium tuberculosis (MTB) transmission. However,

the complexity of the MTB genome (10% repetitive regions and 65% GC content)

challenges short-read mapping and assembly, leading to the exclusion of certain

genomic regions from the analysis. Long-read sequencing can overcome these

limitations, giving access to these regions, generally uninterrogated. Our study

aims to evaluate the potential of long-read sequencing in redefining long-term

MTB transmission clusters, previously characterized by short-read sequencing. We

selected 78 cases from eight long-term clusters (5-17 years; 7 to 16 cases),

from a population-based genomic epidemiology program in Almería, Spain. The

clusters were carefully selected to ensure cases i) infected by identical

strains (0 SNPs), ii) exhibiting pairwise-SNP-based distances from 1 to 16 SNPs

and iii) distributed along different branches in the genomic networks. Long-read

analysis increased the distances of each cluster from the reference by an

average of 258 SNPs and intercluster distances by 113 SNPs. Within-cluster

diversity also increased, with pairwise distances rising from 1 to 22 SNPs

across 1-7 network branches. In one cluster, the acquisition of diversity led to

overpass the 12-SNP threshold to consider a transmission cluster. Additionally,

in four clusters, 1-2 cases previously classified as infected by identical

strains were now reclassified due to the identification of additional SNP

differences. Thanks to the identification of new diversity between the cases we

could identify index cases, reconstruct transmission chronologies, precise

patient-to-patient relationships and propose new epidemiological interpretations

among the cases in cluster.

DOI: 10.1080/20477724.2025.2555926

PMID: 40986624

**44. Proc Natl Acad Sci U S A. 2025 Sep 30;122(39):e2516660122. doi:**

**10.1073/pnas.2516660122. Epub 2025 Sep 23.**

Structural and functional analysis of the Mycobacterium tuberculosis MmpS5L5

efflux pump presages increased bedaquiline resistance.

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Bedaquiline, an antitubercular drug that targets ATP-synthase, is a key

component of a new oral drug regimen that has revolutionized the treatment of

multidrug-resistant tuberculosis. Clinical bedaquiline resistance in

Mycobacterium tuberculosis has rapidly emerged, primarily due to mutations in

the transcriptional repressor Rv0678 that result in upregulation of the

resistance-nodulation-division (RND) efflux pump MmpS5/MmpL5 (MmpS5L5). Here, to

understand how MmpS5L5 effluxes bedaquiline, we determined the structure of the

MmpS5L5 complex using cryo-electron microscopy, revealing a trimeric

architecture distinct from the canonical tripartite RND efflux pumps of

gram-negative bacteria. Structure prediction modeling in conjunction with

functional genetic analysis indicates that it uses a periplasmic coiled-coil

tube to transport molecules across the cell wall. Structure-guided genetic

approaches identify MmpL5 mutations that alter bedaquiline transport; these

mutations converge on a region in MmpL5 located in the lower portion of the

periplasmic cavity, proximal to the outer leaflet of the inner membrane,

suggesting a route for bedaquiline entry into the pump. While currently known

clinical resistance to bedaquiline is due to pump upregulation, our findings

that several MmpL5 variants increase bedaquiline efflux may presage the

emergence of additional modes of clinical resistance.

DOI: 10.1073/pnas.2516660122

PMID: 40986343 [Indexed for MEDLINE]

**45. J Exp Med. 2025 Dec 1;222(12):e20250466. doi: 10.1084/jem.20250466. Epub 2025**

**Sep 23.**

Type I IFN drives neutrophil swarming, impeding lung T cell-macrophage

interactions and TB control.

Branchett WJ(1), Stavropoulos E(1), Shields J(1), Al-Dibouni A(1), Cardoso M(2),

Fernandes AI(2)(3), Moreira-Teixeira L(1), Slawinski H(4), Mikolajczak A(5),

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The early immune mechanisms determining Mycobacterium tuberculosis infection

outcome are unclear. Using bulk and scRNA-seq over the first weeks of infection,

we describe an unexpected, higher early pulmonary type I IFN response in

relatively resistant C57BL/6 as compared with highly TB-susceptible C3HeB/FeJ

mice. C57BL/6 mice showed pronounced early monocyte-derived macrophage (MDM)

accumulation and extensive CD4+ T cell-MDM interactions in lung lesions,

accompanied by high expression of T cell-attractant chemokines by MDMs.

Conversely, lesions in C3HeB/FeJ mice were dominated by neutrophils with high

expression of pro-inflammatory chemokines, from which CD4+ T cells were

spatially segregated. Early type I IFN signaling blockade reduced bacterial load

and neutrophil swarming within early TB lesions while increasing CD4+ T cell

numbers in both C57BL/6 and C3HeB/FeJ mice, with later more pronounced effects

on bacterial load in C3HeB/FeJ mice. These data suggest that early type I IFN

signaling during M. tuberculosis infection favors neutrophil accumulation and

limits CD4+ T cell infiltration into developing lesions.

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DOI: 10.1084/jem.20250466

PMCID: PMC12456410

PMID: 40986319 [Indexed for MEDLINE]

**46. Dig Dis Sci. 2025 Sep 23. doi: 10.1007/s10620-025-09421-0. Online ahead of**

**print.**

EUS-Guided Diagnosis of Hepatic Tuberculosis Presenting as Postoperative

Fistula.

Acharya R(1), Soundararajan R(2), Gupta P(3), Gupta R(4), Rana SS(5).

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DOI: 10.1007/s10620-025-09421-0

PMID: 40986151

**47. J Clin Microbiol. 2025 Sep 23:e0091225. doi: 10.1128/jcm.00912-25. Online ahead of print.**

Off-label evaluation of the BD MAX MDR-TB assay for rapid diagnosis of

rifampicin and isoniazid resistance of Mycobacterium tuberculosis clinical

isolates in a high-volume reference laboratory.

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Drug-resistant tuberculosis (TB) remains a primary global health concern.

Multidrug-resistant TB is defined by resistance to at least rifampicin (RIF) and

isoniazid (INH), the two key drugs used in TB treatment. The BD MAX Multi-Drug

Resistant Tuberculosis (BD MAX) assay is a fully automated real-time PCR

platform recommended by the World Health Organization for the initial diagnosis

of TB and RIF and INH resistance (RIF-R and INH-R) directly from pulmonary

clinical samples. This study aimed to assess the off-label performance of BD MAX

in clinical M. tuberculosis complex (MTBC) isolates under routine laboratory

conditions. The assay was first validated using non-tuberculous mycobacteria

(NTM) and MTBC isolates with known mutations. For real-world validation, it was

compared to the GenoType MTBDRplus by testing 1,440 clinical isolates

prospectively. The BD MAX assay correctly excluded MTBC from all NTM cultures.

Among MTBC isolates with known mutations, it identified 19 of 20 RIF-R isolates

and 14 of 15 INH-R isolates. In prospective testing, BD MAX achieved 99.6%

sensitivity (1,403/1,409), 96.8% specificity (30/31), and 99.5% overall accuracy

(1,433/1,440) for MTBC detection. For drug resistance detection, it showed 95.2%

(40/42) concordance for RIF, 96.8% (30/31) for INH, and 81.3% (13/16) for MDR

when compared to MTBDRplus. Discrepancies between MTBDRplus and BD MAX included

heteroresistant cases and unreportable resistance results by BD MAX due to

infrequent mutations or low bacterial load. Overall, this study confirms BD MAX

as an accurate and reliable tool for MTBC detection and drug resistance

profiling in clinical isolates in high-volume TB laboratories.IMPORTANCEThis

study highlights the importance of the BD MAX Multi-Drug Resistant Tuberculosis

assay (BD MAX) applied in clinical isolates for the detection of

multidrug-resistant tuberculosis (MDR-TB), i.e., Mycobacterium tuberculosis

resistance to rifampicin and isoniazid. TB is a global health issue, and

drug-resistant TB makes treatment more difficult, favoring transmission and

disease amplification. The BD MAX platform offers a faster and more automated

way to detect TB and drug resistance. The study showed that BD MAX, applied

off-label in clinical isolates, accurately identified TB and resistance to

rifampicin and isoniazid, with results comparable to those of the widely used

line probe assay. This is significant in a high-volume laboratory because it is

more straightforward and more rapid than the line probe assay. BD MAX showed

some limitations, especially in detecting rare mutations and in cases of low

bacterial levels. Overall, this tool could improve TB care, especially in

high-volume laboratories.

DOI: 10.1128/jcm.00912-25

PMID: 40985744

**48. ChemMedChem. 2025 Sep 22:e202500673. doi: 10.1002/cmdc.202500673. Online ahead of print.**

New Structure Activity Relationship Insight into the Role of the C-3 Extension

on Rifamycin Antimycobacterial Activity.

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Herein, the antimycobacterial screening of a series of rifamycin analogues,

modified at their C-3 extension, is reported. Overall, these compounds display

potent activity against a wild-type Mtb strain assayed in three different growth

media. Several promising C-3 extensions are identified through this screen, with

compounds featuring rigid tertiary alicyclic hydrazones displaying superior

activity to amino compounds. In addition, a general correlative trend between

logP and biological activity is observed. This study adds to the growing

literature surrounding structure activity relationship pertaining the important

C-3 extension of rifamycin, which in addition to a poorly understood role in

target engagement, has utility for modulating physicochemical properties, a key

condition in antimycobacterial drug discovery.

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DOI: 10.1002/cmdc.202500673

PMID: 40983322

**49. JMIR Res Protoc. 2025 Sep 22;14:e64037. doi: 10.2196/64037.**

Perceptions of Occupational Risk and Adherence to Tuberculosis Prevention Among

Health Care Workers: Protocol for a Scoping Review.

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University, Pontianak, Indonesia.

**BACKGROUND:** Tuberculosis (TB) is a major public health problem around the world.

Health care workers (HCWs) are at a much higher risk of contracting TB because

they are often working around sick people in clinical settings. Even though HCWs

play a key role in controlling TB, we still do not fully understand how they see

this risk and how it affects their willingness to follow preventive measures.

**OBJECTIVE:** This study aims to examine the existing body of knowledge on HCWs'

perceived risks of TB and how these perceptions impact their adherence to TB

prevention measures. The results of this scoping review will identify gaps in

the current literature that should inform policy and practice and guide future

research studies to optimize TB prevention among HCWs.

**METHODS:** This scoping review will be conducted following the framework proposed

by Arksey and O'Malley, incorporating the recent advancements. This approach

involves 6 key stages: identifying the research question; identifying relevant

studies; selecting studies; charting the data; collating, summarizing, and

reporting the results; and consulting with stakeholders.

**RESULTS:** As of June 2024, 1345 records were identified (1234 from databases and

111 from other sources), and 667 duplicates were removed. The remaining 678

records were screened by title and abstract, with 216 progressing to full-text

review. After applying the eligibility criteria, 42 studies were included in the

final analysis. Screening and full-text assessments were conducted between

September and October 2024. Data extraction and thematic analysis were performed

in winter 2024. The final data synthesis stage is expected to be completed by

2025.

**CONCLUSIONS:** HCWs' perceptions of risk have a considerable effect on how well

they follow TB prevention measures such as using personal protective equipment

and undergoing health screenings. Lack of resources, lack of training, and the

stigma around TB are some of the main barriers to TB prevention adherence. The

thematic analysis showed that adherence levels were different depending on the

support offered by the institution and the TB knowledge level and perception of

each HCW. Although TB treatment has become more effective, nosocomial infections

are still a big concern, especially in low- and middle-income countries like

Indonesia, where HCWs are more likely to have latent TB infections. This review

shows how important it is for HCWs to understand how TB prevention behaviors

work. To improve HCW adherence, the gaps in institutional support, stigma, and

training must be filled. Future interventions should be based on the specific

problems found in low- and middle-income countries. This will make health care

safer for everyone around the world.

INTERNATIONAL REGISTERED REPORT IDENTIFIER (IRRID): DERR1-10.2196/64037.

©Agus Fitriangga, Alex Alex, Eka Ardiani Putri. Originally published in JMIR

Research Protocols (https://www.researchprotocols.org), 22.09.2025.

DOI: 10.2196/64037

PMID: 40982797 [Indexed for MEDLINE]

**50. Proc Natl Acad Sci U S A. 2025 Sep 30;122(39):e2503966122. doi:**

**10.1073/pnas.2503966122. Epub 2025 Sep 22.**

Inorganic sulfate is critical for Mycobacterium tuberculosis lung tissue

colonization and redox balance.

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Tuberculosis remains the deadliest infectious disease caused by a single

pathogen, highlighting the urgent need for novel therapies. A deeper

understanding of Mycobacterium tuberculosis metabolism could uncover specific

vulnerabilities and inform the development of new treatments. Sulfur, essential

for bacterial growth and survival, fuels key pathways including redox buffering

and coenzyme production. Although previous studies suggest that M. tuberculosis

utilizes various substrates to meet its sulfur requirements, the primary sources

of sulfur exploited during in vivo infection remain unclear. Here, we reveal

that M. tuberculosis acquires inorganic sulfate through the SubI-CysTWA

transporter during macrophage infection. Using nanoSIMS (high spatial resolution

Secondary Ion Mass Spectrometry) analysis, we observed significant

sulfate-derived 33S enrichment in intracellular bacteria, correlating with

metabolic activity. Deletion of subI abolished sulfate uptake, impairing

bacterial growth in vitro and reducing M. tuberculosis survival in murine

macrophages and lungs of infected mice. Finally, our data demonstrate that

sulfate acquisition is essential for maintaining mycobacterial redox balance and

resisting nitrosative stress in vitro and in vivo. Thus, unlike many

intracellular pathogens, M. tuberculosis depends on an energetically costly

inorganic sulfate assimilation pathway to survive in the nutrient-limited host

environment. These findings challenge prior assumptions that organic reduced

sulfur sources, such as methionine, fuel M. tuberculosis sulfur metabolism

during infection. Since animal cells lack a sulfate assimilation pathway,

uncovering the critical role of SubI-CysTWA-mediated sulfate import in M.

tuberculosis pathogenesis highlights this pathway as a promising

pathogen-specific therapeutic target. Targeting this system could either

directly impair M. tuberculosis survival during infection or sensitize bacilli

to antibiotic-induced oxidative stress by disrupting redox homeostasis.

DOI: 10.1073/pnas.2503966122

PMID: 40982672 [Indexed for MEDLINE]

**51. PLOS Glob Public Health. 2025 Sep 22;5(9):e0005109. doi:**

**10.1371/journal.pgph.0005109. eCollection 2025.**

TB stigma in India: A narrative review of types of stigma, gender differences,

and potential interventions.

Carwile ME(1), Prakash Babu S(2), Cintron C(1), Dauphinais M(1), Pan SJ(3),

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In India, persons with tuberculosis (PWTB) and their households experience

significant disease-related stigma. The objective of this narrative review was

to conduct a review of existing literature related to the types of stigma

experienced by PWTB and their household members, with a focus on the effects of

stigma, possible interventions, and gender differences. A literature search was

conducted on PubMed, EMBASE, and Web of Science using key search terms. We found

that tuberculosis (TB)-related stigma has negative effects on emotional and

mental health, relationships, and treatment adherence. Women experience a higher

burden of TB stigma compared to men. Moreover, TB stigma can affect mental

well-being and lead directly to reductions in the number of PTWB seeking

treatment, treatment adherence, and treatment completion. All these factors can

lead to negative health outcomes for the PWTB, higher costs to the government,

and even the spread of the infectious disease to other members of the community.

The consequences of TB-related stigma require additional attention.

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DOI: 10.1371/journal.pgph.0005109

PMCID: PMC12453202

PMID: 40982550

**52. PLoS One. 2025 Sep 22;20(9):e0331904. doi: 10.1371/journal.pone.0331904.**

**eCollection 2025.**

"If we lose it, we are worried": Individual and provider level perceptions

towards weight change among people living with HIV who undergo TB screening in

routine health care settings in Gauteng Province, South Africa.

Dube TN(1), Mboniswa F(1), Qwana SE(2), Charalambous S(1)(3), Ndlovu N(1), Grant

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Africa.

**BACKGROUND:** HIV weakens the immune system, increasing the risk of tuberculosis

(TB) in people with living HIV (PLHIV). People living with HIV and on

antiretroviral treatment (ART) often experience physical body size changes.

Studies have found a significant discrepancy between PLHIV's self-reported

weight loss and their measured weight loss when being screened for TB using the

WHO tool. To understand this inconsistency, a qualitative sub-study was

conducted to explore perceptions and attitudes towards weight change among

adults attending HIV care, as well as health care workers in public clinics in

Gauteng, South Africa.

**METHODS:** Our qualitative study was nested within the XPHACTOR study. A total of

seven focus group discussions were conducted, five with adult participants

attending for HIV care and two with health care workers and research staff in

clinics around Gauteng. Inductive thematic analysis was used to analyse the

data.

**FINDINGS:** The majority of PLHIV preferred to gain weight due to fear of stigma

associated with weight loss. Weight loss is associated with HIV/AIDS, suggesting

that people attending HIV care may underreport weight loss in the context of a

TB symptoms screening tool because they fear stigma. Participants reported that

weight changes impacted their daily lives and had psychological effects on them.

Some PLHIV described lipodystrophy as disproportional weight gain. Culture and

media have an influence on the perception of ideal body size and shape for both

men and women.

**CONCLUSIONS:** Underreporting weight loss might result in poor sensitivity of the

WHO TB screening tool and suggests that we need either alternative ways to

determine weight loss or screening tools for TB that are less dependent on

reported symptoms.

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DOI: 10.1371/journal.pone.0331904

PMCID: PMC12453174

PMID: 40982432 [Indexed for MEDLINE]

**53. Antimicrob Agents Chemother. 2025 Sep 22:e0048125. doi: 10.1128/aac.00481-25. Online ahead of print.**

Epetraborole pharmacokinetics/pharmacodynamics in the hollow fiber system model

of Mycobacterium tuberculosis.

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In the hollow fiber system model of tuberculosis (TB), the ratio of area under

the concentration-time curve to MIC (AUC0-24/MIC) of 327.1 was identified as the

epetraborole optimal exposure target for Mycobacterium tuberculosis kill. Monte

Carlo simulation experiments showed that even the intravenous dose of 1,500

mg/twice daily would fail in the majority of patients, and the dose needed for

good efficacy for TB may likely not be safe for patients.

DOI: 10.1128/aac.00481-25

PMID: 40980919

**54. Antimicrob Agents Chemother. 2025 Sep 22:e0111325. doi: 10.1128/aac.01113-25. Online ahead of print.**

In vitro exposure to clofazimine can select for delamanid and pretomanid

resistance in Mycobacterium tuberculosis.

Rupasinghe P(#)(1)(2), Ismail N(#)(3), Mulders W(1), Warren RM(3), Joseph L(4),

Ngcamu D(4), Gwala T(4), Omar SV(4), Vereecken J(1), de Jong BC(1), Rigouts

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In vitro experiments with Mycobacterium tuberculosis showed that clofazimine

exposure selected for delamanid and pretomanid resistance and mutations in fbiA,

fbiC, or fbiD-after the acquisition of Rv0678 mutations where this could be

determined. Whether this is also possible in vivo and in an Rv0678 wild-type

background has to be studied further. Based on the available evidence, however,

we propose that nitroimidazole resistance should not be considered an exclusion

criterion for the use of clofazimine.

DOI: 10.1128/aac.01113-25

PMID: 40980917

**55. Antimicrob Agents Chemother. 2025 Sep 22:e0098025. doi: 10.1128/aac.00980-25. Online ahead of print.**

Thienopyrimidine amide analogs target MmpL3 in Mycobacterium tuberculosis.

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The identification of novel agents with mechanisms of action distinct from those

currently utilized in tuberculosis treatment remains a significant challenge.

The mycobacterial protein MmpL3 has emerged as a promising drug target due to

its essential role in the synthesis of the cell wall of Mycobacterium

tuberculosis. We previously identified novel thienopyrimidine amides(TPAs) with

good anti-tubercular activity. We profiled a subset of TPAs, determining

activity against intracellular bacteria and bactericidal activity against

replicating bacteria. We ran assays to determine the mode of action by measuring

cell wall stress, ATP production, and bacterial cytological profiling. We

determined activity against a strain of M. tuberculosis with mutations in MmpL3.

We isolated and sequenced resistant mutants. We tested five analogs against a

strain of M. tuberculosis with mutations in MmpL3 and determined that they lost

potency. Analogs induced PiniBAC, a reporter for cell wall stress, and led to an

ATP boost characteristic of cell wall inhibitors. Bacterial cytological

profiling of a representative compound revealed a morphological profile

consistent with other MmpL3 inhibitors. Together, our data support MmpL3 as the

most probable drug target for the TPA analogs and add to the growing list of

scaffolds that can inhibit this vulnerable transporter.

DOI: 10.1128/aac.00980-25

PMID: 40980915

**56. mSphere. 2025 Sep 22:e0057125. doi: 10.1128/msphere.00571-25. Online ahead of print.**

Rapid, accurate, and reproducible de novo prediction of resistance to

antituberculars.

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As one of the deadliest infectious diseases in the world, tuberculosis is

responsible for millions of new cases and deaths reported annually. The rise of

drug-resistant tuberculosis, particularly resistance to first-line treatments

like rifampicin, presents a critical challenge for global health, which

complicates the treatment strategies and calls for effective diagnostic and

predictive tools. In this study, we apply an ensemble-based molecular dynamics

computer simulation method, TIES\_PM, to estimate the binding affinity through

free energy calculations and predict rifampicin resistance in RNA polymerase. By

analyzing 61 mutations, including those in the rifampicin resistance-determining

region, TIES\_PM produces reliable results in good agreement with clinical

reference and identifies abnormal data points indicating alternative mechanisms

of resistance. In the future, TIES\_PM is capable of identifying and selecting

leads with a lower risk of resistance evolution and, for smaller proteins, it

may systematically predict antibiotic resistance by analyzing all possible codon

permutations. Moreover, its flexibility allows for extending predictions to

other first-line drugs and drug-resistant diseases. TIES\_PM provides a rapid,

accurate, low-cost, and scalable supplement to current diagnostic pipelines,

particularly for drug resistance screening in both research and clinical

domains.**IMPORTANCE** Antimicrobial resistance (AMR), a global threat, challenges

early diagnosis and treatment of tuberculosis (TB). This study employs TIES\_PM,

a free-energy calculation method, to efficiently predict AMR by quantifying how

mutations in bacterial RNA polymerase (RNAP) affect rifampicin (RIF) binding. On

simulating 61 clinically observed mutations, the results align with WHO

classifications and reveal ambiguous cases, suggesting alternative resistance

mechanisms. Each mutation requires ~5 h, offering rapid, cost-effective

predictions. An ensemble approach ensures statistical robustness. TIES\_PM can be

extended to smaller proteins for systematic codon permutation analysis, enabling

comprehensive antibiotic resistance prediction, or adapted to identify

low-resistance-risk drug leads. It also applies to other TB drugs and resistant

pathogens, supporting personalized therapy and global AMR surveillance. This

work provides novel tools to refine resistance mutation databases and phenotypic

classification standards, enhancing early diagnosis while advancing

translational research and infectious disease control.

DOI: 10.1128/msphere.00571-25

PMID: 40980905

**57. Chem Commun (Camb). 2025 Sep 22. doi: 10.1039/d5cc04932f. Online ahead of print.**

Harnessing conserved G-quadruplexes for fluorescence detection of Mycobacterium

tuberculosis.

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We report the fluorescence detection of the conserved G-quadruplex (GQ) motif in

Mycobacterium tuberculosis (MTB) DNA, ensuring high specificity with minimal

interference from human and non-MTB DNA sequences. The duplex-to-GQ reliable

conformational polymorphism (GQ-RCP) enables its application in

amplification-compatible MTB detection, offering a platform for precise

diagnostic assays.

DOI: 10.1039/d5cc04932f

PMID: 40980899

**58. J Postgrad Med. 2025 Sep 22. doi: 10.4103/jpgm.jpgm\_222\_25. Online ahead of**

**print.**

Pediatric sternal tubercular osteomyelitis presenting as a subcutaneous abscess:

A rare entity.

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Pediatric sternal abscess with associated osteomyelitis is an infrequent but

challenging clinical entity. Atypical presentations and negative bacterial

cultures compound its diagnosis. This report details a case of a 5-year-old boy

who presented with a progressively increasing lower sternal swelling for 1

month. Upon examination, the lesion was suggestive of a sternal abscess. Work-up

revealed leukocytosis and a raised erythrocyte sedimentation rate. Magnetic

resonance imaging depicted a hyperintense collection in the subcutaneous tissue,

extending into the retrosternal space, accompanied by osteomyelitic changes in

the manubrium. Surgical drainage of the superficial abscess and curetting of the

bony edges of the manubrium, including excision of the sinus tract, were

performed. The patient was initiated on anti-tubercular therapy, to which he

exhibited a favorable response. The follow-up visits showed adequate healing and

new bone formation. Anti-tubercular therapy is a cornerstone for a successful

treatment modality for pediatric sternal abscess with tubercular osteomyelitis.

Timely intervention and interdisciplinary collaboration are essential for

achieving optimal outcomes.

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DOI: 10.4103/jpgm.jpgm\_222\_25

PMID: 40977615

**59. Multimed Man Cardiothorac Surg. 2025 Sep 22;2025. doi: 10.1510/mmcts.2025.035.**

Robotic-assisted bronchial reimplantation for post-tuberculosis bronchial

stenosis: surgical technique.

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This report presents a novel robotic-assisted surgical technique for bronchial

reimplantation in patients with complete bronchial stenosis after tuberculosis

treatment. A 34-year-old female patient with progressive dyspnoea was diagnosed

with complete bronchial stenosis and total left lung atelectasis. After

unsuccessful bronchial dilation attempts, robotic-assisted bronchial

reimplantation with veno-venous extracorporeal membrane oxygenation support was

undertaken. Intra-operative bronchoscopy ensured airway patency throughout the

procedure. At 1-year follow-up, the patient remained asymptomatic in daily

activities, with no late complications or restenosis, reinforcing the long-term

efficacy of the procedure. This technique demonstrates the potential for

enhanced surgical outcomes in managing complex bronchial stenosis. The findings

highlight the viability of this advanced technique in improving respiratory

function and patient recovery.

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Cardio-Thoracic Surgery. All rights reserved.

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PMID: 40977491 [Indexed for MEDLINE]

**60. Trans R Soc Trop Med Hyg. 2025 Sep 22:traf100. doi: 10.1093/trstmh/traf100.**

**Online ahead of print.**

Effect of introducing ethambutol and integrating drugs into fixed-dose tablets

on mortality in tuberculosis patients.

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**BACKGROUND: I**n response to increasing primary resistance to isoniazid, the

Brazilian Ministry of Health modified the tuberculosis (TB) treatment regimen at

the end of 2009. The changes included adding ethambutol to the intensive phase,

using fixed-dose combination tablets and adjusting isoniazid and pyrazinamide

dosages. This study aimed to estimate the effect of the regimen change on

all-cause mortality and, secondarily, on TB-specific mortality, treatment

success and loss to follow-up.

**METHODS:** We analysed cohorts of individuals ≥10 y of age who initiated TB

treatment before (n = 145 528) and after (n = 161 264) the regimen change. Data

were obtained from the national notifiable disease and mortality information

systems. Missing data were imputed and effects were estimated using multilevel

logistic regression models with states as the clustering level. Covariates were

selected using a directed acyclic graph.

**RESULTS:** The regimen change was not associated with all-cause mortality

(relative risk [RR] 1.01 [95% confidence interval {CI} 0.98 to 1.04]) or

TB-specific mortality (RR 0.98 [95% CI 0.95 to 1.02]). The treatment success

rate was lower, and loss to follow-up was higher during the modified regimen

period compared with the previous one. However, sensitivity analyses suggest

that changes in the handling of transfers and missing outcome data may partly

explain these findings.

**CONCLUSION:** We concluded that the modified regimen did not adversely affect

survival among TB patients.

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DOI: 10.1093/trstmh/traf100

PMID: 40977297

**61. Folia Microbiol (Praha). 2025 Sep 22. doi: 10.1007/s12223-025-01319-8. Online**

**ahead of print.**

Flurbiprofen restores rifampicin and isoniazid sensitivity in

multidrug-resistant Mycobacterium tuberculosis putatively by inhibiting efflux

pumps Rv0194 and Rv0933.

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Multidrug-resistant tuberculosis remains a global health challenge,

necessitating novel therapeutic approaches. Efflux pumps, including Rv0194 and

Rv0933, contribute to Mycobacterium tuberculosis resistance by actively

extruding first-line drugs such as rifampicin and isoniazid. This study aimed to

identify small-molecule inhibitors that target these pumps to restore drug

susceptibility. Through in silico screening, six lead compounds were selected

and evaluated for antimicrobial activity against ten MDR-TB clinical isolates.

Among them, flurbiprofen and trichlorocarbinalide exhibited significant

inhibitory effects, enhancing rifampicin and isoniazid activity in checkerboard

synergy assays. These combinations reduced the minimum inhibitory concentrations

of both drugs, confirming their potential to reverse resistance. Cytotoxicity

assessments of peripheral blood mononuclear and THP-1 cells demonstrated

favourable safety profiles. Mechanistic studies revealed increased expression of

Rv0194 and Rv0933 upon rifampicin and isoniazid exposure, underscoring their

role in drug resistance. Flurbiprofen and trichlorocarbinalide may enhance

intracellular drug retention by inhibiting these efflux pumps, improving

therapeutic efficacy. However, trichlorocarbinalide did not restore rifampicin

or isoniazid sensitivity as efficiently as flurbiprofen did. These findings

highlight flurbiprofen as a promising efflux pump inhibitor that could

potentiate standard TB treatments and counteract resistance. Further studies

using diverse clinical isolates and in vivo models are needed to validate its

therapeutic potential.

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v.v.i.

DOI: 10.1007/s12223-025-01319-8

PMID: 40976821

**62. J Infect Dis. 2025 Sep 22:jiaf482. doi: 10.1093/infdis/jiaf482. Online ahead of print.**

Activin A mediated KAT8 expression induces ferroptosis during Mycobacterium

tuberculosis infection.

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Activin A, a secretory glycoprotein, is upregulated in tuberculosis (TB)

patients, and its levels are correlated with disease severity. During infection,

Mycobacterium tuberculosis (Mtb) induces ferroptosis, an iron-induced mode of

cell death, that aids in dissemination and survival. Here, we identify a

functional role for activin A and the downstream SMAD2/3 signalling in

Mtb-induced ferroptosis and disease progression. Molecular assays, including

ChIP and loss-of-function analysis, demonstrated that Activin A regulates the

expression of KAT8, which in-turn regulates levels of HO-1. Mechanistically, we

identify that KAT8-mediated acetylation of NRF2 during Mtb infection enhances

its nuclear availability leading to increased HO-1 expression. Finally,

utilizing an in vivo mouse model of TB, we show that the pharmacological

inhibition of activin A receptor and KAT8 restricts Mtb burden, limits

dissemination and ameliorates TB pathology. Thus, we report a novel role for

activin A in regulating NRF2 localisation and outline its potential consequences

during TB.

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PMID: 40976643

**63. Comput Biol Chem. 2025 Sep 21;120(Pt 2):108691. doi:**

**10.1016/j.compbiolchem.2025.108691. Online ahead of print.**

Methyl 2-(7-hydroxy-3-methyloctyl)-1,3-dimethyl-4-oxocyclohex-2-enecarboxylate

as a natural and potent antitubercular lead: An in silico study integrating

molecular docking, molecular dynamics, FMO, and DFT analyses.

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The currently marketed antitubercular drugs have limited efficacy with the

potential to cause organ toxicity. Thus, there is a need for new drug therapies

to combat tuberculosis. Methyl

2-(7-hydroxy-3-methyloctyl)-1,3-dimethyl-4-oxocyclohex-2-enecarboxylate (PE14)

and (E)-3,7,11,15-tetramethylhexadec-2-en-1-ol (EA8) are the natural

antitubercular lead-like molecules isolated from petroleum ether and ethyl

acetate leaf extracts of Ipomea sepiaria, respectively. Extensive research has

demonstrated the wide range of health benefits associated with this plant.

However, the antitubercular effects of phytocompounds isolated from this species

have not been systematically investigated. To evaluate the antitubercular effect

of the natural compound, in silico prediction of binding affinity against

selected antitubercular target proteins was conducted, and this was compared

with co-crystallized ligands as a standard. Additionally, the physicochemical

properties, pharmacokinetics, and various toxicity-related parameters were also

predicted. Two ligand docking complexes were selected for molecular dynamics

simulations to calculate the binding free energy over 250 ns. Moreover, FMO and

DFT were also investigated. PE14 complies with RO5 and exhibits suitable ADMET

profiles. The molecular docking scores in kcal/mol showed comparatively more

potency against antitubercular drug targets compared to the co-crystalized

ligand of the target protein as well as EA8. Overall, the strength of

interaction between the ligands with their selected target proteins from the

molecular docking study, heat change that occurs during the ligand-target

interactions from a molecular dynamic simulation study, the electronic

reactivity trend was established as STD > PE14 > CIP > EA8 from FMO analysis and

other multi-parametric druggability profiles of target proteins suggests that

PE14 can be considered as a suitable antitubercular lead-like for the treatment

of M. tuberculosis. The results of the current study were closely correlated

with those of our previous study on Ipomea sepiaria in the LRP assay. However,

necessary in vitro and in vivo studies on the synthesized pure compound must be

carried out to participate in a clinical trial, where the in silico results

would help expedite the process of drug development.

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PMID: 41016330

**64. Tuberculosis (Edinb). 2025 Sep 5;155:102688. doi: 10.1016/j.tube.2025.102688.**

**Online ahead of print.**

Diagnosis of extrapulmonary tuberculosis by Truenat® MTB/MTB Plus assay.

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Diagnosis of extrapulmonary tuberculosis (EPTB) is challenging. During the last

two decades, several nucleic acid amplification tests have been deliberated to

diagnose TB (including EPTB) and drug resistance (DR), i.e. in-house

PCR/multiplex-PCR, commercial real-time PCR (e.g. Cobas TaqMan/LightCycler),

line probe assay (e.g. GenoType MTBDRplus), GeneXpert®/GeneXpert® Ultra and

Truenat®MTB/MTB Plus (TruPlus). However, we still need a simple and reliable

diagnostic test especially for remote areas. Markedly, both GeneXpert/Xpert

Ultra require a constant power supply and their high cost is a major hindrance

in resource-limited settings. To overcome this, Molbio Diagnostics, India,

introduced a Truenat/TruPlus assay (the WHO endorsed), which is chip-based micro

real-time PCR system that targets nrdB, while TruPlus targets IS6110+nrdZ for

the identification of Mtb within 1 h. After a positive result, an 'add-on' chip,

i.e. Truenat® MTB-RIF Dx (TruRif) is utilized to detect rifampicin-resistance

(RIF-R) that takes another 1 h. Although there is adequate literature on the

diagnosis of pulmonary TB by Truenat/TruPlus, limited information is available

on EPTB diagnosis. In this review, we assessed the performance of

Truenat/TruPlus in different EPTB types, i.e. TB lymphadenitis, TB pleuritis, TB

meningitis, osteoarticular TB, etc. that exhibits moderate to good

sensitivity/specificity. Meanwhile, few false negative/positive RIF-R results

are obtained by TruRif. Since Truenat/TruPlus is portable, battery-operated and

relatively cost-effective as compared to GeneXpert/Xpert Ultra, it can be

utilized for preliminary screening of EPTB specimens in peripheral settings,

which may be further confirmed by other tests.

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PMID: 41014808

**65. Pathogens. 2025 Sep 12;14(9):924. doi: 10.3390/pathogens14090924.**

Immune Sensitization to Mycobacterium tuberculosis Among Young Children with and

without Tuberculosis.

Gutierrez J(1), Malone LL(1)(2), Mohammadi M(3), Mukisa J(2), Atuhairwe M(2),

Mwesigwa SPG(2), Athieno S(2), Buwule S(2), Ameda F(4), Nalukwago S(5), Mupere

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97239, USA.

Identification of young children with Mycobacterium tuberculosis (Mtb) infection

is critical to curb pediatric morbidity and mortality. The optimal test to

identify young children with Mtb infection remains controversial. Using a

tuberculosis (TB) household contact (HHC) study design among 130 Ugandan

children less than 5 years of age with Mtb exposure, this study was conducted to

determine the following: (1) the prevalence of Mtb immune sensitization in young

children heavily exposed to TB using both the tuberculin skin test (TST) and

QuantiFERON Gold Plus (QFT-Plus) interferon gamma release assay, and to examine

the concordance of these two tests; and (2) the diagnostic accuracy of TST and

QFT-plus for confirmed and unconfirmed TB in young children. Prevalence of Mtb

immune sensitization was determined using TST at both 5 mm and 10 mm thresholds

for positivity; manufacturer's thresholds were utilized to establish QFT-Plus

positivity. Concordance analysis between TST and QFT-Plus results was performed,

including correlation between QFT-Plus tube TB.1 and tube TB.2. The sensitivity

and specificity of TST and QFT-Plus for confirmed and unconfirmed TB was

determined, and a logistic regression model was utilized to estimate the odds of

TB. A 5 mm TST threshold identified the most children with Mtb sensitization

(49.2%) and had moderate agreement with QFT-Plus (Cohen's Kappa 0.59). The odds

of TB were two times higher among children with a positive TST using a 5 mm

threshold. Concordance between 10 mm TST threshold and QFT-Plus was substantial

(Cohen's Kappa 0.65), with higher concordance observed among older children (2-5

years). The QFT-Plus tube TB.1 and tube TB.2 results were highly correlated.

Positive TST using a 5 mm threshold demonstrated the highest sensitivity for TB

(60%), whereas QFT-Plus testing demonstrated the highest specificity (72%).

Overall, our findings support that among a population of young, BCG-vaccinated

children with heavy household exposure to TB, the TST using a 5 mm threshold

identified more children with evidence of Mtb immune sensitization, and children

with TB disease, than the QFT-Plus. These findings are highly relevant for

children who are TB HHCs in endemic settings, and most at risk for TB following

an exposure. We recommend that TST testing continue to be performed to assess

for Mtb sensitization in young, TB-exposed children in TB-endemic settings to

both prioritize provision of preventive therapy and to aide in diagnosis of

pediatric TB.

DOI: 10.3390/pathogens14090924

PMCID: PMC12472572

PMID: 41011824 [Indexed for MEDLINE]

**66. Molecules. 2025 Sep 12;30(18):3708. doi: 10.3390/molecules30183708.**

Natural Products with Potent Antimycobacterial Activity (2000-2024): A Review.

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Tuberculosis (TB), an infection caused by Mycobacterium tuberculosis, affects

nearly one-third of the world's population. It is estimated that TB infects

around ten million people worldwide, with no less than two million fatalities

annually. It is one of the treatable infections due to improved diagnostic tools

and therapeutic agents. However, the disease remains a threat to humankind due

to the emergence of multidrug- and extensively drug-resistant strains of M.

tuberculosis. This has driven many researchers to look for new antitubercular

medications with better efficacy, safety, and affordability. As has always been

the case, natural products have provided huge potential as a source of remedies

for various infectious and non-infectious diseases. This review aims to report

discoveries and updates of antitubercular natural products with minimum

inhibitory concentration (MIC) values of less than or 10 µg/mL or 50 µM and

selectivity indices of greater than 10. The review discusses 36 naturally

occurring compounds from various classes, isolated from both terrestrial and

aquatic organisms, including higher plants and microorganisms. Perusal of the

literature reveals that most of these promising compounds are alkaloids,

terpenoids, steroids, and peptides. Rufomycin I, a cyclic heptapeptide from

Streptomyces sp., showed potent activity against drug-sensitive and

isoniazid-resistant M. tuberculosis H37Rv (MIC < 0.004 µM), surpassing isoniazid

(MIC = 0.23 µM), likely by inhibiting ClpC1 transcription. Hapalindole A also

displayed strong activity (MIC < 0.6 µM). Current TB drugs have become less

effective; therefore, natural products such as hapalindole A and rufomycin I,

owing to their potent activity, selectivity, and novelty, are increasingly

recognized as potential lead compounds against TB.

DOI: 10.3390/molecules30183708

PMCID: PMC12473002

PMID: 41011600 [Indexed for MEDLINE]

**67. Microorganisms. 2025 Sep 17;13(9):2163. doi: 10.3390/microorganisms13092163.**

Characterization of Drug Resistance Mutations in Mycobacterium tuberculosis

Isolates from Moroccan Patients Using Deeplex Targeted Next-Generation

Sequencing.

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Tuberculosis (TB) is a major public health concern worldwide and in Morocco,

particularly considering the increasing burden of drug-resistant Mycobacterium

tuberculosis (MTB) strains. In this study, we report the first nationwide

molecular characterization of MTB clinical isolates using the Deeplex-MycTB

targeted next-generation sequencing (tNGS) assay. A total of 71 culture-derived

DNA samples from Moroccan TB patients were analyzed to detect

resistance-associated mutations across 18 genes and to determine phylogenetic

lineages. Of the 68 interpretable samples, 75% harbored either confirmed or

uncharacterized mutations linked to drug resistance. Among these, 78% were

classified as multidrug-resistant TB (MDR-TB) including 25.5% that met the

criteria for pre-extensively drug-resistant TB (pre-XDR-TB). Mutations were most

frequently identified in rpoB, katG, inhA, and pncA, consistent with resistance

to rifampicin, isoniazid, and pyrazinamide. Phylogenetic analysis revealed a

predominance of Lineage 4.3 (Euro-American) with a high representation of the

LAM9 and T clades, some of which showed associations with specific resistance

profiles. These findings highlight the utility of tNGS as a powerful tool for

rapid resistance detection and molecular surveillance, with potential

implications for guiding individualized treatment and informing national TB

control strategies in Morocco.

DOI: 10.3390/microorganisms13092163

PMCID: PMC12472841

PMID: 41011494

**68. Life (Basel). 2025 Sep 19;15(9):1472. doi: 10.3390/life15091472.**

Expression of a Tuberculosis-Associated Immunogenic Protein in Escherichia coli.

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It is estimated that one in four people worldwide carries Mycobacterium

tuberculosis bacteria. MPT64 is a protein exclusively secreted by Mycobacterium

tuberculosis complex (MTC) bacteria. It serves as a crucial diagnostic marker

and plays a role in the bacterium's survival by modulating the host immune

response. Consequently, the development of innovative diagnostic tools based on

MPT64, as well as the production of high-purity MPT64 protein to support

research on tuberculosis pathogenesis and the advancement of novel therapeutic

strategies, is of great importance. In this study, optimization experiments were

conducted to produce this protein in E. coli with high yield and purity. First,

a gBlock was designed by codon optimization and then cloned into a plasmid

vector using the LIC method. For more efficient production, E. coli

BL21(DE3)-R3-pRARE2 strain, which carries rare tRNAs for rare codons, was used

as the host. Five different culture media were tested to maximize protein

production, with the highest yield obtained in eBHI medium. The resulting

protein yield was 4.9 mg/L. To the best of our knowledge, this study provides

the most detailed information on the recombinant production and characterization

of MPT64 to date. Therefore, these results contribute important data for future

studies on the MPT64 protein.

DOI: 10.3390/life15091472

PMCID: PMC12471812

PMID: 41010413

**69. Life (Basel). 2025 Sep 13;15(9):1435. doi: 10.3390/life15091435.**

Intensive Management of a Patient with HIV, Active Tuberculosis, and COVID-19: A

Multidisciplinary Approach in the Intensive Care Unit.

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Coinfection with HIV, active tuberculosis, and COVID-19 is rare but markedly

increases mortality risk and complicates treatment due to the interactions

between these infections. Management requires a multidisciplinary approach that

integrates antiretroviral therapy, antituberculous drugs, antibiotics, and

supportive care for COVID-19. We report the case of a 28-year-old male with HIV

(viral load 30 copies, CD4 count 303), active tuberculosis, and a history of

resolved syphilis, who presented with severe respiratory decompensation and

hypoxemia (SpO2 55%), requiring orotracheal intubation. Initial treatment

included broad-spectrum antibiotics, antiretrovirals, and antituberculous

therapy. Despite the critical illness, the patient demonstrated progressive

clinical improvement, was successfully extubated after a spontaneous breathing

trial, and continued recovery under supplemental oxygen. This case underscores

the clinical complexity of triple coinfection and highlights the potential for

favorable outcomes when management is timely and multidisciplinary.

DOI: 10.3390/life15091435

PMCID: PMC12471700

PMID: 41010377

**70. Antibiotics (Basel). 2025 Aug 30;14(9):875. doi: 10.3390/antibiotics14090875.**

Trends in Antituberculosis Drug Resistance and Associated Factors: A 31-Year

Observational Study at a Tertiary Hospital in Barcelona.

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**Objective:** To analyze trends in resistance to antituberculous drugs over a

31-year period (1991-2022) at a hospital in Barcelona and to identify associated

epidemiological determinants. **Methods:** This study included culture-confirmed

tuberculosis cases diagnosed between 1991 and 2022. Drug susceptibility testing

was conducted with clinical data from hospital records and epidemiological data

from the Barcelona Public Health Agency. The primary outcome was resistance to

first-line drugs. A subset of isolates was tested for second-line drugs. Trends

were compared between the periods 1991-2000 and 2001-2022, aligning with

increased immigration. Factors associated with resistance were examined using

multivariate regression analysis. **Results:** Among the 2448 patients included,

tuberculosis cases peaked in the 1990s and subsequently declined, while drug

resistance increased. Overall, 12.2% of isolates showed resistance to at least

one drug: 8.5% were monoresistant, 2.3% multiresistant, and 1.4% polyresistant.

The 2001-2022 period had a higher resistance rate (OR 1.63; 95%CI 1.28-2.09) but

lower multiresistance (OR 0.40; 95%CI 0.23-0.69). Resistance among new cases

doubled from 6.4% to 12.8%, while rates among previously treated cases remained

stable. The predictors of resistance were foreign-born (OR 1.52; 95%CI

1.21-1.91) and previous tuberculosis treatment (OR 2.88; 95%CI 2.17-3.81). A

total of 90% of isolates remained susceptible to fluoroquinolones and

aminoglycosides. **Conclusions:** Although tuberculosis incidence has declined over

the past three decades, antibiotic resistance has increased, driven by

foreign-born and retreatment cases. Ongoing drug susceptibility testing, access

to second-line therapies, and targeted public health interventions for high-risk

populations are essential to maintain control in low-incidence settings.

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PMCID: PMC12466672

PMID: 41009854

**71. Diagnostics (Basel). 2025 Sep 16;15(18):2343. doi: 10.3390/diagnostics15182343.**

Interferon-Gamma Release Assays Versus Tuberculin Skin Test for Active

Tuberculosis Diagnosis: A Systematic Review and Diagnostic Meta-Analysis.

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**Background:** The world health goal of eliminating tuberculosis (TB) is heavily

hinged on timely and efficient diagnosis and treatment. The interferon-γ release

assays (I.G.R.A.s) can diagnose Mycobacterium tuberculosis infection and offer

an alternative to the centuries-old tuberculin skin test (T.S.T.). Yet there is

disagreement over replacing the T.S.T. with I.G.R.A.s as a standard tool.

**Objective:** We aim to assess the diagnostic ability of I.G.R.A.s compared with

T.S.T. for detecting active TB cases. **Methods:** A systematic review identified

relevant studies from four databases. In the diagnostic meta-analysis conducted

with OpenMeta Analyst software, we calculated the sensitivity (SN) and

specificity (SP) for active TB detection via I.G.R.A. and T.S.T. methods

compared to TB culture. Results included pooled estimates for SN and SP with 95%

confidence intervals (CI), stratified by age, immunity, I.G.R.A. type, and

T.S.T. cut-off. **Results:** Our meta-analysis revealed that TB diagnosis using

T.S.T. showed an SN of 72.4% and SP of 79.3%, while I.G.R.A. demonstrated higher

accuracy with an SN of 78.9% and SP of 85.7%. Subgroup analysis by age indicated

that I.G.R.A. consistently outperformed T.S.T. in both adult and pediatric

populations. Among immunocompromised individuals, T.S.T. had low SN (23%) but

high SP (91.2%), whereas I.G.R.A. had higher SN (65.6%) but lower SP (81.9%).

Immunocompetent subjects showed that T.S.T. had SN of 72% and SP of 87.3%, while

I.G.R.A. had higher SN (82.9%) and SP (89.1%). Evaluation by I.G.R.A. type

revealed that T-SPOT.GIT demonstrated a higher SN but lower SP compared to

QFT-GIT. Assessing T.S.T. cut-offs, SP was highest (88.8%) at ≥15 mm, while SN

peaked (71.6%) at ≥5 mm. **Conclusions:** I.G.R.A. consistently showed higher

diagnostic accuracy than T.S.T. across most studied subgroups, indicating its

potential superiority in active TB diagnosis.

DOI: 10.3390/diagnostics15182343

PMCID: PMC12468246

PMID: 41008717

**72. Diagnostics (Basel). 2025 Sep 14;15(18):2327. doi: 10.3390/diagnostics15182327.**

Diagnostic Modality Influences Tuberculosis Detection in People Living with HIV:

Eight Years of Data from a Thai Referral Center.

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**Background:** Tuberculosis (TB) remains a leading cause of death among people

living with HIV (PLWH), yet diagnostic methods vary in accuracy, accessibility,

and implementation. Understanding how diagnostic modality influences TB

detection is essential to optimizing co-infection management. **Methods:** We

conducted a retrospective analysis of institutional data from Bamrasnaradura

Infectious Diseases Institute (BIDI), Thailand, covering 2016-2023. TB detection

rates were assessed across five diagnostic methods-chest radiography (CXR),

smear microscopy, acid-fast bacilli (AFB) staining, culture, and GeneXpert

MTB/RIF-relative to annual HIV-related visit volumes. **Results:** Among 56,599

HIV-related visits, TB detection rates varied substantially by diagnostic

method. CXR was the most commonly used tool, detecting TB in up to 99 cases out

of 6964 visits (1.42%) in 2016, though declining to 23 cases out of 6947 visits

(0.33%) in 2023. GeneXpert was employed more consistently, yielding between 7

cases out of 7577 visits (0.09%) and 13 cases out of 6593 visits (0.20%)

annually. Smear microscopy and AFB staining declined markedly, falling below

0.22% after 2020. These patterns reflect a gradual transition toward molecular

diagnostics, which offer improved accuracy but remain underutilized in

lower-tier settings. To address these gaps, we incorporated trend analyses

confirming significant temporal shifts and propose a tiered TB screening

framework tailored to resource availability across healthcare levels.

**Conclusions:** TB detection among PLWH is strongly influenced by the diagnostic

method used. Unlike HIV diagnosis-which is definitive and standardized-TB

diagnosis remains fragmented and resource-dependent. Context-sensitive screening

protocols are urgently needed to improve TB case detection and management,

particularly in lower-level HIV care facilities.

DOI: 10.3390/diagnostics15182327

PMCID: PMC12468846

PMID: 41008699

**73. Diagnostics (Basel). 2025 Sep 12;15(18):2314. doi: 10.3390/diagnostics15182314.**

Prevalence of Tuberculosis in Central Asia and Southern Caucasus: A Systematic

Literature Review.

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**Background:** In 2023, tuberculosis (TB) caused 1.25 million deaths globally,

remaining a leading infectious killer. Central Asia and Southern Caucasus face

high TB burdens, particularly Mongolia. This review synthesizes TB prevalence

data and diagnostic capabilities in these regions to support public health

strategies. **Methods:** This systematic review aimed to synthesize current data on

TB prevalence in Central Asia, Southern Caucasus, and Mongolia to support public

health strategies and research priorities. A comprehensive search of PubMed and

Google Scholar was conducted for English-language articles published up to 2023.

Studies were assessed using a modified Newcastle-Ottawa Scale. Nine studies met

the inclusion criteria, covering Kazakhstan, Kyrgyzstan, Uzbekistan, Tajikistan,

Turkmenistan, Mongolia, Georgia, Armenia, and Azerbaijan. **Results:** TB incidence

ranged from 67 per 100,000 in Kazakhstan to 190 per 100,000 in Kyrgyzstan, with

the highest prevalence of 68.5% in Mongolia. TB affected men more frequently

(65.3%), and the key risk factors included HIV (30.5%), comorbidities, and

undernutrition. Diagnostic performance varied significantly (microscopy

sensitivity, 45-65%; GeneXpert MTB/RIF, 89-96% sensitivity and 98% specificity

for rifampicin resistance). Diagnostic turnaround times ranged from hours

(molecular) to weeks (conventional). Only 58% of TB facilities had GeneXpert

technology, with urban-rural disparities in diagnostic access. Drug-resistant TB

imposed a significant economic burden, with treatment costs ranging from USD 106

to USD 3125. **Conclusions:** Strengthening surveillance, improving data collection,

and conducting longitudinal studies are essential for designing effective TB

control strategies in these regions. Significant diagnostic gaps persist across

these regions, especially with regard to drug-resistant strains. Point-of-care

molecular diagnostics, improved algorithms, and expanded laboratory training

show promise. Future research should focus on rapid biomarker-based diagnostics,

field-deployable technologies for settings with limited resources, and AI

integration to enhance diagnostic accuracy and efficiency.

DOI: 10.3390/diagnostics15182314

PMCID: PMC12468312

PMID: 41008686

**74. Biomolecules. 2025 Sep 11;15(9):1305. doi: 10.3390/biom15091305.**

Isoniazid-Derived Hydrazones Featuring Piperazine/Piperidine Rings: Design,

Synthesis, and Investigation of Antitubercular Activity.

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Isoniazid (isonicotinic acid hydrazide, INH) is a key drug used to treat

tuberculosis (TB), which continues to be the world's most lethal infectious

disease. Nevertheless, the efficacy of INH has diminished because of the

emergence of Mycobacterium tuberculosis (Mtb) strains that are resistant to INH.

Our goal in this study was to modify INH to reduce this significant resistance

chemically. We synthesized INH-based hydrazones (IP1-IP13) through the reaction

of INH with in-house obtained benzaldehydes carrying a piperidine or piperazine

ring in refluxing ethanol. Upon confirmation of their proposed structures by

various spectral techniques, IP1-IP13 were evaluated for their antimycobacterial

capacity against Mtb H37Rv strain and INH-resistant clinical isolates with katG

and inhA mutations using the Microplate Alamar Blue Assay (MABA). The compounds

were additionally tested for their cytotoxicity. The obtained data indicated

that the compounds with moderately increased lipophilicity compared to INH

(IP7-IP13) were promising antitubercular drug candidates, exhibiting drug-like

properties and negligible cytotoxicity. Out of these, IP11

(N'-(4-(4-cyclohexylpiperazin-1-yl)benzylidene)isonicotinohydrazide) emerged as

the most promising derivative, demonstrating the lowest MIC values against all

Mtb strains tested. Subsequently, the target molecules were evaluated for their

capacity to inhibit enoyl acyl carrier protein reductase (InhA), the main target

enzyme of INH. Except for IP11 demonstrating 81% InhA inhibition at a

concentration of 50 μM, direct InhA inhibition was shown not to be the primary

mechanism responsible for the antitubercular activity of the compounds. The

binding mechanism of IP11 to InhA was analyzed through molecular docking and

molecular dynamics simulations. Altogether, our research identified a novel

approach to modify INH to address the challenges posed by the rising prevalence

of drug-resistant Mtb strains.

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PMCID: PMC12467433

PMID: 41008612 [Indexed for MEDLINE]

**75. Trop Med Infect Dis. 2025 Aug 30;10(9):248. doi: 10.3390/tropicalmed10090248.**

Alcohol Consumption of Male Tuberculosis Index Cases and Tuberculosis

Transmission Among Social Contacts in Puducherry, India: A Cross-Sectional

Analytical Study.

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We aimed to compare the proportion of tuberculosis infection among social

contacts of male tuberculosis Index case with and without alcohol use in the

Puducherry district. A cross-sectional study using ego-centric approach was

conducted between November 2023 and May 2024. A total of 713 social contacts of

106 male pulmonary tuberculosis index cases were enrolled, stratified by

alcohol-use (AUDIT ≥ 8): 358 contacts from 45 alcohol-using cases and 355 from

61 non-alcohol-use cases. Social contacts were defined based on the frequency

and duration of shared indoor exposure with index cases within the past three

months. Tuberculosis infection was screened with Cy-Tb skin test (≥5 mm

induration) at the third month of index case treatment. Univariate and

multivariable analysis were conducted to identify factors associated with

tuberculosis transmission. Among the 358 social contacts of alcohol-use index

cases, 33.8% (n = 121; 95% CI, 29.1-38.8%) tested positive for tuberculosis

infection, significantly higher than 21.7% (n = 77; 95% CI, 17.7-26.3%) among

355 contacts of non-alcohol-use cases. Regression analysis revealed that

contacts of alcohol-using index cases (aOR = 1.6, p < 0.05), were significantly

associated with tuberculosis infection. Alcohol-use among tuberculosis patients

significantly increases the risk of tuberculosis infection in their social

networks.

DOI: 10.3390/tropicalmed10090248

PMCID: PMC12474472

PMID: 41003558

**76. Trop Med Infect Dis. 2025 Aug 29;10(9):247. doi: 10.3390/tropicalmed10090247.**

Impaired Lung Function and Quality of Life Outcomes in Patients with

Tuberculosis: A Cross-Sectional Study.

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Tuberculosis (TB) continues to be the world's deadliest infectious disease, with

an estimated 10.8 million new cases reported in 2023, of which India alone

accounted for 28% of the global burden. This study aims to evaluate the impact

of tuberculosis on pulmonary function and exercise tolerance, and to examine how

these impairments affect health-related quality of life (HRQoL). In a

cross-sectional design, 96 bacteriologically confirmed TB patients and 96 age-

and sex-matched community controls underwent spirometry, six-minute-walk test (6

MWT), and HRQoL evaluation. DR-TB was detected in 27 patients (28.1%): Isoniazid

monoresistance 59.3%, rifampicin monoresistance 11.1%, and XDR-TB 29.6%.

Dyspnoea (70.8%) and cough (37.5%) were the most commonly reported symptoms

among TB patients. Mean values of FEV1, FVC, and FEV1/FVC were significantly

lower in TB patients compared to controls (62.8%, 65.97%, and 70.08% vs. 82.55%,

80.09%, and 78.08%, respectively; p < 0.001). Recurrent or DR-TB was associated

with reduced spirometric indices and 6 MWT distances (241 m vs. 358 m in

drug-sensitive TB). St. George's respiratory questionnaire (SGRQ) scores

indicated significantly poorer health-related quality of life (HRQoL) in

patients compared to controls across all domains-symptoms (23.7 vs. 10.7),

activity (33.3 vs. 14.2), and impact (20.6 vs. 9.4; p < 0.05). SGRQ scores were

inversely correlated with lung function parameters (r = -0.42 to -0.56). These

findings underscore the persistent health burden TB poses post-therapy,

highlighting the need for routine post-TB functional screening and robust DR-TB

control to achieve End-TB goals.

DOI: 10.3390/tropicalmed10090247

PMCID: PMC12474510

PMID: 41003556

**77. J Fungi (Basel). 2025 Sep 11;11(9):665. doi: 10.3390/jof11090665.**

Virulence of Candida Isolates in Patients with Tuberculosis and Oral/Oesophageal

Candidiasis: Co-Infection Evaluation.

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Tuberculosis (TB) is an infection caused by Mycobacterium tuberculosis complex

(MTBC), which can be exacerbated by fungal infections. This study evaluated the

clinical characteristics and virulence of Candida spp. in patients with

tuberculosis. Antifungal sensitivity, phospholipase and proteinase production,

biofilm formation, phagocytic index, and reactive oxygen (ROS) and nitrogen

(RNS) species were assessed. Candida spp. were isolated from 14 patients, 28.5%

women and 71.4% men, mainly from sputum and tracheal secretions. Five (35.7%)

patients were co-infected with Mycobacterium, Candida, and HIV. Candida albicans

(78.6%) and Candida tropicalis (21.4%) were identified in all 14 patients. All

isolates showed sensitivity to amphotericin B and dose-dependent responses to

fluconazole (16 μg/mL). Phospholipase activity was detected in 35.7% of the

isolates, whereas all isolates showed proteinase activity (100%). A significant

difference in phospholipase activity, phagocytosis, and production of reactive

oxygen species (ROS) and nitrogen species (RNS) was observed when Candida

isolates from patients with TB, living with or without HIV, were compared to

Candida isolates from healthy individuals. All isolates were biofilm producers.

This study highlights the relevance of mycoses diagnosis in patients with TB,

since Candida spp. may be more virulent and contribute to the deterioration of

the clinical condition.

DOI: 10.3390/jof11090665

PMCID: PMC12470509

PMID: 41003211

**78. Biosensors (Basel). 2025 Sep 15;15(9):607. doi: 10.3390/bios15090607.**

Gold Nanoparticle-Enhanced Recombinase Polymerase Amplification for Rapid Visual

Detection of Mycobacterium tuberculosis.

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

resource-limited settings where access to rapid and reliable diagnostics is

limited. Conventional diagnostic methods, such as smear microscopy and culture,

are either time-consuming or lack adequate sensitivity. This study optimized

recombinase polymerase amplification (RPA) using 16 primer combinations

targeting IS6110 highly specific to the Mycobacterium tuberculosis complex

(MTC). A novel naked-eye assay, TB-GoldDx, was developed by integrating RPA

combined with gold nanoparticles (AuNPs), enabling equipment-free diagnostics.

TB-GoldDx demonstrated a detection limit of 0.001 ng of MTB H37Rv DNA (~210

bacilli) per 25 µL reaction. Among 100 bacterial strains, it achieved 95.83%

sensitivity and 100% specificity among 100 bacterial strains, comprising 72 MTB

isolates and 28 nontuberculous bacterial species. In 140 sputum samples, the

assay showed 81.43% sensitivity and 58.57% specificity versus acid-fast bacilli

(AFB) smear microscopy, with sensitivity improving to 95.45% in high-load AFB 3+

specimens. Compared to a commercial line probe assay (LPA), TB-GoldDx exhibited

slightly higher sensitivity (84.78% vs. 82.61%) but lower specificity (54.05%

vs. 78.38%). Delivering rapid, visual results in under an hour, TB-GoldDx offers

a low-cost, easily deployable solution for point-of-care tuberculosis detection,

especially in underserved regions, reinforcing global End TB efforts.

DOI: 10.3390/bios15090607

PMCID: PMC12467982

PMID: 41002347 [Indexed for MEDLINE]

**79. Tuberk Toraks. 2025 Sep;73(3):227-230. doi: 10.5578/tt.2025031095.**

Disseminated tuberculosis despite preventive treatment in patients treated with

tumor necrosis factor inhibitors: A report of two cases.

[Article in English]

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DOI: 10.5578/tt.2025031095

PMID: 41002065

**80. Tuberk Toraks. 2025 Sep;73(3):165-177. doi: 10.5578/tt.2025031113.**

Enhancing tuberculosis diagnosis: A deep learning-based framework for accurate

detection and quantification of TB bacilli in microscopic images.

[Article in English]

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**INTRODUCTION:** Tuberculosis (TB), a highly contagious disease, remains one of the

leading causes of death globally. The proposed computer-assisted TB detection

system enhances diagnostic accuracy and efficiency by integrating deep learning

and segmentation techniques.

**MATERIALS AND METHODS:** It consists of two key subsystems: Automated field-ofview

(FOV) recognition and TB bacilli segmentation. Using a motorized microscopic

stage, the system systematically captures Ziehl-Neelsen-stained sputum smear

images at 100x magnification. A customized Inception V3 model with transfer

learning identifies FOVs containing TB bacilli, reducing variability and manual

effort. Segmentation techniques, including coarse-level thresholding and shape

descriptors like area, perimeter, and eccentricity, refine bacilli detection and

eliminate artifacts.

**RESULT:** This study highlights the significant potential of deep learning and

image processing techniques in advancing medical diagnostics, particularly TB

detection. This framework has the potential to improve clinical outcomes and

support global TB eradication efforts by providing a reliable tool for early TB

diagnosis.

**CONCLUSIONS:** The system achieved a mean receiver operating characteristic score

of 0.9505, a precision of 0.924, a recall of 0.882, and an F1 score of 0.902,

demonstrating its potential to improve TB screening, particularly in

resource-limited settings. By minimizing reliance on skilled technicians and

enhancing diagnostic reliability, this approach offers a scalable solution for

effective TB detection and severity assessment.

DOI: 10.5578/tt.2025031113

PMID: 41002059 [Indexed for MEDLINE]

**81. Res Sq [Preprint]. 2025 Sep 15:rs.3.rs-7466214. doi:**

**10.21203/rs.3.rs-7466214/v1.**

The pH gradient contributes to persistence in Mycobacterium tuberculosis.

Sherman D, Eldesouky H, Adams K, Brache J, Aguila L, Garcia M, Xing E, Li PK.

Tuberculosis (TB) remains difficult to cure due in part to poorly defined

drug-tolerant persister cells formed by Mycobacterium tuberculosis (Mtb), which

survive antibiotic treatment without evidence of genetic resistance. To better

define this phenotype, we screened 2,336 FDA-approved drugs for compounds that

target persistence. Unexpectedly, we identified a strong inducer of drug

tolerance -- the antiparasitic niclosamide (NCA), which is known to disrupt

proton motive force. In contrast to earlier reports that it harbors promising

anti-TB activity, we found that NCA protected Mtb from bactericidal doses of

isoniazid, rifampicin, and other standard TB drugs. Investigating further, we

showed that disruption of the pH gradient and consequent intracellular

acidification is needed to induce tolerance, while disruption of membrane

potential is not, and also that protection is tunable by external pH .

Transcriptomic analysis of these chemically-induced persister (CIP) cells

implicated specific genes in this phenotype, and targeted knockdowns confirmed

roles for three genes in either promoting or mitigating the tolerance state.

These findings highlight that chemical disruption of the pH gradient is a facile

and rapid means to induce drug tolerance, offering a potentially useful tool to

probe persister biology in TB and other infectious diseases.

DOI: 10.21203/rs.3.rs-7466214/v1

PMCID: PMC12458573

PMID: 41001543

**82. medRxiv [Preprint]. 2025 Sep 21:2025.09.19.25336212. doi:**

**10.1101/2025.09.19.25336212.**

Combining blood transcriptomic signatures improves the prediction of progression

to tuberculosis among household contacts in Brazil.

Lundell S, Kaipilyawar V, Johnson WE, Dietze R, Ellner JJ, Ribeiro-Rodrigues R,

Salgame P.

Tuberculosis remains a major health threat, infecting nearly a third of the

world's population. Of those infected, 5-10% progress from latent infection to

active tuberculosis (TB) disease and biomarkers to identify which individuals

will progress are needed to allow targeted prophylactic treatment. Several risk

biomarkers have been developed to predict progression but have not been tested

head-to-head on the same platform. Here, we used the NanoString platform and

compared the performance of 15 published gene signatures in predicting

progression at baseline in a household contact cohort. Expression of gene

signatures was profiled in RNA extracted from whole blood and scored using GSVA

and PLAGE. We found that specificity is enhanced by combining signatures and

report that the performance of a combined signature that includes a newly

derived parsimonious signature through machine learning and a published

signature met WHO TPP levels for a triage test. The combined signature had a

90.9% sensitivity and 88% specificity with a PPV of 0.24 and NPV of 1. This

combined signature has potential clinical utility in identifying high-risk

individuals for targeted prophylaxis to prevent TB morbidity and mortality.

DOI: 10.1101/2025.09.19.25336212

PMCID: PMC12458966

PMID: 41001497

**83. medRxiv [Preprint]. 2025 Sep 19:2025.09.18.25335917. doi:**

**10.1101/2025.09.18.25335917.**

Do no harm - re-evaluating the risks of overtreatment in community-wide

tuberculosis screening.

Houben RMGJ, Veeken LD, Schwalb A, Grint DJ, Wasserman S, van Crevel R, Horton

KC.

**BACKGROUND:** Community-wide screening is a crucial strategy to end tuberculosis

(TB), but a common concern is potential harm from overtreatment following false

positive diagnoses. However, current reference standards determining test

performance have limitations, with implications for prevalence thresholds and

treatment decisions for community-wide screening.

**METHODS:** We estimated coverage of community-wide screening at a prevalence

threshold of 0.5% (current global standard), 0.25%, and 0.1% for adult pulmonary

TB. We considered test performance for Xpert Ultra against different reference

standards (sputum culture, plus clinical evaluation, plus disease progression

within two years). Potential harm was estimated through disability adjusted life

years (DALYs) incurred or averted by treatment. We report net specificity,

positive predictive value (PPV), the ratio of false positives to true positives,

and DALYs averted for (non-)treatment based on different reference standards.

**RESULTS:** A lower threshold would increase screening coverage from the current

42% to 84% (0.25% threshold) and 89% (0.1% threshold) of the global TB burden.

In a population of 100,000 with 0.5% prevalence, specificity was 99.5% for

community screening, but increased to 99.7% using disease progression as

reference standard, with PPV increasing from 45 to 66%. In addition, estimated

harm of withholding appropriate treatment was approximately 1,200 times higher

compared to providing inappropriate treatment, with treatment initiation after a

positive Xpert Ultra increasing overall DALYs averted (median 5,977 versus

3,750).

**DISCUSSION:** The benefit of TB treatment following a positive molecular test in

community-wide screening likely outweighs the harm associated with possible

overtreatment, supporting expanding coverage of simplified community-wide

screening.

**BRIEF SUMMARY:** A concern with community-wide tuberculosis screening is the

potential for overtreatment. We evaluated diagnostic reference standards and

relative health costs of (non-)treatment, finding that after a positive

molecular test, the benefit of initiating tuberculosis treatment likely

outweighs its harm.

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PMCID: PMC12458509

PMID: 41001492

**84. Cureus. 2025 Aug 25;17(8):e90979. doi: 10.7759/cureus.90979. eCollection 2025**

**Aug.**

Asymptomatic Miliary Tuberculosis in a Patient With Polymyalgia Rheumatica.

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Miliary tuberculosis (TB), a severe form of TB caused by lymphohematogenous

dissemination from a Mycobacterium tuberculosis focus, usually presents with

systemic symptoms including fever and malaise. Here, we report the case of an

87-year-old woman treated with low-dose prednisolone and methotrexate for

polymyalgia rheumatica, incidentally diagnosed with small miliary nodules in her

lungs on chest computed tomography without any symptoms. Moreover, the patient

reported being full of energy. The acid-fast bacterial culture and polymerase

chain reaction test from various sites, including the transbronchial lung biopsy

(TBLB) and bronchoalveolar lavage fluid, were negative; however, the histology

of the TBLB specimen revealed epithelioid granuloma without acid-fast bacteria.

One and a half months later, she was admitted to our hospital with fever and

somnolence. The cerebrospinal fluid culture test was positive for Mycobacterium

tuberculosis, and the patient was diagnosed with miliary TB complicated by

tuberculous meningitis. This report suggests that although systemic symptoms

usually accompany miliary TB, patients can be asymptomatic, and careful

follow-up is important when suspected.

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PMCID: PMC12459996

PMID: 41001330

**85. Cureus. 2025 Aug 25;17(8):e90958. doi: 10.7759/cureus.90958. eCollection 2025**

**Aug.**

Evaluation of the GenoType Mycobacterium CM/AS Assay for Species Identification

of Mycobacteria.

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**BACKGROUND:** The early differentiation of Mycobacterium tuberculosis (MTB) from

nontuberculous mycobacteria (NTM) and the identification of species among NTM

are crucial for the immediate implementation of the appropriate therapy because

susceptibility to drugs varies widely among different species. Identification to

the species level by classical biochemical methods is time-consuming, requires a

large battery of tests to be run, and results are obtained in four to six weeks

of obtaining the isolate. The introduction of molecular biological methods has

greatly improved the speed and accuracy of the process. Recently, DNA strip

assays for the identification of Mycobacterium to the species level have been

developed. These assays are based on reverse hybridization of a polymerase chain

reaction (PCR) product to a nitrocellulose strip with immobilized probes for

different mycobacterial species. One such assay is GenoType Mycobacterium CM/AS

assay (Hain Lifescience GmbH, Nehren, Germany).

**AIM:** To evaluate the diagnostic accuracy of the GenoType Mycobacterium CM/AS

assay for the species identification of mycobacteria in the culture isolates in

comparison with conventional phenotypic and biochemical methods.

**MATERIAL AND METHODS:** A total of 160 mycobacterial isolates on solid

Lowenstein-Jensen media or liquid MGIT 960 were subjected to species

identification by GenoType Mycobacterium CM/AS assay and biochemical methods.

**RESULTS:** Sensitivity, specificity, positive predictive value (PPV) and negative

predictive Value (NPV) were found to be 100% for all the mycobacterialisolates

except M. terrae, where sensitivity and NPV were 0% but specificity was 100% and

PPV was 98.13%. Hence the overall sensitivity of the GenoType Mycobacterium

CM/AS assay was 98.13% and the specificity was 100%.

**CONCLUSION:** The GenoType assay is a simple, rapid and reliable method for the

identification of clinically important mycobacteria, and it is well suited for

use in a routine laboratory.

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DOI: 10.7759/cureus.90958

PMCID: PMC12459858

PMID: 41001312

**86. bioRxiv [Preprint]. 2025 Sep 15:2025.09.15.676370. doi:**

**10.1101/2025.09.15.676370.**

Genes required for Mycobacterium tuberculosis to survive the transition from

aerosol to pulmonary alveolar lining fluid and early infection in a model of

transmission.

Singh PR, Mishra S, Jinich A, Jiang X, Tsang F, DeJesus M, Rhee KY, Kaner RJ,

Leopold PL, Crystal RG, Nathan C.

Mycobacterium tuberculosis (Mtb) must withstand physical and chemical stresses

during airborne transmission, including during the desiccation of aerosols small

enough to reach pulmonary alveoli in a new host. There, Mtb encounters an

antimicrobial pulmonary alveolar lining fluid (ALF) before it is engulfed by

macrophages. To study the genes involved in Mtb's ability to survive the

transition from desiccated droplet to pulmonary alveolus in an in vitro model,

we formulated a model alveolar lining fluid (MALF) that mimics the composition

of ALF as inferred from human bronchoalveolar lavage fluid (BALF). We compared

the transcriptome of log-phase Mtb in MALF to the transcriptome of Mtb in BALF

as BALF from the lungs of healthy adults was reconstituted to compensate for the

dilution of ALF by lavage (rcBALF). Mtb from log-phase culture in a standard

laboratory medium survived quantitatively in MALF and rcBALF for at least 24

hours. In contrast, Mtb that had passed through earlier stages of transmission

began to succumb after 3 hours in MALF, past the time when particles have been

observed to be phagocytized by alveolar macrophages. Screening of a genome-wide

CRISPRi library of Mtb identified 35 genes as uniquely required by Mtb to

survive the transition from desiccated microdroplet into rehydration in MALF.

Thirty-one of these genes are non-essential under conventional laboratory

conditions and seven have unknown functions. Thirteen of the 35 genes were

additionally required for Mtb to survive in macrophage-like cells cultured at

the air-liquid interface with pulmonary epithelial cells. This study nominates

additional members of the transmission survival genome of Mtb, illustrates that

different genes may contribute to the survival of Mtb at different stages of

transmission, and suggests that modeled transmission can shed light on the

functions of Mtb genes whose contributions have been unknown.

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PMCID: PMC12458190

PMID: 41000987

**87. Int J Med Microbiol. 2025 Sep 16;321:151674. doi: 10.1016/j.ijmm.2025.151674.**

**Online ahead of print.**

Genomic insights into pyrazinamide and fluoroquinolone resistance in

multidrug-resistant tuberculosis in Khyber Pakhtunkhwa, Pakistan.

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**BACKGROUND:** Tuberculosis (TB), caused by bacteria of the Mycobacterium

tuberculosis complex (MTBC), remains a global health challenge, exacerbated by

multidrug-resistant (MDR) and extensively drug-resistant (XDR) strains.

**OBJECTIVES:** This study employs whole-genome sequencing (WGS) to characterise

genetic mutations associated with pyrazinamide (PZA) and fluoroquinolone (FQ)

resistance in MDR-TB isolates from KPK.

**METHODOLOGY:** MDR and pre-XDR TB samples were collected and processed at the

Provincial Tuberculosis Reference Laboratory under Biosafety Level III

conditions. Samples underwent microscopy, GeneXpert MTB/RIF assay, culture, and

drug susceptibility testing. DNA was extracted from positive cultures and

subjected to WGS. Bioinformatics tools were used to analyse sequencing data,

identify resistance-associated mutations, and assess genetic diversity among

isolates.

**RESULTS:** Out of the 78 MTBC isolates analysed, 67 (85.9 %) were identified as

MDR-TB, with 48 categorized as pre-XDR, while 11 were drug-susceptible. The

isolates predominantly came from young patients (mean age: 29.5 years, SD

±12.64), with a higher proportion of female patients (61.53 %). Mutations in the

pncA gene, associated with PZA resistance, were identified in 51 isolates.

Resistance to fluoroquinolones was linked to mutations in the gyrA and gyrB

genes in 48 isolates. WGS confirmed PZA resistance in 51 isolates, 39 (76.47 %)

of which also exhibited FQ resistance.

**CONCLUSION:** Phylogenetic analysis revealed that Lineage 3 (L3) was predominant

(58.97 %), followed by L4, L2, and L1 strains. The clustering of drug-resistant

strains within L3 suggests ongoing localized transmission. These findings

underscore the urgent need for targeted interventions, including enhanced

molecular surveillance and tailored treatment strategies, to combat MDR-TB in

KPK.

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**eCollection 2025.**

Increased circulating Th17 cells and altered CD4 T cell maturation and

differentiation in active tuberculosis with type 2 diabetes: a pilot study.

Ogongo P(1), Martinez-Lopez YE(2), Tran A(1), Lindestam Arlehamn CS(3)(4), Sette

A(3)(5), Dominguez-Trejo IA(2), Garza L(6), Cruz-Gonzalez AM(7), Loera-Salazar

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**INTRODUCTION:** Type 2 diabetes (T2D) is a major risk factor for developing

tuberculosis (TB). However, understanding the role of defective T cell responses

in T2D and TB has been difficult, largely due to inconsistencies across studies.

These discrepancies often stem from T cell subset classification primarily

relying on cytokine expression profiles, which may not fully capture the

complexity of T cell maturation, differentiation, and function in TB patients

with T2D.

**OBJECTIVE AND METHODS:** In this pilot study, we sought to identify alterations in

phenotypic and ex vivo responses of CD4 T cells to Mycobacterium tuberculosis

(Mtb) antigens in people with TB with or without T2D. We evaluated peripheral

blood mononuclear cells (PBMC) by high-parameter spectral flow cytometry and

assessed T cell differentiation using a cytokine agnostic approach based on

validated cell surface markers expression.

**RESULTS:** We found major alterations in specific CD4 T cell properties by T2D

status, despite no difference in the frequency of bulk CD4 or CD8 T cells.

TB-T2D patients (vs TB alone) had fewer circulating naïve CD4 T cells, higher

frequency CD4 T cell responses to Mtb antigens, and increased circulating Th1

and three subsets of Th17 cells. Multivariable analysis confirmed that T2D was

independently associated with these alterations in maturation state,

differentiation phenotype, and the activation of Mtb antigen-responsive CD4 T

**cells.**

**CONCLUSION:** This pilot study reveals CD4 T cell alterations in T2D that likely

worsen TB outcomes. A reduced naïve CD4 T cell pool, increased central memory

and antigen-activated CD4 T cells, and elevated Th1 and three Th17 cell subsets

suggest a pro-inflammatory environment favoring responses that may promote,

rather than control TB. These findings highlight immune dysfunctions that could

be targeted by host-directed therapies to prevent TB and improve outcomes in T2D

patients.

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Dominguez-Trejo, Garza, Cruz-Gonzalez, Loera-Salazar, Rodríguez-Herrera,

Aguillón-Durán, Garcia-Oropesa, Ernst and Restrepo.

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**eCollection 2025.**

In vitro assessment of Brazilian red propolis against mycobacteria:

antibacterial potency, synergy, inhibition of biofilm formation, and

intramacrophage effects.

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EAV(2), Martins CHG(1).

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**BACKGROUND:** Tuberculosis persists as a major global health threat and remains

the leading cause of death from infectious disease. Efforts to control the

disease are increasingly hampered by the emergence of drug-resistant

Mycobacterium tuberculosis strains. At the same time, non-tuberculous

mycobacteria are an expanding clinical concern, with few effective therapies

available. Brazilian red propolis (BRP) has shown broad-spectrum antibacterial

activity, yet its efficacy against mycobacteria is poorly characterized.

**METHODS:** This study evaluated the in vitro antimycobacterial potential of a

crude hydroalcoholic extract of BRP (CHEBRP). Minimum inhibitory concentrations

were determined against drug-susceptible and rifampicin-resistant M.

tuberculosis strains (M. tuberculosis H37Rv-ATCC 27294, clinical isolate, and

rifampicin-resistant clinical isolate; M. kansasii ATCC 12478 and clinical

isolate; M. avium ATCC 25291 and clinical isolate). Fractional inhibitory

concentration indices were calculated to assess interactions with isoniazid and

rifampicin. Biofilm inhibition was measured, and cytotoxicity was assessed in

RAW 264.7 macrophages. Intracellular activity was quantified using infected

macrophage cultures.

**RESULTS:** CHEBRP exhibited potent activity against most M. tuberculosis strains

tested, including rifampicin-resistant strains. Its combination with isoniazid

or rifampicin yielded an indifferent interaction, supporting the feasibility of

co-administration. CHEBRP significantly inhibited biofilm formation, showed

minimal cytotoxicity toward macrophages, and achieved substantial clearance of

intracellular bacilli.

**CONCLUSION:** These in vitro findings highlight CHEBRP as a promising candidate

for adjunctive antimycobacterial therapy. Further studies should investigate its

in vivo efficacy, pharmacokinetics, and activity against a broader range of

mycobacterial species.

Copyright © 2025 Martins, Teixeira, de Souza, Alhatlani, Abdallah, Ambrosio,

Silva, Bastos, Tanimoto, Barbosa, Ferro and Martins.

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**90. Vet Immunol Immunopathol. 2025 Sep 17;289:111001. doi:**

**10.1016/j.vetimm.2025.111001. Online ahead of print.**

A DIVA-compatible Mycobacterium bovis triple mutant vaccine confers protection

against bovine tuberculosis in mouse model.

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Bovine tuberculosis (bTB) is a pulmonary infectious disease caused by

Mycobacterium bovis, affecting cattle and a wide range of mammals, including

humans. Despite its significant impact on global livestock production, no

commercial vaccine is currently available, partly due to potential interference

with standard diagnostic tests. In this study, we evaluated the protective

efficacy of a triple M. bovis mutant lacking the immunodominant antigens ESAT-6

and CFP-10, as well as the virulence factor Ag85A. This mutant is compatible

with DIVA (Differentiation of Infected from Vaccinated Animals) diagnostics

based on ESAT-6 and CFP-10 detection. The triple mutant was assayed both alone

and in a heterologous prime-boost regimen using recombinant Ag85A conjugated to

chitosan nanocapsules. Protection was assessed by quantifying M. bovis

colony-forming units (CFUs) in the lungs and spleen following challenge. Organ

homogenates were cultured on solid media, and CFUs were enumerated at five and

ten weeks post-plating. At five weeks, all vaccinated groups demonstrated

comparable protection in the lungs. In the spleen, both the triple mutant and

BCG groups showed reduced CFU counts compared to the unvaccinated group. By ten

weeks, lung protection was most pronounced in the prime-boost and BCG groups,

whereas spleen protection was restricted to the prime-boost group. At this

stage, persistence of the triple mutant was detected in both lungs and spleen,

highlighting the need for further evaluation of its residual virulence.

Post-challenge immune responses were assessed by measuring CD4 +KLRG1-CXCL3 + T

cells, a subset previously associated with protective immunity against

tuberculosis, among other T cell populations evaluated. Vaccinated mice

exhibited a significant expansion of this population compared to unvaccinated

controls. Notably, higher frequencies of these cells correlated with reduced

pulmonary bacterial burden, reinforcing their potential as a biomarker of

protective immunity.

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**ahead of print.**

Diagnostic accuracy of low-complexity, manual nucleic acid amplification tests

for the detection of pulmonary and extrapulmonary tuberculosis in adults and

adolescents: a systematic review and meta-analysis∗.

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**BACKGROUND:** Low-complexity, manual nucleic acid amplification tests, such as

loop-mediated isothermal amplification for tuberculosis (TB-LAMP), are among the

molecular WHO-recommended rapid diagnostics and can provide results within a few

hours, even in resource-limited settings. We aimed to synthesise evidence on the

accuracy of these tests for the detection of pulmonary and extrapulmonary

tuberculosis, to inform the 2024 update of the WHO consolidated guidelines on

tuberculosis.

**METHODS:** For this systematic review and meta-analysis, we searched the Cochrane

Central Register of Controlled Trials, MEDLINE, Embase, the Science Citation

Index and BIOSIS previews, WHO Global Index Medicus, and Scopus databases, for

articles published from Jan 1, 1946, to Oct 2, 2023, using specific search terms

such as "Tuberculosis", "mycobacterium tuberculosis", "pulmonary tuberculosis",

"extrapulmonary tuberculosis", "Loopamp", "diagnostic test", "smear microscopy",

and "TB-LAMP". We also examined the reference lists of the included articles to

identify potentially eligible studies that were not found in the electronic

searches. Additionally, we searched ClinicalTrials.gov and the WHO Clinical

Trials Registry Platform for ongoing and unpublished studies. We also examined

studies and data received through a WHO public call, made between Nov 30, 2023,

and Feb 15, 2024, for eligibility. We included studies that evaluated

design-locked, marketed technologies belonging to the class of low-complexity,

manual nucleic acid amplification tests (ie, TB-LAMP) against microbiological or

composite reference standards, in adults and adolescents (aged ≥10 years) with

presumptive pulmonary or extrapulmonary tuberculosis. We excluded studies with

case-control designs and those that used in-house methods, screening studies

aimed at identifying individuals with active tuberculosis in community settings,

and drug-resistance surveys. We extracted data using a standardised form and

assessed risk of bias and applicability using the revised Quality Assessment of

Diagnostic Accuracy Studies tool. We contacted study authors for further

information and data as required. We conducted meta-analyses using bivariate

random-effects models to estimate summary sensitivities and specificities for

detecting pulmonary and extrapulmonary tuberculosis, and assessed the certainty

of evidence using the GRADE approach. This study is registered with PROSPERO,

CRD42023471548.

**FINDINGS:** Our searches identified 2806 records from databases and seven records

from other sources. Of these, we screened the full text of 151 articles and

ultimately included 29 studies in our systematic review: 27 on pulmonary

tuberculosis and three on extrapulmonary tuberculosis (one study evaluated

both). The studies generally had low risk of bias and applicability concern.

From 26 studies involving 18 297 participants, the summary sensitivity for the

detection of pulmonary tuberculosis from respiratory specimens was 84·1% (95% CI

78·3-88·6) and the summary specificity was 96·1% (95% CI 94·2-97·4), both with high certainty of evidence. Three studies, involving 95 participants, assessed the accuracy of TB-LAMP for detecting lymph node tuberculosis using lymph node tissue from biopsy. The summary sensitivity was 94·3% (79·8-98·6) and the

summary specificity was 90·0% (79·5-95·4), both with low certainty of evidence.

**INTERPRETATION:** TB-LAMP has satisfactory performance for detecting pulmonary

tuberculosis in adolescents and adults and is a potential alternative to

molecular tests that require more advanced infrastructure. However, the

inability to detect rifampicin resistance is an important limitation of TB-LAMP.

Future research should focus on well powered studies to establish the diagnostic

accuracy of TB-LAMP for extrapulmonary tuberculosis sites.

FUNDING: WHO.

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**92. Proteomes. 2025 Sep 12;13(3):43. doi: 10.3390/proteomes13030043.**

Proteomic Analysis of Sputum from Patients with Active Tuberculosis.

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**BACKGROUND:** Patients with pulmonary tuberculosis (TB) typically produce sputa,

which are used to identify the pathogen. Sputum also contains host proteins that

may aid in diagnosis. We hypothesized that sputa from TB patients will have

unique proteomes when compared to other lung diseases.

**METHODS:** Sputa were collected from 219 patients with suspected TB.

Neutrophil-derived protein calprotectin (CP), which was used as a marker for

lung damage, was quantified and compared between TB and non-TB groups. Three

sputa with high or low CP from each group were selected and analyzed using

label-free proteomics.

**RESULTS:** There was no difference in CP amounts between TB and non-TB groups.

However, TB samples had other differentially abundant neutrophil-associated

proteins. Compared to low CP, samples with high CP had much smaller number of

proteins that could differentiate between TB and non-TB groups. Only two

proteins, MUC5AC and MMP8, were more abundant in TB samples, regardless of CP

levels.

**CONCLUSIONS:** Our findings suggest that TB sputa may have unique proteomes that

depend on CP levels, which should be further validated due to the small sample

size. Therefore, controlled and more advanced TB may need a different set of

biomarkers to reliably distinguish TB from other lung diseases.

DOI: 10.3390/proteomes13030043

PMCID: PMC12452556

PMID: 40981203

**93. Cureus. 2025 Sep 16;17(9):e92421. doi: 10.7759/cureus.92421. eCollection 2025**

**Sep.**

A Fatal Case of Anti-PL-7 Antibody-Associated Rapidly Progressive Interstitial

Lung Disease Complicated by Tuberculosis: A Case Report.

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The anti-PL-7 antibody is an anti-aminoacyl-tRNA synthetase antibody. Patients

who test positive for anti-PL-7 antibodies present with various clinical

symptoms, including myositis, polyarthritis, and interstitial lung disease

(ILD). The anti-PL-7 antibody also causes rapidly progressive ILD (RP-ILD),

which may be fatal. In this report, we present the case of a 92-year-old woman

with anti-PL-7 antibody-positive RP-ILD, complicated by Mycobacterium

tuberculosis infection. Treatment for anti-PL-7 antibody-positive RP-ILD

typically requires combination therapy with corticosteroids and

immunosuppressive agents; however, we were unable to escalate immunosuppression

due to concomitant M. tuberculosis infection, and the patient died due to

respiratory failure. To our knowledge, this is the first report to present the

progression of chest computed tomography findings and clinical course of

anti-PL-7 antibody-positive RP-ILD complicated by pulmonary tuberculosis.

Anti-PL-7 antibody-positive RP-ILD complicated by pulmonary tuberculosis can be

fatal. Therefore, clinicians should closely monitor for pulmonary tuberculosis

in anti-PL-7 antibody-positive ILD and provide preventive treatment when

appropriate.

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**94. Open Forum Infect Dis. 2025 Sep 8;12(9):ofaf563. doi: 10.1093/ofid/ofaf563.**

**eCollection 2025 Sep.**

Costs of 4 Months of Rifampin Versus 2 Months of Double-dose Rifampin for

Tuberculosis Infection: Post-Hoc Analysis of a Phase 2b Randomized Trial.

Romanowski K(1)(2), Pham Ngoc Y(3), Barss L(4), Jabbour E(5), Johnston JC(6),

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University, Montreal, Quebec, Canada.

**BACKGROUND:** Cost is an important consideration when implementing tuberculosis

preventive treatment regimens (TPT). We used data from a phase 2b randomized

trial of TPT to estimate overall cost and key drivers of costs for two TPT

regimens.

**METHODS:** We did a post-hoc analysis of 915 participants aged ≥10 years who were

randomized 1:1 to 2 rifampin-based regimens: a four-month daily regimen at

10 mg/kg (4R10) and a 2-month daily regimen at 20 mg/kg (2R20; 461

participants). We collected country-specific costs for medications, evaluations,

and medical follow-ups from the three participating countries (Canada,

Indonesia, and Viet Nam), and converted all costs to 2024 Canadian dollars. We

report the overall costs of each regimen and cost drivers.

**RESULTS:** Overall, 454 participants received 4R10 and 461 participants received

2R20. We found no difference in the cost of 2R20 versus 4R10, with a cost ratio

of 0.93 (95% CI: .79-1.07); this was consistent in analyses limited to only

those who completed treatment and stratified by country. Costs for medications

and the baseline visit accounted for 68%, 49%, and 55% of all costs in Canada,

Indonesia, and Viet Nam, respectively. Corresponding costs of routine follow-up

visits accounted for approximately 26%, 45%, and 42% of all costs. In all

countries, a minority of costs (<10%) were due to additional visits or

evaluations not specified in the protocol.

**CONCLUSIONS:** Most costs associated with TPT are due to medications and the

baseline treatment initiation visit. TPT regimens requiring fewer follow-up

visits may reduce overall cost, but the magnitude of this reduction varies by

country.

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**95. SAGE Open Med. 2025 Sep 17;13:20503121251376150. doi: 10.1177/20503121251376150. eCollection 2025.**

The overlapping coinfection of hepatitis B virus and anti-hepatitis C virus

antibody in tuberculosis patients: Unraveling co-infection patterns and clinical

implications.

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**AIMS:** Viral hepatitis and tuberculosis are major public health concerns with

shared risk factors, especially in marginalized communities. Despite this,

routine hepatitis B and C viruses screening in tuberculosis patients is

uncommon. This study, conducted in Golestan Province, where tuberculosis and

hepatitis B virus have high incidence rates, aimed to assess the rates and

prevalence of hepatitis B and anti-hepatitis C viruses testing among active

tuberculosis patients.

**MATERIALS AND METHODS:** Our cross-sectional study was conducted between March

2018 and March 2023 and included patient records of 2283 tuberculosis cases

registered in the database of Golestan University of Medical Sciences. Hepatitis

B and anti-hepatitis C viruses were tested among patients with confirmed

tuberculosis. Clinical and demographic data were collected by taking patient

records and performing structured interviews. Exclusions were limited to

patients with a confirmed tuberculosis diagnosis. Patients who did not consent

to participate and had incomplete information were excluded from the study.

**RESULTS:** Among 2280 tuberculosis patients, 50.1% were male, with a mean age of

46.22 years. Hepatitis B virus surface antigen was detected in 10.57%, and 2.32%

tested positive for anti-hepatitis C virus antibodies. Men were more frequently

tested for anti-hepatitis C virus positivity than women (62.15% versus 37.85%,

p > 0.3). Most co-infected patients resided in rural areas, with pulmonary

tuberculosis being the predominant manifestation. Co-infection rates among

chronic hepatitis B virus patients varied by family structure: 6.7% in

three-generation families, 15% in two-generation families, and 15% in

intrafamilial cases. Additionally, 20% of mother-child pairs and 7.5% of

intrafamilial hepatitis B virus patients tested positive for anti-hepatitis C

virus. Liver function test abnormalities were more common in hepatitis B virus

and tuberculosis patients, especially in hepatitis B/anti-hepatitis C viruses

positive tuberculosis cases (p = 0.05). Hepatitis B virus DNA levels were higher

in CHB/tuberculosis patients compared to CHB-only patients (p = 0.02).

**CONCLUSIONS:** Tuberculosis patients were more likely to test positive for

hepatitis B and anti-hepatitis C viruses than the general population. These

results emphasize the need for regular screening and coordinated care for

co-infected patients.

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**2025 Dec.**

Protocol- Comprehensive Care Package to reduce deaths among adult persons

diagnosed with Tuberculosis in Kerala, India (CCp-K)-An implementation project.

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Melfha J(5), Vijayalekshmi AP(1), Sukumaran V(1), Anaswara N(1), Sukumaran S(1),

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This implementation project aims to reduce TB mortality by at least 25% through

early triaging and integrated management of co-morbidities in Kerala, India. The

package will be implemented across Kerala's public health facilities, targeting

all adult TB patients for systematic triaging for severe illness, uncontrolled

diabetes mellitus, alcohol dependence, and tobacco dependence. Triage-positive

individuals will be referred for comprehensive assessment and inpatient care to

nodal treatment centres. This research will follow a mixed-methods approach with

quantitative components assessing feasibility, burden, and programmatic

outcomes, and qualitative interviews exploring facilitators and barriers.

Triaging will be integrated into routine workflows with healthcare worker

training and system monitoring using customized indicators. If found feasible

and effective in improving programmatic outcomes such as early triaging and

inpatient referral, this model offers potential for scale-up across India to

reduce preventable TB deaths through differentiated care and targeted

comorbidity management. • Implements a comprehensive care package to reduce TB

deaths through early triaging and comorbidity management • Leverages existing

public health infrastructure to deliver enhanced TB care within routine

programme settings.

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**97. Front Pediatr. 2025 Sep 5;13:1559240. doi: 10.3389/fped.2025.1559240.**

**eCollection 2025.**

Case Report: Use of extracorporeal support to treat a fulminant Mycobacterium

bovis infection and complex broncho-oesophageal fistula in a child.

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K(3), Snowden C(3), Beeman A(4), Shetty P(4), Muthialu N(4).

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Tuberculosis (TB), caused by Mycobacterium tuberculosis remains a significant

public health issue. Human TB caused by Mycobacterium bovis (M. bovis) is rare

accounting for less than 1% of TB cases in UK annually. Tuberculosis secondary

to immunomodulating agents is well described. We present a case of airway and

pulmonary TB caused by M. bovis, likely due to zoonotic transmission, in an

immunocompromised child due to medical management of Crohn's disease. Management

required extracorporeal membrane oxygenation for complex surgical interventions

on airway and oesophagus.

© 2025 Hussein, Paget, Grandjean, Bamford, Pandey, Fidler, Snowden, Beeman,

Shetty and Muthialu.

DOI: 10.3389/fped.2025.1559240

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PMID: 40980132

**98. Front Cell Infect Microbiol. 2025 Sep 4;15:1638577. doi:**

**10.3389/fcimb.2025.1638577. eCollection 2025.**

Population structure and emergence of resistance to new and repurposed drugs in

XDR-TB: insights from a 10-year genomic study in the Western Cape, South Africa

review.

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Town, South Africa.

**BACKGROUND:** Extensively drug-resistant tuberculosis (XDR-TB) is a global health

threat, being expensive and difficult to treat, with high mortality rates. The

Western Cape Province (WCP), South Africa, has a particularly high burden of

XDR-TB (>800 cases in the past ten years). Drug resistance genotypes and

transmission present substantial regional variability. Thus, a better

understanding of genetic diversity, clustering and the factors related to

transmission can aid in prioritising resources to effectively target high-risk

populations and regions that are disproportionately affected. We describe

genetic diversity, drug resistance profiles and identify potential factors

associated with the spread of XDR-TB strains collected in the WCP.

**METHODS:** We included 729 XDR-TB samples (one per patient), identified through

routine diagnosis spanning 2010 to 2019, from six healthcare districts (HCDs) in

the WCP. Genomic DNA from cultured isolates was sequenced using the Illumina

platform. Sequences were analysed for strain type, drug resistance mutations,

and genomic clustering using the TBProfiler and MTBseq pipelines. We conducted

logistic regression analysis to identify potential factors associated with

genomic traits related to the spread of XDR-TB strains.

**RESULTS:** Of the 729 XDR-TB strains, sublineage 2.2.2 (Atypical Beijing: n=378,

58.79%) strains were predominant, followed by Sublineage 2.2.1 (Typical Beijing:

n=260, 40.43%). Atypical Beijing strains were more likely to cluster than

Typical Beijing strains. Most of the clusters were small, with a few large and

very large clusters, and the strains within very large clusters (primarily

Atypical Beijing) were more likely to be found within Cape Town Metropole, Cape

Winelands and Garden Route HCDs. Certain Atypical Beijing strains were found

resistant to new and repurposed drugs recently introduced in the WHO treatment

guidelines and clustered, indicating potential transmission.

**CONCLUSIONS:** Near-untreatable Atypical Beijing strains are prevalent in the WCP.

Hence, hotspot areas for clustering in Cape Town Metropole, Cape Winelands and

Garden Route HCDs should be prioritised for targeted intervention to prevent

ongoing XDR-TB transmission.

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Klopper, Warren and Streicher.

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**99. Infect Drug Resist. 2025 Sep 15;18:4901-4915. doi: 10.2147/IDR.S542287.**

**eCollection 2025.**

Genetic Analysis of Molecular Mechanisms of Drug Resistance in Mycobacterium

tuberculosis Against Four Major First-Line Anti-Tuberculosis Drugs (Isoniazid,

Rifampin, Ethambutol, and Pyrazinamide).

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Tuberculosis (TB) is a highly contagious and devastating disease that claims

millions of lives annually. According to the World Health Organization (WHO),

approximately 10.8 million people worldwide will be affected by TB in 2023,

highlighting that TB remains the deadliest infectious disease globally. It is

the second leading cause of death due to infectious disease. Additionally, the

emergence of drug-resistant strains has created a significant challenge for the

treatment of this disease. Approximately 25% of TB-related deaths are attributed

to antimicrobial drug resistance. Various mechanisms contribute to the

development of drug resistance in Mycobacterium tuberculosis; however, this

resistance is primarily due to mutations in the target genes of antibiotics,

which reduce the efficacy of anti-TB drugs. This study aimed to provide

up-to-date and valuable information on the genetic mechanisms of M. tuberculosis

resistance to major first-line anti-TB drugs. Understanding these mechanisms can

open new avenues for researchers to treat TB and to overcome drug resistance.

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**eCollection 2025 Sep.**

Isolated pancreatic tail and splenic hilum tuberculosis: a rare case report.

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Abdominal tuberculosis (TB) is a rare extrapulmonary manifestation, with

pancreatic and splenic involvement being extremely uncommon and often

misdiagnosed as malignancy. We present the case of a 22-year-old female with

chronic epigastric pain, weight loss, and fever. Imaging revealed a necrotic

lymph node mass near the pancreatic tail and splenic hilum with splenic

infarction. Fine-needle aspiration cytology confirmed TB, and the patient

responded well to anti-tubercular therapy, avoiding surgical intervention. This

case underscores the importance of considering TB in the differential diagnosis

of upper abdominal masses in endemic regions to prevent unnecessary surgeries.

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Ltd.

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**101. Cureus. 2025 Aug 20;17(8):e90615. doi: 10.7759/cureus.90615. eCollection 2025 Aug.**

From Blinding Vitreous Hemorrhage to 20/20: Multimodal Management of Presumed

Tubercular Retinal Vasculitis in a Tuberculosis-Endemic Setting.

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of Indonesia, Jakarta, IDN.

Tubercular retinal vasculitis (TRV) is an ocular manifestation of Mycobacterium

tuberculosis that can lead to vision-threatening complications such as recurrent

vitreous hemorrhage and cystoid macular edema (CME). Even after completing a

full course of anti-tubercular therapy (ATT), persistent intraocular

inflammation may drive delayed recurrences of CME, highlighting the need for

vigilant, escalation-based management. We report a case of a 31-year-old

Indonesian woman who presented with sudden-onset hand motion vision in her left

eye. Fundus examination was obscured by dense vitreous hemorrhage, and B-scan

ultrasonography confirmed an attached retina. Diagnostic workup revealed a

positive interferon-γ release assay and apical infiltrates on chest radiography,

with no alternative etiology, supporting a diagnosis of presumed TRV. The

patient was treated with a standard nine-month course of ATT and tapering oral

corticosteroids. Due to progressive retinal ischemia, pan-retinal

photocoagulation was performed. Recurrent vitreous hemorrhages and persistent

CME necessitated a posterior sub-Tenon triamcinolone injection and 23-gauge pars

plana vitrectomy with endolaser at month 9. Fifteen months postoperatively,

best-corrected visual acuity had improved to 20/20, with complete CME

resolution. The purpose of this case report is to describe the management of TRV

through a progressive escalation of therapy and to outline practical treatment

considerations for clinicians working in tuberculosis (TB)-endemic regions. This

case also illustrates that early ATT alone may be insufficient to prevent

structural complications in TRV. A stepwise, multimodal approach combining

systemic therapy, laser photocoagulation, periocular corticosteroids, and timely

vitrectomy can restore excellent vision and reduce the risk of recurrent CME.

Clinicians managing patients in TB-endemic areas should maintain close optical

coherence tomography (OCT)-guided monitoring of CME and be prepared to escalate

treatment promptly to prevent irreversible visual loss.

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**102. Cureus. 2025 Aug 19;17(8):e90491. doi: 10.7759/cureus.90491. eCollection 2025 Aug.**

Clinical Presentation, Diagnosis, and Management of Abdominal Tuberculosis in

Pediatric Population: A Prospective Descriptive Study From a Tertiary Care

Centre in North India.

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Aims Abdominal tuberculosis (TB) continues to be a common and challenging

abdominal disease in children, with a nonspecific clinical presentation and poor

outcomes in delayed diagnosis and complicated cases. We aimed to prospectively

evaluate the clinical features and diagnostic workup of children with suspected

abdominal TB, with a focus on early initiation of medical and surgical treatment

and monitoring of therapeutic outcomes. Materials and methods A time-bound

prospective observational study of all patients ≤ 17 years requiring admission

with symptoms suggestive of abdominal TB from February 2020 to May 2023 was

conducted. All necessary routine blood tests and imaging were done, and

endoscopies and surgeries as needed by the patient were carried out. The data of

the patients who were diagnosed as abdominal TB - probable or definitive - were

analyzed. Results Forty-seven patients were recruited with a suspected diagnosis

of abdominal TB. Thirty-four patients (24 females and 10 males) were diagnosed

as abdominal TB - definite in 18/34 patients (52.94%) and probable in 16/34

patients (47.06%). The mean age was 12.20 ± 3.82 years (4-17 years). Median

duration of the symptoms was three months (IQR = 1-5 months). The commonest

symptoms were abdominal pain (94.11%), fever (73.52%), and loss of appetite and

weight (70.58%). Twelve patients (35.29%) gave a positive history of contact

with TB. There were 13/34 (38.23%) patients who had concomitant pulmonary and

abdominal TB, and 21/34 (61.76%) patients who had only abdominal TB. Mantoux

tuberculin skin test was performed in 20 patients, of which 9/20 (45%) were

positive. A Cartridge-Based Nucleic Acid Amplification Test (CBNAAT) was

performed in 30/34 patients (88.23%) from fluid or tissue samples, of which 11

patients (35.48%) showed CBNAAT positivity. Fifteen patients (44.11%) underwent

surgery, 12 for intestinal perforation and three for intestinal obstruction. Out

of the 18 definite cases of abdominal TB, 11/18 (61.111%) were CBNAAT positive,

and 10/18 (55.55%) had histopathology suggestive of TB. The 16 probable cases of

abdominal TB had a strong history and imaging suggestive of TB abdomen. A total

of seven patients who underwent surgery for intestinal perforation expired. One

patient developed a relapse, and four patients developed drug-induced liver

injury (DILI). Conclusion Abdominal TB remains a common cause of acute abdomen

in the pediatric population, often presenting with non-specific features and

lacking a definitive diagnostic modality. Early detection through recognition of

common clinical features, guided imaging, and timely sampling for confirmation

is vital for initiating antitubercular therapy (ATT) and improving outcomes in

abdominal TB.

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**103. Int J Burns Trauma. 2025 Aug 15;15(4):171-176. doi: 10.62347/PBRZ2450.**

**eCollection 2025.**

From suspected joint tuberculosis to gouty arthritis: a diagnostic journey.

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Gout is a metabolic disorder characterized by hyperuricemia, leading to the

deposition of monosodium urate crystals in joints and soft tissues. It commonly

affects the first metatarso-phalangeal (MTP) joint, but atypical presentations

can pose significant diagnostic challenges. In this report, we describe a rare

case of gouty arthritis affecting the proximal interphalangeal (PIP) joint of

the second toe, which was initially suspected to be a case of joint

tuberculosis. A 38-year-old male presented with a painful swelling over the

second toe for two months, with imaging and laboratory findings suggesting an

infectious etiology. Despite clinical suspicion of tuberculosis,

histopathological examination of the lesion confirmed the presence of amorphous

eosinophilic material with chronic inflammatory infiltrate and giant cell

reaction, indicative of gout. Subsequent serum uric acid evaluation revealed

hyperuricemia, leading to a definitive diagnosis. The patient underwent surgical

evacuation of the tophaceous deposits followed by medical management with

colchicine, nonsteroidal anti-inflammatory drugs (NSAIDs), and allopurinol.

Postoperative follow-up demonstrated complete resolution of symptoms with no

recurrence. Aim of the study: This case report aims to highlight the diagnostic

challenges of atypical gout presentations, particularly when mimicking

infectious conditions such as tuberculosis. It underscores the importance of

maintaining a broad differential diagnosis, utilizing histopathology for

confirmation, and considering gout even in uncommon anatomical locations.

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DOI: 10.62347/PBRZ2450

PMCID: PMC12444417

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**104. Bioinformation. 2025 Jun 30;21(6):1602-1605. doi: 10.6026/973206300211602.**

**eCollection 2025.**

Clinical spectrum of tuberculosis among HIV infected patients in India:

Correlation with immunological status using CD4 counts.

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Tuberculosis (TB) remains a common and serious opportunistic infection among

HIV-infected individuals, with clinical presentation closely tied to immune

status. In this prospective study of 100 HIV-positive patients with TB,

pulmonary TB predominated in those with CD4 counts >200, while extra pulmonary

and disseminated TB were strongly associated with CD4 counts <200. Symptoms such

as cough and fever were prevalent and radiographic findings varied with immune

suppression levels. CD4 counts served as a critical marker in determining the

clinical spectrum and severity of TB. These findings underscore the importance

of CD4-based assessment in guiding timely diagnosis and targeted management of

TB in HIV patients.

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DOI: 10.6026/973206300211602

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PMID: 40978657

**105. ACS Omega. 2025 Sep 4;10(36):41221-41232. doi: 10.1021/acsomega.5c03832.**

**eCollection 2025 Sep 16.**

Mycolic Acid-like Lipids Act as Substrates for Mycobacterium marinum melH.

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Mycobacterium tuberculosis (M. tuberculosis), the pathogenic bacterium that

causes tuberculosis, has developed its own mechanism to evade defense mechanisms

to counteract the lethal effects of reactive oxygen species (ROS) generated

within host macrophages during infection. The melH gene present in Mycobacterium

tuberculosis and Mycobacterium marinum plays an important role in reducing ROS

generated during infection. The melH gene encodes an epoxide hydrolase.

Bioinformatics data suggests that the encoded enzyme utilizes lipid substrates

for its function. To identify potential physiological substrates of MelH in

Mycobacterium marinum (M. marinum), we employed a lipid fractionation approach

combined with liquid chromatography-mass spectrometry and treatment using the

active MelH enzyme. We found classes of mycolic acids (MA), predominantly epoxy

MA, accumulate in the melH mutant and upon treatment with MelH are reduced in

the lipid fraction. These results provide insight into how MelH, encoded in the

mel2 operon, contributes to M. marinum and M. tuberculosis persistence by

converting epoxides to diols within the host, thereby alleviating toxicity and

stress responses. Furthermore, these findings offer additional evidence

supporting the potential mechanisms of action if MelH is targeted for

antitubercular drug discovery.

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PMCID: PMC12444526

PMID: 40978362

**106. Case Rep Otolaryngol. 2025 Sep 11;2025:6485801. doi: 10.1155/crot/6485801.**

**eCollection 2025.**

Laryngeal Mycobacterium bovis: A Unique Cause of Airway Compromise in a

27-Year-Old Male With Down Syndrome.

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**Introduction:** Laryngeal tuberculosis (TB) due to Mycobacterium bovis is an

extremely rare cause of airway obstruction. This case report describes a unique

instance of acute airway obstruction in an immunocompetent 27-year-old male with

down syndrome caused by laryngeal Mycobacterium bovis, shedding light on the

challenges of diagnosis and treatment. Case: A 27-year-old male with trisomy 21

presented with progressive shortness of breath, productive cough, dysphonia, and

dysphagia. After a failed workup for pneumonia and other conditions, imaging

revealed likely epiglottitis and a right upper lung lesion. A tracheostomy was

performed due to worsening airway compromise. Biopsy results confirmed

granulomatous inflammation and identified Mycobacterium bovis, which was

resistant to pyrazinamide. The patient was treated with a modified RIPE regimen

and successfully decannulated 2 months later. Conclusion: This case emphasizes

the importance of a comprehensive diagnostic approach, including tissue biopsy

and culture, in patients with airway compromise of unclear etiology.

Mycobacterium bovis, though rare, should be considered in the differential

diagnosis of laryngeal TB, especially in cases with progressive symptoms and

atypical findings. Early recognition and tailored treatment are critical for

favorable outcomes.

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PMID: 40978283

**107. Am J Clin Exp Urol. 2025 Aug 15;13(4):301-305. doi: 10.62347/QURJ3771.**

**eCollection 2025.**

Tuberculous spondylodiscitis with ureteral involvement: a rare case report.

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**BACKGROUND: T**uberculosis spondylitis, also known as Pott's disease, is a form of

osteomyelitis that primarily affects the vertebral bodies and can lead to severe

complications such as paravertebral abscesses, kyphosis, and degenerative spinal

changes. Although it typically involves the skeletal system, contiguous spread

to adjacent organs, such as the genitourinary tract, is rare.

**METHODS:** We report the case of a 64-year-old male with chronic back pain who

underwent a renal protocol abdominopelvic CT scan following ultrasound findings

of right kidney stasis.

**RESULTS:** The CT revealed obstructive uropathy with a dilated and tortuous

ureter, a 27×30 mm intraluminal lesion, intraluminal gas, and periureteric

fibrosis. Fusion of the L3-L5 vertebrae with gibbous deformity and degenerative

changes suggested tuberculous spondylodiscitis with extension to the ureter.

Urinalysis was positive for acid-fast bacilli, confirming genitourinary

tuberculosis. The patient underwent right ureteronephrectomy due to pyonephrosis

and extensive adhesions precluding ureteral reconstruction.

**CONCLUSION:** This case highlights a rare but serious complication of spinal

tuberculosis involving direct spread to the ureter. Timely diagnosis using

imaging and microbiological testing, followed by appropriate surgical

intervention, is critical to prevent long-term morbidity.

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PMCID: PMC12444390

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**108. FEBS J. 2025 Sep 21. doi: 10.1111/febs.70265. Online ahead of print.**

Lung organoids as a human system for Mycobacteria infection modeling and drug

testing.

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Mycobacterial infections remain a global public health challenge. Each year,

high rates of morbidity and mortality worldwide are a consequence of chronic

respiratory infections due to Mycobacteria. According to the World Health

Organization (WHO), in 2023, 10.8 million individuals fell ill with

Mycobacterium tuberculosis (Mtb), resulting in an estimated 1.25 million deaths.

This positions tuberculosis (TB) as the leading cause of death from a single

pathogen worldwide after the coronavirus disease (COVID-19) pandemic. On the

other hand, the cases of people affected by nontuberculous mycobacteria (NTM)

have risen globally, but the precise incidence and prevalence of both pulmonary

and extrapulmonary disease remain unknown. In Europe, nontuberculous

mycobacterial pulmonary diseases affect between 0.2 and 2.9 per 100 000

individuals, mainly patients with cystic fibrosis (CF) and non-CF

bronchiectasis. The diagnosis and treatment of mycobacterial infections are

challenging and complex, frequently requiring long-duration treatments with

several antibiotics, which in most cases leads to poor patient outcomes. As the

role of immune cells has been extensively assessed, in this Review, we summarize

the current knowledge about the contribution of epithelial cells in the early

steps of Mycobacteria infections. Additionally, we describe how human lung

organoid technology provides new tools to better understand host-Mycobacteria

interactions in the airways and test new therapeutic targets.

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behalf of Federation of European Biochemical Societies.

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**109. IJTLD Open. 2025 Sep 10;2(9):512-518. doi: 10.5588/ijtldopen.24.0571.**

**eCollection 2025 Sep.**

TB treatment support strategies for children, adolescents, and young adults in a

low-incidence setting.

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**BACKGROUND:** Globally, TB programmes should pay attention to the treatment

support needs of children and adolescents (0-24 years) given the high disease

burden and specific care requirements. We examine how health care workers in a

low-incidence setting monitor and support TB treatment and TB preventive

treatment (TPT) in this population.

**METHODS:** A quantitative web-based cross-sectional survey was conducted from 1

December 2023 to 31 January 2024 among Dutch health care workers routinely

caring for persons (0-24 years) in community- and hospital-based TB services.

**RESULTS:** Ninety-three health care workers participated. The most common

strategies to monitor TB treatment and TPT were 1) verbal questioning on

adherence (100% vs. 99%) and 2) evaluating clinical response to TB treatment

(91%). Additional strategies were always used for TB treatment, with a pill

organiser being the preferred method, while 50% seldom used extra strategies for

TPT. Digital support technologies were rarely used for TB treatment and TPT by

78% and 90% of respondents, respectively.

**CONCLUSION:** Dutch health care workers relied on traditional methods to support

TB treatment adherence with limited use of digital technologies and greater

focus on disease than infection. Further research is needed to assess whether

these strategies meet young people's needs in TB care and improve outcomes.

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PMID: 40959790

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**eCollection 2025 Sep.**

An economic analysis of BPaL for multidrug-resistant TB in South Africa and the

Philippines.

Masuku SD(1)(2), Nattey C(1), Coetzee L(1), Hirasen K(1), Mabhula A(1), Casalme

DJ(3), Gler MT(4), Gupta A(5), Juneja S(5), Ndjeka N(6)(7), Evans D(1), Nichols

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**BACKGROUND:** The WHO endorses bedaquiline, pretomanid, and linezolid (BPaL)-based

regimens for multidrug-resistant/rifampicin-resistant TB, and both the

Philippines (PH) and South Africa (SA) have adopted these regimens.

**METHODS:** Using a Markov model, we assessed the cost per successful treatment and

5-year budgetary and economic impact of BPaL-based regimens in SA and PH.

Treatment outcomes were informed by national electronic registries, SA BPaL

Clinical Access Program, and PH operational research. Costs were estimated from

the provider perspective.

**RESULTS:** Over 5 years, BPaL-based regimens reduce total costs by 20%-25% in SA

and 9%-11% in PH compared with a standard short oral regimen (SSOR) when

achieving the same number of successful treatments, due to lower cost per

successful treatment from reduced loss to follow-up and mortality. BPaL-based

regimens improve treatment success by 22%, leading to more patients completing

full treatment and higher overall resource use. Therefore, the budget for

BPaL-based regimens is projected to increase by 7%-8% (SA) and 6% (PH) from

2023/24 to 2027/28.

**CONCLUSION:** BPaL-based regimens reduce cost per successful treatment compared

with SSOR and require smaller budgets for similar treatment outcomes.

Implementation may involve initial budget increases, but improvements in

treatment success and long-term health outcomes outweigh these costs, presenting

a strong rationale for rollout.

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PMCID: PMC12435464

PMID: 40959787

**111. IJTLD Open. 2025 Sep 10;2(9):542-544. doi: 10.5588/ijtldopen.25.0263.**

**eCollection 2025 Sep.**

Bedaquiline and levofloxacin replacing rifampicin for the treatment of TB.

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DOI: 10.5588/ijtldopen.25.0263

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**112. IJTLD Open. 2025 Sep 10;2(9):552-554. doi: 10.5588/ijtldopen.25.0203.**

**eCollection 2025 Sep.**

Host-protein biomarkers distinguish asymptomatic TB in an active case finding

study.

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Strengthening the TB response with artificial intelligence and the right to

health.

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Spoligotyping-based molecular typing of Mycobacterium tuberculosis complex

isolated from Metahara sugar factory workers in Central Ethiopia.

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**BACKGROUND:** Understanding the genetic makeup of Mycobacterium tuberculosis

complex (MTBC) strains is crucial, as lineage differences influence

transmissibility, pathogenicity, and drug resistance patterns, all of which are

essential for understanding MTBC transmission dynamics and designing effective

TB control strategies. The present study investigated the genetic diversity of

Mycobacterium tuberculosis complex among pulmonary tuberculosis (TB) patients

employed at Metahara Sugar Factory, located in Fentale district, East Showa Zone

Oromia, central Ethiopia.

**METHODS:** A cross-sectional study was conducted among 390 suspected pulmonary TB

patients. Sputum samples were examined using Ziehl-Neelsen staining and

cultured, followed by molecular characterizations of the isolates using region

of difference 9 (RD9) deletion typing and spoligotyping.

**RESULTS:** Out of 390 participants, 96 (24.6%) were smear positive, and 89 (22.8%)

were culture positive. RD9 deletion typing confirmed 88 isolates as M.

tuberculosis. Further characterization of the 88 isolates using spoligotyping

revealed 28 distinct spoligotyping patterns of which 15 unique (single

isolates), and 13 shared among 73 clustered isolates. Among these, 19 matched

shared international type (SITs) in the SpolDB4 database, while, 9 were novel

(orphan) patterns. The predominant SITs were SIT523 (19.32%), SIT53 (13.6%),

SIT149 (9.1%) and SIT289 (7.95%). Lineage analysis using TB-insight RUN

TB-Lineage classified the strains primarily as Euro-American (63.64%), followed

by Indo-Oceanic (20.45%), East-African-Indian (14.77%) and M. africanum (1.14%).

**CONCLUSION:** The high clustering rate observed may suggest recent transmission;

however, this must be interpreted cautiously due to the limited discriminatory

power of spoligotyping, which may overestimate clustering and underestimate

diversity. This underscores the need for targeted TB control strategies informed

by enhanced molecular surveillance.

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A Rare Concurrent Presentation of Typhoid Fever with Bacteremia and Pulmonary

Tuberculosis.

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This case report describes an unusual presentation of concurrent typhoid fever

and pulmonary tuberculosis (TB) in an 82-year-old female. She was admitted with

syncope and dehydration and initially suspected of having pneumonia and a

urinary tract infection (UTI). Urine and blood cultures rapidly identified

gram-negative rods, while CT imaging showed cavitary lesions in the bilateral

upper lobes and left lower lobe. The gram-negative rods were identified as

Salmonella enterica subspecies enterica Typhi, and sputum acid-fast bacilli

(AFB) PCR and cultures confirmed the presence of Mycobacterium tuberculosis

complex. The patient was treated for both typhoid fever and pulmonary

tuberculosis. This rare case highlights the clinical challenge of distinguishing

whether a single disease process is responsible for multiple symptoms (Occam's

Razor) or if multiple diseases are concurrently affecting the patient (Hickam's

dictum). Here, two distinct infections explained the complex presentation.

Although typhoid fever was diagnosed first and could rarely be associated with

pulmonary abscesses, cavitary lung lesions are more commonly seen in pulmonary

tuberculosis. This case underscores the importance of considering multiple

concurrent infections in complex clinical scenarios.

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