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**境外学者发表的结核病英文文章摘要**

**（89篇）**

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

**1. Clin Microbiol Infect. 2025 Sep 11:S1198-743X(25)00453-7. doi:**

**10.1016/j.cmi.2025.09.003. Online ahead of print.**

High rates of acquired resistance to fluoroquinolones, bedaquiline and linezolid

in patients failing treatment against drug-resistant tuberculosis in the

Republic of Moldova.

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**OBJECTIVES:** Mycobacterium tuberculosis with rifampicin resistance rank among the

four critical antimicrobial-resistant pathogens needing priority attention as

identified by the World Health Organization (WHO) in 2024. Our objective was to

identify causes of treatment failure in patients diagnosed with

multidrug-resistant/rifampicin-resistant tuberculosis (MDR/RR-TB) in a

nation-wide cohort in the Republic of Moldova, a WHO high-burden country of

MDR/RR-TB.

**METHODS:** A retrospective cohort study analyzed national tuberculosis

surveillance data (2021-2022) on patients diagnosed with MDR/RR-TB with

available baseline and follow-up drug susceptibility testing for WHO Group A

drugs. Treatment failure was defined as the absence of sputum culture conversion

after six months. Logistic regression was used to identify risk factors

associated with treatment failure.

**RESULTS:** Of 1034 patients initiating MDR/RR-TB treatment, 55 (5.3%) experienced

treatment, failure, while 693 (67.1%) were successfully treated. Baseline

resistance to WHO Group A drugs was significantly higher in patients with

treatment failure than in those with successful outcomes: fluoroquinolones

((32/48 (66.7%) vs. 86/471 (18.3%), p<0.0001), bedaquiline (6/42 (12.5%) vs.

3/468 (0.6%), p<0.0001), and linezolid (12/48 (25.0%) vs. 3/468 (0.6%),

p<0.0001). Acquired resistance occurred in 19/48 (39.6%) of those failing

treatment but none with successful outcomes, particularly to bedaquiline 13/42

(30.9%), linezolid 6/36 (16.7%), and fluoroquinolones 4/16 (25.0%). Baseline

fluoroquinolone resistance (OR 4.7, 95% CI 2.0 - 11.2) and acquired resistance

to any WHO Group A drug (OR 63.5, 95% CI 7.7 - 8311.7) were associated with

treatment failure.

**CONCLUSIONS:** While frequencies of treatment failure in MDR/RR-TB are low on

bedaquiline-containing treatment regimens, we find alarmingly high rates of

baseline and acquired drug resistance to key second-line anti-TB drugs as a

driver for treatment failure in MDR/RR-TB. Strengthening resistance monitoring,

improving adherence, and optimizing individualized regimens are urgently needed

to prevent the emergence of extensively drug-resistant (XDR)-TB in high-burden

settings of MDR/RR-TB.

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**2. Clin Microbiol Infect. 2025 Sep 11:S1198-743X(25)00452-5. doi:**

**10.1016/j.cmi.2025.09.002. Online ahead of print.**

Diagnostic performance of Xpert MTB/RIF Ultra assay with pulmonary and

extrapulmonary specimens: a retrospective evaluation in a low incidence setting

in Finland.

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Helsinki and Helsinki University Hospital, Helsinki, Finland.

**OBJECTIVE:** The aim was to evaluate the sensitivity and specificity of Xpert

MTB/RIF Ultra (Xpert Ultra) assay in detection of extrapulmonary tuberculosis

(TB) in comparison to pulmonary TB in a low incidence setting in the Helsinki

capital area of Finland.

**METHODS:** The retrospective analysis included results from 1112 pulmonary and 705

extrapulmonary samples collected between 2018 and 2023, of which 193 and 136

were culture-positive for Mycobacterium tuberculosis (MTB), respectively. Xpert

Ultra results were compared to mycobacterial culture. PCR positive, culture

negative cases were separately compared to available clinical data (composite

reference standard, CRS).

**RESULTS:** Compared to culture, Xpert Ultra demonstrated 95.3% (95% CI:

91.3-97.7%) sensitivity and 94.5 % specificity (95% CI: 92.8-95.8%) with

pulmonary samples, 47.1% (95% CI: 26.2-69.0%) and 96.7% (95% CI: 93.8-98.4%)

with pleural fluid, 100% (95% CI: 86.9-100%) and 81.8% (95% CI: 72.4-88.6%) with

tissue, 96.6% (95% CI: 81.4-100%) and 75.0% (95% CI: 62.2-84.6%) with pus, and

95.1% (95% CI: 83.0-99.5%) and 67.5% (95% CI: 51.9-80.0%) with lymph node

samples, respectively. Other less common sample types were also included. When

CRS was also considered, specificity exceeded 93% for all sample types.

Sensitivity was 100% with both smear-positive pulmonary and smear-positive

extrapulmonary samples. No false rifampicin susceptibility testing results or

cross-reactivity with nontuberculous mycobacteria were detected.

**CONCLUSIONS:** Xpert Ultra detected MTB in lymph node, tissue, and pus samples

with high accuracy comparable to analysis of pulmonary samples while reducing

time to diagnosis by up to several weeks compared to mycobacterial culture.

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PMID: 40945716

**3. Med. 2025 Sep 12;6(9):100705. doi: 10.1016/j.medj.2025.100705.**

A metabolic syndrome: Understanding host factors that drive mortality in

tuberculosis meningitis.

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Cerebrospinal fluid metabolomics uncovered distinct short chain fatty acids and

amino acids strongly associated with mortality in persons with tuberculosis

meningitis (TBM). These findings from Nhat et al. highlight the critical role of

energy metabolism in the host response to TBM and provide new avenues to explore

and target for host-directed therapy.

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PMID: 40945505

**4. Int J Surg Case Rep. 2025 Sep 9;135:111917. doi: 10.1016/j.ijscr.2025.111917.**

**Online ahead of print.**

Isolated splenic tuberculosis mimicking a solid splenic neoplasm in an

immunocompetent patient: A surgical case report.

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**INTRODUCTION AND IMPORTANCE:** Tuberculosis is the leading cause of death by an

infectious agent globally, especially among immunocompromised patients.

Extrapulmonary tuberculosis (EPTB) can occur as a sequela of pulmonary

tuberculosis through lympho-hematogenous or miliary spread, or can occur in

isolation. EPTB rarely occurs in isolation in a single organ, especially in

immunocompetent patients. Limited data exist on the incidence of isolated

splenic tuberculosis in immunocompetent patients.

**CASE PRESENTATION:** This report highlights a case of a 45-year-old

immunocompetent female with a one-month history of dull left upper quadrant

pain. A contrast-enhanced abdominal CT scan revealed a solitary hypodense,

heterogeneous, solid splenic mass occupying most of the splenic parenchyma, with

an initial preoperative diagnosis of a splenic hemangioma. A near-total

splenectomy was done, with histopathology revealing chronic granulomatous

infection, suggesting tuberculous infection. In our scenario, the patient had a

favourable outcome, receiving a six-month course of anti-tuberculous therapy and

no surgical complications postoperatively.

**CLINICAL DISCUSSION:** Splenic tuberculosis, although rare, can be classified as

either micro-nodular, macro-nodular, miliary, or mixed types. The other subtypes

commonly occur. However, macro-nodular splenic tuberculosis is rare and mimics

benign and malignant splenic neoplasms radiologically, providing diagnostic

challenges.

**CONCLUSION:** Isolated splenic tuberculosis should be considered in the

differential diagnosis of solitary splenic lesions, even in immunocompetent

patients in TB-endemic areas. While timely diagnosis and anti-tubercular therapy

may preserve splenic tissue in selected cases, surgery remains inevitable when

diagnosis is uncertain, complications arise, or medical therapy fails. The case

further highlights the importance of multidisciplinary team management.

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**5. Biomed Pharmacother. 2025 Sep 12;191:118537. doi: 10.1016/j.biopha.2025.118537.**

**Online ahead of print.**

Novel antitubercular agents based on 2,4-disubstituted

5-(aryl-2-ylmethyl)-5H-pyrrolo[3,2-d]pyrimidines.

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Soukup O(4), Hympanova M(4), Sorf A(5), Benkova M(4), Bartacek J(2), Drabina

P(2), Kufa M(6), Kovar O(6), Fikejzlová L(7), Hruby M(8), Ozhelevska O(4), Jagob

J(6), Zdarova-Karasova J(7), Odvarkova J(7), Kaderavková I(7), Rozsypal T(9),

Ewa Greber K(10), Ciura K(11), Janousek J(4), Kratky M(5), Igreja Sa IC(12),

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

health challenge, especially with the rise of multidrug-resistant (MDR) and

extensively drug-resistant (XDR) strains. Current treatment regimens are

prolonged and associated with significant toxicity, underscoring the need for

novel therapeutic agents. This study investigates a new series of

2,4-disubstituted 5-(aryl-2-ylmethyl)-5H-pyrrolo[3,2-d]pyrimidine derivatives as

potential antitubercular agents. The most promising compound, 74, exhibited

potent anti-TB activity, including against MDR strains, with a MIC99 of 2 µM.

Structure-activity relationship studies identified critical substitutions at

positions 2- and 4- of the core scaffold that enhanced antimycobacterial

potency, while bulkier aromatic moieties at position 5- were preferred. Despite

its high efficacy, 74 demonstrated significant cytotoxicity, inhibition of

cytochrome P450 enzymes and cardiotoxicity through hERG channel inhibition,

highlighting challenges in further development. Pharmacokinetic studies of 74

revealed favorable systemic exposure with a prolonged half-life, suggesting its

potential for less frequent dosing. Nonetheless, in vitro assays demonstrated

rapid metabolic turnover, likely due to high intrinsic clearance, and the

compound's elevated logD values further indicate the need for structural

modifications to improve both solubility and metabolic stability. Efforts to

introduce more polar substituents at the 4-position led to a loss of anti-TB

activity, emphasizing the complexity of balancing potency and safety.

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**6. ACS Infect Dis. 2025 Sep 12. doi: 10.1021/acsinfecdis.5c00365. Online ahead of print.**

Metabolic Tagging Reveals Surface-Associated Lipoproteins in Mycobacteria.

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Mycobacteria such as the causative agent of tuberculosis, Mycobacterium

tuberculosis (Mtb), encode over 100 bioinformatically predicted lipoproteins.

Despite the importance of these post-translationally modified proteins for

mycobacterial survival, many remain experimentally unconfirmed. Here we

characterized in Mtb and M. smegmatis (Msm) the metabolic incorporation of

several modified fatty acids as a facile method of adding chemical groups that

enable downstream applications such as detection and enrichment of

lipid-modified proteins. We further showed for azido palmitic acid in Msm that

incorporation is an active process dependent on the lipoprotein biosynthesis

pathway and that a subset of these lipid-modified proteins are associated with

the mycobacterial cell surface. Because mycobacteria do not encode known

lipoprotein transporters, these data have implications for uncovering the roles

of lipoproteins and the possible transport processes involved. Our findings and

the tools we validated will enable the further study of pathways related to

lipoprotein function in mycobacteria and other bacteria in which lipoproteins

remain poorly understood.

DOI: 10.1021/acsinfecdis.5c00365

PMID: 40940670

**7. Int J Infect Dis. 2025 Sep 10:108054. doi: 10.1016/j.ijid.2025.108054. Online**

**ahead of print.**

Longitudinal epidemiology of pulmonary nontuberculous mycobacteria and

tuberculosis in Singapore (2006 - 2024): Emerging dominance of Mycobacterium

abscessus.

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**BACKGROUND:** Nontuberculous mycobacteria (NTM) are increasingly recognised as

important pulmonary pathogens, with rising incidence reported globally as

tuberculosis (TB) declines. While epidemiology is well described in temperate

regions, long-term data from tropical, high-density cities such as Singapore

remain scarce. Prior local studies suggested a shift from Mycobacterium avium

complex (MAC) to M. abscessus as the predominant NTM species, but comprehensive

longitudinal analyses are lacking.

**METHODS:** We performed a retrospective review of all respiratory mycobacterial

cultures at Singapore General Hospital between 2006 and 2024. Pulmonary NTM

(pNTM) was defined using 2007 ATS/IDSA microbiologic criteria (≥2 specimens with

same species or one positive BAL/biopsy), and pulmonary TB (pTB) as a single

culture-positive respiratory specimen. Only the first isolate per patient per

species was included. ICD-10 coding data (2018-2024) were also analysed to

verify trends.

**RESULTS:** A total of 3,877 pTB and 1,825 pNTM cases met inclusion criteria.

Incidence of pNTM increased from 35 to 65 per 100,000 patient-years, while pTB

declined from 225 to 70 per 100,000 patient-years. ICD-10 coding data confirmed

similar trends, with pTB incidence declining from 185 to 41 per 100,000

patient-years between 2018-2024, while pNTM remained stable at 40-43. Species

distribution, derived from microbiological isolates, showed a steady decline in

MAC and a marked rise in M. abscessus, which surpassed MAC as the most common

species after 2014.

**CONCLUSION:** pNTM incidence has risen substantially in Singapore, now approaching

that of TB. The emergence of M. abscessus as the predominant NTM species has

important clinical and public health implications, underscoring the need for

ongoing integrated surveillance and tailored management strategies in tropical

urban environments.

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PMID: 40939955

**8. Chest. 2025 Sep 10:S0012-3692(25)05171-2. doi: 10.1016/j.chest.2025.05.055.**

**Online ahead of print.**

Contribution of Key Comorbidities to Unfavorable Treatment Outcomes among Adults

with Drug-sensitive Pulmonary Tuberculosis in India: a Prospective Cohort

Analysis.

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JA(6), Christopher DJ(10), Viswanathan V(11), Ellner JJ(12), Kornfeld H(13),

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**BACKGROUND:** The population-level impact of risk factors for unfavorable

tuberculosis treatment outcomes depends on their relative prevalence in the

population. We calculated unadjusted and adjusted attributable fractions (AFs)

to estimate the proportion of unfavorable tuberculosis treatment outcomes that

can be attributed to key risk factors in India.

**RESEARCH QUESTION:** What proportion of unfavorable tuberculosis treatment

outcomes can be attributed to key risk factors in India?

**STUDY DESIGN:** and Methods: Adults with drug-sensitive pulmonary tuberculosis

were enrolled from 5 diverse clinical sites at treatment initiation and

prospectively evaluated for 24 months. The primary outcome was a composite

unfavorable treatment outcome of failure, recurrence, or death. We estimated the

unadjusted and adjusted AFs for potentially modifiable risk factors of

unfavorable treatment outcomes.

**RESULTS:** 2930 adults contributed 32912 person-months of follow-up. Median age

was 43 (IQR 31-52) years, 2136 (72.9%) were male, 1609 (55.5%) were

undernourished, 1182 (40.4%) ever-smoked, 956 (32.8%) had diabetes, 437 (14.9%)

reported alcohol misuse, and 65 (2.2%) were HIV positive. Overall, 129 failed

treatment, 80 had recurrence, and 101 died. In our unadjusted analysis, 32.2%

(95% Confidence Interval [CI]: 23.1-40.3) of all unfavorable outcomes were

attributable to undernutrition, 19.4% (95%CI 12.3-25.8) were attributable to

ever-smoking, 8.5% (95% CI: 4.3-12.6) to alcohol misuse and 1.6% (95%CI 0.1-3.0)

to HIV coinfection. After adjusting for simultaneous presence of multiple risk

factors, we found 29.0% (95% CI: 17.6-38.8) of all unfavorable outcomes were

attributable to undernutrition. Alcohol misuse and ever-smoking accounted for

15.4% (95% CI: 7.9-22.3) and 17.9% (95% CI: 1.1-31.9) of treatment failures.

**INTERPRETATION:** Undernutrition, ever-smoking, and alcohol misuse accounted for

over a third of all unfavorable treatment outcomes and may present high-yield

intervention targets to improve tuberculosis treatment outcomes in India.

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**9. Lancet Microbe. 2025 Sep 9:101235. doi: 10.1016/j.lanmic.2025.101235. Online**

**ahead of print.**

Xpert MTB/RIF Ultra stool assay for diagnosing pulmonary tuberculosis in HIV

patients: the tip of the iceberg.

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DOI: 10.1016/j.lanmic.2025.101235

PMID: 40939605

**10. PLoS One. 2025 Sep 12;20(9):e0332161. doi: 10.1371/journal.pone.0332161.**

**eCollection 2025.**

Transient vascular occlusions in a zebrafish model of mycobacterial brain

infection.

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Mycobacterial brain infection, for example tuberculous meningitis (TBM), caused

by Mycobacterium tuberculosis, is a severe manifestation of tuberculosis that

occurs when the bacteria invade the brain. In addition to extensive

inflammation, vascular complications such as stroke frequently arise,

significantly increasing the risk of disability and death. However, the

mechanisms underlying these vascular complications remain poorly understood, as

current knowledge is derived exclusively from human studies. To date, no animal

model has been established to investigate the onset and progression of vascular

pathology in TBM. Here, we use transparent zebrafish larvae to investigate

vascular pathology during the early stages of TBM, establishing a model for

studying vascular complications from mycobacterial brain infection. We find that

mycobacteria preferentially attach to the lumen of vessel bifurcations and

induce vessel enlargement. These attached microcolonies are sufficient to

occlude brain blood vessels in the absence of an organized thrombus. The

majority of microcolony-associated occlusions are transient and contribute to

global hypoperfusion of the brain. These vascular disruptions lead to

accumulation of oxidative stress and cell death in both the vasculature and

neurons. Taken together, these findings demonstrate the occurrence of ischemic

events during the early stages of mycobacterial brain infection and establish an

animal model for studying vascular complications in TBM.

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Creative Commons CC0 public domain dedication.

DOI: 10.1371/journal.pone.0332161

PMCID: PMC12431238

PMID: 40938925

**11. Am J Respir Crit Care Med. 2025 Sep 12. doi: 10.1164/rccm.202506-1477RL. Online ahead of print.**

Oral Rinse versus Facemask Capture for Non-Sputum Diagnosis of Pulmonary

Tuberculosis.

Mendelsohn SC(1), Jackson GT(2), Wessels E(3), Beyers E(2), Visagie S(2), Steyn

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DOI: 10.1164/rccm.202506-1477RL

PMID: 40938650

**12. Am J Respir Crit Care Med. 2025 Sep 12. doi: 10.1164/rccm.202503-0723RL. Online ahead of print.**

Oral Rinse as an Alternative Diagnostic Specimen for Detection of Tuberculosis.

Gordhan BG(1), Sewcharran A(2), Waja Z(3), Martinson N(3), Araujo-Pereira M(4),

Saboia AS(5), Lourenço MCS(6), Gomes-Silva A(7), Rolla VC(7), Kana B(8);

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DOI: 10.1164/rccm.202503-0723RL

PMID: 40938622

**13. Microbiol Spectr. 2025 Sep 12:e0113125. doi: 10.1128/spectrum.01131-25. Online ahead of print.**

Assembly of the Mycobacterium tuberculosis type VII ESX-1 secretion system in

Mycobacterium smegmatis identifies a new transcriptional activator of esx-1

genes and a novel TB vaccine.

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Mycobacterium tuberculosis (M. tb) uses its type VII secretion system (T7SS)

ESX-1 to export immunogenic, virulence-mediating protein effectors. In this

study, the fast-growing, non-pathogenic model mycobacteria Mycobacterium

smegmatis mc2-155 was engineered to express the M. tb T7SS ESX-1 system. We

found that M. smegmatis transformed with M. tb esx-1 locus genes only, as well

as M. smegmatis transformed with M. tb esx-1 and espACD operon genes (designated

MSX-1), produces and secretes the M. tb ESX-1 protein effectors EsxA, EsxB, and

EspB. However, the abundance of these proteins was higher inside the cell and

culture filtrate of the MSX-1 strain. Although ESX-1 is critical for M. tb

pathogenesis, expression of M. tb ESX-1 did not make the recombinant M.

smegmatis strains virulent in macrophages. Serendipitously, transformation of M.

smegmatis with a modified esx-1 locus in this study revealed rv3860, a gene of

previously unknown function, to be required for the transcription of pe35,

ppe68, esxB, and esxA genes. Finally, mice vaccinated with MSX-1 were found to

be as protected as mice vaccinated with Mycobacterium bovis BCG against M. tb

infection, without becoming sensitized to tuberculin. These results show that a

functional M. tb ESX-1 system can be assembled in M. smegmatis to uncover novel

facets of the secretion machinery and that the modified M. smegmatis strain can

function as a tuberculosis (TB) vaccine. Unlike BCG, however, its deployment may

be compatible with tests currently used to diagnose TB.IMPORTANCEIn this study,

we modified Mycobacterium smegmatis, which is often used as a surrogate model

organism in mycobacterial research, to produce and assemble a functional

Mycobacterium tuberculosis (M. tb) ESX-1 protein secretion system. One such M.

smegmatis strain named MSX-1 was found to make a functional M. tb ESX-1 system

without becoming virulent. And in using M. smegmatis as a chassis to study the

ESX-1 system, we found that rv3860, an M. tb gene of previously unknown

function, is needed for the production of key ESX-1 proteins. Finally, mice

vaccinated with MSX-1 were as protected from tuberculosis (TB) as mice given

BCG, the only approved TB vaccine. Notably, we found that unlike BCG, MSX-1 does

not sensitize mice to the antigens used in existing TB diagnostic tests. These

observations, taken together, highlight the utility of M. smegmatis as a chassis

to study the M. tb ESX-1 secretion machinery.

DOI: 10.1128/spectrum.01131-25

PMID: 40938095

**14. Elife. 2025 Sep 12;13:RP102441. doi: 10.7554/eLife.102441.**

Tuberculosis susceptibility in genetically diverse mice reveals functional

diversity of neutrophils.

Ravesloot-Chavez MM(1), Van Dis E(2), Fox D(2), Anaya-Sanchez A(1), Espich S(3),

Nguyenla XH(2), Rawal S(2), Samani H(2), Ballinger M(4), Thomas HF(4), Kotov

DI(2), Vance RE(2), Nachman MW(4), Stanley SA(2)(3).

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Update of

 doi: 10.1101/2023.06.29.547125.

 doi: 10.7554/eLife.102441.1.

Tuberculosis is a heterogeneous disease in humans with individuals exhibiting a

wide range of susceptibility. This heterogeneity is not captured by standard

laboratory mouse lines. We used a new collection of 19 wild-derived inbred mouse

lines collected from diverse geographic sites to identify novel phenotypes

during Mycobacterium tuberculosis (Mtb) infection. Wild-derived mice have

heterogeneous immune responses to infection that result in differential ability

to control disease at early time points. Correlation analysis with multiple

parameters including sex, weight, and cellular immune responses in the lungs

revealed that enhanced control of infection is associated with increased numbers

of CD4 T cells, CD8 T cells, and B cells. Surprisingly, we did not observe

strong correlations between IFN-γ production and control of infection. Although

in most lines high neutrophils were associated with susceptibility, we

identified a mouse line that harbors high neutrophil numbers yet controls

infection. Using single-cell RNA sequencing, we identified a novel neutrophil

signature associated with failure to control infection.

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PMCID: PMC12431774

PMID: 40937719

**15. Gates Open Res. 2025 Sep 9;9:69. doi: 10.12688/gatesopenres.16362.1. eCollection 2025.**

Mycobacterium tuberculosis growth inhibition by peripheral blood mononuclear

cells from household contacts is not affected by previous SARS-CoV-2 infection.

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van Rensburg I(1), Shabangu A(1), Smith B(1), Noor F(1), Walzl G(1), Urdahl

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Update of

 doi: 10.12688/verixiv.514.3.

**BACKGROUND:** There is a concern that SARS-CoV-2 infection may drive poor outcomes

after Mycobacterium tuberculosis Mtb exposure and infection. We performed an ex

vivo Mtb killing assay using peripheral blood mononuclear cells (PBMC) from

three groups: healthy household contacts of people with active TB with and

without serologic evidence of previous SARS-CoV-2 infection (COV+HHC and

COV-HHC), and participants with active TB and previous SARS-CoV-2 (COV+TB+).

**METHODS:** Twenty participants per group from Cape Town, South Africa were

classified according to SARS-CoV-2 anti-S and anti-N antibody tests. We infected

PBMC from each participant at a MOI of 0.001 with Mtb strain H37Rv in a 4-day

growth inhibition assay. Mycobacteria were quantified through inoculation into

Bactec Mycobacteria Growth Indicator Tube (MGIT) liquid culture. PBMC from a

subset of participants were infected in the presence of autologous time-matched

serum and Mtb-uninfected control PBMCs were included.

**RESULTS:** There was no difference in the time to detection of Mtb or the

normalised Mtb growth ratio (log10CFUsample - log10CFUcontrol) between groups in

the standard protocol, or when infected cells from the COV+HHC and COV+TB+ (n=10

each) groups were cultured with autologous time-matched serum. The group with

active TB demonstrated the best Mtb growth control. Extracellular Mtb measured

by culturing the supernatants of the infected cell cultures also did not show

any difference between groups. Five (14.3%) uninfected controls were culture

positive.

**CONCLUSION:** Our results show that previous SARS-CoV-2 does not affect the Mtb

killing ability of circulating mononuclear immune cells in vitro. Previous

SARS-CoV-2 is unlikely to affect the outcome of Mtb infection through this

mechanism.

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DOI: 10.12688/gatesopenres.16362.1

PMCID: PMC12420909

PMID: 40936501

**16. Sci Total Environ. 2025 Sep 10;1000:180408. doi:**

**10.1016/j.scitotenv.2025.180408. Online ahead of print.**

Quantitative microbial risk assessment of drug-resistant tuberculosis exposure

from wastewater systems across Sub-Saharan Africa.

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Tuberculosis (TB), especially in its drug-resistant form, remains a critical

public health challenge in sub-Saharan Africa, where conventional airborne

transmission has been well-characterized. However, wastewater systems prevalent

across urban centres may serve as overlooked environmental reservoirs for

Mycobacterium tuberculosis, posing occupational and environmental health risks.

Despite this, the health implications of wastewater exposure remain

underexplored, particularly in high TB-burden settings. To address this research

gap, we applied the Quantitative Microbial Risk Assessment (QMRA) framework,

incorporating Disability-Adjusted Life Years (DALYs), to assess the health risks

of exposure to drug-resistant TB pathogens in wastewater. Our study uniquely

focuses on three exposure scenarios: untreated wastewater at the head of works,

aerosols from aeration tanks, and reuse of treated wastewater for irrigation,

across six African countries: Ghana, Nigeria, Kenya, Uganda, Cameroon, and South

Africa. The study found the highest concentrations of M. tuberculosis in Ghana,

with rifampicin-resistant strains present at lower levels across all countries.

Infection risks ranged from 3 % to 100 %, with irrigation posing the highest

median infection risk (0.77). The greatest disease burdens were observed at the

head of works (112.46 DALYs) and during irrigation (105.31 DALYs). Our findings

highlight wastewater as a significant and previously underestimated route for TB

transmission. This study underscores the urgent need for enhanced treatment

technologies, occupational safety protocols, and environmental surveillance.

Integrating wastewater-based epidemiology into national TB monitoring could

provide a valuable early-warning system, especially in regions reusing

wastewater for agriculture, and may significantly strengthen global TB control

strategies.

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**17. Antimicrob Agents Chemother. 2025 Sep 11:e0079525. doi: 10.1128/aac.00795-25. Online ahead of print.**

Incorporation of macrophage immune stresses into an intracellular assay of drug

tolerance in Mycobacterium tuberculosis.

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Development of new and improved tuberculosis (TB) chemotherapies is hampered by

antibiotic resistance and drug tolerance by Mycobacterium tuberculosis (Mtb).

Phenotypic drug tolerance, a phenomenon where Mtb populations can temporarily

survive therapeutic antibiotic concentrations, represents a significant hurdle

to TB treatment and is indeed one of the factors responsible for prolonged TB

therapy. Assays that can identify compounds with improved efficacy against

drug-tolerant Mtb are urgently required to improve TB treatment regimens. Here,

we report the development of a 96-well plate assay capable of identifying

anti-Mtb drugs with activity against drug-tolerant Mtb in physiologically

relevant intracellular environments within macrophages. Primary murine

macrophages, modified either by immunological activation or specific CRISPR/Cas9

gene knockouts to generate tolerance-inducing environments, were infected with

an Mtb strain constitutively expressing luciferase. Following drug exposure,

differences in bacterial survival were measured by bacterial outgrowth after

lysis of the host macrophages. By monitoring Mtb luciferase in infected

macrophages before, during, and after drug treatment, we confirmed earlier

observations that host immune stresses trigger induction of drug tolerance.

However, while host stresses induced tolerance against some anti-TB compounds,

the same host stresses were synergistic with other anti-TB drugs. Our assay

provides the ability to profile the activities of anti-TB drugs on bacteria in

intracellular host environments, which is critical to the rational design of

drug combinations that provide optimal coverage of the Mtb sub-populations in

the infected host.

DOI: 10.1128/aac.00795-25

PMID: 40934365

**18. PLoS Pathog. 2025 Sep 11;21(9):e1013183. doi: 10.1371/journal.ppat.1013183.**

**Online ahead of print.**

HIV-1 Tat favors the multiplication of Mycobacterium tuberculosis and Toxoplasma

by inhibiting clathrin-mediated endocytosis and autophagy.

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S(2), Besteiro S(2), Bordat Y(2), Nguyen-Chi M(2), Audemard N(1), Mesleard-Roux

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HIV-1 and Mycobacterium tuberculosis (Mtb) coinfections are a major public

health problem but are not well characterized. HIV-1 Tat is secreted by infected

cells, generating nanomolar concentrations of Tat in the sera of people living

with HIV. Circulating Tat enters cells, binds to PI(4,5)P2 then undergoes

palmitoylation, thereby becoming resident on this phosphoinositide. Here, we

found that Tat favors the multiplication of Mtb in macrophages. Moreover, Tat

renders zebrafish larvae more sensitive to mycobacterial infection. We found

that Tat binding to PI(4,5)P2 and palmitoylation enable Tat to inhibit the

recruitment of the AP-2 adaptor, thereby inhibiting clathrin-mediated

endocytosis and in turn autophagy. This inhibition prevents the degradation of

intracellular pathogens such as Mtb and opsonized Toxoplasma gondii, but also of

lipid droplets, thereby facilitating the access of these pathogens to lipids. We

thus identified a mechanism enabling HIV Tat to favor the multiplication of

intracellular pathogens such as Mtb.

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DOI: 10.1371/journal.ppat.1013183

PMID: 40934260

**19. PLOS Glob Public Health. 2025 Sep 11;5(9):e0005062. doi:**

**10.1371/journal.pgph.0005062. eCollection 2025.**

A broader lens on tuberculosis cost-effectiveness analysis: How patient-incurred

costs and post-tuberculosis outcomes reshape estimates in a multi-country study.

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Tuberculosis (TB) remains a major public health challenge, with financial and

health impacts extending beyond treatment. Both the perspective adopted in

cost-effectiveness analyses-which critically determines choices such as the

inclusion of patient-incurred costs-and the extent to which long-term

post-treatment considerations are incorporated have important policy

implications. This study examines how the choice of timeframe and cost

perspectives influence the estimated cost-effectiveness of TB interventions,

particularly preventative measures. Using data from 19 WHO TB patient cost

surveys and global epidemiological databases, we modelled a hypothetical

preventative TB intervention, generating four incremental cost-effectiveness

ratios (ICERs) per country under different analytical approaches. These included

a conventional timeframe up to treatment completion, an extended timeframe

incorporating post-TB effects, and two perspectives that either included or

excluded patient-incurred costs. The approach yielding the lowest ICER (societal

perspective; extended timeframe) was anchored in the primary analysis to a 1×GDP

per capita threshold. Using this benchmark simplified cross-country comparisons

and removed the need for health system cost estimates. Sensitivity and scenario

analyses explored how threshold values influenced the relative impact of

timeframe and costing perspective. ICERs were higher when patient costs were

omitted or the post-TB period was excluded, peaking when both were absent.

However, across all countries, post-TB considerations had a far greater impact

on cost-effectiveness. On average, removing the post-TB period increased ICERs

by over 50% (ranging from +19.3% in Ghana to +108% in Mongolia, societal

perspective). Including patient-incurred costs increased the likelihood that

prevention was cost-effective, particularly in low-GDP settings with lower

willingness-to-pay thresholds. However, their impact was minimal above 2×GDP.

Our study highlights how narrowly defining the financial and health burden of

tuberculosis in cost-effectiveness analyses risks underestimating the benefits

of interventions-particularly in lower-GDP countries where the socioeconomic

burden of tuberculosis is greatest-which could lead to misguided policy

decisions that overlook the full impact of tuberculosis.

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PMID: 40934257

**20. Trop Med Int Health. 2025 Sep 11. doi: 10.1111/tmi.70022. Online ahead of print.**

Expanding the Lens: Functional and Epidemiological Contexts in Genotypic

Surveillance of Drug-Resistant Tuberculosis.

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Punjab, Pakistan.

DOI: 10.1111/tmi.70022

PMID: 40931972

**21. J Bras Pneumol. 2025 Sep 8;51(3):e20250154. doi: 10.36416/1806-3756/e20250154.**

Scaling up tuberculosis preventive treatment in Brazil: the ExpandTPT way

forward.

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DOI: 10.36416/1806-3756/e20250154

PMCID: PMC12401115

PMID: 40929487

**22. J Bras Pneumol. 2025 Sep 8;51(3):e20250153. doi: 10.36416/1806-3756/e20250153.**

Post-tuberculosis and postinfected bronchiectasis: data from global registries.

Oscullo G(1)(2), Martinez-García MA(1)(2), Centis R(3), D'Ambrosio L(4),

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PMCID: PMC12401148

PMID: 40929486

**23. PLOS Glob Public Health. 2025 Sep 10;5(9):e0005050. doi:**

**10.1371/journal.pgph.0005050. eCollection 2025.**

Potential impact, costs, and benefits of population-wide screening interventions

for tuberculosis in Viet Nam: A mathematical modelling study.

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L(1)(2), Veeken LD(5), Garden FL(6)(7), Nguyen HV(8), Nguyen TA(9)(10)(11)(12),

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Population-wide screening may accelerate the decline of tuberculosis (TB)

incidence, but the optimal screening algorithm and duration must weigh resource

considerations. We calibrated a deterministic transmission model to TB

epidemiology in Viet Nam. We simulated three population-wide screening

algorithms from 2025: sputum nucleic acid amplification tests (NAAT, Xpert

MTB/RIF Ultra) only; chest radiography (CXR) followed by NAAT; and CXR-only

without microbiological confirmation. We determined the annual screening rounds

required to reduce pulmonary TB prevalence below 50 per 100,000 people.

Cost-effectiveness was assessed using incremental cost-effectiveness ratios

(ICERs), representing the additional costs (in US$) per disability-adjusted life

year (DALY) averted compared to business-as-usual by 2050. Additionally, we

evaluated the impact of NAAT cartridges costing US$1 each. NAAT-based algorithms

required at least six rounds to reach the prevalence threshold, while CXR-only

required three. NAAT-only achieved a prevalence reduction consistent with the

ACT3 trial after three rounds. The CXR+NAAT algorithm averted 4.29m DALYs

(95%UI:2.86-6.14) at US$225 (95%UI:85-520) per DALY averted compared with

business-as-usual. The front-loaded investment of US$161m (95%UI:111-224)

annually during the intervention resulted in average annual cost savings of

US$12.7m (95%UI:6.7-21.4) up to 2050 compared to the business-as-usual

counterfactual. Reducing the cost of NAAT to US$1 led to a 50% and 15% reduction

in budget impact and a 63% and 26% reduction in the estimated ICER for the

NAAT-only and CXR+NAAT algorithms, respectively. In Viet Nam, population-wide

screening could achieve ambitious policy goals. Substantial front-loaded

investment is immediately followed by persistent cost savings and could be

further offset by more affordable NAATs.

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original author and source are credited.

DOI: 10.1371/journal.pgph.0005050

PMCID: PMC12422431

PMID: 40929179

**24. Pediatr Infect Dis J. 2025 Sep 11. doi: 10.1097/INF.0000000000004981. Online**

**ahead of print.**

Mycoplasma pneumoniae Infection Mimicking Pediatric Tuberculosis: A Case Report.

Sel Coban D(1), Ozbakir H(2), Avci Yavuz B(1), Kahraman Cetin B(2), Gulaslan

Erdogan O(3), Akaslan Kara A(2).

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DOI: 10.1097/INF.0000000000004981

PMID: 40928230

**25. Respirology. 2025 Sep 10. doi: 10.1111/resp.70130. Online ahead of print.**

Letter From the Korean Academy of Tuberculosis and Respiratory Diseases

(KATRD)-Navigating Reform: South Korea's Healthcare System at a Crossroads.

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South Korea.

DOI: 10.1111/resp.70130

PMID: 40927844

**26. Health Policy Plan. 2025 Sep 10:czaf058. doi: 10.1093/heapol/czaf058. Online**

**ahead of print.**

Understanding the financial hardships faced by TB and HIV patients during the

COVID-19 pandemic: A mixed-method study in Bandung and Yogyakarta, Indonesia.

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Wulandari LPL(5), Putra IWCSD(2), Wahyuningtias SD(2), Probandari A(2)(4),

Thabrany H(6), Wiseman V(7)(5), Ahmad RA(2), Boettiger D(5), Liverani

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Mada/Dr. Sardjito General Hospital, Yogyakarta, Indonesia.

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The COVID-19 pandemic had significant widespread financial impacts, resulting in

decreased household income, increased unemployment, and disrupted health

services. Despite the higher prevalence of infections of tuberculosis (TB) and

human immunodeficiency virus (HIV) in poorer populations, research on the

financial challenges faced by these populations during the pandemic is still

limited. Indonesia recorded the highest COVID-19 cases in Southeast Asia

(6,815,156) while contending with the dual burden of HIV and TB. This study

investigates the factors influencing out-of-pocket (OOP) payments and

catastrophic health spending during the pandemic, alongside patients' challenges

and coping mechanisms in Bandung and Yogyakarta, Indonesia. We employed a

parallel convergent mixed-methods approach, combining quantitative analysis of

OOP costs with qualitative interviews. The determinants of OOP payments were

analysed using a two-part cluster-robust regression model. Catastrophic health

spending was defined as OOP payments exceeding 10% of a household's annual

income. Data on OOP spending were recorded via diaries, while qualitative data

were gathered from in-depth interviews with TB and HIV patients and healthcare

workers from January to October 2022. The findings indicated that 5.13% (95% CI:

2.99 to 7.28) of households incurred catastrophically. The median household

spent USD 8.48 OOP, with non-medical expenses comprising the largest share

(median USD 5.93). Key predictors of higher costs included facility location in

Yogyakarta (OOP costs difference USD 23.84, 95% CI: 9.90 to 37.77, P<0.001);

seeking care from public hospitals (USD 17.37, 8.83 to 25.90, P<0.001); and

absence of health insurance (USD 10.49, 2.40 to 18.58, P = 0.011). Patients

reported that job losses during lockdowns exacerbated financial strain, while

coping strategies documented included borrowing, family contributions, and

selling assets. This is the first study to focus on OOP spending and the

financial hardships experienced by TB and HIV patients in Indonesia during the

pandemic, providing insights for targeted policy and preparedness efforts to

alleviate the financial burden during large-scale public health crises.

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The London School of Hygiene and Tropical Medicine.

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**27. J Infect Dis. 2025 Sep 10:jiaf467. doi: 10.1093/infdis/jiaf467. Online ahead of print.**

Rifampin Exposure in Pregnant and Non-Pregnant Women with Tuberculosis in India.

Rao PS(1), Prakash Babu S(2), Ezhumalai K(2), Knudsen S(3), Ramakrishnan J(2),

Joseph N(4), Cintron C(3), Dauphinais MR(3), Narasimhan PB(5), Salgame P(6),

Hochberg NS(3)(7), Hom DL(6), Heysell SK(1), Horsburgh CR Jr(3)(7)(8), Ellner

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This prospective cohort study evaluated rifampin pharmacokinetics in pregnant

and non-pregnant women with tuberculosis in India. Pregnant women had

significantly lower drug exposure, with <20% of the participants achieving

target concentrations at any trimester. Findings highlight potential underdosing

in pregnancy and underscore the need for dedicated pharmacokinetics studies in

pregnancy, and revised rifampin dosing guidelines.

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DOI: 10.1093/infdis/jiaf467

PMID: 40925610

**28. PLoS Biol. 2025 Sep 9;23(9):e3003377. doi: 10.1371/journal.pbio.3003377. Online ahead of print.**

Cathepsin Z is a conserved susceptibility factor underlying tuberculosis

severity.

Meade RK(1)(2), Adefisayo OO(1), Gontijo MTP(1), Harris SJ(1), Pyle CJ(1),

Wilburn KM(1), Ecker AMV(1), Hughes EJ(1)(2), Garcia PD(1), Ivie J(3), McHenry

ML(4), Benchek PH(4), Mayanja-Kizza H(5), Neff JL(6), Ko DC(1)(2), Stout JE(7),

Stein CM(4)(8), Hawn TR(3), Tobin DM(1)(2)(9), Smith CM(1)(2).

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Tuberculosis (TB) outcomes vary widely, from asymptomatic infection to

mortality, yet most animal models do not recapitulate human phenotypic and

genotypic variation. The genetically diverse Collaborative Cross mouse panel

models distinct facets of TB disease that occur in humans and allows

identification of genomic loci underlying clinical outcomes. We previously

mapped a TB susceptibility locus on mouse chromosome 2. Here, we identify

cathepsin Z (Ctsz) as a lead candidate underlying this TB susceptibility and

show that Ctsz ablation leads to increased bacterial burden, pulmonary

inflammation and decreased survival in mice. Ctsz disturbance within murine

macrophages enhances production of chemokine (C-X-C motif) ligand 1 (CXCL1), a

known biomarker of TB severity. From a Ugandan household contact study, we

identify significant associations between CTSZ variants and TB disease severity.

Finally, we examine patient-derived TB granulomas and report CTSZ localization

within granuloma-associated macrophages, placing human CTSZ at the host-pathogen

interface. These findings implicate a conserved CTSZ-CXCL1 axis in humans and

genetically diverse mice that mediates TB disease severity.

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PMID: 40924769

**29. PLoS One. 2025 Sep 9;20(9):e0331958. doi: 10.1371/journal.pone.0331958.**

**eCollection 2025.**

Prevalence and factors influencing drug-resistant tuberculosis in four regions

of Ghana.

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**INTRODUCTION:** The alarming rate of drug-resistant tuberculosis (DR-TB) globally

is a threat to treatment success among positive tuberculosis (TB) cases. Studies

aimed at determining the prevalence, trend of DR-TB and socio-demographic and

clinical risk factors contributing to DR-TB in the four regions of Ghana are

currently unknown. This study sought to determine the prevalence and trend of

DR-TB, identify socio-demographic and clinical risk factors that influence

DR-TB, and analyse the relationship between underweight and adverse drug

reactions and treatment outcomes among DR-TB patients in four regions of Ghana.

**METHOD:** It was a retrospective review conducted over 5 years, from January 2018

to the end of December 2022. The data were retrieved from the DR-TB registers

and folders at the Directly Observed Treatment (DOT) centres in the four

regions. Analysis of the data was conducted using STATA version 17.

**RESULTS:** The prevalence of DR-TB in Ashanti was 10.1%, Eastern 5.3%, 27.8% in

Central, and 2.7% in the Upper West region for the year 2022. The overall

prevalence rate of DR-TB for the period 2018-2022 was 13.8%. The

socio-demographic and clinical risk factors that influence DR-TB in the four

regions are: age, marital status (aOR 3.58, P-value< 0.00, 95% CI 2.86-4.48),

Senior High School (SHS) level of education (aOR 2.09, P-value = 0.01, 95% CI

1.21-3.63), alcohol intake (aOR 0.49, P-value <0.00, 95% CI 0.38-0.63),

previously treated (aOR 22.03, P-value<0.00, CI 16.58-29.26), major adverse drug

reaction (aOR 125.50, P-value<0.00, 95% CI 58.05-271.34), and minor adverse drug

reaction (aOR 23.59, P-value<0.00, 95% CI 18.32-30.39); treatment outcome, cure

(aOR 0.52, P-value<0.00, 95% CI 0.41-0.66), completed (aOR 9.67, P-value<0.00,

95% CI 6.56-14.28), relapsed (aOR 2.62, P-value = 0.01, 95% CI 1.33-5.18),

Lost-to-Follow-up (LTFU) (aOR 0.45, P-value<0.00, 95% CI 0.29-0.70), and failure

(aOR 35.24, P-value<0.00, 95% CI 7.76-159.99). Also, there was an association

between underweight and adverse drug reaction (RRR 5.74, P-value<0.00, 95% CI

4.86-6.79) and treatment outcome (RRR 0.79, P-value<0.00, 95% CI 0.74-0.86).

**CONCLUSION:** The study shows that the prevalence of DR-TB in Ghana is low,

probably not because the cases have reduced but due to inadequate GeneXpert

machines to detect the cases. Age, marital status, education, alcohol intake,

previously treated TB cases, adverse drug reactions, underweight, and treatment

outcome are factors influencing the development of DR-TB. Therefore,

interventions aimed at improving the nutritional status of DR-TB cases and

minimising adverse drug reactions will improve treatment outcomes.

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original author and source are credited.

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PMCID: PMC12419598

PMID: 40924745 [Indexed for MEDLINE]

**30. Infect Immun. 2025 Sep 9:e0040125. doi: 10.1128/iai.00401-25. Online ahead of print.**

Cell death pathways in response to Mycobacterium tuberculosis and other

mycobacterial infections.

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Cell death mechanisms play a fundamental role in mycobacterial pathogenesis. We

critically reviewed 94 research manuscripts, 44 review articles, and 4 book

chapters to analyze important discoveries, background literature, and potential

shortcomings in the field. The focus of this review is the pathogen

Mycobacterium tuberculosis (Mtb) and other Mtb and Mycobacterium avium complex

microorganisms. Virulent strains hijack cell death processes by inhibiting

autophagy, apoptosis, and pyroptosis while eliciting necrosis and ferroptosis to

multiply intracellularly and spread within and between hosts. In addition,

virulent strains may induce apoptosis in epithelial cells or secondary infected

macrophages to spread. Autophagy does not control Mtb intracellular replication

in vivo but suppresses macrophage and T cell responses in Mtb infections, with a

predominant role in preventing neutrophil infiltration. In contrast, attenuated

vaccine strains promote apoptosis in macrophages, leading to the activation of

innate immunity and, eventually, the acquired immune response. Although Mtb

infection activates necroptosis, studies with mutant cell lines have indicated

that this process is not essential for cell lysis and that Mtb promotes

unprogrammed necrosis. Ferroptosis is discussed in the context of necrotic

processes involving lipid peroxidation. Recent research indicated that

pyroptosis is more akin to apoptosis as Mtb proteins induce cell membrane repair

to prevent inflammasome activation. In the supplementary tables, homologs of

mycobacterial cell death pathways and virulence factors were identified using a

basic local alignment search tool protein followed by a conserved domain

database search to determine the presence of functional domains. Finally,

prospects for therapeutic interventions are discussed.

DOI: 10.1128/iai.00401-25

PMID: 40924403

**31. Anesthesiology. 2025 Oct 1;143(4):1137. doi: 10.1097/ALN.0000000000005591. Epub 2025 Sep 9.**

Everything Is Tuberculosis: The History and Persistence of Our Deadliest

Infection.

Johnstone RE(1).

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DOI: 10.1097/ALN.0000000000005591

PMID: 40923839

**32. BMJ Glob Health. 2025 Sep 8;10(9):e019770. doi: 10.1136/bmjgh-2025-019770.**

Taxes for tuberculosis: could tobacco and sugar tax revenue fund tuberculosis

control interventions?

Coleman M(1)(2), Coussens AK(3)(4)(5), Calderwood CJ(6)(7), Schoeman I(8),

Bhargava M(9), Sinha P(10)(11), Marais BJ(2)(12), Kranzer K(13)(6)(7).

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PMCID: PMC12421150

PMID: 40921613

**33. PLoS One. 2025 Sep 8;20(9):e0330345. doi: 10.1371/journal.pone.0330345.**

**eCollection 2025.**

Refining the diagnostic approach to latent tuberculosis Infection with

Quantiferon gold plus: A retrospective analysis of borderline results.

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Spain.

The Quantiferon Gold Plus (QFT) test, a widely used interferon-γ release assay

(IGRA), diagnoses latent tuberculosis infection (LTBI) with a positivity

threshold of ≥0.35 IU/mL. Results near this cut-off can be challenging to

interpret due to variability from immunological, pre-analytical, and technical

factors, prompting recommendations for a borderline range to refine diagnosis

and reduce overtreatment. This retrospective study analyzed QFT results from

9,944 patients (2019-2023), establishing ranges: < 0.2 IU/mL as negative,

0.2-0.35 IU/mL as borderline negative, 0.35-0.7 IU/mL as borderline positive,

and >0.7 IU/mL as positive. Borderline results occurred in 7.6% of patients,

particularly in those born in Africa or South America, and in older individuals.

Of 64 patients retested, 60.9% reverted to negative, while 17.1% of borderline

negatives later converted to positive or borderline positive. Notably, no active

TB cases emerged among those who reverted to negative on repeat testing. These

findings emphasize the need for cautious interpretation of borderline QFT

results, as their link to active TB progression differs from clear results. The

study supports repeat testing of borderline cases to enhance LTBI diagnostic

accuracy and inform treatment decisions.

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PMCID: PMC12416684

PMID: 40920768 [Indexed for MEDLINE]

**34. Clin Infect Dis. 2025 Sep 8:ciaf495. doi: 10.1093/cid/ciaf495. Online ahead of print.**

Cost-effectiveness of Targeted Next Generation Sequencing for TB drug-resistance

testing as an alternative to the standard of care in South Africa.

de Nooy A(1), Omar SV(2), Ockhuisen T(1), Zwerling A(3), Shrestha S(3), Suresh

A(4), Khan S(4), Colman RE(4)(5), Uplekar S(4), Rodwell TC(4)(5), Ismail N(6),

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**BACKGROUND:** South Africa faces emerging resistance to TB drugs like bedaquiline.

Phenotypic drug susceptibility testing (DST), the current reference standard for

bedaquiline DST, has long turnaround times. Targeted next-generation sequencing

(tNGS) offers a comprehensive alternative, potentially delivering faster

results. However, these advantages must be weighed against differences in cost

and test accuracy.

**METHODS:** We used a decision tree model to evaluate the cost-effectiveness of

tNGS against the standard of care (SOC) in South Africa across different levels

of tNGS decentralization. Key outcomes included survival rates, time to a

correct resistance profile, infectious time, and disability-adjusted life years

(DALYs). Sensitivity analyses assessed the impact of drug resistance prevalence,

tNGS sensitivity, and improved DST access on overall cost-effectiveness.

**RESULTS:** tNGS averted 408 DALYs and correctly identified 90.7% of resistance

profiles as compared to 87.7% with SOC. Based on model assumptions for South

Africa, tNGS had a reduced turnaround time and averted 97 years of infectious

time. Centralized tNGS was cost-saving relative to SOC, however decentralization

of tNGS resulted in higher costs per DALY averted ($671- $2,454). tNGS

performance, relative to the SOC, improved at higher bedaquiline resistance and

with increased sensitivity. Any increase in DST access through tNGS would

improve cost-effectiveness in decentralized scenarios.

**CONCLUSIONS:** tNGS could be cost-saving (centralized) or cost-effective

(decentralized) in South Africa and has the potential to improve patient

outcomes by returning a greater number of correct results in a shorter time.

This analysis should be replicated across other settings to evaluate the broader

feasibility of tNGS for DST.

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Infectious Diseases Society of America.

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**35. J Drug Target. 2025 Sep 8:1-35. doi: 10.1080/1061186X.2025.2559006. Online ahead of print.**

"Engineering Rifampicin-Encapsulated Inhalable Microparticles for Precision

Tuberculosis Therapy: In Vivo Distribution and Therapeutic Evaluation".

Tiwari R(1), Jahnavi P(2), Vellingiri D(3), Yadav S(4), Jadhav AB(5), Aparna

TN(6), Sekar V(7), Sharma P(8).

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Tuberculosis (TB) continues to cause significant global mortality, highlighting

the need for improved drug delivery systems. The objective of this paper focuses

in describing the formulation, optimization and in vivo assessment of rifampicin

encapsulated PLGA microparticles for site-specific inhalation therapy.

Microparticles for inhalation were produced by spray drying, and the DoE

methodology was applied to reach the most suitable aerodynamic properties (mass

median aerodynamics diameter (MMAD) 2.5 µm, fine particle fraction (FPF) 62%).

Microparticles encapsulation of rifampicin led to prolongation of the pulmonary

residence time both in BALB/c mice and Wistar rats and was 2.4 times higher than

the concentration of the free oral rifampicin. Further, via Computational Fluid

Dynamics (CFD) simulations and the use of AI-determined predictive modeling,

aerosol deposition was maximized at an inhalation flow rate of 30L/min targeting

the alveolar region indicated by having 52.8% of the aerosol deposition at this

region. The TB-infected mice, which showed the lung tissue bacterial load was

reduced to 3.2 log colony forming unit (CFU) and the levels of TNF-α were

decreased while IL-10 levels were increased. With this kind of accelerated

stability testing it was ascertained that the type of formulation had a

shelf-life of 24 months.

DOI: 10.1080/1061186X.2025.2559006

PMID: 40919741

**36. Trans R Soc Trop Med Hyg. 2025 Sep 8:traf086. doi: 10.1093/trstmh/traf086.**

**Online ahead of print.**

Social inequalities as effect modifiers of active case-finding strategies for

tuberculosis in Brazil: an ecological study.

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**BACKGROUND:** Social inequalities play a crucial role in the incidence of TB,

making it plausible that they act as effect modifiers on the impact of active

case-finding (ACF) strategies in the detection of the disease. We estimated the

association between ACF strategies and TB detection rates and evaluated their

effect modification due to social inequalities in Brazilian municipalities.

**METHODS:** We included 5033 municipalities that reported at least one new TB case.

We defined the TB detection rate as the outcome variable. Our exposure variables

were the proportion of primary care team (PCT) reporting community-based ACF for

TB and household contact investigation (HCI) of new TB cases. We also assessed

the Municipal Human Development Index (MHDI) and the Social Vulnerability Index

(SVI) as potential effect modifier variables.

**RESULTS:** The TB detection rate was positively associated with both the

proportion of PCTs conducting community-based ACF and the proportion conducting

HCI. These associations weakened as MHDI increased (interaction incident rate

ratio [IRR] 0.95, 95% CI 0.90 to 0.98 for ACF; IRR 0.93, 95% CI 0.89 to 0.96 for

HCI) and strengthened with higher SVI values (IRR 1.11, 95% CI 1.02 to 1.22 and

IRR 1.17, 95% CI 1.08 to 1.27, respectively).

**CONCLUSION:** Social inequalities in Brazilian municipalities modify the effect of

ACF strategies on TB detection rates.

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DOI: 10.1093/trstmh/traf086

PMID: 40916767

**37. Toxicol Mech Methods. 2025 Sep 8:1-32. doi: 10.1080/15376516.2025.2554918.**

**Online ahead of print.**

Unveiling the molecular toxicity of Isoniazid and Rifampicin in tuberculosis

therapy: emerging insights and therapeutic strategies.

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Tuberculosis, caused by Mycobacterium tuberculosis, persists as a significant

worldwide health issue, resulting in millions of infections and fatalities each

year. Treatment predominantly depends on first-line antibiotics, including

Isoniazid (INH) and Rifampicin (RIF). Nevertheless, extended use of these

medications is linked to considerable adverse effects, leading to various organ

toxicities, especially hepatotoxicity and nephrotoxicity. INH causes liver and

kidney damage by pathways that include oxidative stress, mitochondrial

malfunction, and inflammation. RIF induces organ damage by blocking

drug-metabolizing enzymes, facilitating lipid peroxidation, and triggering

apoptosis and cholestasis. Although both medications are crucial in TB

treatment, their synergistic effect on organ damage remains little comprehended.

RIF is recognized for exacerbating INH-induced hepatic damage by increasing

CYP2E1 metabolism, indicating intricate interactions. This study analyses the

molecular toxicity processes generated by INH and RIF, summarizes current

clinical and experimental data, and investigates the preventive potential of

natural substances, such as antioxidants and phytochemicals. It also explores

alternative treatment techniques, nanobiotechnology designed to mitigate

drug-induced organ toxicity by giving protective agents at the same time and

targeting specific mechanisms. This review presents an innovative viewpoint on

the management of INH and RIF toxicity and underscores potential avenues for

further research.

DOI: 10.1080/15376516.2025.2554918

PMID: 40916634

**38. J Clin Med. 2025 Aug 24;14(17):5980. doi: 10.3390/jcm14175980.**

History of Pulmonary Tuberculosis Accelerates Early Onset and Severity of COPD:

Evidence from a Multicenter Study in Romania.

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MA(7)(8), Andrei GM(1), Biciusca V(1), Olteanu M(1)(2).

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Bucharest, Romania.

**Background:** Pulmonary tuberculosis (TB) is increasingly recognized as a risk

factor for chronic obstructive pulmonary disease (COPD), but its impact on COPD

onset and severity remains poorly characterized, particularly in low- and

middle-income countries. This multicenter study aimed to assess the impact of

prior pulmonary TB on COPD onset, severity, the timing of the first severe

exacerbation, and progression among Romanian patients with and without a history

of pulmonary TB. **Methods:** This retrospective multicenter study included adults

hospitalized for their first severe COPD exacerbation at two tertiary care

centers in Romania between April 2020 and April 2025. Patients were grouped

based on smoking status and prior TB history. Propensity score matching was used

to control for confounding factors. Clinical characteristics, spirometry, and

radiological TB patterns were analyzed comparatively between patients with prior

TB and TB-naïve patients. **Results:** Among 403 COPD patients, those with prior TB

had significantly earlier COPD onset (mean age 48.67 ± 6.42 vs. 65.61 ± 5.14

years in smokers, p < 0.001) and shorter intervals to their first severe COPD

exacerbation compared to patients without prior TB (6.35 ± 4.71 vs. 15.14 ± 6.93 years in smokers, p < 0.001). COPD prevalence was higher among TB survivors

compared to those without TB history, especially in smokers (OR = 5.73; 95% CI,

3.30-9.94, p < 0.001), versus non-smokers (OR =2.23; 95% CI, 1.37-3.64, p =

0.001). Radiological severity of TB lesions significantly influenced COPD

prevalence among smokers (OR = 10.79, p < 0.001). **Conclusions:** Prior pulmonary

TB substantially accelerates COPD onset, exacerbation timing, and disease

severity, particularly in smokers. This multicenter comparative study

demonstrates that prior pulmonary TB significantly accelerates COPD onset,

exacerbation timing, and disease severity, especially among smokers. Recognizing

TB history as a significant COPD risk factor underscores the importance of

targeted COPD screening and tailored management in populations with high TB

prevalence.

DOI: 10.3390/jcm14175980

PMCID: PMC12429621

PMID: 40943740

**39. J Clin Med. 2025 Aug 22;14(17):5949. doi: 10.3390/jcm14175949.**

The Impact of Social Factors on the Duration of Hospitalization for

Tuberculosis.

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**Introduction:** Tuberculosis (TB) predominantly affects older adults in Japan, and

prolonged hospitalization remains a challenge. This study evaluated both

clinical and social factors influencing hospitalization duration. **Methods:** We

retrospectively analyzed 203 patients with smear-positive pulmonary TB admitted

to NHO Wakayama Hospital (2017-2022). Stepwise multiple regression was used to

identify factors associated with hospitalization duration**. Results:** Key factors

included time to smear negativity, duration from isolation release to discharge,

independence in daily life, and discharge destination. Prolonged stays were

often due to social issues, such as difficulties in arranging transfers to

long-term care homes or family acceptance. **Conclusions:** While Japan is

developing new discharge criteria based on clinical indicators, our findings

highlight the significant impact of non-clinical, social factors on

hospitalization duration. Addressing these factors is essential for effective

discharge planning.

DOI: 10.3390/jcm14175949

PMCID: PMC12429506

PMID: 40943708

**40. Int J Mol Sci. 2025 Sep 2;26(17):8531. doi: 10.3390/ijms26178531.**

Structure-Function Analysis of Mycobacterium tuberculosis Drug Target Cytochrome

P450 125 (CYP125) Enzyme Family.

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Tuberculosis, the deadliest human lung disease caused by Mycobacterium

tuberculosis, continues to be a global health threat, and finding new drugs and

drug targets seems an ongoing battle. The cytochrome P450 CYP125A1 enzyme of M.

tuberculosis H37Rv, which is involved in cholesterol metabolism, is a

well-established target for drug development. Research is ongoing to identify

new compounds that target this enzyme. Understanding the structure-activity

relationship of CYP125 family members is crucial for developing a specific and

efficient inhibitor. In this direction, this study analyzed 21 crystal

structures of CYP125 family enzymes, unraveling the factors responsible for

substrate specificity and the amino acids that play a key role in catalysis. One

of the unique features of CYP125A1 is its active site cavity shape, which

determines the specificity of substrates and inhibitors. The active site cavity

is shaped like a letter box, lined by hydrophobic residues, and it transitions

into a funnel-like shape with a progressive narrowing as it approaches the heme.

Due to this shape, the cholesterol and cholest-4-en-3-one serve as substrates,

but not androstenedione, as the former molecules have an alkyl side chain that

extends down the narrow funnel channels, interacting with the heme iron.

Different binding patterns were observed for substrates and indole-derived

inhibitors. Both type I and type II interactions were observed with the

non-azole P450 inhibitor LP10 and indole-derived compounds, where the side chain

of the indole-derived compound determined the type of interaction. This study

provides a comprehensive understanding of the structure-function analysis of

P450 enzymes and the interactions of CYP125A members with various ligands. Our

findings pave the way for designing new and specific CYP125A1 inhibitors that

will ultimately be developed into novel anti-TB drugs.

DOI: 10.3390/ijms26178531

PMCID: PMC12429392

PMID: 40943450

**41. Int J Mol Sci. 2025 Aug 22;26(17):8117. doi: 10.3390/ijms26178117.**

Paradoxical Use of Benralizumab in Reactive Hypereosinophilia from Toxocariasis

and Tuberculosis Co-Infection-Case Report and Literature Review.

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Tuberculosis and parasitic infections, including Toxocara, frequently coexist in

many regions worldwide, yet their interaction remains poorly understood.

Tuberculosis triggers a type 1 immune response characterized by IL-12, IFN-γ,

and TNF-α production, while toxocariasis elicits a type 2 response, mediated by

cytokines such as IL-4, IL-5, IL-13, and IL-33. The coexistence of these

divergent immune pathways can disrupt immune regulation and impair the host's

ability to control both infections, potentially leading to persistent

hypereosinophilia. We illustrate this complex interplay through a real-world

case involving a heavy smoker in whom Toxocara infection likely reactivated

latent tuberculosis, resulting in severe, unexplained hypereosinophilia and

late-onset asthma with recurrent exacerbations. After excluding other causes and

completing full antituberculosis therapy along with three courses of

antiparasitic treatment and systemic corticosteroids, hypereosinophilia

persisted. The introduction of benralizumab, a biologic therapy targeting

IL-5Rα, led to a rapid reduction in eosinophils to normal ranges and significant

clinical improvement. This case underscores the diagnostic and therapeutic

challenges posed by the intersection of common infections and highlights that

even a neglected parasitic infection such as toxocariasis can underlie severe

respiratory complications with eosinophilia, where paradoxically biologic

therapy may ultimately provide a very effective intervention.

DOI: 10.3390/ijms26178117

PMCID: PMC12428141

PMID: 40943043

**42. Diagnostics (Basel). 2025 Aug 28;15(17):2183. doi: 10.3390/diagnostics15172183.**

Development of SNP-LAMP Combined with Lateral Flow Dipstick to Detect the S531L

rpoB Gene Mutation in Rifampicin-Resistant Mycobacterium tuberculosis.

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Thailand.

**Background:** Tuberculosis (TB) remains a primary global health concern, despite

the widespread availability of effective chemotherapeutic interventions. The

emergence and dissemination of drug-resistant strains of Mycobacterium

tuberculosis, particularly those exhibiting resistance to rifampicin, present

significant obstacles to the success of TB control programs. Consequently, there

is an urgent need for rapid, sensitive, and specific molecular diagnostic tools

to inform timely clinical decision-making and reduce the transmission of

disease. Loop-mediated isothermal amplification (LAMP) has gained attention as a

promising alternative to conventional polymerase chain reaction (PCR)

techniques. This method, which facilitates DNA amplification under constant

temperature conditions, offers advantages including high specificity, rapid

turnaround time, and operational simplicity-features that render it especially

suitable for implementation in resource-limited settings. **Methods:** In this

study, a LAMP assay targeting the rpoB gene was developed, with particular focus

on detecting the codon 531 C→T mutation associated with rifampicin resistance. A set of four to six primers was designed to recognize six distinct regions of the target sequence. Allele-specific amplification was achieved by incorporating a deliberate single nucleotide mismatch at the 3' terminus of the B2 primer to

enable precise discrimination between wild-type and mutant alleles. The assay

was conducted at an optimized temperature of 61 °C for 60 min, followed by

visual detection using a lateral flow dipstick (LFD) within five minutes.

**Results:** The LAMP-LFD assay demonstrated 100% concordance with drug

susceptibility testing (DST) and DNA sequencing. No cross-reactivity with

wild-type strains was observed, underscoring the assay's high specificity.

**Conclusions:** This platform offers a robust, field-deployable solution for

detecting the codon 531 C→T mutation associated with rifampicin resistance in

low-resource settings.

DOI: 10.3390/diagnostics15172183

PMCID: PMC12428009

PMID: 40941669

**43. Healthcare (Basel). 2025 Aug 26;13(17):2120. doi: 10.3390/healthcare13172120.**

Perceived Stigma and Associated Factors Among Patients with Tuberculosis and

Their Families in Jazan Region, Saudi Arabia.

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**Background:** Stigma is a major barrier to tuberculosis (TB) control worldwide.

However, there is limited evidence of TB-related stigma not only toward patients

but also toward their family members in Saudi Arabia. This study aims to assess

the level of TB-related stigma and associated factors among individuals with TB

and their families in Jazan, Saudi Arabia. **Methods:** A cross-sectional survey was

conducted among 404 participants (272 adult patients with TB and their 132

family members). Participants were interviewed using a structured questionnaire

adapted from validated TB-related stigma scales, covering sociodemographic

factors and perceived stigma. Sociodemographic factors were used to compare

stigma grades. Collected data were analyzed using the Statistical Package for

the Social Sciences. Frequencies and percentages were used to describe

qualitative variables, while the χ2-test was applied to compare TB-related

stigma levels according to demographic factors. p < 0.05 was considered

statistically significant. **Results**: Most participant patients had pulmonary TB

(78.7%), while 21.3% had extrapulmonary TB. More than half of them (50.7%)

experienced severe stigma, while 23.5% had mild stigma. Levels of TB-related

stigma differed significantly according to the patients' age groups (p = 0.011),

residence (p < 0.001), occupation (p = 0.022), and type of TB, which was higher

among those with pulmonary TB (p = 0.003). Moreover, 24.2% of family members

experienced severe stigma, while 25% had mild stigma. Perceived stigma showed a

negative impact on the management of TB. Levels of stigma differed significantly

among family members according to their residence (p < 0.001) and marital status

(p = 0.018). **Conclusions:** TB-related stigma is widespread among individuals with

TB and their family members in Saudi Arabia. This stigma has significant

negative impacts on the management of TB. Levels of perceived stigma are higher

among younger patients, those living in urban areas, unemployed patients, and

patients with pulmonary TB. Among family members, the stigma levels are higher

for those living in urban areas and single individuals.

DOI: 10.3390/healthcare13172120

PMCID: PMC12428549

PMID: 40941472

**44. Healthcare (Basel). 2025 Aug 22;13(17):2093. doi: 10.3390/healthcare13172093.**

Strengthening Clinical Governance and Public Health Interventions to Improve

Drug-Resistant Tuberculosis Outcomes in Rural South Africa.

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**Background/Objectives:** Drug-resistant tuberculosis (DR-TB) presents significant

challenges to public health, particularly in rural South Africa, where limited

infrastructure, high HIV co-infection rates, and weak clinical governance

contribute to poor treatment outcomes. This study evaluates treatment

trajectories and the impact of clinical governance and public health

interventions on DR-TB outcomes in the rural Eastern Cape**. Methods:** A

retrospective cohort study was conducted among 323 laboratory-confirmed DR-TB

patients treated between 2018 and 2021. Kaplan-Meier curves and Cox proportional

hazards analysis identified predictors of unfavorable outcomes. Logistic

regression analysis simulated the impact of enhanced clinical governance

scenarios on treatment success. **Results:** Treatment outcomes included cure

(36.2%), completion (26.0%), loss to follow up (LTFU) (9.0%), death (9.3%),

failure (2.2%), and transfer (9.3%). The median treatment duration was 10 months

(IQR: 9-11). Survival analysis indicates the highest risk of death and LTFU

occurred in the first 6-8 months of treatment. Multivariate Cox regression

revealed that primary (HR = 0.39; 95% CI: 0.23-0.68; p = 0.0017) and secondary

education (HR = 0.50; 95% CI: 0.31-0.85; p = 0.0103) were significantly

protective. Paradoxically, patients with pre-XDR (HR = 0.13; p = 0.034) and XDR

TB (HR = 0.16; p = 0.043) showed lower hazard of poor outcomes, likely due to

early mortality or referral. HIV-negative status was associated with higher risk

of poor outcomes (HR = 1.74; p = 0.010). Simulations suggested that improved

clinical governance via better follow-up, TB/HIV integration, and adherence

support could improve treatment success by up to 20 percentage points in

high-impact scenarios. **Conclusions:** Strengthening clinical governance through

targeted interventions could substantially reduce LTFU and mortality, especially

in vulnerable subgroups. A coordinated, patient-centered approach is critical

for improving DR-TB outcomes in rural, high-burden settings.

DOI: 10.3390/healthcare13172093

PMCID: PMC12428479

PMID: 40941444

**45. Animals (Basel). 2025 Sep 2;15(17):2580. doi: 10.3390/ani15172580.**

Fetal Bovine Serum Supplementation Enhances Functional Consistency of IGRA

Results in Bovine Tuberculosis Diagnostics.

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The interferon-gamma release assay (IGRA) is a reliable diagnostic tool for

bovine tuberculosis (bTB) due to its high sensitivity and specificity. However,

the assay relies on viable T-cell function, making it susceptible to

functionally undetectable responses during sample storage. This study aimed to

evaluate whether fetal bovine serum (FBS) supplementation could mitigate

functional deterioration and stabilize immune responses in stored blood samples.

The IGRA was conducted on blood samples from 91 cattle under three conditions:

fresh (Day 0), stored without FBS (FBS X), and stored with 10% FBS (FBS O). A

dual stimulation using bovine PPD (bovis) and mitogen revealed that the FBS O

condition significantly preserved IFN-γ responses, with a higher frequency of

simultaneous bovis and mitogen recovery (dual recovery). Additional correlation

analysis between MTT cell viability and mitogen response further suggested that

FBS contributes to T-cell functionality beyond survival. These findings suggest

that FBS supplementation improves the functional consistency of IGRA results and

reduces the risk of functionally undetectable responses in delayed testing

scenarios.

DOI: 10.3390/ani15172580

PMCID: PMC12427214

PMID: 40941374

**46. Diagn Microbiol Infect Dis. 2025 Sep 7;114(1):117102. doi:**

**10.1016/j.diagmicrobio.2025.117102. Online ahead of print.**

Comparison between Xpert ultra and standard M10 for detection of MTBC in

clinical samples.

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This study compared the STANDARD M10 MDR-TB with GeneXpert® MTB/RIF Ultra test

in detecting tuberculosis on 57 samples. Sensitivity and specificity were 92 %

and 100 % with a positive predictive value of 100 % with a substantial agreement

(0.74) at Kappa agreement test.

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PMID: 40939481

**47. J Public Health Afr. 2025 Aug 6;16(1):1265. doi: 10.4102/jphia.v16i1.1265.**

**eCollection 2025.**

The use of lateral flow lipoarabinomannan for diagnosis of TB in advanced HIV

disease in Abia State, Nigeria.

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Abuja, Nigeria.

**BACKGROUND:** Lateral flow lipoarabinomannan (LF-LAM) test used in the diagnosis

of active tuberculosis (TB) among patients with advanced human immunodeficiency

virus (HIV) disease remains a relatively new approach in the diagnosis of TB in

Nigeria. This study focused on the use of LF-LAM assay Alere Determine™ in the

diagnosis of active tuberculosis among patients with advanced HIV disease in

Abia State.

**AIM:** This study was carried out to identify potential gaps that could be missed

along the LF-LAM implementation cascade, which can be strengthened to improve

quality of patients' care, while gaining insight into health workers'

understanding of the test.

**SETTING:** This study was carried out in Abia State, Nigeria.

**METHODS:** Electronic data were extracted through a query run on health facility

electronic databases, while manual chart abstraction was performed in facilities

without and incomplete electronic medical records. In addition, qualitative

interviews were conducted among health workers to gain insight.

**RESULTS:** Out of 1249 newly enrolled patients who were eligible for the test,

only 605 (48.4%) were tested, and 644 (51.6%) were missed within the study

period (October 2022 - September 2023). Out of this number, 159 (26.3%) were

positive for the test, and only 68 (42%) were sent for further testing with

GeneXpert, while 30 (18.9%) had no testing with GeneXpert and 61 (38.9%) had no

documentation.

**CONCLUSION:** Low awareness and capacity among health workers including poor

documentation practices contributed to missed opportunities for the patients who

could have benefitted from this test.

**CONTRIBUTION:** The study recommends comprehensive training of healthcare workers

on the utilisation of LF-LAM test and improvement of documentation practices in

Abia State and Nigeria.

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DOI: 10.4102/jphia.v16i1.1265

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**48. Public Health Action. 2025 Sep 3;15(3):124-128. doi: 10.5588/pha.25.0021.**

**eCollection 2025 Sep.**

Implementing standardised community-based service package to improve TB outcomes

in six countries.

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**BACKGROUND:** Although the need for community-based support services as part of TB

care is reaffirmed in various strategies, there are no data on the

implementation progress of the recommended standardised package of

community-based support services to improve TB outcomes developed by a

consortium of partners in 2021.

**METHODS:** The study describes country adaptation and initial planned

implementation of the community-based packages in six countries of Eastern

Europe and Central Asia - Azerbaijan; the Republic of Belarus (Belarus); the

Kyrgyz Republic (Kyrgyzstan); the Republic of Moldova (Moldova); Tajikistan; and

Ukraine - using programme review and qualitative data.

**RESULTS:** An analysis of the package adaptation and initial implementation is

presented from the perspective of the country implementers with a focus on

country-specific approaches and lessons learned. The analysis framework is

focused on the following specific areas: 1) adaptation practices; 2) ensuring

quality and supervision of the services; and 3) securing funding. Commonalities

and differences in each of these areas are analysed.

**CONCLUSION:** In all countries, standardised community-based service packages were

adapted and gradually introduced to support clinical TB care. Proper costing and

monitoring of the services delivered at the community levels and integrating the

budgeted packages into national TB programmes are recommended to ensure

sustainability.

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**49. Public Health Action. 2025 Sep 3;15(3):97-102. doi: 10.5588/pha.25.0004.**

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Decentralising DR-TB care: the trade-off between quality of care and service

coverage in the early phase of implementation.

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**BACKGROUND:** A policy of decentralised care for drug-resistant TB (DR-TB) was

introduced in South Africa in 2011. We describe a trade-off between increasing

coverage of services and poor quality of care, in the early phase of policy

implementation.

**METHODS:** This was a mixed methods case study, comparing implementation in

KwaZulu-Natal and Western Cape provinces; with interviews and quantitative

analysis of routine DR-TB programme data. We analysed qualitative data,

thematically organizing findings into inputs, processes, and outputs to explore

how decentralisation influenced quality of DR-TB care.

**RESULTS:** Decentralisation of DR-TB care expanded access across provinces but

there was wide variation in pace, planning and structural readiness. Where rapid

scale-up outpaced capacity-building, weaknesses in resourcing, workforce, and

clinical governance compromised quality of care. Two illustrative examples

highlight that decentralisation to inadequately resourced sites resulted in

morbidity to patients who did not receive effective monitoring for adverse

events; and decentralising services to inadequately capacitated clinicians

resulted in incorrect initiation in more complex cases and late referral of

clinical complications.

**CONCLUSIONS:** Attempts to decentralise DR-TB treatment in the context of complex

treatment algorithms and limited health system capacity resulted in trade-offs

of care quality. We argue that quality of care should be an essential

consideration in early implementation of health programmes.

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**50. Public Health Action. 2025 Sep 3;15(3):108-112. doi: 10.5588/pha.24.0054.**

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Impact of social franchising on TB contact investigation and uptake of TB

preventive therapy.

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**BACKGROUND:** TB continues to pose significant public health challenges in

high-burden regions such as Kano State, Nigeria, where private health sector

engagement in TB control is notably lacking. The Social Franchising for TB

Contact Investigation (SOFT) model was introduced to leverage private healthcare

to increase the reach and efficacy of TB control efforts.

**METHODS:** This nine-month project supported mapping health facilities, training

of community health workers and systematic TB contact screening. The SOFT model

aimed to enhance TB control by integrating private healthcare facilities and

community-based organisations to improve TB yield, contact investigation and

uptake of TB Preventive Therapy (TPT).

**RESULTS:** The project showed a consistent increase in TB case detection, with a

significant rise in index TB cases identified and their contacts screened each

quarter. There was also a marked increase in the number of household contacts

screened and initiated on TPT, demonstrating the model's effectiveness in

enhancing TB control efforts.

**CONCLUSION:** The integration of social franchising with community and private

healthcare engagement presents a scalable and innovative approach to improving

TB control in high-burden settings. This model contributes significantly to

global TB elimination efforts by improving detection rates and TPT uptake.

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**51. Public Health Action. 2025 Sep 3;15(3):118-123. doi: 10.5588/pha.25.0015.**

**eCollection 2025 Sep.**

Role of triage audit in an ongoing differentiated TB care initiative to reduce

deaths in Tamil Nadu, India.

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**OBJECTIVE:** In the ongoing India's first state-wide differentiated TB care

programme in Tamil Nadu (TN-KET), adults diagnosed with drug-sensitive TB at

public facilities undergo triage. The adults with severe undernutrition,

respiratory insufficiency, or poor performance status are prioritised for

comprehensive assessment and inpatient care. Although the programme met triage

coverage targets, 11 districts failed to achieve the goal of a 30% reduction in

TB death rates. This study compares aggregate triage coverage with actual

coverage and evaluates the quality of programme-reported triaging data against

an investigator-led audit (repeat assessments in the field) within a few weeks

of diagnosis.

**DESIGN:** An ecological study using routine programme data (April 2022-June 2024)

was conducted for the first objective, and a cross-sectional analytical study

with primary and secondary data (August 2024-February 2025) was performed for

the triage audit.

**RESULTS:** Among 48,905 adults with drug-sensitive TB notified, the true triage

coverage was 84% against the reported triage coverage of 113%. The triage audit

showed 35.7% were triage-positive, compared with 27.6% through TB SeWA (Severe

TB Web Application). The mean weight and body mass index from the audit were

0.82 kg and 0.63 kg/m2 lower than TB SeWA data, and oedema was unassessed in 65%

of the adults with TB.

**CONCLUSION:** The districts need to address inadequate triage coverage and

suboptimal quality of triaging.

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**52. Public Health Action. 2025 Sep 3;15(3):129-134. doi: 10.5588/pha.25.0011.**

**eCollection 2025 Sep.**

Improving TB care services among coal mine workers and their associated

communities in Pakistan.

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**SETTING:** Five major coal mining districts in Balochistan, Pakistan.

**OBJECTIVES:** To assess burden of TB among coal miners and their associated

communities and establish linkages with TB care services.

**DESIGN:** A cross-sectional study was conducted to find TB cases through active

case finding. The target population included people working at coal mining sites

and surrounding communities residing within 10 km, including coal miners'

families and other individuals. Verbal symptom screening was carried out via

mobile camps and community outreach. Sputum was collected from screened positive

individuals and tested for TB on GeneXpert. TB cases diagnosed were linked with

TB care services.

**RESULTS:** A total of 14,541 individuals including 8,149 (56%) coal miners were

screened. Of the people screened, 81% were male, median age was 31 years, 2,274

(15.6%) had TB symptoms, and 34 confirmed TB cases were diagnosed. All 34 TB

patients were linked to care and 32 completed treatments successfully. The

estimated TB prevalence was 234 cases per 100,000 population (95% confidence

interval: 150.6-316.5), with no significant difference between coal miners and

associated communities.

**CONCLUSION:** Similar TB prevalence among coal miners and associated communities

reflects shared vulnerability. Use of more sensitive screening tools is

recommended to validate prevalence estimates in future studies.

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**53. Public Health Action. 2025 Sep 3;15(3):113-117. doi: 10.5588/pha.24.0044.**

**eCollection 2025 Sep.**

Knowledge, enablers, and barriers to TB preventive treatment among health care

workers.

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**BACKGROUND:** As part of its TB control efforts, the Nigeria National TB Program

has prioritised implementation of TB preventive treatment (TPT) especially among

all contacts of TB patients. This study aims to assess knowledge, perceived

enablers, and barriers to TPT among health care workers (HCWs) in Nigeria.

**METHODS:** This was a cross-sectional descriptive study using mixed methods.

Quantitative data were collected from 434 HCWs and analysed using SPSS version

25, and in-depth interviews were conducted on 36 purposely selected HCWs with

thematic analysis.

**RESULT:** More than half of the respondents (55.7%) had good knowledge of TPT.

Nurses, doctors, and other HCWs working in public tertiary institutions had

better knowledge compared with other cadres. Adequate knowledge of types of TPT

regimens and belief in their effectiveness were elicited as enablers, whereas

barriers included suboptimal contact tracing system, TPT stock-outs, long

duration of TPT, unavailability of TB infection testing before TPT, absence of

transport logistics support for patients to receive TPT, and poor HCW capacity.

**CONCLUSION:** HCWs in public tertiary settings had better knowledge of TPT.

Successful scale-up of TPT services requires competency building for other

cadres and interventions addressing other identifiable barriers.

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**54. Public Health Action. 2025 Sep 3;15(3):103-107. doi: 10.5588/pha.25.0017.**

**eCollection 2025 Sep.**

Implementation of BMI field charts for nutritional assessment in adult patients

with tuberculosis in Karnataka.

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**BACKGROUND:** We tested the operational feasibility of body mass index (BMI) field

charts in nutritional assessment of adult patients with tuberculosis (PwTB),

which obviate calculations and provide nutritional status based on BMI and the

ideal weight (BMI = 21 kg/m2).

**METHODS:** We trained primary health care providers (HCPs) in 39 primary health

centres for nutritional assessment and classification and identifying the ideal

weight using BMI field charts in PwTB. Using the descriptive statistics method,

we analysed the collected data and reported the nutritional status in PwTB and

the uptake of the field charts among the HCPs.

**RESULTS:** The median (interquartile range [IQR]) weight and BMI were 44 kg (37.0,

50.0) and 16.9 kg/m2 (15.2, 18.9), respectively, in 214 PwTB, of which 146

(68.2%) patients had a BMI of <18.5 kg/m2. The HCPs documented the ideal weight

in 155 (72.4%) patients, which was correct in 147 (94.8%) patients. The median

(IQR) weight deficit to achieve the ideal weight was 10.4 kg (7.3, 12.8) in men

and 11.9 kg (7.0, 17.9) in women. For a BMI of 18.5 kg/m2, the deficit was 6.4

kg (3.4, 8.5) in men and 11.3 kg (4.6, 13.6) in women.

**CONCLUSION:** The magnitude and severity of undernutrition in adult PwTB in a

well-performing district of Karnataka in South India were high. A single

training session successfully improved nutritional assessment and BMI field

chart usage among the primary HCPs.

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**55. Public Health Action. 2025 Sep 3;15(3):140-141. doi: 10.5588/pha.25.0023.**

**eCollection 2025 Sep.**

Clinical diagnosis of TB: further examples of under- and over-diagnosis.

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**56. Public Health Action. 2025 Sep 3;15(3):137-139. doi: 10.5588/pha.25.0010.**

**eCollection 2025 Sep.**

Use of trained African giant pouched rats as a predictor of clinical diagnosis

of pulmonary TB.

Soka J(1), Mwimanzi S(1), Fast CD(1)(2), Mwesiga G(1), Edward N(1), Stephen

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For over a decade, trained African giant pouched rats have been employed in

detecting missed pulmonary TB (PTB). However, the relationship between

rat-positive results and subsequent clinical PTB or extrapulmonary TB (EPTB) has

not been previously reported. This report highlights the use of rat-positivity

as a predictor for PTB clinical diagnosis and treatment among presumptive TB.

Treating physicians were 1.39 times more likely to clinically diagnose and treat

rat-positives than rat-negatives: 12% versus 9%, respectively, odds ratio=1.39,

95% confidence interval: 1.05-1.84. No difference was observed among EPTB.

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**57. Front Immunol. 2025 Aug 27;16:1664398. doi: 10.3389/fimmu.2025.1664398.**

**eCollection 2025.**

Effect of co-vaccination of cattle with RB51 and BCG on vaccine-specific CD4(+)

T cell responses.

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**INTRODUCTION:** Brucella abortus and Mycobacterium bovis, the causative agents of

bovine brucellosis and tuberculosis respectively, are zoonotic bacterial

pathogens that both contribute to major economic losses in the cattle industry

and pose a human health risk worldwide. Co-infections of cattle with B. abortus

and M. bovis have been identified in various developing countries, necessitating

the development of an efficacious strategy for controlling both important

zoonotic diseases even in the event of co-infection. Brucella abortus strain

RB51, a live attenuated vaccine for bovine brucellosis that is currently used in

the US, is highly effective at preventing reproductive failure due to

brucellosis in cattle. Bacillus Calmette-Guérin (BCG) is a live attenuated

vaccine strain of M. bovis that provides protection against bovine tuberculosis

in cattle but is not currently licensed for use in the US.

**METHODS:** The study presented here compares functional Th1 responses of RB51 +

BCG vaccinated cattle to responses of RB51-only and BCG-only vaccinated cattle

to evaluate the feasibility of a combined vaccination strategy for controlling

both bovine brucellosis and tuberculosis.

**RESULTS:** This work identified that peripheral blood mononuclear cells (PBMC)

from RB51 vaccinates proliferate not only in response to stimulation with killed

RB51 but also in response to mycobacterial antigen PPDb. Combination vaccinates

show significantly more CD4+ T cell proliferation than single BCG vaccinates

when stimulated with PPDb, while no differences were observed between RB51 and

combination vaccinates stimulated with RB51.

**DISCUSSION/CONCLUSION:** Significantly enhanced BCG-specific Th1 responses in

combination vaccinates compared to BCG-only vaccinates suggest that combining

vaccinations for B. abortus and M. bovis may alter the host CD4+ T cell

response.

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DOI: 10.3389/fimmu.2025.1664398

PMCID: PMC12420227

PMID: 40936934

**58. J Orthop Case Rep. 2025 Sep;15(9):188-193. doi: 10.13107/jocr.2025.v15.i09.6064.**

Total Knee Arthroplasty in Tuberculous Arthritis of the Knee - A Case Report.

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**INTRODUCTION:** Tuberculosis (TB) remains a significant global health challenge,

with 10.6 million new cases and 1.3 million deaths reported in 2022.

Extrapulmonary TB accounts for approximately 16% of all cases, with

osteoarticular TB being a notable subset. Tubercular arthritis of the knee is a

rare manifestation, often misdiagnosed due to its atypical presentation. Total

knee arthroplasty (TKA) is considered the treatment of choice in advanced cases;

however, evidence on outcomes in cases with incidental tubercular findings

remains limited. This report highlights a case of tubercular arthritis of the

knee diagnosed incidentally and evaluates the clinical outcomes following TKA.

**CASE REPORT:** A 55-year-old female patient of South Asian descent presented with

progressive left knee pain and restricted range of motion. Clinical and

radiological investigations revealed signs of inflammatory pathology, including

elevated serum markers and imaging findings consistent with arthritis.

Histopathological examination of the synovial tissue confirmed tubercular

arthritis. The patient underwent surgical debridement followed by TKA.

Postoperatively, the patient demonstrated significant functional improvement and

was closely monitored over a 2-year follow-up period, with no recurrence of

infection or prosthesis-related complications.

**CONCLUSION:** The atypical presentation of tubercular arthritis of the knee poses

a diagnostic challenge and carries a high risk of mismanagement if not properly

evaluated. This case underscores the importance of thorough radiological and

histopathological assessments for accurate diagnosis. Our findings suggest that

a combined approach of debridement and TKA offers effective results, minimizing

the risk of post-operative complications, including periprosthetic joint

infections. This report adds valuable evidence to the orthopedic literature,

demonstrating that TKA is a viable option for managing tubercular arthritis of

the knee, which provided that the diagnosis is confirmed, and appropriate

surgical and medical protocols are followed.

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**59. J Public Health Afr. 2025 Aug 30;16(4):1364. doi: 10.4102/jphia.v16i4.1364.**

**eCollection 2025.**

Burden and determinants of MDR-TB among prisoners in sub-Saharan Africa:

Systematic review and meta-analysis protocol.

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**BACKGROUND:** Tuberculosis (TB) is one of the leading causes of death globally

because of a single infectious pathogen. The rise in prevalence of

multi-drug-resistant tuberculosis (MDR-TB) puts an increased burden on the

health system in terms of cost and longer treatment duration. People living in

correctional facilities are more likely to develop TB and have poor TB treatment

outcomes than the general population, making them a vulnerable group to develop

MDR-TB. However, the burden of MDR-TB and associated treatment outcomes among

prisoners in sub-Saharan Africa (SSA) is poorly documented.

**AIM:** The study aims to investigate the burden and associated factors of MDR-TB

treatment among prisoners in SSA.

**SETTING:** The review will include studies of MDR-TB done in prisons and detention

centers involving prisoners and inmates in sub Saharan Africa.

**METHODS:** Following the Preferred Reporting Items for Systematic Reviews and

Meta-Analyses (PROSPERO), we will conduct a systematic review and meta-analysis.

We will review studies examining MDR-TB patient treatment outcomes among

prisoners reported in published literature in SSA from 2000 to 31 December 2024.

A search on studies reporting MDR-TB treatment outcomes from the databases such

as 'Medline, Embase, CINAHL (EBSCOhost), Scopus and Web of Science' will be

conducted. We will analyse continuous outcomes as mean differences for studies

using the same scales with standard deviation reported and binary outcome data

as odds ratios or risk ratios, all presented with their 95% confidence

intervals. Additionally, the pooled proportions will be used to determine the

prevalence or incidence of specific MDR-TB treatment outcomes. Heterogeneity

will be assessed using the I 2 statistic, and where significant heterogeneity is

detected, a random-effects model meta-analysis will be performed; otherwise, a

fixed-effect model meta-analysis will be carried out. Risk factors will be

determined using the meta-regression analysis technique.

**RESULTS:** After analysis of pooled data, prevalence of MDT-TB in prisons will be

presented as proportions. Meta-analysis outcome will be presented as forest

plots, showing odd ratios and co-responding 95% confidence intervals. Narrative

synthesis of included studies will be presented in a table format.

**CONCLUSION:** This proposed systematic review and meta-analysis will help

consolidate evidence to support the development of public health guidelines to

enhance the reduction of MDT-TB factors among prisoners in the SSA region.

**CONTRIBUTION:** This review will provide evidence to support guideline development

on screening, diagnosis, and clinical management of MDR-TB patients in prisons.

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**60. Spat Spatiotemporal Epidemiol. 2025 Aug;54:100729. doi:**

**10.1016/j.sste.2025.100729. Epub 2025 Jun 5.**

Evaluation of spatial and non-spatial factors on tuberculosis using geospatial

information system and fuzzy logic.

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Tuberculosis is a deadly infectious disease that has not been eradicated yet.

The prevalence of this disease is still very high in some parts of the world, so

it is considered a deadly disease. Iran is one of the countries which has not

yet achieved the ability to eliminate this disease. The prevalence of

tuberculosis is relatively higher in some provinces than in the other ones.

Sistan and Baluchestan is the province with high rates of tuberculosis. In this

paper, the factors affecting tuberculosis are modeled in Sistan and Baluchestan

province using Geospatial Information Systems (GIS) and FL. This research

contains two general analyzes. In the first analysis, three different scenarios

of FL rules are presented. The first two scenarios examine spatial and

non-spatial factors respectively. The third scenario also examines the

combination of spatial and non-spatial factors simultaneously. As a result, the

effect of spatial and non-spatial factors on tuberculosis is obtained. In the

second analysis, a spatial scatter density map of tuberculosis is produced

according to spatial data. This research reveals that the effects of spatial and

non-spatial factors on tuberculosis are 57 % and 43 %, respectively. By

comparing the results with samplings, the scatter rate map of tuberculosis is

obtained with an accuracy of 71 %.

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**61. Biochem Biophys Res Commun. 2025 Sep 5;783:152592. doi:**

**10.1016/j.bbrc.2025.152592. Online ahead of print.**

Crystal structure of N-terminal VapB46 antitoxin and interaction analysis of its

cognate partners from molecular dynamics simulation.

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Toxin-antitoxin (TA) systems are important for persister cell formation in

Mycobacterium tuberculosis (Mtb), which aids their survival during stress

condition. Antitoxins regulate the TA systems by binding to the

promoter-operator region. Among fifty VapBC TA systems in Mtb, few have been

characterized, while remaining needs characterisation to understand the VapBC TA

mechanism. Here, we report the crystal structure of the N-terminal domain of

VapB46 antitoxin at a resolution of 1.64 Å. The protein has a DNA-binding domain

that resembles the N-terminal domain of Phd antitoxin with a βααββ fold.

Simulation study revealed that VapB46 binds as a dimer at two promoter/operator

DNA sites, and tetrameric VapB46 binds to VapC46 toxin via its C-terminal

domain. The analysis of the structure and simulation study provides detailed

insights into the VapBC46 TA system, paving the way for future drug development

targeting this system.

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PMID: 40934556

**62. Radiol Case Rep. 2025 Aug 30;20(11):5762-5768. doi: 10.1016/j.radcr.2025.08.005. eCollection 2025 Nov.**

Tuberculous spondylodiscitis with atypical presentation: A diagnostic challenge:

Case report and review of literature.

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Spinal tuberculosis is the most common form of osteoarticular tuberculosis and

presents significant diagnostic challenges, especially in atypical cases. It may

clinically and radiologically mimic neoplastic lesions, particularly when disc

involvement is absent. We report a case of a 60-year-old woman with a history of

treated lymph node tuberculosis who presented with chronic inflammatory

dorsolumbar pain without systemic symptoms. Initial imaging revealed lytic

lesions of the D11-D12 vertebrae with preservation of the intervertebral disc,

raising suspicion of a neoplastic process. A PET scan demonstrated

hypermetabolism at the affected level, and a first biopsy showed nonspecific

inflammatory lesions. The patient was lost to follow-up but was later readmitted

with worsening symptoms. Further investigations revealed vertebral lysis on

radiographs and D11-D12 spondylodiscitis with a right psoas abscess on MRI. CT

imaging showed lymphadenopathy, disc-vertebral involvement, and a psoas

collection, more suggestive of tuberculosis than malignancy. A second biopsy

confirmed granulomatous inflammation, establishing the diagnosis of a

tuberculous spondylodiscitis. The patient was successfully treated with a

9-month anti-tuberculous regimen, resulting in significant clinical and

radiological improvement. Tuberculous spondylodiscitis should be considered in

the differential diagnosis of isolated spinal lesions suggestive of malignancy,

especially in endemic regions. Early diagnosis and appropriate treatment are

crucial to prevent complications.

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DOI: 10.1016/j.radcr.2025.08.005

PMCID: PMC12419077

PMID: 40934036

**63. Lancet Reg Health Eur. 2025 Aug 29;57:101436. doi: 10.1016/j.lanepe.2025.101436. eCollection 2025 Oct.**

Commentary on: diagnostic accuracy and predictive value of the QuantiFERON-TB

Gold Plus assay for tuberculosis in immunocompromised individuals: a prospective

TBnet study.

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DOI: 10.1016/j.lanepe.2025.101436

PMCID: PMC12418987

PMID: 40933838

**64. Pediatric Health Med Ther. 2025 Sep 4;16:227-236. doi: 10.2147/PHMT.S515071.**

**eCollection 2025.**

Pediatric Non-Cystic Fibrosis Pulmonary Nontuberculous Mycobacterium Infections:

A Global Population Based Study.

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**BACKGROUND:** Nontuberculous mycobacteria (NTM) are Mycobacterial pathogens that

cause pulmonary infections among children, particularly those with underlying

lung conditions or immunosuppression. Clinical presentations include chronic

cough, weight loss, and fatigue. Diagnosis involves clinical assessment,

radiographic imaging, and microbiological confirmation, while treatment often

requires prolonged, multidrug antibiotic regimens. This study aimed to analyze

the epidemiology and clinical outcomes of pulmonary NTM infections in a

non-cystic fibrosis pediatric population from four distinct age groups.

**METHODS:** A retrospective study as cross-sectional design for data collection

from the TriNetX platform, a global electronic health record database. Inclusion

criteria targeted pediatric patients aged 0-18 years with pulmonary NTM, while

exclusion criteria included cystic fibrosis, tuberculosis, smoking history, and

cutaneous NTM infections. The cohort comprised 109 cases among 0-2 years (mean

age 2 years), 401 cases among 3-5 years (mean age 4 years), 1,074 cases among

6-12 years (mean age 9 years), and 760 cases among 13-18 years (mean age 15

years). Demographics, comorbidities, and inflammatory markers were analyzed.

Logistic and binomial regression models were used to evaluate associations

between age group and five-year outcomes of pediatric pulmonary NTM, reporting

odds ratios (OR), risk ratios (RR), 95% confidence intervals (CI), and p-values.

**RESULTS**: Of the total 2,344 records of pediatric patients examined, the most

common comorbidities included malignancies (36%), acute pharyngitis (78%),

asthma (46%), unspecified pneumonia (46%), and immunodeficiencies (22%). Female

patients represented 53.31% of cases. Key inflammatory markers (eg C-reactive

protein (CRP), mean white blood cell count, ferritin) were elevated among older

age groups.

**CONCLUSION:** This study highlights age-specific variations in risk factors,

clinical outcomes, and inflammatory responses, offering potential insights for

improved diagnosis and management of NTM in children. These results underscore

the importance of further research in pediatric cohorts with NTM to better

understand its role in pediatric pulmonary conditions and comorbidities.

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**65. Infect Med (Beijing). 2025 Aug 12;4(3):100197. doi: 10.1016/j.imj.2025.100197.**

**eCollection 2025 Sep.**

Diagnostic yield of polymerase chain reaction on induced sputum for pulmonary

tuberculosis: A single-center retrospective cross-sectional study.

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University, Bangkok 10400, Thailand.

**BACKGROUND:** Data on tuberculosis-polymerase chain reaction (TB-PCR) diagnostic

yield in induced sputum (IS) samples is limited. This study was conducted to

evaluate the diagnostic yield of TB-PCR in IS samples from patients with

pulmonary TB and to identify factors that are associated with positive TB-PCR

results.

**METHODS:** This retrospective cross-sectional study was conducted at the Faculty

of Medicine Ramathibodi Hospital. Patients who underwent IS collection for the

diagnosis of pulmonary TB were included. Sputum specimens were obtained for

acid-fast bacilli (AFB) smear, TB-PCR (Anyplex Seegene MTB/NTM real-time

detection assay or Xpert MTB/RIF assay), and TB culture. Multivariate logistic

regression analysis was performed to identify factors associated with IS TB-PCR

positivity. The McNemar test was used to compare the diagnostic yield of each

test.

**RESULTS:** A total of 124 IS specimens of patients with pulmonary TB were

evaluated. There were 65 (52.4%) men, with a mean age of 55.3 ± 19.5 years. The

diagnostic yield of IS TB-PCR for the diagnosis of pulmonary TB was 31.5% (95%

confidence interval [CI]: 23.2-39.7). The diagnostic yields were 34.4% (95% CI:

22.0-46.0) for Xpert MTB/RIF and 28.6% (95% CI: 17.8-40.2) for Anyplex MTB/NTM,

with no significant difference between the two assays (p = 0.49). TB-PCR had a

higher diagnostic yield than AFB smear (31.5% vs. 6.5%, p < 0.01). Logistic

regression analysis showed that moderately advanced (adjusted odds ratio [aOR] =

3.73, 95% CI: 1.24-11.21, p = 0.019) and far advanced (aOR = 3.95, 95% CI:

1.05-14.82, p = 0.042) radiographic extent of disease were associated with

positive IS TB-PCR.

**CONCLUSIONS:** Induced sputum TB-PCR is an effective initial method for patients

with suspected pulmonary TB who are unable to produce reliable sputum,

especially those with moderately advanced or far advanced radiographic extent of

disease.

© 2025 The Authors.

DOI: 10.1016/j.imj.2025.100197

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**66. Front Public Health. 2025 Aug 26;13:1598269. doi: 10.3389/fpubh.2025.1598269.**

**eCollection 2025.**

Scaling up tuberculosis case finding via private providers in Ghana: an impact

evaluation using interrupted time series.

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Environmental Health (HMGU), Neuherberg, Germany.

**BACKGROUND:** Although TB services are free in Ghana, TB case detection remains

low and mostly limited to public facilities. To address this, a Public-Private

Mix (PPM) Directly Observed Therapy (DOT) model was introduced, involving

community private healthcare providers and the National Health Insurance Scheme

(NHIS) to boost TB case detection rates.

**METHODS:** This impact evaluation focuses on four key interventions targeting

vulnerable populations in Ghana's two largest metropolitan areas between the

last quarter of 2018 and the first quarter of 2020. Screening and TB register

data were collected from implementing facilities, along with TB case

notifications from 2015 to 2022 for both intervention and control areas.

Comparative interrupted time series (ITS) analysis was used to evaluate the

effect of the interventions on quarterly TB case notifications.

**RESULTS:** During the intervention period, a total of 563,868 persons were

screened for TB, 12,121 of these were presumptive for TB and 590 persons were

diagnosed with TB. Of the diagnosed TB cases, 95.3% (562) were bacteriologically

confirmed. The overall TB screening yield was 104.6 cases per 100,000

population. In the intervention area, TB case notifications increased from 1,392

cases in 2018 to 1,462 cases in 2019 while they decreased from 853 to 778 in the

control area. The ITS analyses detected positive post-intervention trend

differences in all forms of TB and bacteriologically confirmed TB notification

case rates between the intervention and control areas.

**CONCLUSION:** Expanding free TB services through a PPM DOT model and sustained

community engagement can increase TB case detection in urban areas. National TB

programs should adopt and scale this approach to enhance TB surveillance and

control.

Copyright © 2025 Hayibor, Kenu, Mensah, Awalime, Anaman, Asante-Poku, Ivanova,

Abhishek, Rachow and Hanson-Nortey.

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PMCID: PMC12417460

PMID: 40933408

**67. Infez Med. 2025 Sep 1;33(3):329-332. doi: 10.53854/liim-3303-10. eCollection**

**2025.**

A destruent case of recurrent primary naso-pharyngeal tuberculosis in a migrant.

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A 24-year-old Ukrainian man with post-natal developmental disability was treated

for presumptive facial cutaneous TB in 2018 in his home country. After moving to

Italy, his nostril lesion recurred in 2021, expanding to the upper lip, but he

was lost to follow-up before a diagnosis was made. In 2023, when symptoms

worsened, a biopsy was performed showing chronic inflammation and negative

microbiological molecular tests and culture. By 2024, the lesion spread to the

eyelids with worsening ulcerations. After surgical resection, histology revealed

a vegetative, haemorrhagic mucosa with necrotic granulomatous inflammation and

rifampin-susceptible Mycobacterium tuberculosis (Mtb) was detected at molecular

testing. Diagnosis of recurrent primary cutaneous TB without pulmonary

involvement was made and treatment for drug susceptible TB was initiated,

leading to complete remission of the facial lesions. Primary cutaneous TB

without pulmonary involvement is rare, presenting as nodules, plaques, papules,

or ulcers. Diagnosis requires systemic evaluation, imaging, infection screening

and expert consultation. Cutaneous TB (CTB) is uncommon in Ukraine and accounts

for less than 2% of extrapulmonary TB cases with frequent association with

immunosuppression and delayed presentation. Although infrequent, CTB mirrors the

wider TB scenario, that is also characterized by MDR-TB in 27% of new and 45% of

retreatment cases, and XDR-TB in 13% of MDR-TB cases. In individuals coming from

TB endemic areas with strong clinical suspicion, empirical TB diagnosis should

always be considered despite negative microbiology to enable timely treatment

and prevent progression. A multidisciplinary approach is essential for accurate

diagnosis and optimal management.

DOI: 10.53854/liim-3303-10

PMCID: PMC12419177

PMID: 40933222

**68. Infez Med. 2025 Sep 1;33(3):321-328. doi: 10.53854/liim-3303-9. eCollection**

**2025.**

Impact of the COVID-19 pandemic on tuberculosis services in a rural area of

Senegal.

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**BACKGROUND:** The Coronavirus (COVID-19) pandemic significantly impacted on

tuberculosis (TB) services (TB) services in both high and low TB burden

countries. Objectives: This study aimed to investigate the impact of COVID-19 on

TB outpatient services in terms of new TB case notifications and treatment

outcomes in a rural area of Senegal.

**METHODS:** A retrospective observational study was conducted at the Health Care

Centre of Diofior (HCD) in the Fimela district, Fatick Region (Senegal),

covering the period from January 1st, 2018, to December 31st, 2022. Data were

divided into pre-COVID-19 (until March 31st, 2020) and during-COVID-19 (from

April 1st, 2020) periods for analysis.

**RESULTS:** Among the 246 TB cases included (63.4% male, median age 38.4 years), 94

(38.2%) had been diagnosed in the pre-COVID-19 period and 152 (61.8%) in the

during-COVID-19 period. In 2020, TB case notifications dropped by 24.4% compared

to 2019, followed by an increase of 70.6% in 2021 and 91.2% in 2022. The TB

treatment success rate decreased from 85.1% before COVID-19 to 77.6% in

during-COVID-19 period. Moreover, mortality increased from 2.1% to 5.3%, and the

lost-to-follow-up rate rose from 8.5% to 14.5% between the pre- and

during-COVID-19 periods.

**CONCLUSIONS:** Although the number of COVID-19 cases reported in Senegal was

relatively low in the study period compared to other settings, our study

indicates that the pandemic had a significant impact on TB services in this

rural area of Senegal.

DOI: 10.53854/liim-3303-9

PMCID: PMC12419176

PMID: 40933219

**69. Cureus. 2025 Aug 10;17(8):e89742. doi: 10.7759/cureus.89742. eCollection 2025**

**Aug.**

A Rare Case of Pleural Melanoma Masquerading as a Tubercular Pleural Effusion.

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This case report highlights the case of an extremely rare case of primary

pleural melanoma in a 15-year-old female with left-sided exudative pleural

effusion with pleural fluid adenosine deaminase (ADA) in the tuberculosis range.

Melanoma is an aggressive malignant tumor mainly arising from the skin, but very

few cases have been reported of a primary melanoma arising from the pleura. In

addition, this patient's pleural fluid ADA was in the tuberculosis suspect

range, but a detailed analysis of the pleural fluid and pleural biopsy helped in

pinpointing the diagnosis. Through this case, the entire pleural fluid analysis,

including the pleural fluid routine microscopy, pleural fluid cytology, and even

pleural biopsy in select cases, needs to be assessed in order to avoid

misdiagnosis of tuberculosis.

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**70. Cureus. 2025 Aug 10;17(8):e89732. doi: 10.7759/cureus.89732. eCollection 2025**

**Aug.**

The Prevalence and Clinical Presentation of Abdominal Tuberculosis in Patients

With Acute Surgical Abdomen: A Prospective Observational Study.

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**Background and objective** The diagnosis of abdominal tuberculosis (ATB) poses

significant difficulty in the context of acute abdomen cases, especially in

regions where it is endemic. This study aimed to determine the frequency and

clinical manifestations of ATB among adults with an acute surgical abdomen at a

tertiary care center in Ranchi, India, focusing on the means of arriving at the

diagnosis and subsequent treatment results. **Methods** Our study involved 60

patients with acute abdominal symptoms and was conducted during the year

2023-2024 at the Rajendra Institute of Medical Sciences, Ranchi. We collected

demographic data along with imaging studies such as X-ray, ultrasound, CT scan,

acid-fast bacilli (AFB) smear, cartridge-based nucleic acid amplification test

(CBNAAT), intraoperative findings, histopathological examination (HPE), and

symptomatology to perform relevant and timely diagnosis. The association between

clinical symptoms of the patients and ATB was assessed using the chi-square

test. **Results** The confirmation rate of ATB was five (8.3%) among the patients. A significant association was observed with fever and weight loss (p<0.01),

although all patients did report some degree of abdominal pain. HPE showed high

accuracy with 90% sensitivity and 95% specificity. For CT imaging, sensitivity

and specificity were reported at 70% and 85%, respectively, while ultrasound

sensitivity lagged at approximately 60%. Anti-tuberculosis therapy (ATT) had

demonstrable benefits for all ATB patients. Common intraoperative findings

involved lymphadenopathy along with ascites. **Conclusions** The data indicate that

ATB was present in five (8.3%) cases, manifesting as acute abdomen presenting

surgically; we identified weight loss and fever as main symptoms that

contributed to our diagnostic approach, leading us to diagnose it more

effectively than would otherwise be possible in unexplained abdominal pain

cases. HPE-based imaging tests performed alongside appropriate medications

showed excellent results in endemic areas.

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PMID: 40932962

**71. Swiss Med Wkly. 2025 May 29;155:4187. doi: 10.57187/s.4187.**

Sex distribution in tuberculosis disease in children, adolescents, and adults in

a low-incidence country: a retrospective population-based cohort study.

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**AIM:** Globally, tuberculosis incidence shows notable sex disparity, with higher

rates observed in males. While this pattern is well documented in adults from

high-incidence countries, the influence of sex on tuberculosis incidence in

children and adolescents, particularly in low-incidence settings, remains

unclear. This study investigated sex-specific tuberculosis incidence rates

across all age groups, focusing on adolescents, in a low-incidence country.

**METHODS:**  In this retrospective cohort study, data from the Swiss Federal Office

of Public Health (FOPH) tuberculosis database, which centrally consolidates

mandatory notifications from physicians and laboratories across Switzerland,

were analysed from 2000 to 2021. Tuberculosis incidence rates and male-to-female

ratios were calculated and stratified by sex and age. Adolescence was divided

into early (10-14 years) and late (15-19 years) stages for detailed analysis.

**RESULTS:** Over 22 years, the average tuberculosis incidence in Switzerland was

6.78 per 100,000 population, with an overall male-to-female ratio of 1:0.75 (p

<0.001). Among the 11,872 notified cases, 832 occurred in adolescents, yielding

an incidence rate of 4.39 per 100,000. In late adolescence, males had a

significantly higher tuberculosis incidence rate (5.73 per 100,000) than females

(2.97 per 100,000, p <0.001), resulting in a male-to-female ratio of 1:0.5.

Additionally, data on asylum seekers revealed nearly twice as many males as

females arriving in Switzerland in late adolescence.

**CONCLUSIONS:** This study reveals significant sex disparity in tuberculosis

incidence in a country with low tuberculosis incidence, with males showing

higher rates than females beginning in late adolescence. This discrepancy is

likely influenced by the higher influx of male asylum seekers in adolescence.

DOI: 10.57187/s.4187

PMID: 40931799 [Indexed for MEDLINE]

**72. Open Res Eur. 2025 Apr 25;4:212. doi: 10.12688/openreseurope.18175.3.**

**eCollection 2024.**

Post-trial access practices in conducted clinical trials for Malaria,

Tuberculosis, and Neglected Tropical Diseases (NTDs) across Sub-Saharan African

countries:  A quantitative study.

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**BACKGROUND:** According to the Council of International Organizations and Medical

Sciences (CIOMS) 2016, post-trial access (PTA) refers to the ethical imperative

that requires the sponsor, researchers, and relevant public health authority,

"to make available as soon as possible any intervention or product developed,

and knowledge generated, for the population or community in which the research

is carried out." Law, policy, and practical guidance for PTA has so far been

vague but has recently attracted and increased attention in the context of

benefit sharing of scientific research results with low- and middle-income

countries (LMICs).Although the number of clinical trials conducted in the Sub

Saharan (SSA) countries has increased in the past two decades, plans and

practices for PTA are underreported. The study examines PTA planning and

implementation in clinical trials focused on TB, Malaria, and Neglected Tropical

Diseases (NTDs) in Sub-Saharan African countries, conducted between 2008 and

2019.

**OBJECTIVE:** The study aims to identify gaps in PTA planning and implementation,

highlight challenges, and suggest strategies for improving access to trial

interventions and knowledge post-research.

**METHOD:** A quantitative, cross-sectional study was conducted, using a

self-administered online questionnaire to assess the PTA planning and

implementation practices of Principal Investigators (PIs), co-PIs, trial

coordinators, and sponsors involved in clinical trials in malaria, tuberculosis

and NTDs across Sub-Saharan African countries. Of the 300 invited potential

participants, 37 provided complete responses.

**FINDINGS:** Nearly half (43%) of the study respondents did not provide PTA plans

for TB, Malaria, and NTDs in clinical trials. The findings highlight an overall

lack of formalized PTA policies and commitments in clinical trials for TB,

Malaria, and NTDs in Sub-Saharan Africa. Most of the study participants (70.3%)

expressed the need for PTA training.

**CONCLUSION:** Although the study offers valuable insights into PTA planning and

practices, its generalizability may be limited by factors such as geographical

and disease focus, reliance on self-reported data, and stakeholder

representation. Despite these limitations, the study underscores an urgent need

for structured PTA policy training programs, stakeholder collaboration, and

effective training. Its findings can serve as a foundation for further research

and policy development to enhance PTA in LMICs.

Copyright: © 2025 Seralegne Y et al.

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PMID: 40931749

**73. Clin Case Rep. 2025 Sep 7;13(9):e70868. doi: 10.1002/ccr3.70868. eCollection**

**2025 Sep.**

Black Hairy Tongue as a Rare Adverse Effect of Linezolid in Multidrug-Resistant

Tuberculosis: A Case Report.

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Black hairy tongue (BHT), or lingua villosa nigra, is a rare adverse effect of

linezolid, an antibiotic frequently used in the treatment of multidrug-resistant

tuberculosis (MDR-TB). We present a case of a 24-year-old female who developed

BHT while receiving linezolid as part of a longer regimen for MDR-TB. The

patient exhibited a typical BHT presentation, with painless brown-to-black

discoloration on the posterior dorsal surface of her tongue, appearing 25 days

after initiating linezolid therapy. There were no other identifiable

contributing factors. Upon discontinuation of linezolid and a shift to a

modified regimen, the BHT completely resolved within 10 days. A Naranjo Adverse

Drug Reaction Probability Scale score of 5 suggested a probable causal

relationship between linezolid and BHT. This report represents the first

documented case of linezolid-associated BHT from Nepal, highlighting the

importance of clinicians' awareness of this rare but clinically significant side

effect, especially within the context of MDR-TB treatment, to provide prompt

diagnosis, reassurance, and appropriate management.

© 2025 The Author(s). Clinical Case Reports published by John Wiley & Sons Ltd.

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PMCID: PMC12414800

PMID: 40927404

**74. Front Med (Lausanne). 2025 Aug 25;12:1602370. doi: 10.3389/fmed.2025.1602370.**

**eCollection 2025.**

Case Report: Sarcoidosis or tuberculosis? A continuous challenge.

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Sarcoidosis is a multisystem granulomatous disorder of unknown etiology,

characterized by the formation of non-caseating granulomas in affected tissues

and organs. In over half of the cases, the disease undergoes spontaneous

remission. In contrast, tuberculosis (TB) is an infectious disease caused by

Mycobacterium tuberculosis, which, if left untreated, can be fatal. Sarcoidosis

and tuberculosis exhibit numerous overlapping clinical, radiological, and

histopathological features, including the presence of epithelioid cell

granulomas with multinucleated giant cells. Historically, a potential

etiological role of M. tuberculosis in sarcoidosis has been proposed; however,

this hypothesis has not been conclusively supported by current evidence or

therapeutic outcomes. Differentiating between these two entities presents a

significant diagnostic challenge, particularly in regions with a high prevalence

of tuberculosis. The diagnostic complexity is further heightened in cases where

a concomitant occurrence of both conditions is suspected. In such scenarios, the

absence of a definitive biomarker hampers the ability to discern whether the

diseases coexist independently or share a pathogenic link. This article reviews

current evidence on the association between sarcoidosis and tuberculosis and

explores potential pathways to elucidate their etiological interrelationship.

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**75. Front Med (Lausanne). 2025 Aug 25;12:1596579. doi: 10.3389/fmed.2025.1596579.**

**eCollection 2025.**

Advancing the fight against tuberculosis: integrating innovation and public

health in diagnosis, treatment, vaccine development, and implementation science.

Elbehiry A(1), Marzouk E(1), Edrees HM(2), AlShaqi R(3), Ellethy AT(4), Alzaben

F(5), Anagreyyah S(6), Algarni A(6), Almuhaydili K(7), Alotaibi I(8), Albaqami

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Tuberculosis (TB) remains one of the leading causes of infectious disease

mortality worldwide, increasingly complicated by the emergence of drug-resistant

strains and limitations in existing diagnostic and therapeutic strategies.

Despite decades of global efforts, the disease continues to impose a significant

burden, particularly in low- and middle-income countries (LMICs) where health

system weaknesses hinder progress. This comprehensive review explores recent

advancements in TB diagnostics, antimicrobial resistance (AMR surveillance),

treatment strategies, and vaccine development. It critically evaluates

cutting-edge technologies including CRISPR-based diagnostics, whole-genome

sequencing, and digital adherence tools, alongside therapeutic innovations such

as shorter multidrug-resistant TB regimens and host-directed therapies. Special

emphasis is placed on the translational gap-highlighting barriers to real-world

implementation such as cost, infrastructure, and policy fragmentation. While

innovations like the Xpert MTB/RIF Ultra, BPaLM regimen, and next-generation

vaccines such as M72/AS01E represent pivotal progress, their deployment remains

uneven. Implementation science, cost-effectiveness analyses, and health equity

considerations are vital to scaling up these tools. Moreover, the expansion of

the TB vaccine pipeline and integration of AI in diagnostics signal a

transformative period in TB control. Eliminating TB demands more than biomedical

breakthroughs-it requires a unified strategy that aligns innovation with access,

equity, and sustainability. By bridging science with implementation, and

integrating diagnostics, treatment, and prevention within robust health systems,

the global community can accelerate the path toward ending TB.

Copyright © 2025 Elbehiry, Marzouk, Edrees, AlShaqi, Ellethy, Alzaben,

Anagreyyah, Algarni, Almuhaydili, Alotaibi, Albaqami, Alamri, Ibrahem,

Almuzaini, Dhahri and Abu-Okail.

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PMID: 40927186

**76. Cureus. 2025 Aug 8;17(8):e89662. doi: 10.7759/cureus.89662. eCollection 2025**

**Aug.**

Disseminated Tuberculosis Complicated by Pulmonary Thromboembolism.

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Tuberculosis (TB) is a multisystem infectious disease with both pulmonary and

extrapulmonary manifestations. TB can also induce a hypercoagulable state,

setting off a cascade of changes in the body, including systemic inflammation,

endothelial dysfunction, and abnormalities in the coagulation and fibrinolytic

pathways. Collectively, these factors significantly increase the risk of venous

thromboembolism, such as deep vein thrombosis and pulmonary embolism. These

complications can worsen the overall disease course and complicate TB

management. We report the case of a 27-year-old man presenting with high-grade

fever, abdominal pain, and significant weight loss. Imaging suggested

tuberculous peritonitis, and computed tomography pulmonary angiography revealed

pulmonary thromboembolism, a rare but serious TB-associated complication.

Omental biopsy confirmed TB based on histopathology and GeneXpert. Despite the

initiation of anti-tubercular therapy and anticoagulation, the patient developed

osteomyelitis of the right iliac bone with an intramuscular abscess, which

tested positive for Mycobacterium tuberculosis. This case highlights the

thrombotic and multisystemic nature of TB and the need for vigilance in

identifying its uncommon complications.

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PMID: 40926907

**77. Chem Biol Drug Des. 2025 Sep;106(3):e70171. doi: 10.1111/cbdd.70171.**

Rationally Designed InhA Inhibitors: A Comparative Anti-Tubercular Activity

Study of Sulfonate Esters of Isoniazid Hydrazones and Their Structurally

Flexible Benzyl Analogues.

Kadima MG(1), Mishra S(2), Kumar G(2), Seboletswe P(2), Roquet-Banères F(3),

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Molecular hybridization of isoniazid with hydrophobic aromatic moieties

represents a promising strategy for the development of novel anti-tubercular

therapeutics. In this study, a series of hybrid molecules (5a-i) was synthesized

by linking isoniazid with aromatic sulfonate esters via a hydrazone bridge.

Molecular docking studies revealed that these compounds interact effectively

with the catalytic triad of the InhA enzyme (Y158, F149, and K165), suggesting

their potential as InhA inhibitors. To enhance molecular flexibility and improve

binding interactions with both NADH and the catalytic residues, a second

generation of derivatives (8a-k) was designed and synthesized. All synthesized

compounds were structurally characterized using spectroscopic techniques,

including nuclear magnetic resonance (NMR), Fourier transform infrared

spectroscopy (IR), and high-resolution mass spectrometry. As anticipated, these

new compounds exhibited enhanced anti-tubercular activity compared to their

precursors. Notably, compound 8b demonstrated significant potency with an MIC of

0.078 μg/mL, approximately twofold more active than its precursor 5b

(MIC = 0.156 μg/mL) against Mycobacterium tuberculosis (Mtb). However, both

generations of compounds (e.g., 5a, 5b, 8a, 8b, 8c, and 8 k) lost activity

against INH-resistant Mtb strains harboring katG mutations. Importantly, no

cytotoxicity was observed for these compounds in THP-1 human monocytic cells at

a concentration of 10 μg/mL. The structural integrity of the lead compound 8b

was confirmed via 1H NMR stability studies. The ADME/T parameters (absorption,

distribution, metabolism, excretion, and toxicity) were also explored to

determine their drug likeness and safety profile. Collectively, these hybrid

molecules present valuable scaffolds for further optimization in the pursuit of

new anti-tubercular agents.

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**78. Acta Ortop Mex. 2025 Jul-Aug;39(4):236-241.**

Tuberculosis tenosynovitis in the wrist: a case report.

[Article in English]

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Articular tuberculosis is a rare condition, with extrapulmonary presentations

most commonly appearing in joints such as the hip or knee. It is usually

associated with conditions like immunosuppression or a history of pulmonary

tuberculosis. Diagnosis involves imaging or pathology, and treatment typically

involves surgical intervention along with medication. Here is the case of a

25-year-old male from Barranquilla, Colombia. He lacks classical risk factors

for pulmonary tuberculosis but has a history of open reduction of a traumatic

fracture in his right distal radius four years ago. He presented with persistent

pain, joint swelling, and limited movement, leading to removal of the

osteosynthesis material. Despite this, the pain persisted, prompting further

investigation with X-ray and MRI of the wrist. These imaging studies revealed

findings compatible with tuberculosis. Based on these results, the medical team

opted for a surgical procedure. An oncological resection of the synovium was

performed, and the material that was removed was used for histological studies

to confirm suspicions of extrapulmonary tuberculosis. Following these

procedures, the patient underwent physical therapy and began tuberculosis

medication, resulting in significant improvement of his symptoms.

PMID: 40925851 [Indexed for MEDLINE]

**79. Int J Infect Dis. 2025 Sep 7:108051. doi: 10.1016/j.ijid.2025.108051. Online**

**ahead of print.**

Disseminated Mycobacterium simiae infection causing rhinosinusitis in a severely

immunocompromised patient.

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**BACKGROUND:** Mycobacterium simiae is a slow-growing environmental nontuberculous

mycobacterium (NTM), commonly isolated from soil and water. M. simiae is not

known to transmit zoonotically or via human-to-human contact; infection is

presumed to occur through direct environmental exposure. Although M. simiae

represents a small proportion of NTM isolates globally, its clinical relevance

is increasingly recognised. Extrapulmonary manifestations are rare, and to date,

no cases of rhinosinusitis attributable to M. simiae have been reported.

**CASE PRESENTATION AND MANAGEMENT:** A 33-year-old male with advanced human

immunodeficiency virus infection (HIV) (CD4⁺ count 6 cells/µL), who completed

tuberculosis treatment two months prior to the current admission, presented with

right eye proptosis, pain, restricted ocular movement, nasal discharge, and

fever. Three weeks earlier, he was hospitalized and discharged for chronic

diarrhea complicated by acute-on-chronic kidney injury and pancytopenia. Imaging

showed sinus opacification with bony erosion extending into the orbit. Cultures

from blood and sinus aspirate identified Mycobacterium simiae, confirmed by

line-probe assay. Despite multidisciplinary care, minimal improvement occurred,

and he died two weeks after admission.

**CONCLUSION:** This case represents the first documented instance of M. simiae

associated rhinosinusitis and highlights the pathogenic potential of

environmental NTM in causing destructive and disseminated disease in severely

immunocompromised patients.

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**80. Allergol Immunopathol (Madr). 2025 Sep 1;53(5):69-77. doi:**

**10.15586/aei.v53i5.1427. eCollection 2025.**

Antituberculosis drug-induced hypersensitivity: clinical characteristics and

risk factors.

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Training and Research Hospital, İstanbul, Turkey.

**BACKGROUND:** Antituberculosis drugs can cause hypersensitivity reactions that

interrupt treatment and increase morbidity. Early identification and management

are essential to prevent complications and drug resistance.

**OBJECTIVE:** To evaluate the clinical characteristics, risk factors, and outcomes

of antituberculosis drug-induced hypersensitivity reactions over a 10-year

period in a tertiary referral center.

**METHODS:** We retrospectively analyzed 449 patients hospitalized for

antituberculosis drug-induced hypersensitivity between 2015 and 2024. A control

group of 478 tuberculosis patients without hypersensitivity was included.

Demographic features, comorbidities, hypersensitivity types, causative drugs,

and treatment outcomes were compared.

**RESULTS:** The prevalence of hypersensitivity was 12.1%. Female gender, older age,

Turkish nationality, and history of other drug allergies were significant risk

factors. Type 1 reactions (77.7%) were more common and associated with shorter

treatment interruption and higher cure rates. Pyrazinamide was the most

frequently implicated drug. Desensitization was successful in the majority of

patients.

**CONCLUSION:** This large cohort study highlights key risk factors and clinical

outcomes in tuberculosis drug hypersensitivity. Close monitoring of high-risk

patients in the early treatment phase may reduce delays and improve outcomes.

Copyright: Zeynep YK, et al.

DOI: 10.15586/aei.v53i5.1427

PMID: 40923422 [Indexed for MEDLINE]

**81. Monaldi Arch Chest Dis. 2025 Sep 4. doi: 10.4081/monaldi.2025.3562. Online ahead of print.**

Diagnostic utility of flexible bronchoscopy in smear-negative and atypical lung

infections: identifying tuberculosis, fungal, and non-tuberculous mycobacteria

infections and malignancy.

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Fiber-optic bronchoscopy (FOB) plays a crucial role in the diagnosis and

management of various pulmonary diseases by offering direct visualization of the

airways and enabling targeted sampling for microbiological and histopathological

evaluation. This study aimed to assess the clinical, radiological,

microbiological, and histopathological profiles of patients undergoing FOB. A

retrospective analysis of 103 participants who underwent the procedure over one

year was conducted. After obtaining informed consent, demographic and clinical

information was recorded, and relevant radiological findings were noted. The

procedure was performed under local anesthesia. In all cases with inconclusive

sputum evaluation, bronchoalveolar lavage (BAL) was conducted, with additional

brushing and biopsy performed in selected participants. The collected samples

were analyzed to determine the underlying etiology. Among the 103 individuals

studied, 52.4% were female, with a mean age of 54.82 years, and the majority

(82.5%) were over 40 years old. Cough was the most common symptom (73.78%),

followed by breathlessness. The frequent comorbidities included diabetes

(27.18%) and hypertension (18.4%). Radiological patterns commonly included

consolidation (59%) and cavitary lesions (30.1%). On bronchoscopy, secretions

(67%) and inflamed mucosa (26%) were the most frequent findings. BAL cultures

were positive in 48% of cases, with Klebsiella being the predominant organism.

Tuberculosis was confirmed in 32% of the cases. Histopathology confirmed

malignancy in 5.8%, mainly adenocarcinoma. In 24.2% of participants, the

procedure was inconclusive. Overall, FOB was found to be a safe and valuable

tool in diagnosing a spectrum of pulmonary conditions, especially in

smear-negative tuberculosis, fungal and atypical infections, and malignancies,

aiding targeted therapy and better clinical outcomes.

DOI: 10.4081/monaldi.2025.3562

PMID: 40923354

**82. Int J Epidemiol. 2025 Aug 18;54(5):dyaf154. doi: 10.1093/ije/dyaf154.**

Body mass index and tuberculosis risk: an updated systematic literature review

and dose-response meta-analysis.

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Hygiene & Tropical Medicine, London, United Kingdom.

**BACKGROUND:** The relationship between nutritional status and tuberculosis is

critically important but poorly understood. We extended a 2009 review

characterizing the relationship between body mass index (BMI) and tuberculosis

risk.

**METHODS:** We systematically searched for new studies published between 2009 and

2024 investigating BMI and tuberculosis risk in adults. We extracted estimates

of risk in BMI categories, used resampling to assign a median BMI 'dose' within

each category, and included these in one-stage dose-response meta-analyses,

stratifying results by population group and country tuberculosis burden. We

fitted linear models for comparability with the 2009 review and restricted cubic

spline models to investigate nonlinear relationships and piecewise linear

models.

**RESULTS:** Our analyses showed an inverse dose-response relationship between BMI

and tuberculosis risk across all populations in the full underweight to obese

range (15.0-35.0 kg/m2). The spline and piecewise linear models showed a

nonlinear relationship-in 22 general-population cohorts (n = 24 921 531), there

was a steep per-unit reduction in risk for BMI of <25.0 kg/m2 [18.0%, 95%

confidence interval (CI): 16.4-19.6], which decreased more gradually for BMI

of ≥25.0 kg/m2 (6.9%, 95% CI: 4.6-9.2). In 18 cohorts of people with HIV

(n = 162 609), the reduction was 15.3% for BMI of <23.0 kg/m2 (95% CI:

13.1-17.5) and 2.6% (95% CI: -3.1-7.9) for BMI of ≥23.0 kg/m2. In three cohorts

of people with diabetes (n = 1 118 424), the reduction was 20.5% for BMI

of <24.0 kg/m2 (95% CI: 18.4-22.6) and 13.4% (95% CI: 3.9-22.0) for BMI

of ≥24.0 kg/m2. Based on the global BMI distribution, we estimated a relative

risk of tuberculosis associated with undernutrition (BMI < 18.5 kg/m2) of 5.0

(95% CI: 4.2-5.9).

**CONCLUSION:** Our results highlight the independent importance of nutritional

status as a driver of the tuberculosis epidemic.

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International Epidemiological Association.

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**83. Cureus. 2025 Aug 4;17(8):e89383. doi: 10.7759/cureus.89383. eCollection 2025**

**Aug.**

Tuberculous Meningitis in a One-Year-Old Child With Isoniazid-Induced

Hepatotoxicity: A Case Report.

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Tuberculous meningitis (TBM) is predominantly observed in developing countries

but remains relatively rare in developed countries. Therefore, if a clinician

does not suspect TBM, its diagnosis may be delayed. Furthermore, drug-induced

hepatotoxicity is common and can become severe during TBM treatment. Given the

importance of multidrug regimens for TBM management, alternative drugs with

favorable cerebrospinal fluid (CSF) penetration and high safety in terms of side

effects are urgently required. We report a case of a one-year and 10-month-old

Japanese boy who presented with an eight-day history of fever and altered

consciousness. Contrast-enhanced magnetic resonance imaging revealed brainstem

infarction, hydrocephalus, and basilar meningeal enhancement. CSF analysis

showed an increased cell count with a predominance of mononuclear cells. On the

basis of these findings, we suspected TBM and initiated antituberculosis

treatment, including isoniazid, rifampicin, ethambutol, and pyrazinamide, along

with steroids and aspirin. TBM was confirmed based on a combination of clinical

findings and a positive sputum culture for Mycobacterium tuberculosis. During

treatment, the patient developed isoniazid-induced hepatotoxicity, characterized

by elevated levels of hepatic transaminases and hyperbilirubinemia. Substituting

isoniazid with linezolid and levofloxacin in the initial treatment successfully

ameliorated the hepatic injury without additional adverse events. This suggests

that even in developed countries, clinicians must maintain a high suspicion of

TBM when evaluating children with subacute neurological symptoms and consider

performing additional imaging studies and CSF examinations. Further, this case

demonstrated that linezolid and levofloxacin can be useful alternatives to

isoniazid in preventing associated hepatotoxicity.

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**84. Cureus. 2025 Aug 5;17(8):e89419. doi: 10.7759/cureus.89419. eCollection 2025**

**Aug.**

Evaluation of Late Postoperative Pulmonary Function Following Lobectomy in

Patients With Tubercular and Non-tubercular Lung Diseases.

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**BACKGROUND:** Pulmonary function testing, especially spirometry, is essential for

assessing patients after pulmonary resection for tubercular and non-tubercular

diseases. Tuberculosis (TB) remains a major cause of death globally, while other

non-tubercular conditions such as lung abscess, bullous disease, and

bronchiectasis also require lobectomy. This study aimed to compare late

postoperative pulmonary function following lobectomy between TB and non-TB

patients.

**METHODS:** This cross-sectional study included 60 patients (30 TB, 30 non-TB) who

underwent lobectomy at the National Institute of Diseases of the Chest and

Hospital between January 2022 and June 2023. Pulmonary function was evaluated

using spirometry, measuring forced vital capacity (FVC) and forced expiratory

volume in one second (FEV1). The FEV1/FVC ratio was also calculated to assess

the presence and severity of obstructive or restrictive lung patterns. Data were

collected using a semi-structured questionnaire via face-to-face interviews.

**RESULTS:** Among TB patients, 86.67% had postoperative forced expiratory volume in

one second (FEV1) <2 L, compared to 60% in non-TB patients (p<0.05).

Postoperative forced vital capacity (FVC) ≥2 L was found in 40% of TB and 43.33%

of non-TB patients (p<0.05). Although FEV1/FVC improved in both groups, the

difference was not statistically significant. Hospital stay, intraoperative

bleeding, lobe involvement, and underlying disease showed significant

differences between groups.

**CONCLUSION:** Non-TB patients demonstrated better postoperative pulmonary function

than TB patients. These findings may guide perioperative planning and help

reduce complications following lobectomy.

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**Aug.**

Cerebral Tuberculoma in a Patient With Pre-extensively Drug-Resistant

Tuberculosis and AIDS: Diagnostic and Management Challenges.

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Extrapulmonary tuberculosis (TB), particularly when it involves the central

nervous system (CNS), remains a significant clinical challenge. Cerebral

tuberculoma, though rare, can present with complex symptoms that overlap with

other neurological conditions, making timely diagnosis difficult. The condition

demands a multidisciplinary approach for accurate diagnosis and effective

management, especially in patients with multiple comorbidities. This report

describes a complex case of pre-extensively drug-resistant TB affecting both the

lungs and CNS in a 54-year-old immunocompromised male with AIDS, chronic

hepatitis B and C, COVID-19, and reactivated varicella. The patient presented

with systemic symptoms and new-onset neurological deficits, including seizures

and right-sided paresis. Brain MRI revealed a cerebral tuberculoma with

surrounding edema. Sputum testing confirmed Mycobacterium tuberculosis resistant

to multiple first- and second-line agents. Treatment included a five-drug

anti-tuberculosis regimen followed by initiation of antiretroviral therapy. The

clinical course was complicated by immune reconstitution inflammatory syndrome,

hepatic decompensation, and varicella reactivation. Despite profound

immunosuppression and multisystem involvement, the patient achieved a favorable

outcome through aggressive, multidisciplinary management. This case underscores

the diagnostic complexity of CNS TB in patients with advanced HIV infection and

multiple viral coinfections and highlights the critical role of early

neuroimaging and coordinated care.

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**Aug.**

Beyond Post-tuberculosis Sequelae: Uncovering Common Variable Immunodeficiency

in an Adult.

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Common variable immunodeficiency (CVID) is a rare immunodeficiency syndrome

presenting with wide manifestations and leading to a delayed diagnosis. A

40-year-old male, a case of old treated tuberculosis, presented with a

productive cough and hemoptysis. He had a history of recurrent respiratory

symptoms previously attributed to post-tuberculosis sequelae with bilateral

bronchiectasis, which can also occur as a manifestation of underlying common

variable immunodeficiency (CVID). After a detailed evaluation, serum

immunoglobulin levels were markedly reduced, confirming CVID. The patient was

started on intravenous immunoglobulin (IVIG) therapy every month. After a

six-month follow-up, the patient was symptomatically better and had reduced

hospitalizations.

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Revisiting the therapeutic threshold in tuberculosis Care: Lessons from Southern

Africa's dual-method approach.

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**eCollection 2025.**

Enhancing diagnostic efficiency of pyrazinamide resistance in Mycobacterium

tuberculosis via modified MGIT assay and genotypic correlation.

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Pyrazinamide (PZA) plays a crucial role in the treatment of both active and

latent tuberculosis, particularly in regimens designed to treat drug-resistant

TB. However, diagnosing resistance to PZA poses challenges for managing TB,

highlighting the need for accurate detection methods. This study aims to address

the challenges in detecting PZA resistance by modifying the standard MGIT960 PZA

drug susceptibility testing method by optimizing the inoculum dilution. Briefly,

three MGIT DST versions were evaluated: the standard method, the reduced

inoculum (RI) method employing a 1:20 inoculum dilution and the sparse dilution

(SD) method using a 1:50 dilution of the inoculum for growth control tube, while

the undiluted MGIT positive culture was used for the PZA test tube. The SD MGIT

DST approach minimized the number of false-resistant PZA results to (31/401) 7.7

% against 27 % by standard MGIT DST and 11.7 % by RI MGIT DST approach, thereby

reducing the false-positivity rate by 19.3 %. Targeted sequencing of pncA gene

identified mutations in only 14/401 isolates (3.5 %). Whole genome sequencing

(WGS) of the 31 phenotypically resistant isolates identified resistance

-associated mutations in pncA gene (45 %), panD (9.6 %), mas (12.9 %), glpK (3.2

%), and lprG (3.2 %), and others efflux associated genes like Rv1258c (3.2 %),

Rv0191c (3.2 %), and Rv3008 (6.45 %), except for 4 isolates, for which no

mutations were detected in the target genes. These genes are involved in various

resistance mechanisms including cell wall synthesis, metabolic pathways, and

drug tolerance, which are essential for PZA efficacy. Notably, new mutations in

glpK and mas were detected in isolates with wild-type pncA and were absent in

the sensitive isolates. Our study substantiates the improvement of phenotypic

testing methods and enhances the detection of PZA resistance even in

resource-limited settings and direct research towards improving the diagnostic

accuracy in TB drug resistance management.

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**ahead of print.**

New Indazole Derivatives as Potential Scaffolds for the Development of

Anticancer, Antiviral, and Anti-tuberculosis Chemotherapeutic Compounds.

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**INTRODUCTION:** Chemotherapy remains essential despite advances in immunotherapy,

radiotherapy, and biological therapy. However, the wide range of chemical drugs

is limited by a narrow therapeutic index, low selectivity, and the development

of resistance. In this regard, new high-efficiency drugs are in extremely high

demand. The indazole moiety, a scaffold found in many biologically active

compounds, was selected for use in new drug design.

**METHODS:** Six new indazole derivatives were synthesized via Suzuki-Miyaura

coupling starting from bromoindazole. Their antiviral (against influenza A and

SARS-CoV-2), antibacterial (against M. tuberculosis), and antiproliferative

activities (against neuroblastoma, glioma, leukemia cell lines) were evaluated

in vitro. Acute toxicity was assessed in mice of both sexes via single

intragastric administration, with toxicometric parameters and pathomorphological

changes studied.

**RESULTS:** 6-(1H-pyrazol-4-yl)-1H-indazole (8) suppressed the reproduction of the

influenza virus at non-toxic doses to the MDCK cells and showed cytotoxicity

against cancer cell lines, with an IC50 between 4 and 14 μM. However, it

exhibited significant acute toxicity in mice (LD50 40 mg/kg), causing systemic

organ damage.

**DISCUSSION:** Derivative 8 demonstrated promising antiviral and antiproliferative

activities but exhibited considerable acute toxicity in vivo. The antiviral

efficacy, although lower than oseltamivir, is meaningful and justifies further

optimization and investigation. Its antibacterial activity against M.

tuberculosis adds to its potential as a multifunctional agent.

**CONCLUSION:** While derivative 8 has shown potential as an antiviral and

anticancer agent, its high toxicity highlights the need for further studies to

define a safe and effective therapeutic window. Overall, the indazole scaffold

remains a valuable platform for the development of new therapeutic compounds.

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