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**境外学者发表的结核病英文文章摘要**

**（107篇）**

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

**1. Nature. 2025 Jun 18. doi: 10.1038/s41586-025-09177-7. Online ahead of print.**

Targeting de novo purine biosynthesis for tuberculosis treatment.

Lamprecht DA(#)(1)(2), Wall RJ(#)(3), Leemans A(#)(4), Truebody B(5), Sprangers

J(4)(6), Fiogbe P(4)(6), Davies C(3), Wetzel J(4), Daems S(4), Pearson W(3),

Pillay V(5), Saylock S(7), Ricketts MD(7), Davis E(3), Huff A(7), Grell T(7),

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C(11), Sans S(11), Desorme A(11), Chappat N(11), Ray A(11), Pereira Moraes

M(12), Washington T(12), D'Erasmo H(12), Sancheti P(9), Everaerts M(9),

Monshouwer M(4), Esquivias J(13), Larrouy-Maumus G(14), Draghia Akli R(7)(15),

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Tuberculosis remains the leading cause of death from an infectious disease1,2.

Here we report the discovery of a first-in-class small-molecule inhibitor

targeting PurF, the first enzyme in the mycobacterial de novo purine

biosynthesis pathway. The lead candidate, JNJ-6640, exhibited nanomolar

bactericidal activity in vitro. Comprehensive genetic and biochemical approaches

confirmed that JNJ-6640 was highly selective for mycobacterial PurF.

Single-cell-level microscopy demonstrated a downstream effect on DNA

replication. We determined the physiologically relevant concentrations

of nucleobases in human and mouse lung tissue, showing that these levels were

insufficient to salvage PurF inhibition. Indeed, proof-of-concept studies using

a long-acting injectable formulation demonstrated the in vivo efficacy of the

compound. Finally, we show that inclusion of JNJ-6640 could have a crucial role

in improving current treatment regimens for drug-resistant tuberculosis.

Together, we demonstrate that JNJ-6640 is a promising chemical lead and that

targeting de novo purine biosynthesis represents a novel strategy for

tuberculosis drug development.

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**2. Microb Pathog. 2025 Jun 20:107827. doi: 10.1016/j.micpath.2025.107827. Online**

**ahead of print.**

Association of viral exposure with tuberculosis disease progression: A

systematic review.

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**INTRODUCTION:** Viral infections have been found to affect the outcome of

bacterial infections, but for the case of tuberculosis, much emphasis has been

on HIV and less attention has been given to other viruses. We conducted a

systematic review to identify studies that investigated the association of viral

infection other than HIV and HIV coinfection with tuberculosis disease

susceptibility and progression.

**METHODS:** We searched PubMed, Ovid Embase, and Scopus electronic databases using

search terms "tuberculosis, viral disease, not HIV, TB, virus" in text words and

MeSH terms for cohort and cross-sectional case-control studies by design that

associated virus infections other than HIV-1 and HIV-2 with the development of

TB disease.

**RESULTS:** Ten articles (three for cohort and seven for cross-sectional

case-control studies) were included in this review. An association with TB

disease was established for infections with Human Cytomegalovirus (HCMV, 3

studies), Human T-Lymphotropic virus type 1 (HTLV-1, 3), Hepatitis C virus (HCV,

2) and Human Herpesvirus-8 virus (HHV-8, 1). Published studies failed to

establish an association with Herpes Simplex virus-1 and 2 (1), Epstein Barr

virus (2), and Influenza A virus (1). Majority of these studies (7 studies) were

scored high quality in appraisal, one intermediate and two were scored low. The

variation in viral pathogens, study designs and methods of measurement precluded

meta-analysis.

**CONCLUSION:** This limited data suggests that infections with HCMV, HTLV-1, HCV

and possibly HHV-8 may be associated with TB disease, either through increasing

susceptibility to infection or through enhancing progression from infection to

disease. More data are needed on the potential role of other viral infections

than HIV in tuberculosis disease progression, in order to be considered in the

programmatic control of tuberculosis disease.

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Treatment outcomes of bedaquiline-resistant tuberculosis: a retrospective and

matched cohort study.

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**BACKGROUND:** Rising prevalence of bedaquiline resistance undermines benefits from

this life-saving drug for rifampicin-resistant tuberculosis (RR tuberculosis).

Despite increasing awareness, patient-level outcomes for bedaquiline-resistant

tuberculosis have not been well characterised and case management has been

poorly defined.

**METHODS:** We did a retrospective cohort study of bedaquiline-resistant

tuberculosis with matched RR tuberculosis controls at a tuberculosis referral

hospital in East London, South Africa. Cases included patients aged 13 years or

older with a phenotypic bedaquiline-resistant Mycobacterium tuberculosis isolate

identified between Jan 1, 2018 and June 30, 2023. Controls with confirmed

bedaquiline-susceptible tuberculosis, matched 1:1 by baseline culture status,

age, and HIV status, were selected from a prospective observational study

conducted during an overlapping period at the same facility. Primary outcomes

included time to sputum culture conversion (SCC), a modified WHO-defined

unfavourable outcome, and tuberculosis-free survival (alive, with SCC, and in

care or treatment completed) up until 18 months. Adjusted analyses used Cox

proportional hazards and logistic regression models.

**FINDINGS:** 82 patients with bedaquiline-resistant tuberculosis were included, 57

(70%) of whom were HIV positive. Bedaquiline was prescribed for 72 (88%) of 82

patients and meropenem (plus amoxicillin-clavulanate) for 32 (39%) of 82.

Together with bedaquiline, the most frequently prescribed drugs included

clofazimine, linezolid, and terizidone. Median time to SCC after treatment

initiation was 175 days (IQR 100-254) in the bedaquiline-resistant cohort and 32

days (30-42) in matched controls. In the analysis of the combined cohorts,

bedaquiline resistance (adjusted hazard ratio 0·03, 95% CI 0·0023-0·29, p=0·003) was associated with longer time to SCC when adjusted for baseline microscopy grade and baseline fluoroquinolone resistance. WHO treatment outcomes in those with bedaquiline-resistant tuberculosis were unfavourable in 54 (67%) of 81 patients, driven by treatment failure in 35 (43%) of 81. At 18 months, 43 (52%)

of 82 patients had reached tuberculosis-free survival, 19 (23%) of 82 had died,

and 50 (79%) of 63 survivors were still on treatment.

**INTERPRETATION**: Current treatment options for bedaquiline-resistant tuberculosis

result in prolonged therapy, delayed microbiological responses, and poor

clinical outcomes. Implementation of more rapid resistance testing, including

targeted next-generation sequencing, and access to novel treatment options

within randomised controlled trials for bedaquiline-resistant tuberculosis, are

priorities for tuberculosis programmes.

FUNDING: The South African Medical Research Council.

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Unified global action needed to tackle bedaquiline-resistant tuberculosis.

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**5. BMC Infect Dis. 2025 Jun 20;25(1):806. doi: 10.1186/s12879-025-11220-x.**

Drug resistance profile of Mycobacterium tuberculosis complex isolated from

pulmonary tuberculosis patients and their household contacts in central

Ethiopia.

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**BACKGROUND:** There is a gap between tuberculosis (TB) infection and the onset of

clinical TB disease, which makes identifying TB transmission dynamics a

prominent challenge. Different reports were made on the concordance of

drug-resistance profiles between the household contact and the purported index

case. This study investigated the drug-resistance pattern concordance of the

index-household contact pair in central Ethiopia.

**METHOD:** A laboratory-based cross-sectional study was conducted on Mycobacterium

tuberculosis isolates identified from bacteriologically confirmed pulmonary TB

patients and their household contacts (HHCs) in central Ethiopia from January to

December 2023. Sputum specimens were collected from index cases and presumptive

HHCs and examined using the Xpert Ultra assay, Xpert XDR assay, and

Mycobacterium tuberculosis culture. Descriptive statistics were used to

summarize the data.

**RESULT:** Among 902 TB symptoms screened HHCs of 303 index cases, 20.17% (182/902)

had Presumptive TB, and 7.14% (13/182) developed active tuberculosis. In index

cases, 23.52% (64 /272) showed resistance to at least one of the five first-line

anti-TB drugs. The prevalence of mono-resistant to STR, INH, RIF, and PZA was:

2.20% (6 /272), 2.20% (6/272), 6.25% (17/272), and 1.47% (4/272), respectively.

Any first-line anti-TB drug resistance was higher among relapse cases than new

cases, at 41.67% (10/24) and 21.77% (54/248), respectively. Among the RR/MDR-TB

cases tested with the Xpert MTB/XDR assay, 56.81% (25/44) cases showed

resistance to INH. Among these 25 INH resistance samples, 5 had no melting point

on the wild ahpc gene as well as on the ahpc gene mutant. In HHCs with positive

cultures, 23.07% (3/13) displayed resistance to any first-line anti-TB

medication. Only 69.23% (9/13) of HHCs had isolates that aligned with the pDST

pattern of the index case for all five first-line anti-TB drugs.

**CONCLUSION:** Nearly one-third of the household contacts have discordant

drug-resistance profiles from the index patients. This study offers compelling

proof that it is not advisable to treat close contacts without DST results based

on the DST results of the supposed source case. The low drug resistance rate to

new oral second-line drugs in this study did not guarantee the absence of

resistance to each drug.

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**6. Int J Biol Macromol. 2025 Jun 18:145279. doi: 10.1016/j.ijbiomac.2025.145279.**

**Online ahead of print.**

Structural analysis of M. tuberculosis EccC1 and its complex with EsxAB

virulence factor using X-ray crystallography, molecular docking, and dynamics

simulation techniques.

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M. tuberculosis ESX-1 system secretes virulence factors into host macrophages

during infection, however, the mechanism of secretion is currently unknown.

Here, we have determined the crystal structure of MtbEccCb1-D2 protein

(Leu34-Ser313 residues, Mw ~ 31.4 kDa) in complex with ATPγS and Mg2+, which

adopts a classical Ftsk/SpoEIII type fold. The EccCb1-D2 showed two melting

temperatures, Tm1 at 37.64 ± 0.08 °C and Tm2 at 65.85 ± 0.12 °C, during the

unfolding pathway. Modeled ∆EccC1 and ∆EccC1 + EsxAB hexamers showed a channel

(~34 Å) involved in EsxAB (~29 Å) translocation toward the inner membrane. At

the entrance gate of the channel, the LxxxMxF motif of the EsxB export arm binds

to the substrate binding pocket of the EccCb1-D3 protein. Inside the channel,

the PL-1 and PL-2 pore loops, close to the α7-helix and the loop between β8-β9

strands in EccCa1-D1, EccCb1-D2, and EccCb1-D3 may be involved in EsxAB factor

translocation. Stability, fluctuation, and compactness parameters in 100 ns

dynamics simulation analysis showed the highest flexibility in ΔEccCa1, ∆EccC1,

and ∆EccC1 + EsxAB hexamers and stability in ΔEccCb1 hexamer. Our EccCb1-D2

structure and dynamics simulation analysis on four modeled systems have revealed

the mechanism involved in EsxAB translocation, a key target for the development

of antivirulence inhibitors against M. tuberculosis.

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**7. PLoS One. 2025 Jun 20;20(6):e0324838. doi: 10.1371/journal.pone.0324838.**

**eCollection 2025.**

The prevalence of undernutrition and associated risk factors in people with

tuberculosis in Lao People's Democratic Republic.

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**OBJECTIVE:** Undernutrition is common in individuals with tuberculosis (TB). There

is a bidirectional association between having TB and undernutrition;

undernutrition increases the risk of having active TB, and having TB worsen

undernutrition by reducing appetite and food intake. Despite World Health

Organization (WHO) recommendations for comprehensive nutritional assessment and

counselling for people with TB, systematic implementation is lacking in Lao

People's Democratic Republic (Lao PDR), leading to an insufficient understanding

of undernutrition prevalence in this population.

**METHODS:** A facility-based cross-sectional survey was conducted between March

2022 and March 2023 in six central and provincial hospitals in Lao PDR. We

assessed the prevalence of undernutrition in 312 people diagnosed with TB at TB

diagnosis using body mass index (BMI). Undernutrition was defined as a

BMI < 18.5 kg/m2, and severe undernutrition as a BMI below 16.5 kg/m2. Data on

demographic, clinical and economic information and nutritional status were

extracted from an intervention study assessing the effect of nutritional

counselling and feeding on the financial burden of TB and TB treatment outcomes.

**RESULTS:** Of 312 participants, 40.7% (n = 127) were with undernutrition

(BMI < 18.5 kg/m2) at the time of TB diagnosis. 20.5% (n = 64) with severe

undernutrition (BMI < 16.5 kg/m2). Factors significantly associated with

undernutrition included age group 15-24 years (Adjusted odds ratio (AOR) 6.9,

95% confidence interval [95%CI]: 2.2-23.2), drug-resistant TB (AOR 3.2, 95%CI:

1.0-11.8), experiences of hospitalization until TB diagnosis (AOR 3.4, 95%CI:

2.0-5.9), self-reported weight loss (AOR 7.8, 95%CI: 2.3-36.4), and below the

poverty line at TB diagnosis (AOR 1.9, 95%CI: 1.0-3.6).

**CONCLUSION:** A high prevalence of undernutrition was observed in people diagnosed

with TB at their diagnosis in Lao PDR. The findings underscore the urgent need

for systematic nutritional assessment and counselling as integral components of

TB care to identify and address undernutrition, thereby enhancing overall health

outcomes for individuals with TB.

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**10.1371/journal.pgph.0004212. eCollection 2025.**

Non-communicable diseases and resistant tuberculosis, a growing burden among

people living with HIV in Eastern Kenya.

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Human Immunodeficiency Virus (HIV) and tuberculosis (TB) continue to pose a

significant health burden in Kenya. Countries with the highest rates of people

living with HIV (PLWH) also have a high prevalence of non-communicable diseases

(NCDs), including type 2 diabetes (T2D) and hypertension (HPT). This study

evaluated the burden and factors associated with T2D, HPT, and TB, including

resistant strains among PLWH receiving antiretroviral therapy (ART) in Eastern

Kenya. Blood and sputum samples, and baseline information were collected from

280 consenting PLWH. The participants' blood pressure (BP), glycated hemoglobin

(HbA1c), CD4 cell counts, HIV viral load, full blood count, blood chemistry, and

Rifampicin resistance were assessed. The mean (SD) age of the participants was

35.6 (±9.8) years, and a median (IQR) duration of living with HIV of 7 (4 -8)

years. Most participants, 179 (63.9%), were HIV mono-infected, with 58 (20.7%)

HIV/TB, 42 (15%) HIV/T2D, and 33 (11.8%) HIV/HPT dual comorbidities reported.

Triple comorbidities reported included 18 (6.4%) HIV/T2D/HPT, 9 (3.2%)

HIV/TB/T2D, and 9 (3.2%) HIV/TB/HPT, with 4 (1.4%) HIV/TB/T2D/HPT quadruple

comorbidity reported. Six (2.1%) multidrug-resistant TB coinfections were

detected. In multivariate analyses, being on ARV only (aOR 0.5; 95% CI 0.4 -

0.6, p = 0.0001) and achieving virological suppression (aOR 0.8; 95% CI 0.6 -

0.9, p = 0.017) were protective against HIV/TB coinfection. Previous hospital

admission (aOR 1.2; 95% CI 1.1 - 1.4, p = 0.049) and previous TB infection (aOR

1.6; 95% CI 1.0 - 3.0, p = 0.034) were associated with HIV/TB coinfection. The

PLWH in Eastern Kenya continues to experience a syndemic of NCDs and TB,

including resistant strains. Consistent adherence to ART is crucial for

achieving viral suppression; these are protective against NCDs and TB among

PLWH. The findings highlight the necessity of integrating NCD management with

HIV and TB treatment programs in Kenya.

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Mycobacterium tuberculosis Infection and Acute or Subclinical Coronary Artery

Disease: the Swiss HIV Cohort Study.

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**BACKGROUND:** In tuberculosis medium/high prevalence countries, Mycobacterium

tuberculosis (MTB) infection has been associated with acute coronary artery

disease (CAD) events and subclinical atherosclerosis. We aimed to examine

whether MTB infection contributes to clinical and subclinical CAD in people with

HIV (PWH) in tuberculosis low incidence settings.

**METHODS:** Regarding CAD events, cases were Swiss HIV Cohort Study (SHCS)

participants with a first CAD event (2000-2022). CAD-free SHCS controls were

matched on sex, age and observation time. Regarding subclinical atherosclerosis,

SHCS participants underwent (2013-2019) non-contrast CT for detection of

coronary artery calcification (CAC) and coronary CT angiography (CCTA) for the

detection of coronary soft, mixed, or high-risk plaque (SMHRP). We obtained

univariable/multivariable odds ratios (OR) for CAD events, CAC, and SMRHP, in

participants with negative TB status, MTB infection, and active TB, analyzed in

the context of traditional and HIV-related CAD risk factors.

**RESULTS:** We included 465 patients with acute CAD events and 1123 controls

(median age 56 years, 14% women, 86% with suppressed HIV RNA). MTB infection was

not associated with CAD events in multivariable analysis (odds ratio [95%

confidence interval], 0.92 [0.55-1.52]) vs. participants with negative TB

status. In 402 participants undergoing CAC/CCTA (median age 53 years, 14% women,

96% with suppressed HIV RNA), MTB infection was not associated with SMHRP

(OR=0.55 [0.19-1.55]) or with CAC (OR=0.38 [0.1-1.41]) in multivariable

analysis.

**CONCLUSIONS: I**n PWH in Switzerland, a tuberculosis low prevalence country, we

found no evidence of any association between MTB infection and acute CAD events

or subclinical coronary atherosclerosis.

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DOI: 10.1097/QAI.0000000000003714

PMID: 40539759

**10. Vet Rec. 2025 Jun 21;196(12):e5696. doi: 10.1002/vetr.5696.**

Bovine TB infection status in cattle in Great Britain in 2023.

George BM(1), Duncan D(1), Waller E(1), Marriott E(1), Payne MC(1), Withenshaw

S(1), Brouwer A(1), Harris KA(1), May HE(1), Avigad R(1).

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In 2023, 3078 cattle herds experienced a new bovine tuberculosis (TB) incident

out of a total of 68,895 registered cattle herds in Great Britain (GB). This was

a 13.6 per cent decrease in the number of new TB incidents and a 3.3 per cent

decrease in the number of registered herds compared with 2022. Similarly, the

number of TB incidents in England fell by 16.9 per cent and the number of herds

reduced by 4.3 per cent. In Scotland, there was also a decline in the number of

TB incidents (-18.2 per cent) and herds (-0.5 per cent). In contrast, Wales

experienced a 2.3 per cent increase in the number of new TB incidents, and a 2.0

per cent decrease in the number of herds. In GB the herd incidence rate of TB

decreased for the third consecutive year, with 6.5 new cases per 100 herd years

at risk (100 HYR) in 2023, compared with 7.2 in 2022 (incidence rate ratio

[IRR]=0.90, P<0.001). Similarly, the herd incidence rate in England decreased

significantly in 2023 compared with 2022, from 8.4 to 7.3 new TB incidents per

100 HYR (IRR=0.87, P<0.001). This decrease was mainly observed in the High risk

area. The herd incidence rate in Wales increased non-significantly in 2023

compared with 2022, from 6.5 to 6.8 incidents per 100 HYR (IRR=1.05, P=0.38).

Changes in incidence rate were not universal across Wales TB areas, with a

significant increase observed in the High TB Area West, and a significant

decrease in the Intermediate TB Area North. Scotland remained Officially TB Free

in 2023, with an annual herd incidence rate of 0.6 TB incidents per 100 HYR,

slightly lower than in 2022 (0.7) (IRR=0.84, P=0.51). At GB level, there was a

slight decrease in TB prevalence from 3.9 per cent in 2022 to 3.6 per cent in

2023. TB prevalence in England in 2023 declined in all TB risk areas relative to

2022. There was a small increase in TB prevalence in Wales in 2023 (5.4 per

cent) compared with 2022 (5.3 per cent). TB prevalence in Scotland remained

unchanged between 2022 and 2023 (0.1 per cent).

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DOI: 10.1002/vetr.5696

PMID: 40539673

**11. ACS Infect Dis. 2025 Jun 20. doi: 10.1021/acsinfecdis.5c00077. Online ahead of print.**

Playing Telephone: How Secondary Messengers Influence Host-Pathogen Interactions

in Tuberculosis.

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Secondary messengers are small, diffusible signaling molecules that transmit

information from environmental cues detected at the cell surface by

extracellular signaling molecules (primary messengers) to effector proteins,

thereby enabling an appropriate cellular response. These molecules include

cyclic nucleotides, alarmones, and lipid-derived metabolites and are ubiquitous

regulators, influencing processes such as growth, metabolism, and

neurotransmission in mammalian cells, as well as chemotaxis, biofilm formation,

and metabolism in prokaryotes. Mycobacterium tuberculosis encodes an extensive

array of genes dedicated to the synthesis and degradation of a diverse range of

secondary messenger molecules. Given its highly intricate intracellular

lifestyle and its ability to endure and persist in hostile and fluctuating

environments, there is significant potential for crosstalk between host and

bacterial secondary messengers. M. tuberculosis has likely co-opted these

signaling processes within the host cell to facilitate its own pathogenesis and

virulence. Recent studies have begun to elucidate the complex and multifaceted

roles played by some of these secondary messengers, highlighting their capacity

to regulate mycobacterial physiology while simultaneously modulating host immune

responses. This review summarizes the current understanding of secondary

messenger signaling in M. tuberculosis and explores how this knowledge is being

leveraged to develop improved vaccines and therapeutic strategies.

DOI: 10.1021/acsinfecdis.5c00077

PMID: 40539596

**12. Pharmacogenomics. 2025 Jun 20:1-15. doi: 10.1080/14622416.2025.2509479. Online ahead of print.**

Genetic polymorphisms and adverse reactions to antituberculosis therapy.

Gunter HM(1), Choshi P(2), Chimbetete T(2), Pedretti S(3), Lehloenya RJ(4)(5),

Sinxadi PZ(1)(6), Ritchie MD(7)(8)(9), Phillips EJ(10)(11), Haas DW(11)(12),

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Tuberculosis is the leading cause of death from a single infectious agent

globally, with the highest burden in low-and middle-income countries. Successful

treatment requires prolonged administration of multiple drugs. The increasing

threat of multidrug-resistant tuberculosis has prompted the development of a

robust pipeline for new drugs. While generally safe and well tolerated, adverse

drug reactions (ADRs) to TB drugs have a considerable impact on treatment

outcomes. Pharmacogenetic testing has been implemented for some diseases to

identify at-risk individuals and prevent ADRs. For tuberculosis treatment, the

use of pharmacogenetic testing to optimize complex regimens and avoid ADRs is

appealing, but there has been minimal implementation. To improve the use of

pharmacogenetics, understanding both the pharmacology of relevant drugs and

population-specific pathophysiology of ADRs are essential. This review

highlights the major treatment-limiting ADRs with TB drugs, the current

understanding of drug metabolic pathways, ADR pathophysiology, and known

pharmacogenetic risk alleles. We highlight research gaps and barriers to

meaningful clinical use and implementation of pharmacogenomic testing to prevent

adverse reactions to TB drugs.

DOI: 10.1080/14622416.2025.2509479

PMID: 40538374

**13. Infect Dis Poverty. 2025 Jun 20;14(1):53. doi: 10.1186/s40249-025-01324-6.**

The social determinants of tuberculosis: a case-control study characterising

pathways to equitable intervention in Peru.

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**BACKGROUND:** Despite being key components of global tuberculosis policy, poverty

reduction and social protection interventions have been inconsistently

implemented. We aimed to characterise how poverty and interrelated personal risk

factors increase tuberculosis risk in Peru to inform the design of locally

appropriate, person-centred, equity-oriented interventions.

**METHODS:** We undertook a case-control study among people aged 15 years and over

in 32 communities in Peru between 2016 and 2019. Cases (n = 2337) were people

diagnosed with any form of tuberculosis. Controls (n = 981) were people living

in randomly selected households in the same communities. We derived measures of

household poverty from three dimensions (physical, human, and financial capital)

and investigated the associations between these; personal risk factors more

specifically linked to health (e.g. smoking); and tuberculosis. We used logistic

regression to calculate adjusted odds ratios (aOR), 95% confidence intervals

(95% CI), and population attributable fractions (PAF). A directed acyclic graph

was used to inform the analytical approach.

**RESULTS:** Household poverty was strongly associated with tuberculosis (aOR = 3.1;

95% CI: 2.3-4.2 for people from the 'poorer' versus 'less poor' half of

households). There was a non-linear social gradient across deciles of household

poverty, with odds of tuberculosis increasing exponentially as poverty deepened

(aOR = 12.6; 95% CI: 6.8-23.2 for the 'poorest' decile versus the 'least poor'

decile). Overall, tuberculosis burden could be halved by reducing poverty in the

'poorer' half of households to the level of the 'less poor' half (PAF = 47%; 95%

CI: 40-54). For key personal risk factors, we estimated PAF for alcohol excess

(PAF = 12.3%, 95% CI: 7.2-17.2); underweight (PAF = 10.3%, 95% CI: 8.7-11.8);

smoking (PAF = 8.8%, 95% CI: 3.8-13.5); HIV (PAF = 5.7%, 95% CI: 4.6-6.7); and

diabetes (PAF = 4.6%, 95% CI: 3.3-6.0). We also identified other important risk

factors including previous tuberculosis (PAF = 14.8%, 95% CI: 11.6-17.9);

incarceration (PAF = 9.5%, 95% CI: 6.8-12.1); and lower social capital

(PAF = 4.1%, 95% CI: 2.6-5.6). Most personal risk factors, particularly

education and substance misuse, tuberculosis exposures (e.g. incarceration and

homelessness), and undernutrition, exhibited a social gradient across quintiles

of household poverty and were more prevalent in people living in poorer

households (Cochran-Armitage test for linear trend P < 0.001 for variables

showing these social gradients).

**CONCLUSIONS:** Interventions addressing multidimensional household poverty and

interrelated personal risk factors could substantially reduce tuberculosis

burden. Our results provide an evidence base for designing person-centred,

equity-oriented interventions; and support more effective implementation of

poverty reduction and social protection within the global tuberculosis response.

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PMCID: PMC12180230

PMID: 40537847

**14. Thorax. 2025 Jun 19:thorax-2025-223594. doi: 10.1136/thorax-2025-223594. Online ahead of print.**

Dual sequential testing for latent tuberculosis infection in BCG-vaccinated

contacts: is it worth it?

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DOI: 10.1136/thorax-2025-223594

PMID: 40537216

**15. Eur Respir J. 2025 Jun 19;65(6):2401126. doi: 10.1183/13993003.01126-2024. Print 2025 Jun.**

WHO online guide on the use of digital technologies for tuberculosis programmes.

Akkerman OW(1)(2)(3), Falzon D(4)(3), Migliori GB(5)(3), Konstantynovska O(6),

Eyuboglu FO(7), Sismanidis C(4), Kanchar A(4), Duarte R(8)(9)(10)(11).

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DOI: 10.1183/13993003.01126-2024

PMID: 40537167

**16. Immunology. 2025 Jun 19. doi: 10.1111/imm.70006. Online ahead of print.**

Acute Plasmodium yoelii 17XNL Infection During BCG Vaccination Limits T Cell

Responses and Mycobacterial Growth Inhibition.

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Tuberculosis and malaria overlap in many sub-Saharan African countries where

Bacillus Calmette Guérin (BCG) vaccination is routinely administered. The aim of

this study was to determine whether the timing of BCG vaccination in relation to

a malaria infection has implications for BCG vaccine efficacy. Mice were

intradermally vaccinated with BCG either 4 weeks before infection with

blood-stage Plasmodium yoelii 17XNL, at 13 days post-infection (during an acute

blood-stage malaria infection) or 21 days post-infection (after clearance of P.

yoelii 17XNL infection). Ex vivo control of mycobacterial growth by splenocytes

was used as a surrogate of protective efficacy, and PPD-specific T-cell

responses were quantified by flow cytometry. No differences in mycobacterial

growth control were detected between BCG vaccinated mice and groups receiving

vaccination prior to or after clearance of P. yoelii 17XNL infection. Poorer

control of mycobacterial growth was observed following BCG vaccination

administered during an acute malarial infection compared to BCG vaccination only

or BCG vaccination after blood-stage malaria infection, and mycobacterial growth

negatively correlated with the magnitude of total cytokine production from

PPD-specific CD4+ T cells (p < 0.0001). Delayed BCG vaccination beyond the

neonatal period may increase the risk of concurrent malarial infections with the

potential to reduce BCG efficacy in children in malaria-endemic areas.

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DOI: 10.1111/imm.70006

PMID: 40537144

**17. Indian J Gastroenterol. 2025 Jun 19. doi: 10.1007/s12664-025-01795-3. Online**

**ahead of print.**

Urinary lipoarabinomannan for gastrointestinal tuberculosis: Another tool in the

kit.

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DOI: 10.1007/s12664-025-01795-3

PMID: 40536573

**18. Respirol Case Rep. 2025 Jun 18;13(6):e70252. doi: 10.1002/rcr2.70252.**

**eCollection 2025 Jun.**

When Teratoma Masquerades: A Rare Case of Intrapleural Mature Cystic Teratoma

Mimicking Tuberculous Empyema.

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Teratomas are germ cell tumours generally gonadal in origin and very rare,

arising from extra gonadal tissue. The most common extragonadal teratomas are

mediastinal, and the majority are benign. We report a case of a 49-year-old lady

with recurrent right complex pleural effusion occurring a month after the

completion of treatment for tuberculous empyema. Imaging from ultrasound of the

thorax and contrasted enhanced computed tomography (CECT) thorax revealed

multiseptated and loculated effusion in the thorax without any mediastinal and

lung involvement. Surprisingly, pleural fluids were negative for tuberculosis.

Despite chest drainage and initial treatment for bacterial empyema without

improvement, she underwent video assisted thoracoscopy and decortication of the

right pleura, and histopathological analysis revealed a mature cystic teratoma.

She was discharged in good health and under yearly surveillance. The rarity of

intrapleural mature cystic teratoma and its misleading presentation due to the

concurrent tuberculous empyema make this case noteworthy.

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Australia, Ltd on behalf of The Asian Pacific Society of Respirology.

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PMID: 40535730

**19. Respirol Case Rep. 2025 Jun 18;13(6):e70244. doi: 10.1002/rcr2.70244.**

**eCollection 2025 Jun.**

Catastrophic Hemoptysis in Concurrent Laryngeal and Endobronchial Tuberculosis

in an Immunocompetent Host: Survival Following Brief ECMO Support.

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We present a case of a 45-year-old previously healthy Filipino domestic helper

who presented with life-threatening hemoptysis due to disseminated tuberculosis

(TB) involving the larynx, tracheobronchial tree, and pulmonary parenchyma. She

presented with acute respiratory distress from massive hemoptysis, necessitating

emergent intubation and subsequent veno-venous (V-V) extracorporeal membrane

oxygenation (ECMO) support. Initial chest radiography revealed bilateral upper

lobe infiltrates and right middle lobe collapse. Bronchoscopic evaluation

demonstrated active haemorrhage and airway obstruction secondary to clot

formation. An incidental epiglottic mass was identified during laryngoscopy.

Given the failure of conservative measures to control bleeding, she underwent

emergent right middle and lower lobectomies. Histopathological analysis

confirmed necrotizing granulomatous inflammation, and Mycobacterium tuberculosis

was detected via polymerase chain reaction (PCR) testing. She was treated with a

multi-drug anti-tuberculosis regimen and successfully weaned from ECMO. The

epiglottic mass resolved, and there was no tracheal stenosis. This case

illustrates the complexities of managing tuberculosis-related respiratory

failure. It demonstrates the strategic role of ECMO in handling massive

hemoptysis, especially in cases of concurrent laryngeal TB (LTB) and

endobronchial TB (EBTB).

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Australia, Ltd on behalf of The Asian Pacific Society of Respirology.

DOI: 10.1002/rcr2.70244

PMCID: PMC12174960

PMID: 40535727

**20. Health Sci Rep. 2025 Jun 17;8(6):e70867. doi: 10.1002/hsr2.70867. eCollection**

**2025 Jun.**

Predictors of Longitudinal Viral Load count and Survival Time to Death Among

Adult TB/HIV Coinfected Patients Treated at Two Selected Amhara Region

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**BACKGROUND AND AIMS:** The most prevalent opportunistic illness among people

living with HIV/AIDS is tuberculosis. The aim of this study was to determine

predictors of longitudinal viral load and survival time to death among adult

TB/HIV coinfected patients treated at two selected Amhara region Comprehensive

Specialized Hospitals, Ethiopia.

**METHODS:** A retrospective follow-up study design was conducted from March

2018-2022 in the University of Gondar Comprehensive Specialized Hospital and

Felege Hiwot Comprehensive Specialized Hospital. Descriptive statistics,

separate Cox PH model, separate generalized linear mixed model, and joint model

were employed to analyze the coinfected patient data.

**RESULTS:** Among 253 TB/HIV coinfected participants, 26.5% mortality and the rest

were censored. Random intercept and slope model for the longitudinal viral load

count Cox PH model for time to death were selected based on AIC and BIC values.

The estimate of the association parameter due to the slope ( γ1 = 0.4981) and

due to the viral load count variability through time is positive ( γ2 = 0.6247

).

**CONCLUSIONS: T**hese results concluded that the joint model is not only the

simplest model, but also provided a better fit to the coinfected patients' data

than the separate model. The parameter estimation under the joint model revealed

that INH, residence, CD4 cell count, functional status, and BMI were considered

as significant joint predictors of viral load count and time to death among

TB/HIV coinfected patients. Furthermore, the results of the association

parameter concluded that the higher the viral load count of the patient, the

higher the chance of mortality, and correspondingly, patients with lower viral

load count have a lower chance of mortality. In this study, important potential

joint predictors should be given special attention by adult TB/HIV coinfected

patients and health professionals to minimize viral load and risk of mortality.

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PMCID: PMC12174616

PMID: 40535517

**21. Trop Med Health. 2025 Jun 18;53(1):84. doi: 10.1186/s41182-025-00766-w.**

Factors influencing the health-seeking behavior of Vietnamese migrants in Japan:

a cross-sectional study on knowledge, attitudes, and practices towards

tuberculosis.

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**BACKGROUND:** Addressing tuberculosis (TB) among migrants from high-burden

countries is important for the health of migrants and for public health in

low-TB-burden countries. Therefore, approaches that enable migrants to access TB

diagnostic services and care early are required. To develop TB risk

communication for migrants from high-TB-burden countries, this study aimed to

assess Vietnamese migrants' knowledge, attitudes, and practices (KAP) towards TB

and its association with health-seeking behaviors.

**METHODS:** A cross-sectional study was conducted among Vietnam-born migrants aged

18 years and older in two cities in Japan. A self-administered online survey

consisted of questions on demographics, health-related issues and behaviors, and

the KAP towards TB. Participants who would not seek healthcare even if they had

TB symptoms were categorized as having "non-health-seeking behavior", and

related factors were examined using multiple logistic regression analysis.

**RESULTS:** A total of 230 Vietnamese migrants participated in this study.

Technical intern trainees (46.1%) and workers (28.7%) comprised the majority of

the participants. Overall, 73.9% believed that persons infected with TB were

infectious, and 46.1% reported concerns about being diagnosed with TB. Their

concerns included maintaining employment and continuing schooling during

treatment. Ten percent of the participants stated that they would not consult a

doctor even if they developed TB symptoms. Multiple logistic regression analysis

revealed that participants who believed that TB could not be cured were

significantly more likely to exhibit non-health-seeking behavior (adjusted odds

ratio: 3.12, 95% confidence interval 1.14-8.52) compared to those who believed

TB could be cured.

**CONCLUSIONS:** Tailored TB risk communication should address migrants'

misconceptions and concerns regarding TB in the host countries. Further efforts

are needed to improve TB knowledge through TB education and to disseminate

information before and after migration. Creating a supportive environment, such

as language assistance and work- and school-related social support, is also

needed to facilitate the early detection of TB and healthcare access among

migrants.

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PMCID: PMC12175359

PMID: 40533807

**22. Indian J Gastroenterol. 2025 Jun 19. doi: 10.1007/s12664-025-01764-w. Online**

**ahead of print.**

Urinary lipoarabinomannan: A novel diagnostic tool for distinguishing

gastrointestinal tuberculosis from Crohn's disease.

Singh M(1), Goyal MK(1), Narang H(1), Mubbunu M(1), Kumar P(1), Kante B(1),

Vuyyuru SK(1), Upadhyay AD(2), Das P(3), Goyal A(4), Sharma R(4), Singh UB(5),

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**BACKGROUND:** The differentiation between gastrointestinal tuberculosis (GITB) and

Crohn's disease (CD) is challenging. Detection of urinary lipoarabinomannan

(LAM), a glycolipid component of the Mycobacterium tuberculosis cell wall, has

shown potential as a non-invasive diagnostic marker for tuberculosis.

**OBJECTIVE:** We evaluated the diagnostic accuracy of urinary LAM in distinguishing

GITB from CD.

**METHODS:** This prospective study included patients diagnosed with GITB, CD or

those with indeterminate conditions (January 2021 to April 2022). Comprehensive

clinical evaluations, laboratory investigations, computed tomography (CT)

enterography, colonoscopy and histopathological analyses were performed. First

morning midstream urine samples were collected and analyzed using TB LAM antigen

kit. The analytical team was blinded from the clinical data. Sensitivity,

specificity, positive predictive value (PPV), negative predictive value (NPV)

and overall diagnostic accuracy of urinary LAM were determined.

**RESULTS:** Of 98 patients, 36 were diagnosed with GITB and 62 with CD. Urinary LAM

was positive in nine out of 36 GITB patients, yielding a sensitivity of 25% (95%

C.I. 12.12-42.20%) and a PPV of 100% (95% C.I. 66.37-100.00%). None of the CD

patients tested positive for urinary LAM, resulting in a specificity of 100%

(95% C.I. 94.22-100.00%) and NPV of 69.66% (95% C.I. 65.54-73.50%). Overall

diagnostic accuracy of urinary LAM in differentiating GITB from CD was 72.45%

(95% C.I. 62.54-80.99%). Notably, the addition of urinary LAM testing to the

existing diagnostic criteria improved the accurate identification of GITB from

44% to 55.6%.

**CONCLUSION:** Urinary LAM testing exhibits high specificity and PPV, making it a

significant adjunct in the diagnostic process for GITB.

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DOI: 10.1007/s12664-025-01764-w

PMID: 40533713

**23. Pediatr Surg Int. 2025 Jun 18;41(1):175. doi: 10.1007/s00383-025-06080-0.**

Abdominal tuberculosis in children: a systematic review on current advances.

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Liver and Biliary Sciences, New Delhi, India. drshilpas@gmail.com.

**AIM:** To study the published literature on abdominal tuberculosis in children in

the last 10 years.

**METHOD:** A PubMed search was done on 27th March 2025 with keywords "pediatric

abdominal tuberculosis", using the filter of last 10 years. The articles were

screened for relevance and the data were compiled on gender, age, presenting

complaints, diagnosing criteria, associated pathologies, surgical management,

complications and outcomes.

**RESULTS:** The search yielded 194 articles. After screening for relevance, 143

articles were excluded. 51 articles were studied. A total of 807 cases were

studied in 51 articles, with female preponderance. The largest series was of 218

children. The age was predominantly in the adolescent period. The youngest child

was an 8-day neonate with congenital tuberculosis. Predominant symptoms included

fever, pain abdomen, abdominal distension, constipation, diarrhea, ascites and

weight loss. Unusual presentations included splenic microabscess, liver abscess

in HIV positive cases, deep vein thrombosis, mesenteric artery stenosis and

intracranial sinus thrombosis. Mycobacterial cultures showed 50-75% positivity.

Concomitant pulmonary tuberculosis was reported in 6 studies. The management

included medical with or without surgical management. The main indication for

surgical management was intestinal perforation.

**CONCLUSION:** Pediatric abdominal tuberculosis is an enigma due to the vague

symptoms and needs to be differentiated from other conditions.

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**24. Int Immunopharmacol. 2025 Jun 17;161:115047. doi: 10.1016/j.intimp.2025.115047. Online ahead of print.**

Long-term omega-3 fatty acids modulate immune responses more effectively than

ibuprofen in Mtb-infected mice: An in silico functional analysis approach.

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Tuberculosis (TB) remains a major global public health threat, necessitating

alternative and novel treatments to modulate inflammation and shorten drug

treatment periods. The potential of omega-3 long-chain polyunsaturated fatty

acids (EPA/DHA) and ibuprofen as adjunct therapies in TB treatment was

demonstrated recently in Mycobacterium TB (Mtb) C3HeB/FeJ mice, but the

underlying molecular mechanisms of the immune response pathways remain largely

unknown. Here, we used in silico predictive functional network modelling to

predict underlying molecular relationships and functional network interactions

associated with inflammatory and immune response pathways. We focused on Th1,

Th2 and Th17 cell pathways in the lung tissue when administering adjunct EPA/DHA

or ibuprofen to Mtb-infected C3HeB/FeJ mice. Mice (n = 36) initially received

Rifafour® (rifampicin, isoniazid, pyrazinamide, and ethambutol) for three days

before transitioning to rifampicin and isoniazid alone for the remainder

(11 days) of the experiment, with or without EPA/DHA (1.6:1) or ibuprofen

(0.05 g/L) supplementation. Standard TB drug treatment alone downregulated Th1

cell responses, shifting toward a Th2-skewed immune profile, which may impact

long-term host immune competence. Adjunct ibuprofen resulted in excessive

inflammation as indicated by increased pro-inflammatory cytokines and neutrophil

recruitment (via Th17 cell activity), which was associated with higher lung

bacterial loads and reduced alveolar space compared to TB drugs alone or the

adjunct EPA/DHA group. In contrast, supplementing EPA/DHA maintained a Th1/Th2

immune balance and reduced excessive Th17 activity, yielding lower bacterial

loads. These findings suggest that EPA/DHA supplementation holds promise as a

safe and more effective host-directed therapy, adjunct to TB drugs, by enhancing

immune balance and mitigating excessive lung damage. Further investigation into

the clinical applicability of EPA/DHA as an adjunct in TB treatment is

warranted.

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PMID: 40532324

**25. N Engl J Med. 2025 Jun 19;392(23):2391-2392. doi: 10.1056/NEJMc2502735.**

Levofloxacin for the Prevention of Multidrug-Resistant Tuberculosis. Reply.

Hesseling AC(1), Schaaf HS(1), Purchase SE(1).

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Comment on

N Engl J Med. 2024 Dec 19;391(24):2304-2314. doi: 10.1056/NEJMoa2314325.

DOI: 10.1056/NEJMc2502735

PMID: 40532166

**26. N Engl J Med. 2025 Jun 19;392(23):2390-2391. doi: 10.1056/NEJMc2502735.**

Levofloxacin for the Prevention of Multidrug-Resistant Tuberculosis. Reply.

Fox GJ(1), Nhung NV(2), Marks GB(3).

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(3)Burnet Institute, Melbourne, VIC, Australia.

Comment on

N Engl J Med. 2024 Dec 19;391(24):2304-2314. doi: 10.1056/NEJMoa2314325.

DOI: 10.1056/NEJMc2502735

PMID: 40532165

**27. N Engl J Med. 2025 Jun 19;392(23):2389-2390. doi: 10.1056/NEJMc2502735.**

Levofloxacin for the Prevention of Multidrug-Resistant Tuberculosis.

Lubelchek R(1).

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Comment on

N Engl J Med. 2024 Dec 19;391(24):2304-2314. doi: 10.1056/NEJMoa2314325.

DOI: 10.1056/NEJMc2502735

PMID: 40532163

**28. N Engl J Med. 2025 Jun 19;392(23):2389. doi: 10.1056/NEJMc2502735.**

Levofloxacin for the Prevention of Multidrug-Resistant Tuberculosis.

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Comment on

N Engl J Med. 2024 Dec 19;391(24):2304-2314. doi: 10.1056/NEJMoa2314325.

DOI: 10.1056/NEJMc2502735

PMID: 40532162

**29. PLOS Glob Public Health. 2025 Jun 18;5(6):e0003955. doi:**

**10.1371/journal.pgph.0003955. eCollection 2025.**

Evaluating InferVision's Computer-Aided Detection (CAD) algorithm for

Tuberculosis (TB) screening, Lusaka, Zambia.

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Author information:

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The objective of this study was to evaluate the diagnostic performance of

InferRead DR Chest for tuberculosis (TB) screening in a high HIV and TB burden

setting. The study assessed the performance of InferRead DR Chest using

anonymized chest X-ray images from an active TB case finding study in Lusaka,

Zambia, for individuals aged 15 and older. The Xpert MTB/RIF or MTB culture was

the composite reference standard. Performance was evaluated using the Area Under

the Receiver Operating Characteristic Curve (AUC), and a binary classification

point was selected where the sensitivity aligned with the WHO target product

profile for TB screening tools. Of the 1,890 chest X-ray images that met the

inclusion criteria, 91.5% of participants reported at least one TB symptom. The

median age was 38 years (IQR: 29-47), and 1,186 (62.8%) were male. From the

study sample, 449 participants (23.8%) reported a history of previous TB, and

704 (37.2%) were HIV positive. Among the analyzed images, 289 (15.3%) were

classified as TB positive based on the composite reference standard test

results. The overall area under the curve (AUC) was 0.81 (95% CI: 0.78-0.83).

Among individuals with a history of previous TB and those who were HIV positive,

the AUCs were 0.71 (95% CI: 0.63-0.79) and 0.77 (95% CI: 0.72-0.82),

respectively. At a sensitivity of 90.3% (95% CI: 86.3%-93.5%), InferRead DR

Chest achieved a specificity of 39.2% (95% CI: 36.8%-41.7%) at TB score cut

point of 0.12. InferRead DR Chest had acceptable performance in our population.

Additional training and piloting of InferRead DR Chest in this population is

recommended.

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

original author and source are credited.

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PMCID: PMC12176154

PMID: 40531944

**30. PLoS One. 2025 Jun 18;20(6):e0319630. doi: 10.1371/journal.pone.0319630.**

**eCollection 2025.**

Verification of emerging genomic mutations in Mycobacterium tuberculosis allows

transmission chains to be distinguished in an epidemiological typing cluster

extending over thirty years.

de Zwaan R(1), de Vries G(2), Ubbelohde E(1)(3), Mulder A(1), Kamst-van

Agterveld M(1), Rebel K(4), Kautz S(5), Kremer K(3), Anthony RM(1), van

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Netherlands.

Whole genome sequencing (WGS) is able to identify epidemiological links between

Mycobacterium tuberculosis isolates. Recent clustering can be ruled out using a

pre-defined single nucleotide polymorphism (SNP) threshold. If WGS clusters grow

significantly over time limited genetic variability hampers epidemiological

investigations. Newly emerging (informative) SNPs in isolates of an extended

cluster growing for more than 30 years to >150 cases in the Netherlands were

analysed. WGS data was analyzed from 61 sequencing files from 54 patients.

Genomic positions that varied within the cluster isolates were carefully

screened for minority populations in other isolates from the cluster. A

transmission scheme was generated on the basis of WGS data alone then compared

to the epidemiological information available. Fifty-two informative SNPs were

identified, eight of which were also detected as mixed variants. One emerging

SNP in dnaA (1199G > A R400H) has been observed in other transmitted strains and

may be under selection. There was high concordance between the transmission

chains suggested on basis of the newly emerging SNPs and scenarios identified

using classical epidemiological cluster investigations. Analysis of filtered

SNPs accumulating in the genome of M. tuberculosis in large clusters contains

information on transmission dynamics and can be used to support epidemiological

investigations.

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original author and source are credited.

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PMCID: PMC12176192

PMID: 40531890 [Indexed for MEDLINE]

**31. J Acquir Immune Defic Syndr. 2025 Jun 18. doi: 10.1097/QAI.0000000000003713.**

**Online ahead of print.**

Sex and HIV Modify Immune Activation Biomarkers in Ugandans Post-Tuberculosis.

Abelman RA(1), Fitzpatrick J(1), Zawedde J(2), Beck-Engeser G(3), Rn IS(2),

Marzan F(1)(4), Byanyima P(2), Ambayec GC(2), Kaswabuli S(2), Musisi E(2),

Sessolo A(2), Velasquez E(1), Lalitha R(5), Byanova KL(6), Aweeka FT(4),

Deitchman AN(3)(4), Lin J(7), Davis JL(8)(9), Crothers K(10), Worodria W(5),

Hunt PW(3), Huang L(1)(6).

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Washington, Seattle, Washington, USA.

**BACKGROUND:** While there are sex and HIV differences in tuberculosis (TB)

prevalence, the underlying mechanisms are incompletely understood. Few studies

have evaluated whether sex and HIV modify the inflammatory response to TB.

**METHODS:** Adults with pulmonary TB with and without HIV in Kampala, Uganda had 12

immune activation biomarkers measured at TB diagnosis and at completion of

therapy. Associations between biomarkers and sex were assessed using

multivariable regression models at baseline and follow-up after adjusting for

age, HIV status, and AFB smear grade. Given evidence of sex-HIV interaction in

several biomarkers, models were stratified by HIV status.

**RESULTS:** Overall, 151 participants were included and 74 (49%) were female.

Forty-nine (32%) participants had HIV; 21 (43%) of those with HIV were female.

At baseline, biomarkers were overall higher in men whereas at follow-up, suPAR

(p<0.001) and sCD163 were higher in women (p=0.02) and IL-6 (p=0.01) and IFABP

(p=0.02) were higher in men. After stratifying by HIV status, at baseline, the

majority of the biomarkers were higher in men without HIV and there were no sex

differences in those with HIV. At follow-up, women without HIV had higher levels

of suPAR (p=0.01) and sCD163 (p=0.051). Women with HIV had higher levels of

suPAR, CRP, and IP-10 (p<0.05 for all); no other sex differences were observed.

**CONCLUSIONS:** Among adults with pulmonary TB in Uganda, men had greater immune

activation than women only in the absence of HIV. Following treatment, women

tended to have more immune activation than men in the setting of HIV.

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DOI: 10.1097/QAI.0000000000003713

PMID: 40530901

**32. Curr Drug Discov Technol. 2025 Jun 16. doi:**

**10.2174/0115701638364461250603050239. Online ahead of print.**

Computational Investigation of Phytochemicals Targeting Isocitrate Lyase to

Inhibit Mycobacterium tuberculosis.

Chouhan M(1), Kumar M(2), Mishra R(3), Gupta S(4), Tiwari PK(1), Rustagi S(5),

Sharma K(6), Singh DP(7), Kumar S(1).

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**INTRODUCTION:** The global burden of tuberculosis (TB) remains a major concern for

society that is worsening day by day with the emergence of drug-resistant TB as

well as risks associated with latent TB. Isocitrate lyase (ICL) has been shown

as a potential target that plays a role in the la-tent/dormant stage of M.

tuberculosis. Several inhibitors against ICL have been designed and tested,

which have various side effects.

**METHODOLOGY:** This study focuses on the phytochemicals from plant extracts, which

have anti-tuber-cular properties. A total of 1413 phytochemicals were virtually

screened against ICL to identify the promising therapeutic compounds. The top

four lead phytochemicals were selected based on their binding energy and

subjected to redocking and intermolecular interaction analysis. These results

were further validated through 100 ns MD simulation to check the stability of

these complexes. The find-ings of these complexes were compared to the reference

compound VGX.

**RESULTS:** The top selected compound viz., Allantoin, Gallic acid, Citric acid,

and 3,5-Dihydroxyben-zoic acid from virtual screening result displayed better

docking score ranging from -8 kcal/mol to -7.2 kcal/mol than the reference

compound VGX (-7.5 kcal/mol). Moreover, during the MD simula-tion analysis,

gallic acid exhibited greater stability compared to all other compounds,

including the reference compound.

**CONCLUSION:** Among selected phytochemicals, gallic acid exhibited highest

stability and binding af-finity within the active site of ICL as compared to

previously identified compounds, which suggests that it is as potential

candidate against ICL. That can be used for further in vitro and in vivo studies

to evaluate its effectiveness against TB.

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epub@benthamscience.net.

DOI: 10.2174/0115701638364461250603050239

PMID: 40530732

**33. Mol Microbiol. 2025 Jun 17. doi: 10.1111/mmi.15370. Online ahead of print.**

The Mycobacterium tuberculosis Transposon Sequencing Database (MtbTnDB): A

Large-Scale Guide to Genetic Conditional Essentiality.

Jinich A(1)(2), Zaveri A(3), DeJesus MA(4), Spencer A(2), Almada-Monter R(2),

Flores-Bautista E(5), Smith CM(6), Sassetti CM(7), Rock JM(4), Ehrt S(3),

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Medical College, New York City, New York, USA.

Characterizing genetic essentiality across various conditions is fundamental for

understanding gene function. Transposon sequencing (TnSeq) is a powerful

technique to generate genome-wide essentiality profiles in bacteria and has been

extensively applied to Mycobacterium tuberculosis (Mtb). Dozens of TnSeq screens

have yielded valuable insights into the biology of Mtb in vitro, inside

macrophages, and in model host organisms. Despite their value, these Mtb TnSeq

profiles have not been standardized or collated into a single, easily searchable

database. This results in significant challenges when attempting to query and

compare these resources, limiting our ability to obtain a comprehensive and

consistent understanding of genetic conditional essentiality in Mtb. We address

this problem by building a central repository of publicly available Mtb TnSeq

screens, the Mtb transposon sequencing database (MtbTnDB). The MtbTnDB is a

living resource that encompasses to date ≈150 standardized TnSeq screens,

enabling open access to data, visualizations, and functional predictions through

an interactive web app (www.mtbtndb.app). We conduct several statistical

analyses on the complete database, such as demonstrating that (i) genes in the

same genomic neighborhood have similar TnSeq profiles, and (ii) clusters of

genes with similar TnSeq profiles are enriched for genes from similar functional

categories. We further analyze the performance of machine learning models

trained on TnSeq profiles to predict the functional annotation of orphan genes

in Mtb. By facilitating the comparison of TnSeq screens across conditions, the

MtbTnDB will accelerate the exploration of conditional genetic essentiality,

provide insights into the functional organization of Mtb genes, and help predict

gene function in this important human pathogen.

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DOI: 10.1111/mmi.15370

PMID: 40527579

**34. Int J Risk Saf Med. 2025 Jun 17:9246479251353401. doi:**

**10.1177/09246479251353401. Online ahead of print.**

Paradoxical responses to modified, all-oral shorter treatment of tuberculosis in

non-immunocompromised patients: Cases from Armenia.

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**Background** The previous publications presented paradoxical responses to anti-TB

treatment in non-immunocompromised patients. Treatment for extra-pulmonary

tuberculosis was associated with the majority of these responses.ObjectivesIn

this paper, we present three cases of paradoxical radiological worsening in the

HIV-negative patients receiving new modified, all-oral shorter regimens for

pulmonary tuberculosis.**Methods** The treatment effectiveness was assessed based on

the radiological and bacteriological examinations. Each of the three patients

was adherent to treatment.**Results** Anti-TB therapy was effective in all of the

cases, evidenced by bacteriological response. After initiation of treatment, the

chest X-rays showed increased infiltration in the lungs. The patients continued

treatment without adjustments of the shorter regimens. The following chest

X-rays revealed positive dynamics. Despite the lack of specific therapeutic

interventions to address radiological deterioration, the shorter treatment

courses were successful. This means that radiological worsening detected in the

middle of shorter treatment does not always indicate that anti-TB chemotherapy

is ineffective.**Conclusion** Paradoxical deterioration of chest X-ray findings may

happen in HIV-negative patients receiving shorter regimens for

rifampicin-resistant pulmonary tuberculosis but this worsening is not a reliable

indicator for treatment outcome prediction. Additional therapeutic interventions

or modifications of the chemotherapy regimens are not always necessary.

DOI: 10.1177/09246479251353401

PMID: 40527493

**35. mBio. 2025 Jun 17:e0106825. doi: 10.1128/mbio.01068-25. Online ahead of print.**

Ser/Thr phosphorylation of Mycobacterium tuberculosis type II RelK toxin by PknK

destabilizes TA interaction and interferes with toxin neutralization.

Sarah SR(#)(1)(2), Garg A(#)(1)(2), Afroz S(3), Korch S(4), Ray A(3), Gupta

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Toxin-antitoxin (TA) modules represent genetic elements implicated in bacterial

persistence. Mycobacterium tuberculosis encodes 90+ TA modules, the majority of

which are type II, comprising of a toxin component and an antitoxin counterpart

that neutralizes the toxin. Under stressful environments, the antitoxin is

degraded, releasing the toxin which then acts to halt cellular growth. Towards

elucidating the underlying regulatory mechanisms that govern a synchronized TA

cellular program, we explored the regulation of type II TA modules by

post-translational modification. In silico analysis revealed that ~85% of M.

tuberculosis TA proteins possess potential Ser/Thr phosphorylation sites,

implicating them as targets for mycobacterial Ser/Thr protein kinases (STPKs).

We demonstrate that members of the RelBE family interact with PknK, a

stress-responsive STPK using the mycobacterial protein fragment complementation

(M-PFC) assay and are subjected to Ser/Thr phosphorylation in vitro. LC-MS/MS

confirmed multiple sites of phosphorylation in the RelJK module. Results from

molecular dynamics simulations, in vitro binding, and co-expression studies with

RelJK proteins indicate that the secondary structure changes associated with

Thr77 phosphorylation in RelK toxin compromise its binding to the RelJ

antitoxin. Substitution of Thr77 with alanine or glutamate in RelK toxin

resulted in poor binding to the RelJ antitoxin, allowing a partial rescue of

cells co-expressing wild-type RelJ antitoxin and RelK phosphorylation-deficient

(T77A) or phosphomimetic (T77E) mutant toxins vs wild-type RelJK proteins. These

findings implicate the RelK Thr77 residue at the toxin-antitoxin interaction

interface and, more importantly, establish toxin phosphorylation as a novel

mechanism influencing interaction dynamics of the TA module components.

IMPORTANCE: Bacterial pathogens rely on the phenomenon of persistence as a

survival strategy to combat the adverse environmental conditions encountered

during infection. As a stochastic process, the driving force(s) that potentiate

the formation of persisters in a bacterial population are largely unclear. This

study is a step towards the discovery of intricate regulatory mechanisms that

coordinate a synchronized TA cellular program. We propose a model where the TA

module is regulated post-translationally, specifically via Ser/Thr

phosphorylation disrupting the interaction between the toxin and antitoxin

proteins as a mechanism to regulate TA function.

DOI: 10.1128/mbio.01068-25

PMID: 40525867

**36. ACS Infect Dis. 2025 Jun 17. doi: 10.1021/acsinfecdis.5c00150. Online ahead of print.**

Single-Sample Melt-Based Screening for Rifampicin Susceptibility in the Emerging

Mutation Hotspot at rpoB Codon 491.

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Author information:

(1)Department of Biomedical Engineering, Vanderbilt University, Nashville,

Tennessee 37235, United States.

Based on sequencing data, mutations at rpoB codon 491 ofMycobacterium

tuberculosisare associated with rifampicin resistance, but current commercial

and WHO-endorsed genotypic tests fail to detect them. As a result, resistant

infections go untreated, driving transmission and multidrug resistance. A

real-time PCR assay by André et al. specifically screens for I491F but omits

other codon 491 mutations. To address this gap, a single-sample screening method

using asymmetric PCR followed by melt analysis was developed for the three

sequence-identified variants, I491F/N/M. Each sample contained a melt probe

matching the susceptible sequence, which, after asymmetric PCR spanning codon

491, hybridized with the excess strand to form a duplex. The duplex's melt

temperature (Tm) was then measured. To enable single-sample classification, each

reaction also included double-stranded L-DNA identical to the probe and

wild-type PCR product duplex. Susceptibility was determined by the within-sample

Tm difference between the probe-product and L-DNA duplexes. The approach was

evaluated and compared to the André assay across two calibrated PCR instruments

using synthetic rpoB wild-type and variant sequences. As expected, the André

assay distinguished wild-type from I491F samples but misclassified I491N and

I491M samples based on multisample Tm comparison. In contrast, our single-sample

classification strategy used within-sample Tm differences, classifying samples

as rifampicin-susceptible when the within-sample Tm difference was less than

0.83 °C. With this approach, the method achieved 100% sensitivity and 100%

specificity across both PCR instruments. Although demonstrated for rpoB codon

491, this assay design is readily adaptable to any other sequence-identified,

clinically significant mutation hotspot.

DOI: 10.1021/acsinfecdis.5c00150

PMID: 40525806

**37. Anatol J Cardiol. 2025 Jun 16. doi: 10.14744/AnatolJCardiol.2025.5454. Online**

**ahead of print.**

Tricuspid Regurgitation Worsening After Pericardiectomy in Tuberculosis

Constrictive Pericarditis: An Overlooked Prognostic Concern.

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DOI: 10.14744/AnatolJCardiol.2025.5454

PMID: 40525212

**38. J Surg Case Rep. 2025 Jun 16;2025(6):rjaf422. doi: 10.1093/jscr/rjaf422.**

**eCollection 2025 Jun.**

Abdominal tuberculosis in a patient with ankylosing spondylitis and infliximab:

is the risk still too great? A case report.

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Ankylosing spondylitis is a chronic inflammatory spondyloarthropathy that will

cause severe symptoms and complications if left untreated. Anti-TNF-α inhibitor

is the treatment of choice, yet all treatments have difficulties, and

opportunistic infections following this therapy are well known. Reactivation of

latent tuberculosis (TB) and abdominal TB is a serious problem in this therapy

since diagnosis is difficult, as symptoms are nonspecific, and complications can

be fatal. We present the case of a 47-year-old female doctor with a past medical

history of ankylosing spondylitis; she was treated with infliximab. She began

developing abdominal pain that led to an acute abdomen due to abdominal TB.

After successful treatment, she fully recovered, and the patient is doing well

in follow-ups.

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Ltd.

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PMCID: PMC12168116

PMID: 40525094

**39. Clin Nucl Med. 2025 Jun 17. doi: 10.1097/RLU.0000000000005805. Online ahead of print.**

Cutaneous Tuberculosis (CTB) Identified on 18F-FDG PET/CT.

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(2)The University of Texas M.D. Anderson Cancer Center.

As Cutaneous Tuberculosis (CTB) comprises only a small percentage of

extra-pulmonary cases, it is often a challenging diagnosis for dermatologists.

The multitude of clinical manifestations with lesions mimicking other conditions

is further compounded by ambiguous histological and immunohistochemistry

findings. This case of a 69-year-old man with an extensive medical history who

presented with unusual cutaneous lesions unresponsive to treatment and negative

initial histological examination, demonstrated these challenges.

18F-Fludeoxyglucose (FDG) PET/CT imaging was used to identify pulmonary nodules

and tracer uptake in cutaneous tissue, supporting the diagnosis of CTB.

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DOI: 10.1097/RLU.0000000000005805

PMID: 40524368

**40. PLoS Pathog. 2025 Jun 16;21(6):e1013267. doi: 10.1371/journal.ppat.1013267.**

**Online ahead of print.**

APOE protects against severe infection with Mycobacterium tuberculosis by

restraining production of neutrophil extracellular traps.

Liu D(1), Mai D(1), Jahn AN(1), Murray TA(1), Aitchison JD(1), Gern BH(1)(2),

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Mice lacking apolipoprotein E (APOE, Apoe-/- mice) on a high cholesterol (HC)

diet are highly susceptible to infection with Mycobacterium tuberculosis (Mtb)

but the underlying immune dysregulation has been unclear. While neutrophils are

often the predominant cell type in the lungs of humans with severe tuberculosis

(TB), they are relatively scarce in the lungs of some strains of mice that are

used to study the disease. The neutrophil levels in the lungs of Mtb-infected

Apoe-/- HC mice are very high, and thus studies in this model offer the

opportunity to examine the role of specific neutrophil functions in the

pathology of severe TB. We determined that depleting neutrophils, depleting

plasmacytoid dendritic cells (pDCs), or blocking type I interferon signaling

improved the outcome of TB in Apoe-/- HC mice. We also demonstrated that

blocking the activation of peptidylarginine deiminase 4 (PAD4), an enzyme

critical to NET formation, leads to fewer NETs in the lungs and dramatically

improves the outcome of TB in Apoe-/- HC mice without affecting the number of

neutrophils in the lung. We found that the transcriptional profile of

neutrophils in Mtb-infected Apoe-/- HC mice is biased towards a state that

resembles the "N2" phenotype that has been defined in cancer models and has been

implicated in matrix degradation and tissue destruction. Our observations

strongly suggest that the state of the neutrophil when it encounters the

Mtb-infected lung is one of the main drivers of severe disease and implies that

targeted interventions that alter specific states or functions, such as the

production of NETs, may improve outcome while preserving sufficient capacity for

host-defense.

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DOI: 10.1371/journal.ppat.1013267

PMID: 40523023

**41. PLoS One. 2025 Jun 16;20(6):e0325914. doi: 10.1371/journal.pone.0325914.**

**eCollection 2025.**

TBpore cluster: A novel phylogenetic pipeline for tuberculosis transmission

studies using nanopore next-generation sequencing data.

Gagnon S(1)(2), Ametepe E(1)(3), Point F(1), Cloutier Charette W(2), Chakravarti

A(2), Rivest P(4), Akochy PM(5), Soualhine H(6), Iqbal Z(7), Hall MB(7),

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**BACKGROUND:** Molecular typing of Mycobacterium tuberculosis complex isolates

enhances understanding of tuberculosis (TB) transmission dynamics, supporting

public health efforts in outbreak investigations. This study aims to validate

TBpore, a novel bioinformatic pipeline for clustering TB transmission isolates

using Oxford Nanopore Technology (ONT) data and comparing it against

conventional Mycobacterial Interspersed Repetitive-Unit Variable Number

(MIRU-VNTR) typing and Illumina sequencing.

**METHODOLOGY/PRINCIPAL FINDINGS:** This retrospective case-control study included

58 clinical isolates from two TB outbreaks in Canada, previously characterized

by public health investigations and MIRU-VNTR typing. DNA extraction and

sequencing were performed on both Illumina and ONT platforms. Illumina data were

processed using Clockwork and psdm, while Nanopore data were analyzed with

TBpore. SNP distances were used to compare clustering results across methods,

with clusters defined by SNP distance thresholds of ≤5 and ≤12. Both sequencing

methods showed a high degree of concordance in clustering results. All isolates

from the M. africanum outbreak clustered within the defined SNP thresholds,

consistent with MIRU-VNTR and epidemiological data. In the M. tuberculosis

outbreak, 20 out of 21 isolates clustered similarly across methods, with one

exception. Within outbreak pairwise SNP distances were lower with Nanopore.

**CONCLUSION/SIGNIFICANCE:** ONT sequencing and the TBpore pipeline offer an

accurate alternative to Illumina technology for TB molecular epidemiology. This

study suggests potential increased clustering sensitivity with Nanopore

technology, warranting further validation on larger datasets with robust

epidemiological metadata.

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original author and source are credited.

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PMCID: PMC12169557

PMID: 40522986 [Indexed for MEDLINE]

**42. PLoS One. 2025 Jun 16;20(6):e0324614. doi: 10.1371/journal.pone.0324614.**

**eCollection 2025.**

Understanding stigma: The experiences of people with drug-sensitive pulmonary

tuberculosis in Rawalpindi, Pakistan.

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**INTRODUCTION:** Tuberculosis (TB) is a major global health problem and Pakistan is

ranked fifth among the 30 high-burden countries in the world. TB-related stigma

affects health seeking behaviour and treatment adherence, increasing disease

transmission and worsening health outcomes. This study aimed to explore

experiences of stigma among people with TB (PWTB) in Rawalpindi to help inform

targeted stigma reduction interventions that could improve health seeking

behaviour, treatment adherence and the mental well-being of PWTB in Pakistan.

**METHODOLOGY:** In-depth interviews were conducted with 15 people with pulmonary

drug sensitive TB from Rawalpindi, Pakistan. For assessing emerging themes, an

inductive themed analysis approach was used. Next, a deductive approach was

applied by analysing and interpreting the data against the Health Stigma and

Discrimination Framework.

**RESULTS:** TB- related stigma among participants was driven by fear of infection,

which in some cases was due to misconceptions surrounding TB transmission as

well as social judgement and gender norms. Stigma manifested through:

anticipated and perceived stigma in the form of non-disclosure and fear of

social exclusion; enacted stigma among friends and family, in the workplace and

healthcare settings; and internalised stigma, The negative outcomes of stigma

that resulted for some participants included non- adherence and social

exclusion, in the form of loss of marriage prospects and employment.

**CONCLUSION:** This study confirms that TB-related stigma persists in Pakistan,

impacting he well-being, medication adherence and treatment outcomes of PWTB.

The distinct drivers, manifestations and outcomes of stigma in Rawalpindi

Pakistan uncovered from this study, supported by previous research, can help

inform targeted stigma reduction interventions such as public education

programmes.

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PMCID: PMC12169514

PMID: 40522906 [Indexed for MEDLINE]

**43. Chem Biodivers. 2025 Jun 16:e00474. doi: 10.1002/cbdv.202500474. Online ahead of print.**

Synthesis of Phenoxy Substituted Imidazo[1,2-b]Pyridazine-Based Amide

Derivatives for Antibacterial and Anti-Tubercular Activities.

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A series of 10 phenoxy-substituted imidazo[1,2-b]pyridazine amide derivatives

were synthesized from 6-chloro-2-methyl-8-phenoxyimidazo[1,2-b]pyridazine-3-carboxylic acid and respective amines. All these 10 compounds were characterized using spectroscopic analysis (1H, 13C, HPLC, and ESI). Furthermore, the molecular structure obtained with spectroscopic analysis was confirmed by single-crystal x-ray diffraction (SXRD) analysis with a compound 12. All the 10 newly synthesized compounds were screened for in vitro antibacterial activities with the agar dilution method against two Gram-positive bacteria (Staphylococcus aureus and Bacillus subtilis) and two Gram-negative bacteria (Escherichia coli and Pseudomonas aeruginosa). Compounds 11 and 13 both showed MIC values, 6.25 µg/mL, and comparable antibacterial activity to the positive control with the reference drug. Similarly, Mycobacterium tuberculosis H37Rv using the Microplate Alamar Blue Assay (MABA) and compounds 9 and 12 displayed moderate tubercular activities at a concentration of 25 µg/mL. The molecular docking studies correlated with

biological activity against the active sites of PDB ID: 5JZX.

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DOI: 10.1002/cbdv.202500474

PMID: 40522775

**44. Curr HIV/AIDS Rep. 2025 Jun 16;22(1):37. doi: 10.1007/s11904-025-00746-z.**

An Update on the Clinical Management of HIV and Tuberculosis Co-Infection in

Pregnancy: TB Preventative Therapy, Long-Acting ARVs, and Bedaquiline-Based

Regimens.

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**PURPOSE:** This update addresses HIV/TB co-infection management in pregnancy,

focusing on new treatment options.

**RECENT FINDINGS:** Pregnancy with HIV increases TB risk and worsens treatment

outcomes. While long-acting antiretroviral therapies (LA-ART) like

cabotegravir/rilpivirine and lenacapavir exist, data on their safety and

efficacy in pregnant individuals are limited. Treating both HIV and TB is

crucial, but pregnancy's physiological changes complicate drug management.

Standard ART and TB preventive therapy (TPT) with isoniazid are recommended

after excluding active TB, despite some concerns about adverse outcomes when

combined with ARV treatment. For active drug-resistant TB, the new 6-month BPaLM

regimen (bedaquiline, pretomanid, linezolid, moxifloxacin) is not recommended in

pregnancy due to limited safety data on pretomanid. Instead, a 9-month regimen

is preferred, though bedaquiline and pretomanid are likely safe. More research

on these new therapies in pregnant populations is needed. While standard ART

remains the recommended approach for HIV/TB co-infection in pregnancy, further

research is crucial to establish the safety and efficacy of newer LA-ART and

bedaquiline-based TB regimens in this high-risk population. Concerns around the

safety of TPT in pregnancy remain unanswered and further prospective research is

urgently needed.

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DOI: 10.1007/s11904-025-00746-z

PMCID: PMC12170718

PMID: 40522414 [Indexed for MEDLINE]

**45. Ocul Immunol Inflamm. 2025 Jun 16:1-9. doi: 10.1080/09273948.2025.2517309.**

**Online ahead of print.**

Validation of the COTS Calculator for Tubercular Uveitis: Predictive Performance

and Diagnostic Utility in an Indian Cohort.

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**PURPOSE:** Diagnosing ocular tuberculosis (OTB) is clinically challenging due to

its paucibacillary nature and lack of definitive diagnostic tests. The

Collaborative Ocular Tuberculosis Study (COTS) Calculator was developed as a

clinical decision-support tool to guide anti-tubercular therapy (ATT)

initiation. This study externally validates the COTS Calculator in a high-burden

Indian cohort and assesses the additive value of radiological and immunological

testing.

**METHODS:** This retrospective cohort study included 196 OTB patients treated

between 2015 and 2022 at a tertiary eye care center in South India. Inclusion

required complete diagnostic workup, ≥6-month follow-up post-ATT, and at least

one supportive test (TST, IGRA, CT, or CXR). Two thresholds were evaluated: M4I1

(median ≥ 4) and M4I2 (median ≥ 4, IQR ≤ 2). Treatment response and recurrence

were primary outcomes. Diagnostic performance was measured using AUC,

sensitivity, specificity, PPV, and NPV. Composite scores (CT+CXR and TST+IGRA)

were also analyzed.

**RESULTS:** The M4I2 threshold yielded higher sensitivity (83%) than M4I1 (60%)

with comparable AUC (0.60 vs 0.58), though at lower specificity (38% vs 56%).

Both thresholds achieved high PPV (94%) but poor NPV (11-17%). Composite testing

showed similar high PPV (93%) and poor NPV (9-11%). Higher COTS scores and

multiple positive tests correlated with favorable treatment response.

**CONCLUSIONS:** The COTS Calculator, particularly the M4I2 model, provides a useful

clinical tool to guide ATT decisions in OTB. While limited in ruling out TB, its

integration with radiological and immunological testing supports early treatment

decisions in TB-endemic settings. Prospective validation is warranted.

DOI: 10.1080/09273948.2025.2517309

PMID: 40521722

**46. Clin Infect Dis. 2025 Jun 16:ciaf322. doi: 10.1093/cid/ciaf322. Online ahead of print.**

Long-term protection from TB preventive treatment among people with HIV in a

high-burden tuberculosis setting: an observational cohort study from India.

Agarwal R(1), Nyendak M(1), Chava N(2), Allam RR(1), Moonan PK(1), Sriram CS(3),

Ganti R(2), Ragi PK(2), Polsani AR(2), Yeldandi VV(2), Ho C(1), Prasad RP(2),

Kurada J(2), Prasad K(3), Thogarucheeti M(3).

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**BACKGROUND: T**uberculosis (TB) preventive treatment (TPT) is critical to the end

TB strategy. There is limited evidence on its long-term protective effect among

people living with HIV (PLWH) receiving antiretroviral therapy (ART) in

high-burden programmatic settings.

**METHODS:** This observational cohort study included PLWH who initiated a single

TPT course from March 2017 to September 2018 at 14 ART centres in Andhra

Pradesh, India (TB prevalence: 274/100,000). We followed PLWH for 6 years and

censored person-time at TB diagnosis, loss to follow-up, or death. We calculated

TB incidence rates (IR) and mortality rates (MR) per 100 person-years (PY)

stratified by TPT completion and effective ART (viral load<1000 copies/ml).

Cox-proportional hazards models estimated adjusted hazard ratios (aHR) with 95%

confidence limits (95% CL) for TB and mortality.

**FINDINGS:** We followed 4,706 PLWH for 23,414 PY. TB was diagnosed in 135 PLWH

(2.9%)-122 among 4,454 PLWH who completed TPT (IR: 0.55/100PY, 95% CL:

0.46-0.66), and 13 among 252 PLWH who did not (IR: 1.06/100PY, 95% CL:

0.56-1.81). There were 553 all-cause deaths (11.8%)-MR: 2.2/100PY (95% CL:

2.0-2.4) among those who completed TPT compared to 13.5/100PY (95% CL:

11.1-16.3) among those who did not. TPT, combined with effective ART, was

associated with an 87% reduction in TB (aHR: 0.13; 95% CL: 0.05-0.37) and a 94%

reduction in all-cause mortality (aHR: 0.06; 95% CL: 0.04-0.10).

**CONCLUSION:** A single TPT course combined with effective ART conferred durable

protection against TB and significantly reduced mortality among PLWH in a

high-burden TB setting.

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**47. Int J Mycobacteriol. 2025 Apr 1;14(2):204-207. doi: 10.4103/ijmy.ijmy\_19\_25.**

**Epub 2025 Jun 20.**

When Peritoneal Tuberculosis Mimics Carcinomatosis: A Diagnostic Enigma.

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Abdominal tuberculosis (TB) can present with the involvement of the peritoneum,

stomach, intestinal tract, hepatobiliary tree, pancreas, perianal area, or lymph

nodes. Peritoneal TB is one of the most challenging forms to diagnose and

usually occurs through reactivation of latent TB infection or through

hematogeneous spread in the setting of active pulmonary TB. A 25-year-old male

from Guinea-Bissau, with multiple visits to the emergency department in the last

month due to several daily soft stools and generalized abdominal pain. He

returned with an abdominal computed tomography (CT) revealing irregular ascites

and suspected peritoneal carcinomatosis. He was admitted for an etiological

study, and an abdominal CT scan was repeated, which showed diffuse thickening of

the stomach wall. Erythrocyte sedimentation rate of 14 mm/1 h and C-reactive

protein of 1.24 mg/dL. Interferon-gamma release assay was positive. Acid-fast

bacilli smear in sputum and blood and urine cultures in Loewenstein-Jensen

medium were negative. Upper gastrointestinal endoscopy revealed Helicobacter

Pylori infection and colonoscopy was normal. Positron emission tomography-CT

confirmed the abdominal CT findings. Diagnostic laparoscopy was performed to

clarify the etiology, and pathological anatomy revealed findings compatible with

tuberculosis. Treatment with isoniazid, rifampicin, pyrazinamide, and

ethambutolepyridoxine was started. Although abdominal TB continues to be a

significant health problem in the developing world, recently, there has been an

increase in the number of patients diagnosed with abdominal TB in parts of the

world where TB generally was rare. This is partly a result of increasing travel

and migration and also of the rising number of HIV patients who are susceptible

to opportunistic infections.

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Nonfunctioning Kidney Due to Renal Tuberculosis: A Diagnostic Challenge.

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Urogenital tuberculosis (TB) is a common manifestation of extrapulmonary TB,

accounting for approximately 30%-40% of all cases, with the kidneys being the

most frequently affected organ. Despite its prevalence, renal TB often presents

diagnostic challenges due to nonspecific clinical symptoms, which can lead to

delayed diagnosis and treatment. Increased occurrences of extrapulmonary TB have

been observed in recent decades, linked to a rise in organ transplants and the

prevalence of acquired immune deficiency syndrome. The urogenital form of the

disease may arise from either disseminated infection or primary genitourinary

localization. Symptoms typically include pyuria, dysuria, fever, flank pain, and

burning micturition, often revealing a mass related to hydronephrosis of the

affected kidney. Clinicians in regions with high TB prevalence, such as India,

should maintain a high index of suspicion for renal TB, especially in patients

with recurrent urinary tract infections. Early identification and treatment are

crucial to prevent the development of nonfunctioning kidneys and associated

complications. This case report highlights the importance of recognizing the

clinical presentation of renal TB to improve diagnosis and management in

affected patients.

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PPE18 and PepA Variations in Mycobacterium tuberculosis Clinical Isolates from

Makassar, Indonesia: Challenges for Immune Recognition and Vaccine Development.

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Makassar, Indonesia.

**BACKGROUND:** The M72/AS01E tuberculosis vaccine candidate, currently on trial in

Indonesia, includes PPE18 (Rv1196) and PepA (Rv0125) as key antigens. Genetic

variation in these proteins may affect immune recognition and vaccine efficacy.

This study aims to analyse the genetic diversity of Rv1196 and Rv0125 in

Mycobacterium tuberculosis clinical isolates from Indonesia and assess the

structural and immunological implications using in silico methods.

**METHODS**: Rv1196 and Rv0125 genes from clinical isolates were sequenced and

analysed for polymorphisms. PPE18 variants were modelled using I-TASSER

(Iterative Threading ASSEmbly Refinement), and structural stability and HLA

(Human Leukocyte Antigen) binding predictions (HLA-I and HLA-II) were performed

using IEDB (Immune Epitope Database) tools. Molecular docking with TLR2

(Toll-like Receptor 2) was conducted to evaluate receptor interactions.

**RESULTS:** A novel non-synonymous mutation (T22G, Ser8Ala) was identified in

Rv0125, which was otherwise conserved. Rv1196 showed high variability with 58

polymorphic sites, including 38 non-synonymous mutations, a frequent Arg287Gln

substitution, and a ΔThr163-Ala164 deletion. Structural modelling indicated

preserved PPE18 fold but altered epitope binding in an allele-specific manner.

Docking showed stronger TLR2 interactions for variants 6S31 and 6S32, suggesting

enhanced IL-10 induction and a Th2-skewed immune response.

**CONCLUSIONS:** PPE18 genetic variation may influence immune recognition and the

effectiveness of M72/AS01E. Ongoing antigenic surveillance in endemic areas is

essential to guide vaccine design and diagnostics.

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Molecular Characterization of Mycobacterium Tuberculosis in HIV Patients

Receiving Antiretroviral Drugs in Cameroon.

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**BACKGROUND:** Tuberculosis (TB) remains a leading cause of mortality among people

living with HIV/AIDS, who face a tenfold higher risk of Mycobacterium

tuberculosis (MTB) infection. TB-HIV coinfection complicates disease management

due to drug interactions, overlapping toxicities, immune reconstitution

inflammatory syndrome, and high treatment burdens, potentially driving drug

resistance. The emergence of resistant MTB further exacerbates this challenge.

This study evaluated the drug resistance profile of MTB in TB-confirmed samples

from HIV-positive patients.

**METHODS:** An analytical cross-sectional study was conducted on 216 sputum samples

from HIV patients on antiretroviral therapy at Jamot Hospital, Yaoundé, Cameroon

(June-September 2022). Two consecutive samples per patient underwent fluorescent

microscopy (Auramine-Rhodamine stain) and TB-Loop-Mediated Isothermal

Amplification. DNA was extracted using the GenoLyse® kit (Hain Lifescience,

Germany), and drug resistance profiles were assessed via GenoType® MTBDRplus and

MTBDRsl line probe assays.

**RESULTS:** TB was confirmed in 12.04% (26/216) of participants. Rifampicin (RIF)

and isoniazid (INH) resistance were each detected in 50% (13/26) of cases, with

23% (6/26) exhibiting multidrug-resistance (MDR). Predominant mutations included

rpoB MUT2B (15.38%) for RIF and inhA MUT2A (23.06%) for INH. Second-line

resistance analysis revealed 61.54% (8/13) resistance to kanamycin

(KAN)/amikacin (AMK)/viomycin, 7.69% (1/13) to AMK/capreomycin/viomycin, and

7.69% (1/13) to KAN. Notably, 61.54% (8/13) lacked the rrs wild-type probe,

indicating resistance to injectable TB drugs.

**CONCLUSION:** High MDR-TB prevalence was observed among HIV-TB coinfected

patients, underscoring the urgent need for enhanced resistance surveillance and

optimized treatment strategies in TB/HIV-endemic regions like Cameroon. Further

research is warranted to elucidate HIV's role in driving TB drug resistance.

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Influence of Single-nucleotide Polymorphism of INF-γ (rs.2430561, +874 A/T) and

Interleukin-10 (rs.1800896, -1082 A/G) on the Risk of Tuberculosis and Drug

Resistance in Kaduna State, Nigeria.

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**BACKGROUND:** Tuberculosis (TB) remains a global health challenge, necessitating

comprehensive research to understand genetic factors influencing susceptibility

and drug resistance. This study aimed to investigate the presence of drug

resistance, analyze single nucleotide polymorphisms (SNPs) in IFN-γ (reference

SNP. 2430561, +874 Adenine/Thymine) and IL-10 (reference SNP.1800896, -1082

Adenine/Guanine), and assess their associations with age and sex among a cross

section of TB patients in Kaduna state.

**METHODS:** A total of 140 participants, comprising drug-resistant TB (DR-TB)

patients, drug-susceptible TB (DS-TB) patients, and Apparently Healthy controls

(AHCs), were enrolled. Genomic deoxyribonucleic acid was extracted, and SNPs

were genotyped using polymerase chain reaction-based techniques. Associations

between genotypes, alleles, age, and sex were analyzed. Odd ratios and

Hardy-Weinberg equilibrium were employed for demographic and genetic analyses.

**RESULTS:** In DR-TB, significant associations were observed between IFN-γ

genotypes/alleles and increased susceptibility, with thymine thymine (TT)

genotype and T allele showing higher frequency. For IL-10, guanine guanine (GG)

genotype and G allele were prevalent, indicating potential associations with

DR-TB risk. In DS-TB, similar trends were observed, highlighting potential

genetic influences on susceptibility. HWE analysis revealed significant

deviations in some groups, suggesting genetic variations.

**CONCLUSIONS:** The prevalence of specific genotypes and alleles indicates

potential genetic markers for risk assessment. Deviations from HWE suggest

population-specific genetic variations. These findings underscore the importance

of genetic factors in TB outcomes and advocate for tailored interventions for

different populations.

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Use of Whole-genome Sequencing in a Tuberculosis Outbreak among Young Immigrants

in a Japanese Language School, 2024.

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Kitakyushu, Japan.

**BACKGROUND:** In early April 2024, three Nepalese students (Pt1-Pt3) in the

morning classes of a Japanese language school in Western Japan were diagnosed

with sputum smear-positive pulmonary tuberculosis (TB). The smear status of Pt1

and Pt3 was 3+, whereas Pt2 was scanty positive. This study aims at describing

cases with active TB as well as latent TB infection (LTBI) in this outbreak.

**METHODS:** The outbreak cases are epidemiologically described in terms of time,

place, and person.

**RESULTS:** An intensive contact investigation using chest X-rays found 13 cases

with active TB as of January 2025. Ten cases, including Pt1 and Pt2, were found

in Classroom A, whereas one case each was found in the morning classes of

Classrooms B (Pt3) and C and in Classroom D (afternoon class). In addition, 10

other cases of LTBI were found in Classroom A. Whole-genome sequencing (WGS)

revealed that Pt3 and another case in Classroom A had genetically distinct

Mycobacterium tuberculosis strains, with 1072 and 466 single nucleotide

variants, respectively, indicating they were unrelated to the outbreak. On the

other hand, the case of Classroom C shared the outbreak strain, and the person

had frequently visited the apartment of Pt1 and Pt2. The case of Classroom D did

not have close contact with those of Classroom A and was eventually excluded

from the outbreak cases.

**CONCLUSION:** WGS is useful in distinguishing outbreak-related cases from

coincidentally found ones in TB outbreak investigations.

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Potential Role of Whole Genome Sequencing to Predict the Virulence, Anti-TB

Resistance, and Variants of Mycobacterium tuberculosis Strains from

Rifampicin-sensitive Pulmonary Tuberculosis Patients in Surabaya, East Java,

Indonesia.

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**BACKGROUND:** Tuberculosis (TB) is the second concern of a fatal infectious

disease in the world caused by Mycobacterium tuberculosis (MTB). Indonesia has

many regions that is known as a hotspot region for MTB cases, one of the most

cities high newly case detected in 5 years was Surabaya. In 2022, Surabaya

reported a higher pulmonary TB (PTB) prevalence rate of 0.35%. This study aimed

to investigate the genomic and phylogenetic characteristics of MTB from isolates

of rifampicin-sensitive PTB patients in Surabaya using whole genome sequencing

(WGS).

**METHODS:** This study is a cross-sectional study to descriptively analyses WGS

data using bioinformatics. Out of 8 enrolled drug-sensitive PTB patients;

however, only three cultured isolates successfully grew on MB 7H11/OADC agar and

subjected for WGS analysis.

**RESULTS:** Whole genome analysis revealed that all the samples were drug

sensitive. The identified samples were majority belonged to lineage 4.4.1

(Euro-American [S-type]) and we found a novel strain in East Java region known

as Lineage 4.10 (Euro-American [Uganda 1]). In addition, we identified a novel

SNVs predicted to be associated with genomic adaptation in fgd1, embC, embA, and

rv0565c under antibiotic pressures.

**CONCLUSION:** WGS predicts that all the samples from pulmonary

rifampicin-sensitive TB patients in this study were drug sensitive. We report

the first discovery of a novel L4.10 strain, classified as Uganda 1, in

Surabaya, Indonesia.

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Dynamics of the In vitro Growing of Mycobacterium bovis from the Lungs of

Vaccinated and Infected Mice.

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**BACKGROUND:** Bovine tuberculosis (bTB) is a disease primarily caused by

Mycobacterium bovis. Currently, no commercial vaccines exist for controlling

bTB, making the development of effective vaccine candidates and testing models a

high priority. Mouse models are widely used in preclinical trials of anti-TB

vaccines. Determining the appropriate cultivation time to assess the

mycobacterial load in animal organs or biological samples is crucial to

establishing a reliable model that can accurately evaluate the effectiveness of

a vaccine candidate. The aim of this study was to assess the growth dynamics and

the appearance of colony-forming units (CFUs) in lung homogenates from mice

infected with M. bovis. We compared the CFU counts from vaccinated and

challenged mice with M. bovis using data from a previous experiment.

**METHODS:** CFUs obtained from the lungs of vaccinated and M. bovis-challenged mice

of a previous experiment were registered at 3 and 4 weeks of culturing in solid

media. The statistical analysis was performed with Kruskal-Wallis, followed by a

Dunn's multiple comparison test.

**RESULTS:** On analyzing the CFU dynamics from lung homogenates, we found that mice

vaccinated with Bacillus Calmette-Guérin preserved stable CFU counts after 3

weeks of cultivation on a solid medium. In contrast, both the unvaccinated group

and the group vaccinated with an attenuated M. bovis triple mutant strain

reached their final CFU counts only after 4 weeks of culturing.

**CONCLUSION:** These findings underscore the importance of prolonged follow-up to

accurately assess CFU counts, which are crucial for determining vaccine efficacy

in trials.

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Evolutionary Genetic Analysis of the Pyrazinamidase Gene in Seven Global

Populations of Mycobacterium tuberculosis.

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**BACKGROUND:** This study aims to identify the signatures of natural selection in

the pyrazinamidase (pncA) gene to see if genetic adaptations by Darwinian

natural selection have shaped genetic composition of Mycobacterium tuberculosis

(Mtb).

**METHODS:** The present analyses were based on 209 DNA sequences (561 bp) of the

pncA gene of the bacterial pathogen, Mtb from seven different counties (Peru,

Pakistan, South Africa, Mexico, India, China, and Kuwait) endemic to

tuberculosis (TB). Before conducting tests for Darwinian natural selection in

the pncA gene, we conducted several tests for neutrality in all the available

DNA sequences after retrieval from public domains. Several statistical analyses

under different algorithms were conducted and biological/evolutionary inferences

were drawn.

**RESULTS:** The 209 sequences of the pncA gene in Mtb belonging to seven different

countries were found to be perfectly aligned with the reference sequence. Data

analyses under different population genetic models revealed the highest genetic

diversity in India, followed by Peru; the lowest was in China. Interestingly,

four populations; Peru, Pakistan, India, and Kuwait were found to be deviated

from neutral model of evolution based on Tajima'D (TD) values; two populations

(India and Peru) based on Fu and Li's D and F (FLD and FLF) test values and five

populations (India, Peru, Pakistan, South Africa, and Kuwait) based on Fay and

Wu's H (FWH) test. Moreover, based on the statistically significant results of

neutrality tests, evidence for positive selection in three populations (Peru [P

< 0.02945], Pakistan [P < 0.01767], and Kuwait [P < 0.00301]) at P < 0.05 level

of significance] was found.

**CONCLUSION:** The present evolutionary genetic analysis of the pncA gene indicates

different levels of genetic diversity in seven different country populations. As

almost all the global populations showed deviation from neutral model and three

populations showed signatures of natural selection, with no specific hotspot

region identified for PZA resistance, this gene needs to be studied with larger

population size covering countries with TB incidences to study the evolution of

drug resistance in Mtb. This will help in the management of drug resistance and

TB elimination plan.

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Clinical Profile, Outcomes, and Predictors of Outcomes in Patients with

Tuberculosis with Arachnoiditis.

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**BACKGROUND:** Tuberculosis (TB) remains a leading global cause of infectious

disease-related mortality. This study aimed to investigate the clinical

characteristics, outcomes, and prognostic factors in patients diagnosed with

tuberculous arachnoiditis, a serious complication of TB affecting the spinal

cord and nerve roots.

**METHODS:** This is a retrospective analysis of adult patients admitted with

tuberculous arachnoiditis to a tertiary care center between July 2011 and

November 2021. A total of 119 patients were included. Data collected included

demographics, clinical presentation, cerebrospinal fluid (CSF) analysis,

treatment regimens, and outcomes assessed using the Modified Rankin Scale at

presentation and follow-up. Predictors of outcomes, including mortality, were

analyzed using SPSS software.

**RESULTS:** The median age of patients was 34 years (standard deviation ± 14.13),

with a male-to-female ratio of 53:47. Common presenting features included

lower-limb weakness (67% with power ≤3/5) and bowel/bladder dysfunction (61%).

Higher CSF leukocyte counts and human immunodeficiency virus (HIV) co-infection

were significantly associated with worse outcomes; 63.6% of HIV-positive

patients died before review. Elevated CSF protein levels were directly

correlated with mortality. Longer duration of antitubercular therapy (ATT) was

associated with improved outcomes. Statistical analysis identified HIV status

and CSF protein count as independent predictors of mortality in TB

arachnoiditis.

**CONCLUSION:** In this cohort of patients with tuberculous arachnoiditis,

lower-limb weakness and bowel/bladder incontinence were the predominant clinical

features. HIV seropositivity, elevated CSF protein levels, and duration of ATT

significantly influenced patient outcomes. These findings underscore the

importance of early diagnosis, prompt initiation of ATT, and management of

associated factors like HIV in improving outcomes for patients with TB

arachnoiditis.

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Diagnostic Modalities for Detecting Extrapulmonary Tuberculosis and Resistance

Patterns of Rifampicin and Isoniazid at a Referral Hospital: A Retro Prospective

Study.

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**BACKGROUND:** Tuberculosis (TB), caused by Mycobacterium tuberculosis complex,

results in approximately 1.5 million annual deaths globally. Diagnosing

extrapulmonary TB (EPTB) remains challenging due to the invasive nature of

sample collection and limitations in conventional diagnostic sensitivity. This

study evaluates the diagnostic performance of Xpert®Mycobacterium

tuberculosis/Rifampicin (MTB/RIF), a nucleic acid amplification test, against

direct microscopy for EPTB specimens. In addition, we compare the detection of

first-line anti-tubercular drug resistance between Xpert® MTB/RIF and the MTB-DR

plus line probe assay.

**METHODS:** From January 2022, to April 2023, 2839 clinically suspected EPTB

specimens were collected from patients referred to tertiary care hospitals in

Gorakhpur, India. Specimens included lymph node aspirates, pleural fluid,

cerebrospinal fluid, and tissue biopsies, processed according to the Indian

National Tuberculosis Elimination Program protocols. Diagnostic evaluations

employed microscopy (acid-fast bacilli staining), Xpert® MTB/RIF, and MTB-DR

plus assays.

**RESULTS:** Of 2839 specimens, Xpert® MTB/RIF detected M. tuberculosis in 339 cases

(11.9%), significantly outperforming microscopy (183 cases, 6.4%). The highest

positivity rates occurred in tissue biopsies and lymph node aspirates (29%),

while genitourinary TB was least frequent. Rifampicin resistance was identified

in 14 cases (4.13%), all confirmed as multidrug-resistant TB (MDR-TB) by MTB-DR

plus.

**CONCLUSION:** Xpert® MTB/RIF demonstrated superior sensitivity over microscopy,

supporting its utility for EPTB diagnosis in low-resource settings. The high

MDR-TB prevalence (4.13%) underscores the need for rapid molecular diagnostics

to guide treatment. However, global EPTB burden estimates remain inconsistent,

necessitating standardized surveillance and diagnostic protocols to improve

detection accuracy and inform public health strategies.

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Mitigating Tuberculosis Drug-induced Liver Injury: The Role of Moringa oleifera

and Other Herbal Extracts.

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**BACKGROUND:** Tuberculosis (TB) is a significant public health issue, and

drug-induced liver injury (DILI) from anti-TB medications poses a major

challenge to treatment efficacy. This study aims to evaluate the protective

effects of a blended polyherbal extract consisting of Moringa oleifera Lam.,

Camellia sinensis, Curcuma zanthorrhiza, and Caesalpinia sappan L. against DILI

induced by TB drugs.

**METHODS:** A total of 25 male Wistar rats were divided into five groups: a control

group, a DILI group receiving anti-TB drugs, and three groups receiving varying

doses of the polyherbal extract. Key parameters, including CYP450 expression and

liver enzyme levels (alanine aminotransferase [ALT] and aspartate

aminotransferase [AST]), were assessed using colorimetric techniques.

**RESULTS:** The administration of the highest dose of the polyherbal extract

significantly reduced CYP450 expression and lowered ALT and AST levels compared

to the DILI group. These findings suggest that the polyherbal remedy effectively

protects the liver from damage caused by TB medications.

**CONCLUSIONS:** The study concludes that the polyherbal extract MOC3 exhibits

hepatoprotective properties, indicating its potential as a preventive treatment

for DILI in TB therapy. Further clinical investigations are recommended to

explore its applicability in human subjects.

Copyright © 2025 International Journal of Mycobacteriology.

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**59. Int J Mycobacteriol. 2025 Apr 1;14(2):96-102. doi: 10.4103/ijmy.ijmy\_229\_24.**

**Epub 2025 Jun 20.**

The Effect of Sex on Active and Latent Tuberculosis Occurrence Based on

Mannose-Binding Lectin 2 Gene Expression and Mannose-binding Lectin Plasma

Concentration in Indonesia.

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**BACKGROUND:** Studies on the role of mannose-binding lectin 2 (MBL2) in

individuals infected with tuberculosis (TB) remain limited. This study aimed to

compare MBL2 gene expression and protein concentration between active and latent

TB cases and to assess the influence of sex on these differences.

**METHODS:** This cross-sectional study involved 39 newly diagnosed active pulmonary

TB patients and 25 individuals with latent TB who were household contacts. MBL2

gene expression was evaluated using a relative quantitative polymerase chain

reaction method. MBL protein levels were measured using the enzyme-linked

immunosorbent assay.

**RESULTS:** Among female participants, MBL2 gene expression was significantly lower

in those with active TB compared to those with latent TB (P = 0.02). In male

participants, no significant difference was observed (P = 0.333). Similarly, MBL

protein levels tended to be lower in females with active TB than in those with

latent TB, though this difference was not statistically significant (median

[range]: 124.78 [65.62-499.79] vs. 208.49 [99.85-498.65] ng/mL, P = 0.099). In

males, no significant difference in MBL protein levels was detected between the

active TB and latent TB groups (206.86 [59.11-526.77] vs. 143.55 [65.85-290.7]

ng/mL, P = 0.285).

**CONCLUSION:** This study highlights the influence of sex on the expression of the

MBL2 gene and plasma protein levels in TB patients. A lower expression of the

MBL2 gene in active TB cases compared to latent TB cases was observed

exclusively in women.

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**60. Int J Mycobacteriol. 2025 Apr 1;14(2):89-95. doi: 10.4103/ijmy.ijmy\_71\_25. Epub 2025 Jun 20.**

Studying the Effect of Tumor Necrosis Factor-Alpha and Tumor Necrosis Factor

Gene Polymorphisms on the Incidence of Tuberculosis.

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Tuberculosis and its pathogen, Mycobacterium tuberculosis complex, are a major

health challenge. The causative agent of tuberculosis is M. tuberculosis complex

and is transmitted through airborne droplets. Tumor necrosis factor-alpha

(TNF-α) is one of the cytokines that mediate a major role in the cellular immune

response to tuberculosis and is essential for pathogen clearance, control of

mycobacterial growth, and facilitation of apoptosis of infected cells.

Susceptibility to tuberculosis and disease progression are influenced by

environmental factors and the host's genetic predisposition. TNF polymorphisms

affect disease susceptibility and patient response to drugs and treatment.

Various studies have been conducted to associate TNF polymorphisms with

susceptibility to tuberculosis. This activity aims to review the role of TNF-α

cytokine and the impact of its polymorphisms on the occurrence of tuberculosis

and compiles recent mechanistic and epidemiological findings.

Copyright © 2025 International Journal of Mycobacteriology.

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**61. Front Vet Sci. 2025 Jun 5;12:1601267. doi: 10.3389/fvets.2025.1601267.**

**eCollection 2025.**

Genome-wide long non-coding RNA expression profile and its regulatory role in

the ileocecal valve from Mycobacterium avium subsp. paratuberculosis-infected

cattle.

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Bovine paratuberculosis (PTB) is a chronic enteritis caused by Mycobacterium

avium subsp. paratuberculosis (MAP), which results in significant economic

losses to the dairy industry worldwide. Long non-coding RNAs (lncRNAs) play a

crucial role in regulating the host immune response due to their interaction

with transcripts in proximity. However, their annotation in cattle remains

limited, and their role in cattle naturally infected with MAP has not been fully

explored. In this study, lncRNAs were identified in the transcriptome of

ileocecal valve samples from control cows without lesions (N = 4) and with

PTB-associated focal (N = 5) and diffuse (N = 5) lesions in intestinal tissues

using RNA sequencing. The raw reads were uploaded into the CLC Bio Genomics

Workbench, and the trimmed reads were mapped to the Bos taurus ARS\_UCD1.2.109

reference genome using the Large Gap Read Mapping tool. The resulting annotation

allowed the identification of 1,434 LncRNAs, 899 of which were novel, using the

FlExible Extraction of LncRNA pipeline. LncRNA differential expression (DE)

analysis performed with DESeq2 allowed the identification of 1, 6, and 2 DE

lncRNAs in the comparisons of cows with focal lesions versus (vs) controls,

diffuse lesions vs. controls, and diffuse vs. focal lesions, respectively. Best

lncRNA partner analysis identified expression correlations between the

lncRNA1086.1, lncRNA ENSBTAG00000050406, and lncRNA\_2340.1, and the Inactive

Phosphatidylinositol 3-Phosphatase 9 (MTMR9), GM Domain Family member B (RGMB),

and the homeobox A6 (HOXA6), respectively. The MTMR9 negatively regulates

apoptosis, the RGMB positively regulates IL-6 expression, and the HOXA6

regulates cell differentiation and inflammation. The results of the quantitative

trait locus (QTL) enrichment analysis showed that the DE lncRNAs were located in

genomic regions previously associated with clinical mastitis, HDL cholesterol,

bovine tuberculosis, paratuberculosis, and bovine leukosis susceptibility. The

identified DE lncRNAs could allow the development of novel PTB diagnostic tools

and have potential applications in breeding strategies for PTB-resistant cattle.

Copyright © 2025 Badia-Bringué, Asselstine, Cánovas and Alonso-Hearn.

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**62. Indian J Med Res. 2025 Apr;161(4):354-361. doi: 10.25259/IJMR\_1644\_2024.**

A qualitative study on the barriers to tuberculosis treatment adherence using

digital adherence technologies (DATs).

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**Background & objectives** In order to meet the ambitious aim set by the Government

of India as well as the sustainable development goals (SDG) target for

eliminating tuberculosis in 2030, it is important for the healthcare providers

to follow and support the patients throughout the treatment for its successful

completion. For monitoring the tuberculosis treatment compliance, Digital

Adherence Technologies (DATs) play a major role. DATs are digital tools that use

mobile phone, computer, or sensor technologies to support the capture of

detailed, daily, patient-specific adherence information. DATs provide

opportunities for a more patient-centred care model and also help healthcare

workers while treating tuberculosis (TB) patients when compared to traditional

directly observed therapy. Hence, in this study explored the acceptance and

barriers to the use of DATs for monitoring compliance with TB treatment and its

possible solutions. **Methods** A community-based qualitative study was done in two

PHCs in Puducherry, India among TB patients who completed treatment, healthcare

providers such as tuberculosis health visitors, staff nurses, and respective

medical officers. Thirty participants were interviewed using purposive sampling

to explore TB treatment outcomes over two months (Oct-Nov 2023). In-depth

interviews were conducted with the help of a separate interview guide consisting

of broad, open-ended questions with two primary stimulus questions based on the

acceptance and barriers for use of DATs for capturing adherence to TB treatment.

The possible solutions for the barriers to the use of DATs were also explored by

the healthcare providers. Manual content analysis was done for the qualitative

data. **Results** Benefits of the use of DATs included saving time, identification

of loss to follow up patients, information on NIKSHAY, and other direct benefit

transfers. Barriers include financial constraints, level of education, family

issues, and difficulty in the use of gadgets (tab). Some of the solutions to the

barriers were cooperation from family members, distribution of mobile phones,

appointment of ASHA workers, and linking of NIKSHAY IDs with Aadhaar card

numbers to avoid duplication. **Interpretation & Conclusions** Identification of

barriers and potential solutions in DATs can help in the successful monitoring

and completion of tuberculosis treatment which are crucial towards achieving the

tuberculosis elimination goal set by the Government of India as well as the SDG

target for elimination by 2030.

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PMCID: PMC12178189

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**63. Indian J Med Res. 2025 Apr;161(4):346-353. doi: 10.25259/IJMR\_767\_2025.**

Diagnostic accuracy of real-time PCR assay 'Quantiplus® MTB FAST' for detection

of adult pulmonary tuberculosis (PTB): A multi-centric study.

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**Background & objectives** The global target set by the United Nations (UN)

high-level meeting on Tuberculosis (TB) for coverage of rapid molecular tests is

100 per cent by 2027. Rapid, affordable molecular tests for early detection of

TB are the need of the hour. This study aimed to evaluate the diagnostic

accuracy of an open real-time PCR (RT-PCR) assay, Quantiplus®, with reference to

Mycobacteria Growth Indicator Tube (MGIT) liquid culture. **Methods** We conducted a

prospective multi-centric diagnostic accuracy study of Quantiplus® assay

(version 2.0) at three sites in India for the detection of pulmonary TB in

sputum with culture as the reference standard, compared with Xpert® MTB/RIF. A

total of 657 adults (>18 yr) with presumptive TB were enrolled consecutively.

The Quantiplus® assay uses an extraction-free, quick-lysis protocol and three

gene targets for RT-PCR. **Results** Of the 644 samples analysed, 37 per cent were

culture-positive and 32 per cent were smear-positive. The sensitivity and

specificity of Quantiplus® assay with reference to MGIT culture were 86 per cent

[95% confidence interval (CI): 81-90] and 96 per cent (95% CI: 94-98),

respectively, at Ct ≤ 38. The positive and negative predictive values (PPV/NPV)

were 93 per cent (95% CI: 89-96%) and 92 per cent (95% CI: 89-94%),

respectively. Among the 73 smear-negative culture-positive specimens, the

sensitivity and specificity were 61.6 per cent (95% CI: 50-73) and 97 per cent

(95% CI: 92-98.6), respectively. The performance of Quantiplus® assay(v2.0) was

comparable to Xpert MTB/RIF® (κ=0.83, SE=0.02) at Ct ≤38. **Interpretation &**

**conclusions** The flexibility of the open RT-PCR assay to be used in any RT-PCR

machine makes it a very low-cost (<2 US$) alternative to the expensive

cartridge-based tests. This is the first report of validation of an open system

RT-PCR assay for the detection of pulmonary TB.

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PMCID: PMC12178193

PMID: 40536373 [Indexed for MEDLINE]

**64. Infect Dis Model. 2025 Jun 2;10(4):1037-1054. doi: 10.1016/j.idm.2025.05.010.**

**eCollection 2025 Dec.**

Modelling the potential impact of TB-funded prevention programs on the

transmission dynamics of TB.

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Tuberculosis (TB) continues to be a major global health challenge, with millions

of new cases and deaths each year despite the massive efforts and funding put in

the fight against the disease. In this paper, we develop a mathematical model to

evaluate the impact of TB-funded prevention programs on the transmission

dynamics of TB. The model incorporates stages of TB infection (latent and

active), and accounts for the effects of treatment, funding and TB-funded

prevention programs. Our analysis shows that increased funding and enhanced

prevention programs reduce the number of active TB cases, thereby decreasing the

reproduction number and TB endemicity. Specifically, higher funding rates lead

to improved prevention and treatment outcomes, resulting in the lowering of the

effective reproduction number (R0) and reduced transmission. The model's steady

states are determined and it is shown that the model has a disease-free

equilibrium that is locally asymptotically stable whenever R0 < 1 and multiple

endemic equilibria for R0c < R0 < 1 and a unique endemic equilibrium for R0 > 1 . The model is shown to exhibit a backward bifurcation that vanishes as the funding for TB is increased. The paper also highlights that treatment alone,

while beneficial, is less effective than a combined strategy involving funding

and prevention. Numerical simulations are carried out and the influences of

various parameters on the effective reproduction number are investigated. The

implications of TB-funded prevention programs on TB dynamics and control of TB

are discussed and valuable insights for policymakers in designing effective TB

control programs are highlighted.

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**65. Int J Nurs Stud Adv. 2025 Mar 6;8:100316. doi: 10.1016/j.ijnsa.2025.100316.**

**eCollection 2025 Jun.**

Risk factors on length of stay among pulmonary tuberculosis patients: A

systematic review and meta-analysis.

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Tropical Medicine, Mahidol University, Bangkok, 10400 Thailand.

**BACKGROUND:** Pulmonary Tuberculosis (PTB) remains a pressing public health

concern. Long hospital stays for PTB patients can overburden both patients and

healthcare systems.

**OBJECTIVE:** To identify the key factors contributing to extended length of stay

in PTB patients.

**INFORMATION SOURCES:** Four electronic databases (PubMed, Scopus, Embase, and

CINAHL) were systematically searched from inception to January 1, 2023.

**METHODS:** The articles were screened and performed according to Preferred

Reporting Items for Systematic reviews and Meta-Analyses (PRISMA). Inclusion

criteria were PTB patients diagnosed by doctors and studies reporting factors

affecting length of stay. Exclusion criteria were review articles, case study,

conferences abstract, and proceedings. Study quality was assessed using the

Newcastle-Ottawa Scale (NOS). A random-effects model was used to analyzed risk

factors for length of stay. Heterogeneity was employed using I2 and Q

statistics. Forest plots displayed effect sizes (ES) and 95 % confidence

intervals. STATA 14.2 was used for meta-analysis.

**RESULTS:** A total of 1,190 studies were screened from reputable electronic

databases, six studies comprised of 9,231 participants were included.

Meta-analysis revealed that they are six risk factors associated with longer

length of stay including; older age (OR 1.50, 95 % CI 1.07-2.09, p = 0.019),

comorbidity (OR 1.44, 95 % CI 1.17-1.78, p = 0.001), HIV patient (OR 1.40, 95 %

CI 1.16-1.69, p = 0.001), patients with ADR (OR 2.19, 95 % CI 1.47-3.26, p <

0.001), MDR TB (OR 3.16, 95 % CI 2.31-4.32, p < 0.001), and miliary TB (OR 1.37,

95 % CI 1.10-1.70, p = 0.004) with minimal heterogeneity [(I2 = 34.2 %, p =

0.207), (I2 = 43.1 %, p = 0.118), (I2 = 0.0 %, p = 0.573), (I2 = 0.0 %, p =

0.723), (I2 = 0.0 %, p = 0.366), and (I2 = 0.0 %, p = 0.753), respectively].

There was no evidence of publication bias according to Begg's and Egger's test.

**CONCLUSIONS:** In conclusion, six risk factors were identified as significantly

associated with longer hospital stays in PTB patients: older age, comorbidities,

HIV infection, ADR, MDR-TB, and miliary TB. These findings highlight the

importance of targeted interventions for these high-risk groups to reduce length

of stay and alleviate the burden on healthcare systems. The results are based on

a meta-analysis of six studies with minimal heterogeneity, and no evidence of

publication bias was found. Future research should focus on exploring additional

factors influencing length of stay, particularly in diverse populations, and

evaluating the effectiveness of interventions to shorten hospital stays.

Additionally, studies examining the impact of healthcare infrastructure and

resource allocation on length of stay could provide valuable insights for

improving patient outcomes.

REGISTRATION: This study was registered with PROSPERO, CRD4203390615.

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**66. Cureus. 2025 May 19;17(5):e84378. doi: 10.7759/cureus.84378. eCollection 2025**

**May.**

Navigating a Diagnostic Dilemma: A Case Report of Overlapping Presentation of

Granulomatosis With Polyangiitis and Tuberculosis.

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Granulomatosis with polyangiitis (GPA) and tuberculosis (TB) present a

diagnostic conundrum due to their similar clinical manifestations,

histopathological features, and the presence of positive antineutrophil

cytoplasmic antibodies (ANCAs) in both conditions. We present the case of a

54-year-old patient who was initially evaluated for TB but developed a

vasculitic rash during the course of the illness, suggesting an alternative

diagnosis. Further evaluation revealed positive cytoplasmic ANCA (C-ANCA) and

pulmonary nodules with cavitations on chest imaging, shifting the diagnosis

toward GPA. The diagnosis of GPA was confirmed based on the EULAR/ACR (European

League Against Rheumatism/American College of Rheumatology) 2022 classification

criteria. Disease remission was induced with steroid pulse therapy and

intravenous cyclophosphamide. Azathioprine was used for maintenance therapy. The

patient made a remarkable recovery with treatment. We discuss this case due to

the scarcity of reported cases in Sri Lanka to provide insight into the

diagnostic approach for patients presenting with similar clinical phenotypes.

Although TB is more common than GPA in Asian countries, few cases have been

reported with overlapping features of both diseases. In light of this diagnostic

dilemma, clinicians are faced with significant challenges in accurately

distinguishing between the two diseases, which could lead to delays in the

establishment of appropriate treatment and management. Therefore, we highlight

the importance of considering GPA as a differential diagnosis for TB, even in

Asian countries.

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**67. Front Ophthalmol (Lausanne). 2025 Jun 4;5:1610215. doi:**

**10.3389/fopht.2025.1610215. eCollection 2025.**

Exploiting induced pluripotent stem cell-derived retinal pigment epithelium to

unravel host-pathogen interaction in ocular tuberculosis: a reverse

translational in vitro model.

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Mycobacterium tuberculosis (Mtb) can infect the retinal pigment epithelium (RPE)

cells. Current in vitro research models for ocular tuberculosis (OTB) only rely

on RPE cell culture approaches. Until now it remains unclear why only a minority

of patients with active systemic tuberculosis (TB) develops concurrent OTB.

There is significant variation in the clinical manifestations of OTB, which is

potentially influenced by ethnic differences and diversity in mycobacterial

strains. To better understand the immunopathobiology of OTB, particularly an

individual's susceptibility to Mtb-infection and the specific host response,

cell culture systems utilizing induced pluripotent stem cells (iPSC)-derived RPE

cells offer a promising in vitro model to better mimic the disease. With this

technology, RPE cells can be generated from specific patients of interest,

enabling to test hypotheses in a bench to bedside or reverse manner. In this

current study, we explore the utility of iPSC-derived RPE cells as an in vitro

model for OTB. Such an approach would overcome drawbacks associated with the

currently commonly used "general" RPE cell lines as disease model. The

application of iPSC-derived RPE cells offers promising options for the

identification of novel biomarkers and to study individualized drug screening

methods for host-directed therapy of OTB, in order to restore and maintain

vision in OTB patients with sight-threatening disease.

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Steenwinkel, Vingerling, Dik and van Hagen.

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PMID: 40535229

**68. Indian J Thorac Cardiovasc Surg. 2025 Jul;41(7):911-914. doi:**

**10.1007/s12055-024-01875-7. Epub 2024 Dec 19.**

The great masquerade: TB endomyocarditis as left ventricular mass.

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Cardiac masses are rare and often diagnosed via imaging due to difficulties in

obtaining tissue samples. This case highlights an unusual presentation of

tuberculosis (TB) endomyocarditis as a left ventricular mass. A 25-year-old male

presented with intermittent fever, chills, atypical chest pain, and weight loss

over 6 months, with no other cardiac symptoms or TB exposure. Imaging revealed a left ventricular mass (5 × 4 × 2 cm) with a high standardised uptake value (SUV) of 28 and mediastinal lymph nodes with an SUV of 8, raising suspicions of

sarcoma or lymphoma. After multidisciplinary evaluation, the patient underwent

three cycles of ifosfamide and epirubicin, but the mass did not decrease in

size. A biopsy showed necrotising abscesses and epithelioid cell granulomas, but

no atypical cells, ruling out malignancy. A positive tuberculin test prompted

initiation of intensive anti-tubercular treatment (HRZE). Two months later,

follow-up magnetic resonance imaging (MRI) indicated a reduction in mass size by

over 90%. This case illustrates a rare instance of primary intracardiac

tubercular endomyocarditis and emphasizes the need to consider TB in atypical

cardiac masses. The patient continues anti-tubercular therapy and is under

follow-up.

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**69. Pract Lab Med. 2025 May 30;46:e00479. doi: 10.1016/j.plabm.2025.e00479.**

**eCollection 2025 Sep.**

Direct identification of Mycobacterium species from liquid medium (MGIT) using

FastPrep-2 bead beating system and MALDI-TOF mass spectrometry technology: a

comparison with solid media and PCR-based method.

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University, Baltimore, MD, USA.

**BACKGROUND:** Mycobacterial infections present significant global health

challenges. Traditional diagnostic methods are inadequate for the identification

of Mycobacterium species, highlighting the need for more efficient techniques.

Matrix-assisted laser desorption-ionization time-of-flight (MALDI-TOF) mass

spectrometry (MS) technology offers potential advantages in rapid and accurate

pathogen identification.

**OBJECTIVE:** This study evaluates the accuracy and precision of the MALDI-TOF

using the FastPrep-2 bead beating system and VITEK MS version 3.2 for

identifying Mycobacterium species directly from Mycobacteria Growth Indicator

Tube (MGIT), liquid medium, compared to MALDI-TOF (VITEK MS) based on the

traditional solid medium (Lowenstein-Jensen). We also compared the result of the

MALDI-TOF from MGIT to M tuberculosis results by PCR-based method.

METHODS: The study included 16 mycobacterium tuberculosis (MTB) and 37

nontuberculous mycobacteria (NTM). Isolates were grown in LJ solid medium and

MGIT liquid medium, and lysed using the FastPrep-2 bead beating system.

Identification was performed using VITEK MS version 3.2 from liquid.

**RESULTS:** NTM comprised 70 % (37/53) of the total isolates evaluated. Of these,

92 % (34/37) were successfully identified using VITEK MS from MGIT liquid

medium. Overall, the method achieved 88.6 % accuracy for identifying

Mycobacterium species from liquid medium, compared to 96.2 % from solid medium.

The agreement between both methods was moderate (Kappa = 0.470, p < 0.001). MTB isolates were identified with 100 % accuracy, and the approach demonstrated

excellent reproducibility with 100 % intra-assay and inter-day consistency.

**CONCLUSION:** Using VITEK MS version 3.2 to directly identify MTB and NTM from

MGIT liquid medium provides a rapid, cost-effective, and reliable method for

identifying Mycobacterium species. Further optimization and database expansion

are recommended to enhance accuracy for rare and less common mycobacterial

species.

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PMID: 40534832

**70. J Bras Pneumol. 2025 Jun 13;51(2):e20250059. doi: 10.36416/1806-3756/e20250059.**

Exploring perspectives on the benefits of a tuberculosis short-treatment

regimen: a cross-sectional study on treatment experiences and perceptions.

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DOI: 10.36416/1806-3756/e20250059

PMID: 40531736

**71. J Bras Pneumol. 2025 Jun 13;51(2):e20240426. doi: 10.36416/1806-3756/e20240426. eCollection 2025.**

Knowledge of, Attitude towards, and Preventive Behavior towards Tuberculosis

questionnaire: translation and cross-cultural adaptation for use in Brazil.

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Israelita Albert Einstein, São Paulo (SP) Brasil.

**OBJECTIVE:** To translate the Knowledge of, Attitude towards, and Preventive

Behavior towards Tuberculosis questionnaire into Brazilian Portuguese and adapt

it for use in Brazil.

**METHODS:** This methodological study followed internationally recommended

guidelines for translation and cross-cultural adaptation. After permission was

obtained from the original authors, the process of translation and

cross-cultural adaptation began, including translation into Brazilian Portuguese

by bilingual translators, synthesis of the translations, back-translation for

similarity analysis, revision, and preparation of the final version. A pretest

was conducted on 68 medical students.

**RESULTS:** Most of the questionnaire items showed strong content similarity, with

minor semantic differences. The content validity index for the questionnaire was

0.882, and Cronbach's alpha coefficients were 0.682, 0.809, and 0.613 for

knowledge of tuberculosis, attitudes toward tuberculosis, and preventive

behavior toward tuberculosis, respectively. Cronbach's alpha and omega

coefficients were a = 0.717, w1 = 0.673, w2 = 0.673, and w3 = 0.520.

**CONCLUSIONS:** The process of translation and cross-cultural adaptation of the

Knowledge of, Attitude towards, and Preventive Behavior towards Tuberculosis

questionnaire was successful, making the Brazilian Portuguese version of the

questionnaire reliable for reproducibility. It can be used in order to collect

tuberculosis-related data and support changes in health education curricula.

DOI: 10.36416/1806-3756/e20240426

PMID: 40531734 [Indexed for MEDLINE]

**72. J Bras Pneumol. 2025 Jun 13;51(2):e20240327. doi: 10.36416/1806-3756/e20240327. eCollection 2025.**

A polymorphism in the FAM13A gene confers protection against tuberculosis in

Brazilian workers exposed to silica.

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(RJ), Brasil.

**OBJECTIVE:** Tuberculosis (TB) is an infectious disease caused by the bacillus

Mycobacterium tuberculosis, which was recognized by the World Health

Organization (WHO) as a global epidemic in 1993. TB is the leading infectious

disease associated with silicosis, with studies showing an increased risk when

compared to healthy individuals. We conducted an association study to evaluate

the influence of polymorphisms in the ACE, FAM13A, FAS, FASLG, IL1RN, NOS2,

TGFB1, and TNF genes on TB susceptibility.

**METHODS:** Nine polymorphisms were genotyped using Polymerase Chain Reaction (PCR)

in a sample of 143 patients with silicosis in Rio de Janeiro (RJ), Brazil.

**RESULTS:** Seventy (49%) patients had a confirmed prior diagnosis of TB, of whom

25 (35.7%) had simple silicosis and 45 (64.3%) had complicated silicosis. The TG

genotype of rs2609255 in FAM13A showed a protective effect against TB (OR=0.46;

95% CI: 0.22-0.98; p=0.040) compared to the GG genotype, and also when compared

to the two combined homozygous genotypes (TT+GG) (OR=0.43; 95% CI: 0.20-0.90;

p=0.024). Logistic regression analysis, including independent clinical

variables, confirmed the protective effect of the TG genotype.

**CONCLUSION:** This study suggests that the rs2609255 polymorphism in FAM13A may

play a role in TB risk among patients with silicosis. Given the limited research

on genetic polymorphisms and TB susceptibility in silicosis patients, further

studies are needed to validate these findings.

DOI: 10.36416/1806-3756/e20240327

PMID: 40531729 [Indexed for MEDLINE]

**73. Microb Genom. 2025 Jun;11(6):001429. doi: 10.1099/mgen.0.001429.**

An improved catalogue for whole-genome sequencing prediction of bedaquiline

resistance in Mycobacterium tuberculosis using a reproducible algorithmic

approach.

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Bedaquiline (BDQ) has only been approved for use for just over a decade and is a

key drug for treating multidrug-resistant tuberculosis; however, rising levels

of resistance threaten to reduce its effectiveness. Catalogues of mutations

associated with resistance to BDQ are key to detecting resistance genetically

for either diagnosis or surveillance. At present, building catalogues requires

considerable expert knowledge, often requires the use of complex grading rules

and is an irreproducible process. We developed an automated method, catomatic,

that associates genetic variants with resistance (or susceptibility) using a

two-tailed binomial test with a stated background rate and applied it to a

dataset of 11,867 Mycobacterium tuberculosis samples with whole-genome and BDQ

susceptibility testing data. Using this framework, we investigated how to best

classify variants and the phenotypic significance of minor alleles. The genes

mmpS5 and mmpL5 are not directly associated with BDQ resistance, and our

catalogue of Rv0678, atpE and pepQ variants attains a cross-validated

sensitivity and specificity of 79.4±1.8% and 98.5±0.3%, respectively, for

94±0.4% of samples. Identifying samples with subpopulations containing Rv0678

variants improves sensitivity, and detection thresholds in bioinformatic

pipelines should therefore be lowered. By using a more permissive and

deterministic algorithm trained on a sufficient number of resistant samples, we

have reproducibly constructed a catalogue of BDQ resistance-associated variants

that is comprehensive and accurate.

DOI: 10.1099/mgen.0.001429

PMCID: PMC12177157

PMID: 40531177 [Indexed for MEDLINE]

**74. Nucleic Acids Res. 2025 Jun 6;53(11):gkaf529. doi: 10.1093/nar/gkaf529.**

Selective inhibition of Mycobacterium tuberculosis GpsI unveils a novel strategy

to target the RNA metabolism.

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Polyribonucleotide nucleotidyl-transferases (PNPases) play a critical role in

the degradation of mRNA. The mycobacterial PNPase, guanosine penta-phosphate

synthase I (GpsI), is an essential enzyme in Mycobacterium tuberculosis (Mtb),

collaborating with endoribonucleases and helicases to process RNA. In this

study, we identify GpsI as a novel and underexplored drug target. The inhibitor

1-(4'-(2-phenyl-5-(trifluoromethyl) oxazole-4-carboxamido)-[1,1'-biphenyl]-4-caroxamido) cyclopentane-1-carboxylic acid (X1), discovered through a whole-cell screening, specifically inhibits GpsI activity in biochemical assays. Biochemical and physiological analyses of engineered GpsI variants and recombinant Mycobacterium smegmatis pinpoint amino acids 328 and 527 as critical residues for the selective activity of X1 against Mtb complex. High-resolution cryo-electron microscopy analysis of the ternary GpsI-X1-poly(A) complex elucidates the drug-binding pocket, providing insight into its mechanism of action. This study introduces a potent inhibitor targeting the underexplored Mtb-GpsI and offers a molecular explanation for its selective specificity.

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Acids Research.

DOI: 10.1093/nar/gkaf529

PMID: 40530695 [Indexed for MEDLINE]

**75. Case Rep Oncol. 2025 May 20;18(1):751-755. doi: 10.1159/000546368. eCollection 2025 Jan-Dec.**

Cervical Lymphadenopathy in Concomitant CML and Tuberculosis: A Case Report.

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**INTRODUCTION**: Chronic myeloid leukemia is a myeloproliferative disorder

characterized by the uncontrolled proliferation of mature and maturing

granulocytes in the bone marrow, along with the presence of the Philadelphia

chromosome. Lymphadenopathy is an uncommon initial manifestation of CML and is

typically attributed to the disease itself. However, with the use of tyrosine

kinase inhibitors (TKIs), which can affect T-cell-mediated immunity, new or

persistent lymphadenopathy in CML patients warrants investigation to rule out

opportunistic infections, including tuberculosis (TB), or progression to the

blast phase of CML.

**CASE PRESENTATION:** A 35-year-old male diagnosed with chronic-phase CML initially

presented with cervical lymphadenopathy. The lymphadenopathy was initially

attributed to CML. Further evaluation, including a lymph node biopsy, revealed

concurrent TB infection. Treatment with appropriate anti-tuberculous therapy led

to the resolution of the lymphadenopathy.

**CONCLUSION:** This case highlights the importance of considering opportunistic

infections, such as TB, in CML patients presenting with lymphadenopathy,

particularly those on TKI therapy. Prompt investigation and appropriate

management are crucial to avoid complications and ensure optimal patient

outcomes.

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**76. IJTLD Open. 2025 Jun 13;2(6):324-332. doi: 10.5588/ijtldopen.24.0596.**

**eCollection 2025 Jun.**

Progress and challenges to TB elimination in New South Wales, Australia.

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In Australia, TB care and control is delivered by states and territories, with a

National TB Advisory Committee to advise on national surveillance and strategy.

For more than 30 years, New South Wales (NSW), Australia, has maintained TB

incidence rates of <10/100,000 population, but progress toward TB elimination

and 'zero local TB transmission' remains challenging. Reductions in the TB

notification rate have plateaued in recent decades, mainly due to increased

migration from high incidence countries. There is limited awareness of TB among

the public, and a general perception of low risk, at least for Australian-born

people and locally trained healthcare professionals. As in other low TB

incidence settings, migrants and hard-to-reach populations are overrepresented

in TB notifications. Progress in reducing TB among Australia's Aboriginal and

Torres Strait Islander people has been slow, hindered by embedded disadvantage,

limited healthcare access and historical mistrust. Community engagement and

patient advocacy for TB is minimal. Despite excellent progress over many

decades, TB elimination remains out of reach in NSW due to ongoing migration

from high-incidence settings and the reality of competing health priorities.

Here, we critically assess progress towards TB elimination targets and identify

opportunities to further improve TB control.

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PMID: 40530385

**77. IJTLD Open. 2025 Jun 13;2(6):352-358. doi: 10.5588/ijtldopen.25.0014.**

**eCollection 2025 Jun.**

Data-driven targets for reducing the global burden of TB.

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**BACKGROUND:** The proportion of persons with infectious TB that need to be cured

to reduce prevalence is an important but not well characterized target for TB

control.

**METHODS:** We compared infectious TB prevalence from countries with two

population-based surveys since 2000, accounting for persons receiving curative

treatment and those dying or undergoing natural recovery. Annual incidence was

estimated as the proportion of prevalence that, when applied to each year over

the interval between the two surveys, yielded the observed second survey

prevalence. We then determined the relationship between the proportion of people

with TB cured and the change in prevalence in each of the years covered by the

surveys.

**RESULTS:** Achieving a decline in prevalence required curing at least 20% of those

with infectious TB. None of the countries studied reached the 11% annual decline

in prevalence required to yield the END TB goal of a 90% decrease in prevalence

over 20 years; this would require diagnosing and curing 35-40% of people with

prevalent TB each year.

**CONCLUSIONS:** These results provide targets for achieving the goal of a 90%

reduction in TB and indicate that active case finding will be required to reach

these targets.

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DOI: 10.5588/ijtldopen.25.0014

PMCID: PMC12168725

PMID: 40530384

**78. IJTLD Open. 2025 Jun 13;2(6):315-323. doi: 10.5588/ijtldopen.25.0240.**

**eCollection 2025 Jun.**

Clinical best practices for caring for people with expanded resistance to newer

TB drugs.

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Stambekova A(7), Sinha A(8), Rich ML(7), Reuter A(4), Patel J(2), Otto-Knapp

R(9), Motta I(8)(10), Mesic A(8)(11), McKenna L(12), Maru S(13)(14), Lessem

E(15), Lange C(16)(17), Kiria N(18), Kherabi Y(19)(20), Günther G(21)(22),

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**BACKGROUND:** Strains of Mycobacterium tuberculosis with resistance to the new and

repurposed drugs included in the all-oral shorter TB regimens recommended by WHO

for the treatment of multidrug-resistant/rifampicin-resistant TB (MDR/RR-TB) are

becoming increasingly common globally. When strains of M. tuberculosis have

resistance to one or more of these drugs (bedaquiline, linezolid,

third-generation fluoroquinolones, delamanid, pretomanid, or clofazimine), they

are more challenging to treat.

**METHODS:** In the absence of trial data on how to care for these individuals, a

group of clinical, programmatic and civil society experts came together to

generate a series of best clinical practices. These practices are based on the

published literature and on experience caring for individuals with these forms

of TB.

**RESULTS:** We discuss best clinical practices in the following areas: 1) drug

susceptibility testing; 2) regimen design; 3) adverse event monitoring and

management; 4) special populations; 5) shared decision making and informed

consent; 6) holistic packages of support; and 7) pre-approval

access/compassionate use of newer TB compounds.

**CONCLUSION:** While we await systematic studies of treatment approaches to

generate the necessary evidence base, the clinical practices described here can

be used to guide the programmatic care of people with strains of M. tuberculosis

that have expanded resistance.

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PMCID: PMC12168730

PMID: 40530383

**79. IJTLD Open. 2025 Jun 13;2(6):333-338. doi: 10.5588/ijtldopen.25.0031.**

**eCollection 2025 Jun.**

Adolescents and young adults with TB in a low-incidence setting.

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Stellenbosch University, Cape Town, South Africa.

**BACKGROUND:** Adolescents and young adults (AYA) with TB have distinct physical

and social characteristics compared to other age groups. This study describes a

cohort of AYA with TB in a low TB-prevalence, high-income setting and

investigates whether demographic or social factors affect management outcomes.

**METHODS:** A retrospective cohort study was conducted at a TB referral centre in

North West London, including patients aged 10-24 years from 2015 to 2022. Median

days from symptom onset to healthcare presentation were determined and risk

factors for late presentation (>60 days) were assessed.

**RESULTS:** Among 158 patients (median age 20 years, IQR 17-23), 53.6% had

pulmonary TB, 39.9% extrapulmonary disease, and 5.7% disseminated disease; 25.3%

had cavities. Social risk factors were present in 32.3% of patients. Median

delay to presentation was 45 days (IQR 14-96), with 38.7% presenting after two

months. Delays were longer in patients with incarceration, drug misuse, or

mental health issues, though not statistically significant. Patients with social

risk factors were more likely to receive observed therapy (OR 2.65, IQR

1.27-5.64).

**CONCLUSIONS:** AYA with TB in this setting experienced delays in healthcare

presentation and a quarter had cavitary disease. Social risk factors were common

but not significantly related to outcomes.

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PMID: 40530382

**80. IJTLD Open. 2025 Jun 13;2(6):359-365. doi: 10.5588/ijtldopen.24.0687.**

**eCollection 2025 Jun.**

Trends in prevalent TB among persons enrolling for HIV care before and after

'Test and Treat' across East-Africa.

Kalema N(1), Musick B(2), Babirye S(1), Najjemba L(1), Mubiri P(1), Kiragga

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**BACKGROUND:** In 2015, WHO recommended the global adoption of the 'Test and Treat'

strategy (TTS) for all persons living with HIV (PLHIV). While TTS has improved

viral suppression and reduced mortality, its impact on TB in PLHIV remains

unclear.

**METHODS:** We assessed TB prevalence trends 48 months before and after TTS among

PLHIV aged ≥18 years enrolling at HIV primary care sites affiliated with the

East Africa International Epidemiology Databases to Evaluate AIDS (EA-IeDEA)

consortium. We defined prevalent TB as bacteriologically confirmed or

empirically treated TB within 60 days of enrolment. We estimated monthly TB

prevalence trends using Poisson (change point) model.

**RESULTS:** Among 125,647 PLHIV, 37% were male. The prevalence of TB was 8.9% (95%

CI: 8.7-9.1) before and 6.2% (95% CI: 5.9-6.4) after TTS-adoption. Adjusted

analysis showed significant downward trend in TB prevalence before TTS (adjusted

Prevalence Rate Ratio, aPRR=0.989, p<0.001), which plateaued during TTS

(aPRR=0.999, p=0.131). TB was more frequently present among males (aPRR: 2.09,

p<0.001) and adults ≥25 years across both periods.

**CONCLUSION:** This study highlights a plateau in TB prevalence decline during TTS

and persistent disparities in TB by sex and age, underscoring the need for

targeted interventions.

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DOI: 10.5588/ijtldopen.24.0687

PMCID: PMC12168729

PMID: 40530380

**81. IJTLD Open. 2025 Jun 13;2(6):374-376. doi: 10.5588/ijtldopen.25.0155.**

**eCollection 2025 Jun.**

Mycobacterium tuberculosis in patients with hematologic malignancies in a

low-risk setting.

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**82. IJTLD Open. 2025 Jun 13;2(6):366-373. doi: 10.5588/ijtldopen.25.0105.**

**eCollection 2025 Jun.**

Antenatal screening for TB disease: a systematic review and meta-analysis.

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School of Population and Global Health, The University of Melbourne, Grattan

Street, Parkville, Victoria, Australia.

**OBJECTIVES:** TB disease during pregnancy is associated with poor maternal and

neonatal outcomes, and is a leading non-obstetric cause of maternal death.

However, optimal detection strategies remain uncertain. We aimed to identify the

optimal screening approach for TB disease in pregnant women.

**METHODS:** We searched Ovid MEDLINE, Embase + Embase Classic, Web of Science, and

CENTRAL to identify antenatal screening studies for TB disease. The yield,

number needed to screen (NNS), and positive predictive value (PPV) were

calculated for each method. Pooled estimates were generated using random-effects

meta-analyses. Narrative synthesis was conducted to summarise secondary

outcomes.

**RESULTS:** We included 33 studies. Pooled yield for symptom screening (SS) was

7.26 [95% CI: 0.70, 19.25] cases per 1,000 versus 5.12 [95% CI: 0.79, 12.39] for

TST/IGRA. NNS was 138 [95% CI: 51.95, 1,428.57] for SS versus 1,667 [95% CI:

537.63, 1,000,000] for TST/IGRA. SS pooled PPV was 3.85% [95% CI: 1.23-7.57%],

and <0.01% [95% CI: <0.01-0.05%] for TST/IGRA. Narrative synthesis indicated

antenatal SS is low-cost, feasible, and acceptable but poorly implemented.

**CONCLUSION: I**n pregnancy, symptom screening demonstrates highest yield and

lowest NNS, is low-cost, feasible and acceptable. While currently optimal, the

low PPV underscores the need for TB screening tools tailored to pregnant

populations.

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DOI: 10.5588/ijtldopen.25.0105

PMCID: PMC12168728

PMID: 40530378

**83. IJTLD Open. 2025 Jun 13;2(6):339-345. doi: 10.5588/ijtldopen.25.0084.**

**eCollection 2025 Jun.**

Post-TB sequelae and care: a systematic review and synthesis of qualitative

research.

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Pell C(1), Mulder C(1).

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(5)Kibong'oto Infectious Diseases Hospital, Kilimanjaro, Tanzania.

**BACKGROUND:** TB has long-term health and social sequelae. The experiences of TB

survivors are not well understood and there is limited evidence around gaps in

care. This article aims to provide a comprehensive overview of qualitative

research on post-TB sequelae and care, to identify knowledge gaps and inform

future research and interventions to support person-centred care.

**METHODS:** A systematic search strategy, using two search strings incorporating

post-TB and TB-related chronic respiratory disease. Searches were conducted on

PubMed, Web of Science and CINAHL. Sources were screened systematically, data

extracted independently and analyzed thematically.

**RESULTS**: Sixty-six sources were identified. After applying exclusion/inclusion

criteria, 16 articles were included in a qualitative synthesis. Key themes

included the physical, psychological, economic and social impacts of TB. These

included threats to TB survivors' social role. People who suffer from long-term

sequelae are stigmatised. Access to care is limited and tends to focus on acute

respiratory disease. Policymakers indicate that the lack of data regarding the

long-term impacts of TB contributed to insufficient resources being allocated.

**CONCLUSION:** This systematic review underscores the post-TB physical and

psychological impacts and the complexity of post-TB sequelae; it emphasizes the

urgent need for evidence regarding the long-term impact of TB sequelae to

improve care.

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**84. ACS Med Chem Lett. 2025 May 1;16(6):1008-1016. doi:**

**10.1021/acsmedchemlett.5c00073. eCollection 2025 Jun 12.**

New Triazolopyrimidines with Improved Activity against Mycobacterium

tuberculosis.

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Tuberculosis is a major health crisis, and new drugs are required. We previously

identified a triazolopyrimidine series with antitubercular activity acting via

inhibition of the terminal cytochrome oxidase (QcrB). We conducted further

exploration of the series to improve the potency and physicochemical properties.

We synthesized new analogues using a 3-step synthesis: (i) condensation of an

amino-pyrazole with 1,3-diketones or β-ketoester; (ii) conversion of the

hydroxyl group to chloride; and (iii) SNAr with a variety of amines. Analogues

with modifications of the triazolopyrimidine core and novel 5-member

heteroaromatic rings at the C-5 position were tested for activity and

cytotoxicity. We identified several potent molecules (MIC < 1 μM) with a methyl

furan or thiophene moiety at the C-5 position of the triazolopyrimidine ring.

These analogues had excellent selectivity with no cytotoxicity (CC50 > 100 μM)

against the human HepG2 cell line. We identified new analogues with improved

metabolic stability in both human and mouse liver microsomes.

© 2025 The Authors. Published by American Chemical Society.

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PMCID: PMC12169480

PMID: 40529071

**85. ACS Med Chem Lett. 2025 Jun 3;16(6):1139-1146. doi:**

**10.1021/acsmedchemlett.5c00183. eCollection 2025 Jun 12.**

Pyrroloquinolone-Based Compounds as a Novel Antimycobacterial Chemotype.

Clariano M(1), Nunes D(1), Canudo D(1), Maçãs D(1), Castro BJL(1), Jordaan A(2),

Gomes P(1), Contini A(3), Perdigão J(1), Portugal I(1), Madureira M(1), Warner

DF(2), Pieroni M(3), Perry MJ(1), Lopes F(1).

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Tuberculosis, caused by Mycobacterium tuberculosis (Mtb), remains the world's

most lethal infectious disease, posing an uncontained health challenge. The

major hurdles are the long treatments and low patient compliance that leads to

the appearance of resistance, as well as the lack of drugs that effectively

tackle the latent infections. Herein we report the development of compounds with

the ability to target the electron transport chain of Mtb by inhibiting

cytochrome bcc (cyt-bcc) (7a-i) and additionally being capable of inhibiting

cytochrome bd (cyt-bd) (7j and 7k). We present the synthesis, determination of

physicochemical properties, evaluation of the antibacterial activity, and

cytotoxicity assessment of pyrroloquinolone-based compounds. The antibacterial

evaluation of 7a-k showed selectivity toward mycobacteria, and the results

identify cyt-bcc as their target. Compounds 7j and 7k presented promising

results against Mtb and good physicochemical properties. Cytotoxicity assays

revealed a good safety profile regarding the toxicity for human cell lines.

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**86. Antimicrob Steward Healthc Epidemiol. 2025 Jun 12;5(1):e126. doi:**

**10.1017/ash.2025.10040. eCollection 2025.**

Academic children's hospital partnership with public health to address mass

pediatric community tuberculosis exposure.

Sato AI(1)(2), Becken B(1)(2), Chang AJ(1)(2), Delair SF(1)(2), Eguiguren

L(#)(1)(2), Green Hines A(1)(2), Mowrer C(1)(2), Skar GL(1)(2), Zwiener J(1),

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(#)Contributed equally

**OBJECTIVE:** To illustrate how a partnership between an academic medical center

and a public health department successfully responded to a large tuberculosis

(TB) exposure at a community daycare center.

**SETTING:** A multidisciplinary team rapidly established a dedicated TB Exposure

Clinic to evaluate and screen exposed children requiring window prophylaxis.

PATIENTS: The exposure affected 592 individuals, including 359 children under

five-those at highest risk for severe disease.

**INTERVENTIONS:** Given the vulnerability of young children to TB infection, timely

evaluation and initiation of window prophylaxis were prioritized.

RESULTS: Over two days, 162 children were assessed for TB window prophylaxis,

and 110 additional children underwent TB screening.

**CONCLUSIONS:** By leveraging clinical expertise, interdisciplinary collaboration,

and informatics infrastructure, the TB Exposure Clinic delivered rapid,

comprehensive care while minimizing disruption to local healthcare systems. This

model underscores the essential role of academic medical centers in supporting

public health responses.

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PMCID: PMC12171945

PMID: 40528933

**87. Int J Infect Dis. 2025 Jun 15:107955. doi: 10.1016/j.ijid.2025.107955. Online**

**ahead of print.**

VIDAS® TB-IGRA assay for diagnosing tuberculosis infection in people living with

HIV: a preliminary study.

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**BACKGROUND:** The diagnosis of presumed latent TB infection (LTBI) is problematic

in people living with HIV (PLWH) because of sub-optimal sensitivity and high

indeterminate rates, especially in those with advanced immunosuppression. Better

diagnostic tools for LTBI are needed in this sub-population.

**METHODS**: We compared the sensitivity of VIDAS®TB-IGRA, a fully automated

RD1-specific new interferon-ϒ-release assay (IGRA), to QFT®-Plus in 77 PLWH with

active pulmonary TB who had varying CD4 counts. Sputum culture positivity served

as the reference standard for active TB.

**RESULTS:** The sensitivity of VIDAS®TB-IGRA was similar to QFT®-Plus overall

[90,9% (70/77) versus 92.0% (69/75)], in those with CD4 <200 cells/mm3, [88.9%

(40/45) versus 88.6% (39/44)], and in those with CD4 <100 [85.7% (18/21) versus

80.0% (16/20)]. However, VIDAS®TB-IGRA had a higher sensitivity in those with

CD4 <50 [92.3% (12/13) versus 75% (9/12)] and fewer indeterminate results

overall [0 versus 2]. When the indeterminate results in this subgroup were

regarded as negative, the comparative sensitivity was [92.3% (12/13) versus

69.2% (9/13)].

**CONCLUSIONS:** VIDAS®TB-IGRA had a similar sensitivity to QFT®-Plus in PLWH.

Whether VIDAS®TB-IGRA sensitivity is significantly better at lower CD4 counts

remains to be confirmed in a larger study. These data have implications for the

diagnosis of LTBI in those with advanced immunosuppression.

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PMID: 40527449

**88. Dermatol Online J. 2024 Dec 15;30(6). doi: 10.5070/D330664691.**

Drug reaction with eosinophilia and systemic symptoms (DRESS)with

anti-tuberculosis drugs, a rare and serious complication.

Bouhamdi A, Bouhamdi C(1), Tassa JJ, Douhi Z, Tahiri L, Serraj M, El Biaze M,

Benjelloun MC, Mernissi FZ, Amara B.

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Drug hypersensitivity syndrome or DRESS (drug reaction with eosinophilia and

systemic symptoms) is a severe reaction with an estimated mortality of 10%.

Antibacillary drugs are rarely incriminated. A 28-year-old patient with

tubercular miliaria who developed antibacillary-induced DRESS is presented. The

dermatological lesions appeared four weeks after the beginning of the

antitubercular treatment. The diagnosis of DRESS was made when all the Registry

of Severe Toxidermia (RegiSCAR) criteria were present. The treatment was stopped

and the patient was put on symptomatic treatment under supervision in the

intensive care unit, with progressive improvement. Substitution with second-line

antituberculosis drugs was necessary and was done with caution. DRESS with

antituberculosis drugs is rare and its management is not codified.

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PMID: 40526962 [Indexed for MEDLINE]

**89. Microb Pathog. 2025 Jun 14;206:107811. doi: 10.1016/j.micpath.2025.107811.**

**Online ahead of print.**

Global evaluation of tuberculosis and cryptococcosis Co-infection: A systematic

review.

Bagheri-Josheghani S(1), Rafat Z(2), Davoodian P(3), Azad MH(3), Karmostaji

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Co-infection of tuberculosis (TB) and cryptococcosis as a consequence of

impaired cell-mediated immune responses is accompanied by high mortality and

morbidity rates. This study aimed to provide valuable insights into risk

factors, diagnostic tests, and treatment methods used for infected patients to

facilitate rapid diagnosis, prevention, and treatmentA comprehensive and

systematic search was performed in electronic databases including Google

Scholar, Scopus, PubMed, and Web of Science to find all articles relevant to the

scope of this research, published in English from January 2000 to December 2023.

PRISMA (preferred reporting items for systematic reviews and meta-analyses)

search strategy was used to validate the search process and present the eligible

research data. A total of 1418 studies were recognized in the databases, among

them 47 articles meeting the current research inclusion criteria were included

in the study, comprising a total of 68 cryptococcosis/TB co-infected patients.

India was the country with the largest number of co-infected patients (n = 26,

38.23 %). HIV infection was documented as the most prevalent underlying

condition (n = 22, 31.35 %). Also, combination therapy with amphotericin B and

fluconazole (63.23 %) was the most common antifungal treatment used for

cryptococcal infections, and most patients (38.23 %) received rifampicin as an

anti-TB therapy. Comprehensive epidemiological information could be useful in

early diagnosis and prompt treatment to reduce the clinical course and

seriousness of infection and ameliorate overall outcomes.

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**90. J Med Imaging (Bellingham). 2025 May;12(3):034505. doi:**

**10.1117/1.JMI.12.3.034505. Epub 2025 Jun 13.**

Image database with slides prepared by the Ziehl-Neelsen method for training

automated detection and counting systems for tuberculosis bacilli.

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Barroso NV(3), Tarabal JP(3), Augusto CJ(3).

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Foundation, Belo Horizonte, Brazil.

**PURPOSE:** We aim to provide a robust dataset for training automated systems to

detect tuberculosis bacilli using Ziehl-Neelsen stained slides. By making this

dataset available, a critical gap in the availability of public datasets that

can be used for developing and testing artificial intelligence techniques for

tuberculosis diagnosis is addressed. Our rationale is grounded in the urgent

need for diagnostic tools that can enhance tuberculosis diagnosis quickly and

efficiently, especially in resource-limited settings.

**APPROACH:** The Ziehl-Neelsen method was used to prepare 362 slides, which were

manually read. According to the World Health Organization's guidelines for

performing bacilloscopy for tuberculosis diagnosis, experts annotated each slide

to diagnose it as negative or positive. In addition, selected images underwent a

detailed annotation process aimed at pinpointing the location of each bacillus

and cluster within each image.

**RESULTS:** The database consists of three directories. The first contains all the

images, separated by slide, and indicates whether it is negative or the number

of crosses if positive, for each slide. The second directory contains the 502

images selected for training automated systems, with each bacillus's position

annotated and the Python code used. All the image fragments (positive and

negative patches) used in the models' training, validation, and testing stages

are available in the third directory.

**CONCLUSIONS:** The development of this annotated image database represents a

significant advancement in tuberculosis diagnosis. By providing a high-quality

and accessible resource to the scientific community, we enhance existing

diagnostic tools and facilitate the development of automated technologies.

© 2025 Society of Photo-Optical Instrumentation Engineers (SPIE).

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**91. EClinicalMedicine. 2025 May 29;84:103257. doi: 10.1016/j.eclinm.2025.103257.**

**eCollection 2025 Jun.**

Diagnostic accuracy of point-of-care triage tests for pulmonary tuberculosis

using host blood protein biomarkers: a systematic review and meta-analysis.

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Health Sciences, Kampala, Uganda.

**BACKGROUND:** Limited access to accurate and accessible tuberculosis (TB)

diagnostics remains a critical barrier to timely diagnosis and care in high

burden low- and middle-income countries. Point-of-care (POC) TB Triage tests

(POC-TTTs) defined as a test performed near to a patient or at the site of

patient care without need for specialized expertise or infrastructure, may

bridge this gap. We systematically reviewed and meta-analyzed studies on host

blood protein biomarkers for POC-TTTs including C-reactive protein (CRP), 3-gene

host response (3-gene HR), monocyte-to-lymphocyte ratio (MLR), interferon-γ

induced protein 10 (IP-10), hemoglobin, neutrophil-to-lymphocyte ratio (NLR),

tumor necrosis factor alpha (TNF-a) and interleukin 6 (IL-6) for their accuracy

for screening of pulmonary TB (PTB).

**METHODS:** A literature search was conducted in PubMed, EMBASE and in Web of

Science from 1990 to 31st January 2025. The review included studies that used

unstimulated blood of presumptive TB patients who were screened with a POC

device to quantify biomarkers for PTB diagnosis. Sputum mycobacterial culture or

GeneXpert MTB/Rif or Ultra were used as a reference standard. Risk of bias was

assessed using QUADAS-2 tool. Random effect analysis was performed using the

Hartung-Knapp-Sidik-Jonkman (HKSJ) method to calculate summary estimates with

their 95% confidence intervals (CI). Heterogeneity was tested and quantified

using Cochran's Q and Higgin's I2 test. Egger's linear regression test was used

to assess small study effect. The systematic review protocol was registered in

PROSPERO with an ID of CRD42023483281.

**FINDINGS:** We identified 282, 21, 28, 137, 132, 152, 100 and 77 studies from

which 10, 6, 4, 2, 0, 0, 0 and 1 study(s) were included for CRP, 3-gene HR, MLR,

hemoglobin, IP-10, TNF-a, IL-6 and NLR index tests respectively. The

meta-analysis pooled sensitivity (95% CI) was 74% (58-85), 79% (59-90), 64%

(15-95), 75% (18-98) and the pooled specificity was 68% (52-80), 85% (68-94),

69% (30-92) and 71% (18-100) for CRP, 3-gene HR, MLR, and hemoglobin

respectively. Diagnostic odds ratios ranged from 3.70 (MLR) to 20.93 (3-gene HR)

while higgin's I2 value ranged from 87.4% (MLR) to 99.1% (hemoglobin).

Meta-analysis was not performed on NLR.

**INTERPRETATION:** None of the POC-TTT met the WHO target product profile minimum

requirements for a TB triage test of 90% sensitivity and 70% specificity when a

POC device was used for screening in a typical setting studied. Further

research, specifically focusing on head-to-head comparisons and combination

tests are recommended.

FUNDING: Funding was received from the Mr. Willem Bakhuys Roozeboom Foundation.

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PMID: 40521165

**92. J Cytol. 2025 Apr-Jun;42(2):67-74. doi: 10.4103/joc.joc\_123\_24. Epub 2025 May 29.**

Endobronchial Ultrasound-Guided Transbronchial Needle Aspiration Cytology:

Navigating the Diagnostic Challenge between Tuberculosis and Sarcoidosis in

Endemic Regions.

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Sciences and Dr. Ram Manohar Lohia Hospital, New Delhi, India.

**OBJECTIVE:** Endobronchial ultrasound-guided transbronchial needle aspiration

(EBUS-TBNA) plays an important diagnostic role in concealed pulmonary diseases.

However, diagnosing sarcoidosis and differentiating it from tuberculosis is a

diagnostic quandary. We, thus, aimed to evaluate EBUS-TBNA cytology in these

cases in a tubercular-endemic zone.

**METHODS:** A prospective 5-year study was done in a tertiary care center on 118

patients with tuberculosis versus sarcoidosis with mediastinal lymphadenopathy

who underwent EBUS-TBNA. All samples obtained were sent for cytomorphological

and microbiological evaluation. On cytology analysis, demonstration of acid-fast

bacilli was considered diagnostic of tuberculosis. However, in its absence, a

multidisciplinary diagnostic (MDD) approach was followed to establish a

diagnosis.

**RESULTS:** EBUS-TBNA cytology contributed in reaching the final diagnosis in 88.1%

cases. Of the 55 cases of tuberculosis, cytomorphological features were

contributory in 90.9% cases. Out of 29 cases of sarcoidosis, 24 showed

granulomas. Microbiological tests were contributory in the final diagnosis of

tuberculosis in only 21.8% cases as compared to 90.9% by cytology analysis. In

10 cases, a definitive diagnosis could not be made on cytology analysis and were

finally diagnosed on the basis of MDD. A definitive distinction between

tuberculosis and sarcoidosis could not be made despite MDD in four cases.

**CONCLUSION:** While a diagnosis of tuberculosis can be made independently on

cytological features, MDD with contributory cytological findings is essential

for the diagnosis of sarcoidosis. EBUS-TBNA cytology, thus, plays an important

role in the multidisciplinary strategy of approaching thoracic lesions.

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**93. J Cytol. 2025 Apr-Jun;42(2):82-87. doi: 10.4103/joc.joc\_37\_24. Epub 2025 May 29.**

Role of Immunocytochemistry in Detection of Mycobacterium tuberculosis Antigen

by Fine Needle Aspiration Cytology.

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**BACKGROUND:** Detection of extrapulmonary tuberculosis (EPTB) by Ziehl-Neelsen

(Z-N) staining in fine needle aspirates is challenging due to the low yield of

acid-fast bacteria (AFB). Mycobacterial culture, the gold standard, takes 4-8

weeks. Polymerase chain reaction with 100% sensitivity and 92.1% specificity is

expensive. Mycobacterial antigens produced by the tubercle bacilli consist of

several proteins and enzymes. The protein purified from Mycobacterium

tuberculosis is called MPT. The MPT64, a 24-kd protein, has not been detected in

non-tuberculous mycobacteria. We aim to study the role of immunocytochemical

(ICC) in the detection of EPTB in fine needle aspiration cytology materials by

using MPT64 antibody and compare it with culture and Z-N staining, as ICC is not

routinely practiced for diagnosing EPTB.

**MATERIALS AND METHODS**: A total of 134 patients having enlarged nodes with

suspected EPTB were included; however, only 96/134 cases were suitable for

statistical analysis. Papanicolaou, May-Grünwald-Giemsa, Z-N staining, ICC, and

mycobacteria culture were performed.

**RESULTS:** AFB was positive in 16%, 22.9% of culture-positive, and 11% of MPT64

positive. The sensitivity and specificity of ICC compared to mycobacterial

culture were 45.4% and 99%, respectively. ICC and culture had a moderate

agreement with the Kappa value of 0.535. The positive and negative predictive

values of ICC with culture were 91% and 86%, respectively.

**CONCLUSION:** This study tried to improve the technique's sensitivity to

facilitate its use in routine laboratory practice. Nonetheless, our results

showed no significant improvement over the currently popular Z-N stain, although

a comparison between the ICC technique performed on smears and cell block

sections showed better results in the latter.

Copyright: © 2025 Journal of Cytology.

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PMID: 40520666

**94. Comput Struct Biotechnol J. 2025 May 26;27:2208-2218. doi:**

**10.1016/j.csbj.2025.05.030. eCollection 2025.**

Deep learning-based framework for Mycobacterium tuberculosis bacterial growth

detection for antimicrobial susceptibility testing.

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Tuberculosis (TB) kills more people annually than any other pathogen. Resistance

is an ever-increasing global problem, not least because diagnostics remain

challenging and access limited. 96-well broth microdilution plates offer one

approach to high-throughput phenotypic testing, but they can be challenging to

read. Automated Mycobacterial Growth Detection Algorithm (AMyGDA) is a software

package that uses image processing techniques to read plates, but struggles with

plates that exhibit low growth or images of low quality. We developed a new

framework, TMAS (TB Microbial Analysis System), which leverages state-of-the-art

deep learning models to detect M. tuberculosis growth in images of 96-well

microtiter plates. TMAS is designed to measure Minimum Inhibitory Concentrations

(MICs) rapidly and accurately while differentiating between true bacterial

growth and artefacts. Using 4,018 plate images from the CRyPTIC (Comprehensive

Resistance Prediction for Tuberculosis: An International Consortium) dataset to

train models and refine the framework, TMAS achieved an essential agreement of

98.8%, significantly outperformed the 90% threshold established by the

International Organization for Standardization (ISO). TMAS offers a reliable,

automated and complementary evaluation to support expert interpretation,

potentially improving accuracy and efficiency in tuberculosis drug

susceptibility testing (DST).

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**95. Iran J Nurs Midwifery Res. 2025 May 8;30(3):447-448. doi:**

**10.4103/ijnmr.ijnmr\_373\_21. eCollection 2025 May-Jun.**

Assessing Quality of Life in Patients with New and Recurrent Pulmonary

Tuberculosis: A Cross-Sectional Study from Garut, Indonesia.

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**BACKGROUND:** This study compared the Quality of Life (QoL) between new and

recurrent pulmonary tuberculosis (TB) patients, a crucial indicator for those

undergoing treatment.

**MATERIALS AND METHODS:** A cross-sectional comparative study was conducted at

eight community health centres in Garut, West Java, Indonesia. Convenience

sampling was used to recruit patients aged >15 years with new or recurrent

pulmonary TB. QoL was assessed using the WHOQOL tool. Data were analyzed using

an independent t-test.

**RESULTS:** 54 new and 60 recurrent pulmonary TB patients participated. Recurrent

TB patients Mean(SD) scored significantly higher in the psychological domain

58.30 (10.63) compared to new TB patients 53.70 (10.31) (p < 0.05, t-test:

-2.34).

**CONCLUSIONS:** New pulmonary TB patients experience greater psychological burden,

highlighting the need for targeted psychological support to improve their

overall QoL.

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**96. J Clin Tuberc Other Mycobact Dis. 2025 May 24;40:100536. doi:**

**10.1016/j.jctube.2025.100536. eCollection 2025 Aug.**

Operational considerations of select new treatment recommendations for

drug-susceptible and drug-resistant tuberculosis.

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A number of management updates recently have been published for both

drug-susceptible and drug-resistant tuberculosis (TB), TB in children, and

contacts of patients with drug-resistant TB. The operationalization and

application of these recommendations, which reflect favorable clinical trial

outcomes, may vary significantly for different patient groups and in different

settings. Defining the best treatment approach for each patient requires the

integration of multiple data points including organism culture growth and

corresponding drug susceptibility profiles, specific TB syndrome, concurrent

patient co-morbidities and available public health resources. We review several

updated TB treatment recommendations and discuss applicable strengths, select

limitations and corresponding precautions as they pertain to diverging patient

groups, TB syndromes, and public health capacity.

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PMCID: PMC12166396

PMID: 40520337

**97. J Clin Tuberc Other Mycobact Dis. 2025 May 30;40:100538. doi:**

**10.1016/j.jctube.2025.100538. eCollection 2025 Aug.**

Change in lung function abnormalities in patients treated for first ever

pulmonary tuberculosis in Dar es Salaam, Tanzania.

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67497, Dar es Salaam Tanzania.

**OBJECTIVES:** To document abnormalities in pulmonary function (PF) and associated

factors in patients completing treatment for microbiologically confirmed,

first-ever pulmonary tuberculosis (PTB).From August 2020 to May 2021, we

recruited 332 patients aged ≥15 years. PF was evaluated at baseline and at

treatment completion. The Wilcoxon signed-rank test was used to compare median

PF changes between baseline and treatment completion. A log-binomial regression

model was used to determine factors associated with abnormal PF at treatment

completion. Statistical significance was set at p ≤ 0.05.

**RESULTS:** Abnormal PF was observed in 142 of 300 (47.3 %) patients who completed

the study. Being male (RR [95 % CI] = 1.22 [1.19-2.23]), underweight (RR = 1.49 [1.13-1.95]), having lung cavitation (RR = 1.90 [1.29-2.78]), and lung fibrosis at baseline (RR = 2.16 [1.32-3.53]) were significantly associated with abnormal PF. The median (IQR) FEV1 at treatment completion was 2.33 L (0.90-4.23 L) and FVC was 3.05 L (1.10-7.50 L), both significantly higher than FEV1 of 2.18 L (0.20-5.70 L) and FVC of 2.82 L (0.26-7.05 L) at treatment initiation (p < 0.05

for both).

**CONCLUSION:** Approximately half of the patients had abnormal PF at treatment

completion. Underweight patients, males, and those with lung cavitation at

treatment initiation are more likely to have abnormal PF at the end of treatment

and may require special attention.

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**98. J Clin Tuberc Other Mycobact Dis. 2025 Jun 2;40:100539. doi:**

**10.1016/j.jctube.2025.100539. eCollection 2025 Aug.**

Dietary diversity and associated factors among people with tuberculosis in

Kampala, Uganda: A cross-sectional study.

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(2)Institute of Public Health and Management, Clarke International University,

Kampala, Uganda.

**Rationale**.Dietary diversity (DD) is important in enhancing the nutritional

status of people with tuberculosis (TB), but has been understudied in Uganda.

**OBJECTIVE: T**o investigate the frequency of adequate DD and the associated

factors among people with pulmonary TB aged ≥ 18 years in Kampala, Uganda.

**METHODS:** We enrolled people with pulmonary TB across five health facilities in

Kampala, Uganda. The outcome variable was adequate DD, assessed using the World

Food Program's Food Consumption Score (FCS). Participants with FCS values < 35

were categorized as having inadequate DD, whereas those with FCS ≥ 35 were

classified as having adequate DD. Independent variables included

sociodemographic, clinical, and behavioral factors. We used a Generalized

Estimating Equation with a Poisson distribution, log link function, and robust

standard errors, with health facility as a cluster and several variables to

identify the factors associated with adequate DD. We reported adjusted risk

ratios (aRR) and 95 % confidence intervals (CI).

**RESULTS:** Of 818 participants studied, 250 (30.6 %) had adequate DD. The factors

associated with adequate DD included age ≥ 25 years old (aRR 1.12; 95 % CI:

1.04-1.22), being married (aRR 1.77; 95 % CI: 1.51-2.07), self-employed (aRR

1.22; 95 % CI: 1.09-1.36), and low socioeconomic status (aRR 1.48; 95 % CI:

1.15-1.89).

**CONCLUSION:** We found a low frequency of adequate DD. Persons aged ≥ 25 years,

married, self-employed, and of lower socioeconomic status are more likely to

have adequate DD. Findings suggest a complex interplay between socioeconomic

factors and DD. Targeted interventions are needed to improve DD among people

with TB across different demographic groups.

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**eCollection 2025.**

Discrepancies in tuberculosis burden estimates: North Korean defectors vs.

official reports.

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Seoul, Republic of Korea.

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(#)Contributed equally

**OBJECTIVES:** North and South Korea have taken different approaches to

tuberculosis (TB) epidemic control after the Korean War. This study aimed to

compare TB epidemiology in North Korean defectors (NKDs) based on South Korean

National Health Insurance (NHIS) data and assess its implications for

understanding TB prevalence in North Korea.

**METHODS:** We used the NHIS claims data from 2007 to 2019 to evaluate TB epidemics

in NKD and the age-and-sex matched South Korean control group. The number of

participants was 35,620 for defectors and 107,016 for the control group.

**RESULTS:** The prevalence of TB among NKDs decreased from 466/100,000 persons in

2010 to 95/100,000 persons in 2019, while the North Korean TB prevalence as per

the World Health Organization (WHO) report remained approximately 500/100,000

persons. The NKD TB prevalence was 3-7 times higher than that in the South

Korean population. Additionally, the distribution of TB cases in NKDs showed

distinct age-related patterns, with peaks in the 25-34 and 65 + age groups. The

proportion of extrapulmonary TB in NKDs was 36-46%, similar to South Korean

patterns. The estimated and reported multidrug-resistant TB rates in NKDs were

higher than in the control group, highlighting potential underreporting in North

Korean data.

**CONCLUSION:** There were large gaps in TB prevalence between NKD and native North

Korean residents and between the estimated and reported TB burden within North

Korea. These findings underscore the need for targeted TB control strategies

that address both health system disparities and the integration of NKDs into

local healthcare services.

Copyright © 2025 Jang, Han, Lee, Jeong, Lee, Kang, Oh and Lee.

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PMID: 40520323 [Indexed for MEDLINE]

**100. Access Microbiol. 2025 May 12;7(5):000964.v3. doi: 10.1099/acmi.0.000964.v3.**

**eCollection 2025.**

Classification of unsequenced Mycobacterium tuberculosis strains in a

high-burden setting using a pairwise logistic regression approach.

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(4)Department of Mathematics, Simon Fraser University, Burnaby, Canada.

Over the past three decades, molecular epidemiological studies have provided new

opportunities to investigate the transmission dynamics of Mycobacterium

tuberculosis. In most studies, a sizable fraction of individuals with notified

tuberculosis cannot be included, either because they do not have

culture-positive disease (and thus do not have specimens available for molecular

typing) or because resources for conducting sequencing are limited. A recent

study introduced a regression-based approach for inferring the membership of

unsequenced tuberculosis cases in transmission clusters based on host

demographic and epidemiological data. This method was able to identify the most

likely cluster to which an unsequenced strain belonged with an accuracy of 35%,

although this was in a low-burden setting where a large fraction of cases

occurred among foreign-born migrants. Here, we apply a similar model to M.

tuberculosis whole-genome sequencing data from the Republic of Moldova, a

setting of relatively high local transmission. Using a maximum cluster span of

~40 single nucleotide polymorphisms (SNPs) and a cluster size cutoff of n≥10, we

could best predict the specific cluster to which each clustered case was most

likely to be a member with an accuracy of 17.2 %. In sensitivity analyses, we

found that a more restrictive (~20 SNPs threshold) or permissive (~80 SNPs)

threshold did not improve performance. We found that increasing the minimum

cluster size improved prediction accuracy. These findings highlight the

challenges of transmission inference in high-burden settings like Moldova.

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DOI: 10.1099/acmi.0.000964.v3

PMCID: PMC12163731

PMID: 40519974

**101. Cureus. 2025 May 13;17(5):e84016. doi: 10.7759/cureus.84016. eCollection 2025 May.**

Performance of Various Pelvic-Derived Samples for the Diagnosis of Female

Genital Tract Tuberculosis by Conventional and Molecular Methods: A Systematic

Review and Meta-Analysis.

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College, Moradabad, IND.

(3)Department of Microbiology, KMC Medical College, Maharajganj, IND.

Female genital tuberculosis (FGTB) is a challenging extrapulmonary manifestation

of tuberculosis, often presenting with nonspecific symptoms and a paucibacillary

profile, complicating diagnosis. This systematic review and meta-analysis

evaluated the diagnostic performance of various pelvic-derived samples using

conventional and molecular tests. A comprehensive literature search was

conducted across multiple databases from inception up to August 2024, following

the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)

guidelines. Studies assessing the sensitivity, specificity, or positivity rates

of tests such as Ziehl-Neelsen (ZN) staining, culture, histopathology,

polymerase chain reaction (PCR), and GeneXpert MTB/RIF on samples including

endometrial biopsy, aspirates, menstrual blood, and peritoneal fluid were

included. Meta-analysis using bivariate random-effects models was undertaken

where feasible. Endometrial samples were the most commonly evaluated among the

included studies. ZN staining and culture demonstrated high specificity (pooled

specificity: 1.00) but poor sensitivity (ZN: 10%; culture: 23%). Histopathology

exhibited variable sensitivity (2.56-75%) and high specificity (98%). PCR showed

pooled sensitivity and specificity of 54% and 97%, respectively, with

considerable heterogeneity. GeneXpert demonstrated excellent specificity (pooled

100%) but low sensitivity (14%). Menstrual blood and pelvic washings were

explored with variable results; other sample types had limited diagnostic value.

In conclusion, endometrial biopsy/aspirate remains the most suitable specimen

for FGTB diagnosis. Molecular methods, particularly PCR, offer superior

sensitivity over conventional tests, while GeneXpert's high specificity supports

its role in exclusion. A multimodal diagnostic approach is recommended to

enhance diagnostic yield, especially in resource-limited, high-TB-burden

settings.

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PMCID: PMC12162420

PMID: 40519447

**102. Cureus. 2025 May 13;17(5):e84061. doi: 10.7759/cureus.84061. eCollection 2025 May.**

Scrofuloderma and Miliary Tuberculosis in a 27-Year-Old Nurse.

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AG(2), Castillo Gómez AP(3), Arrazola KS(1).

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A previously healthy 26-year-old female nurse presented with fever, diaphoresis,

and occasional cough for over two months. She visited the emergency department

several times and never had a correct diagnosis. Eventually, she presented to

the emergency department of the ISSSTE General Hospital of Querétaro and was

admitted to the Internal Medicine service. On physical examination, she had a

non-painful, mobile, well-defined, and indurated nodule in the left cervical

region, approximately 20 mm in diameter. The skin had erythematous-violaceous

discoloration on top of the nodule with two central ulcerations and discrete

seropurulent discharge when applying pressure. The nodule was biopsied.

Histologic report identified caseous necrosis, and, simultaneously, chest X-ray

and chest CT scan findings of miliary tuberculosis. Subsequently, polymerase

chain reaction identification of Mycobacterium tuberculosis confirmed the

diagnosis of lymph node tuberculosis with contiguous scrofuloderma and pulmonary

miliary tuberculosis. After 12 months of treatment, clinical recovery was

accomplished.

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PMID: 40519446

**103. Cureus. 2025 May 13;17(5):e84063. doi: 10.7759/cureus.84063. eCollection 2025 May.**

Mycobacterium tuberculosis, Streptococcus pneumoniae, and Staphylococcus aureus

Co-infection in a Two-Year-Old Immunocompetent Patient: A Case Report.

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Co-infections in pulmonary tuberculosis are rare among immunocompetent children

in settings with low tuberculosis prevalence. We present a case of a

two-year-old immunocompetent child with necrotic pleuropneumonia caused by

Mycobacterium tuberculosis, Streptococcus pneumoniae, and Staphylococcus aureus

co-infection in a low tuberculosis prevalence setting. A 24-month-old boy

presented with a five-day history of cough, followed by three days of high fever

and dyspnea. Initial laboratory inflammatory markers were elevated. Chest

ultrasound, radiography, and CT scan revealed necrotic changes in the right

upper lobe with bullae, pleural effusion, and subcutaneous emphysema. Initial

therapeutic procedures included the evacuation of 140 mL of hemorrhagic content

from the pleural space. Microbiological analysis revealed Streptococcus

pneumoniae type 3 from pleural effusion and Staphylococcus aureus from blood

culture. Antimicrobial therapy included ceftriaxone and clindamycin for six

weeks. Following flexible bronchoscopy, microbiological culture from aspirated

material detected Mycobacterium tuberculosis. Anamnesis did not clarify any

prior contact with a tuberculosis-infected individual. This case represents an

example of Streptococcus and Staphylococcus superinfection on evolving pulmonary

tuberculosis. To our knowledge, no literature is currently available indicating

the co-existence of tuberculosis, streptococcal, and staphylococcal pulmonary

infection in an immunocompetent patient in a population with low tuberculosis

prevalence.

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DOI: 10.7759/cureus.84063

PMCID: PMC12163197

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**104. Cureus. 2025 May 14;17(5):e84119. doi: 10.7759/cureus.84119. eCollection 2025 May.**

Rare Coexistence of Cardiac Tuberculosis: Effusive-Constrictive Pericarditis

With Right Atrial Tuberculoma and Right Atrial Myocarditis in an Immunocompetent

Patient With Disseminated Tuberculosis.

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Cardiac involvement in tuberculosis (TB) is uncommon, and especially the

concurrent occurrence of effusive-constrictive pericarditis, right atrial

tuberculoma, and right atrial myocarditis is extremely rare in immunocompetent

individuals. We report a case of a 22-year-old immunocompetent male with

disseminated TB, presenting with this rare combination. To our knowledge, this

specific coexistence has not been documented in the literature previously. The

diagnosis was confirmed using 2D echocardiography, CT scan, and

histopathological analysis. Echocardiography revealed pericardial effusion and

signs of constrictive pericarditis, supported by respiratory variation in

ventricular filling. These findings were also consistent with the patient's

clinical presentation. The right atrial tuberculoma was confirmed by

histopathology of the resected tissue, and right atrial myocarditis was also

proven histologically. The patient was treated with standard anti-tubercular

therapy and underwent surgical resection for right atrial tuberculoma, with a

favorable clinical outcome. This case also highlights the diagnostic value of

histopathology when microbiological tests are inconclusive and emphasizes the

need to consider TB in the differential diagnosis of cardiac masses, which can

mimic various neoplastic or thrombotic lesions.

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PMID: 40519395

**105. Infez Med. 2025 Jun 1;33(2):212-220. doi: 10.53854/liim-3302-7. eCollection**

**2025.**

High prevalence and risk factors of positive sputum smear in newly diagnosed

pulmonary tuberculosis patients in Vietnam.

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**OBJECTIVES:** To assess the prevalence and identify risk factors associated with

smear-positive tuberculosis (acid-fast bacilli [AFB]-positive) in newly

diagnosed patients in Vietnam.

**METHODS:** A retrospective study was conducted on patients newly diagnosed with

pulmonary tuberculosis (PTB) from August 2023 to August 2024. Patients were

classified as smear-positive if at least one respiratory sample tested positive

with AFB before starting anti-tuberculosis treatment. Smear-negative individuals

had to submit a minimum of two sputum samples, all of which had to test negative

before treatment initiation.

**RESULTS:** 379 PTB patients were included with 48.3% being AFB-positive. The

proportion of hemoptysis was significantly higher in AFB-positive than in

AFB-negative patients (9.8% versus 4.1%, p=0.04). AFB-negative patients had a

significantly higher rate of fatigue and crackles compared to AFB-positive

patients with 85.7% versus 77.0%, p=0.03 and 36.2% versus 25.7%, p=0.03,

respectively. Cavitary lung lesions were significantly more common in

AFB-positive patients (48.6% versus 29.1%, p<0.0001). In multivariate analysis,

patients with diabetes mellitus and those with long-term corticosteroid use were

respectively three times and six times more likely to be AFB-positive (OR=2.71,

p=0.002 and OR=6.15, p=0.009) more likely to. Cavitation in chest-x-ray was also

associated with 2.5 times of risk for smear-positive (OR=2.53, p <0.0001). All

of three HIV-coinfected patients were AFB-negative.

**CONCLUSION:** Our findings emphasize the importance of screening and early

diagnosis of PTB in individuals with diabetes mellitus and in those on long-term

corticosteroid therapy. Strengthening TB control efforts, particularly among

high-risk populations, is crucial to reducing the burden of smear-positive TB

and preventing further transmission.

DOI: 10.53854/liim-3302-7

PMCID: PMC12160522

PMID: 40519350

**106. J Biol Chem. 2025 Jun 19:110394. doi: 10.1016/j.jbc.2025.110394. Online ahead of print.**

CryoEM Structure of Rv2531c Reveals Cofactor-Induced Tetramer-Dimer Transition

in a Tuberculin Amino Acid Decarboxylase.

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The survival of Mycobacterium tuberculosis relies on its ability to adapt to

dynamic and hostile host environments. Amino acid decarboxylases play a crucial

role in these adaptations, but their structural and mechanistic properties are

not fully understood. Bioinformatic analyses revealed that these enzymes exist

in three distinct forms based on their domain organization. We used cryogenic

electron microscopy (cryoEM) at 2.86 Å resolution to show that Rv2531c exhibits

unexpected oligomeric and conformational flexibility. The enzyme forms a

tetramer with distinct open and closed conformations in its apo state,

suggesting dynamic inter-subunit interactions. Upon binding pyridoxal

5'-phosphate (PLP), the enzyme undergoes a dramatic structural rearrangement,

transitioning into a dimer. These findings reveal a novel mechanism of

oligomeric plasticity. We also uncover an amino-terminal domain that might play

a role in this process. Our results provide critical insights into the

structural adaptations that support bacterial persistence under intracellular

stress. By elucidating the apo and PLP-bound states of Rv2531c, we contribute to

a deeper understanding of how M. tuberculosis navigates its challenging

intracellular environment. These insights into the unique structural features of

Rv2531c offer a foundation for targeting metabolic resilience in tuberculosis

and open avenues for future studies on the role of this domain in pathogenesis.

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DOI: 10.1016/j.jbc.2025.110394

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**107. BDJ Open. 2025 Jun 20;11(1):60. doi: 10.1038/s41405-025-00341-9.**

Dentists' refusal to manage patients with HIV, tuberculosis, HBV, HCV, epilepsy,

and financial limitations in Damascus, Syria: a cross-sectional study.

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**OBJECTIVE:** This study investigates refusal rates of dentists in Damascus, Syria,

to manage patients who disclose that they are carriers of tuberculosis, human

immunodeficiency virus (HIV), hepatitis B and C (HBV/HCV), and patients with

dental phobia, asthma, epilepsy, patients unable to afford dental care, and

children. The aims are to identify to what extent dentists refuse patients who

are diagnosed carriers of certain blood born viruses, require extra measures,

take a lot of time, or do not pay.

**METHODS:** A cross-sectional study was conducted in Damascus by distributing paper

and electronic questionnaires to dental clinics based on the administrative

divisions of the city.

**RESULTS:** A total of 246 responses were collected. The average years of dental

practice among respondents was 9.39 ± 9.8. Rates of refusal were as follows:

children (n = 55, 22.4%), tuberculosis (n = 176, 71.5%), HIV (n = 192, 78.0%),

HBV/HCV (n = 98, 39.8%), dental phobia (n = 58, 23.6%), asthma (n = 12, 4.9%),

and epilepsy (n = 73, 29.7%). Acceptance of patients with tuberculosis, HIV, and

HBV/HCV was positively associated with greater years of experience. Dentists who

graduated outside of Syria were more likely to accept treating patients with HIV

and HBV/HCV. A significant correlation was found between refusal rates for

patients with tuberculosis, HIV and HBV/HCV.

**CONCLUSIONS:** The proportion of dentists in Damascus refusing to treat patients

who disclose that they are carriers of tuberculosis, HIV/AIDS, and HBV/HCV was

notably high. Managing patients who cannot afford treatment often involved

reducing fees. The findings provide valuable insights into the systemic

challenges in healthcare delivery and propose possible improvements in managing

vulnerable population in resource-constrained settings.

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