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**境外学者发表的结核病英文文章摘要**

**（96篇）**

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

**1. Tuberculosis (Edinb). 2025 Sep 19;155:102692. doi: 10.1016/j.tube.2025.102692.**

**Online ahead of print.**

Exploring CHIT1 and YKL-40 in tuberculous pleural effusion: Insights and

implications.

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**BACKGROUND:** Chitinases and chitinase-like proteins are implicated in the

pathophysiology of lung diseases. This study aimed to evaluate the significance

of chitotriosidase (CHIT1) and YKL-40 in tuberculous pleural effusion (TPE),

identify their cellular sources, and assess their diagnostic potential as TPE

biomarkers.

**METHODS:** This observational, retrospective study included 66 patients with

pleural effusion of different origins: malignant (MPE), tuberculous (TPE),

parapneumonic (PPE), and transudative (TE). Pleural fluid levels of YKL-40 and

CHIT1 were measured. Expressions of YKL-40 and CHIT1 in tuberculous pleural

granulomas were also assessed using immunohistochemical staining.

**RESULTS:** We found the highest median CHIT1 and YKL-40 levels for TPE: 70.51

(interquartile range [IQR] 49.65-136.98) ng/mL and 569.84 (IQR 530.32-706.01)

ng/mL, respectively. YKL-40 was significantly higher in TPE than in PPE (387.98

[IQR 262.94-539.09] ng/mL, p < 0.01)] and TE (254.95 [IQR 188.93-334.1 ng/ml]

ng/mL, p < 0.001). There was a strong positive correlation between the YKL-40

level in TPE and the percentage of macrophages (r = 0.73, p = 0.003) and the

adenosine deaminase activity (r = 0.82, p < 0.001). We revealed strong YKL-40 expression in tuberculoid pleural granulomas.

**CONCLUSION:** YKL-40, but not CHIT-1, may contribute to the pleural inflammatory

response associated with tuberculosis.

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**2. Indian J Med Res. 2025 Jul;162(1):15-27. doi: 10.25259/IJMR\_527\_2025.**

Reliable, accessible, cost-effective, & easy (RACE) diagnostic modality: A key

for elimination of tuberculosis.

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Tuberculosis (TB) is still a major health concern. However, each year more than

one-third of all global TB cases remain undetected and unreported. On top of

that, emergence of drug-resistant TB poses a major challenge. Therefore, a

Reliable, Accessible, Cost-Effective, and Easy (RACE) diagnostic modality is

crucial for starting suitable treatment of TB and curtailing its transmission.

In the last two decades, several advances have been made for improved diagnosis,

which include liquid culture and drug susceptibility testing (DST), line probe

assay (LPA) for drug resistance detection at the molecular level, and

cartridge-based nucleic acid amplification tests (CBNAAT) for rapid diagnosis of

TB and rifampicin resistance detection. Newer drugs and treatment regimens have

been introduced and vaccines are in the pipeline. Despite these advances and

opportunities, a precise, affordable, and accessible diagnostic model is yet to

be evolved, especially in rural and difficult-to-reach areas, where the most

desirable test would be a test that is easy to perform, accessible to masses, is

cost-effective, besides being reliable. Only a point-of-care triage test can

meet these requirements, which can be used by an unskilled or minimally trained

healthcare worker or even by the patient (self-testing). This test should be

able to detect all forms of tuberculosis and latent TB infection. Currently, no

such test is available. In this narrative review, we will discuss how such a

diagnostic modality can help eliminate TB.

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**3. Front Immunol. 2025 Sep 8;16:1608065. doi: 10.3389/fimmu.2025.1608065.**

**eCollection 2025.**

Polyfunctionality of CD4(+) T lymphocytes in buffaloes and cattle: comparative

antigen-specific cytokine responses in bovine tuberculosis infection.

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**INTRODUCTION:** Bovine tuberculosis (BTB), caused by Mycobacterium bovis, is a

chronic infectious disease of major veterinary and public health concern. It

affects a broad range of domestic and wild animals, including water buffalo, and

poses a risk to humans due to its zoonotic nature. The economic consequences of

BTB, arising from production losses and trade restrictions, further underline

its global importance. While cattle immune responses to BTB are well

characterized, the immune mechanisms in buffalo remain poorly understood,

despite their increasing role as livestock in endemic regions. Given that

buffaloes and cattle, although closely related, display notable immunological

differences, comparative studies are essential. This study aimed to investigate

and compare antigen-specific cytokine responses in CD4+ T lymphocytes from

buffaloes and cattle exposed to or infected with M. bovis.

**METHODS:** A multicolor flow cytometry assay was established to enable

high-resolution analysis of cytokine-expressing CD4+ T cells. Blood samples were

obtained from 35 buffaloes (17 IGRA-positive from BTB outbreak farms and 18

IGRA-negative, including animals from both outbreak and Officially

Tuberculosis-Free [OTF] herds) and 10 cattle (6 IGRA-positive from a BTB

outbreak farm and 4 IGRA-negative from an OTF herd). Following six hours of in

vitro stimulation with PPD-B or PBS, intracellular cytokine staining was

performed. This approach allowed simultaneous quantification of single and

polyfunctional CD4+ T cell subsets producing IFN-γ, TNF-α, and IL-17A. Data were analyzed using factor analysis of mixed data (FAMD) to explore species- and

infection-related immune response patterns.

**RESULTS:** The multicolor flow cytometry approach successfully identified distinct

cytokine-producing CD4⁺ T cell populations in both species. Overlapping immune

profiles were observed between buffaloes and cattle; however, specific

subsets-including IL-17A+, IFN-γ+IL-17A+, and TNF-α+IL-17A+ cells-contributed to interspecies differences. Importantly, the frequency of IFN-γ+ and TNF-α+

producing CD4+ T cells correlated with IGRA test status, enabling discrimination

between infected/exposed and non-infected animals. These results demonstrate the

ability of cytokine expression patterns to reflect both infection status and

host species.

**DISCUSSION**: The findings indicate that buffaloes and cattle share broadly

similar antigen-specific cytokine responses, although subtle differences in CD4⁺

T cell subsets exist. The study highlights the value of multicolor flow

cytometry as a high-resolution tool for dissecting immune responses in

veterinary immunology. These insights enhance understanding of buffalo immune

mechanisms against BTB and may contribute to improved disease control

strategies.

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Schiavo, Franzoni, Mazzone, Elnaggar, De Carlo, Galiero, Davis and Martucciello.

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**4. Access Microbiol. 2025 Sep 10;7(9):000781.v4. doi: 10.1099/acmi.0.000781.v4.**

**eCollection 2025.**

A hydrocele revealing epididymal tuberculosis.

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Genitourinary tuberculosis is a severe form of extrapulmonary tuberculosis. The

kidneys are the most commonly affected organs, followed by the epididymis,

testicles, bladder, ureter and prostate. Notably, epididymal tuberculosis is one

of the forms of genital tuberculosis presenting with specific clinical features,

which may include epididymitis, orchid-epididymitis or hydrocele. We report the

case of a patient with a hydrocele that revealed epididymal tuberculosis.

Utilizing molecular biology techniques, a diagnostic test for epididymal

tuberculosis was established. The patient was treated conservatively with

tuberculosis medication for 6 months.

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PMCID: PMC12451304

PMID: 40989929

**5. Iran J Otorhinolaryngol. 2025;37(5):287-290. doi:**

**10.22038/ijorl.2025.85739.3877.**

Ipsilateral Oropharyngeal and Cervical Lymph Node Tuberculosis Simulating

Oropharyngeal Malignancy with Regional Lymph Node Metastasis: A Case Report.

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**INTRODUCTION:** Tuberculosis (TB) is an important contagious disease and a major

public health problem globally. It may manifest as pulmonary TB or primary or

secondary extrapulmonary TB. Primary oropharyngeal TB is very rare and may mimic

presentation of oropharyngeal malignancy especially in the negative initial TB

workup.

**CASE REPORT:** We would like to highlight a case of an elderly man presented with

ipsilateral oropharyngeal mass and cervical lymph node (LN) enlargement,

mimicking oropharyngeal malignancy with regional LN metastasis.

**CONCLUSION:** History of TB contact, poor oral hygiene, and poor immunity should

alert the possibility of oropharyngeal TB. Involvement of ipsilateral

oropharyngeal structure and cervical LN may simulate presentation of

oropharyngeal malignancy with regional LN metastasis. Tissue biopsy for

histopathological examination and appropriate staining is considered gold

standard for diagnosis of TB and excluding malignancy. It is an important

communicable disease, thus notification and referral to infectious disease team

should be done without delay.

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PMCID: PMC12451705

PMID: 40989130

**6. Access Microbiol. 2025 Aug 8;7(8):000928.v5. doi: 10.1099/acmi.0.000928.v5.**

**eCollection 2025.**

Genotypic study of isolated resistance to isoniazid in the Mycobacterium

tuberculosis complex in a Moroccan hospital.

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Introduction. Despite the introduction 40 years ago of effective and low-cost

treatment for tuberculosis (TB), morbidity and mortality from this disease

remain substantial worldwide. According to the WHO, TB is once again the leading

cause of death worldwide from a single infectious agent. In 2023, TB caused

~1.25 million deaths, surpassing COVID-19. In Morocco, the number of new TB

cases rose from 30,897 in 2017 to 35,000 in 2019, highlighting a concerning

upward trend that underscores the persistent challenge TB poses to the country's

public health system. The incidence of multidrug-resistant (MDR) or rifampicin

(RIF)-resistant TB was estimated at 1.7 per 100,000 inhabitants. Isoniazid (INH)

is a cornerstone of first-line TB treatment, and resistance to it, even in the

absence of RIF resistance, is associated with delayed treatment response, higher

rates of treatment failure or relapse and increased risk of progression to

MDR-TB if not promptly identified and appropriately managed. Moreover, current

diagnostic algorithms in many settings, including Morocco, may miss INH

monoresistance due to their reliance on rapid molecular tests that primarily

detect RIF resistance, further emphasizing the emerging threat of drug-resistant

TB. Despite this, national data on INH monoresistance remain scarce. Given the

increasing burden of TB and the critical importance of early detection of drug

resistance, it is essential to better understand patterns of resistance beyond

RIF. It is within this context that we conducted the present study, which aims

to investigate INH resistance in TB cases (pulmonary or extrapulmonary, new or

previously treated) over a period of 3 years. Materials and methods. This is a

retrospective study conducted at the Bacteriology Department of Mohammed V

Military Instruction Hospital over a period of 3 years. Data were collected via

the laboratory information system. Clinical samples underwent treatment using

both conventional bacteriological methods and molecular techniques. The study of

resistance to major anti-TB drugs was performed using the reverse hybridization

technique, specifically the HAIN method (GenoType® MTBDR plus by Hain

Lifescience). Statistical analysis was performed using IBM SPSS Statistics 19

and Microsoft Excel 2019. Results. The study involved 464 patients treated for

pulmonary and extrapulmonary TB, including both new cases and those previously

treated with positive cultures. The mean age of the patients was 42.2 years,

with a range from 8 to 88 years. There was a predominance of males at 74%, with

a sex ratio of 2.8. Pulmonary sputum samples accounted for 84.8% of the cases,

whereas extrapulmonary samples represented only 15.2%, and the positivity rates

for direct examination and culture across all samples were 74% and 100%,

respectively. INH resistance had a prevalence of 9% (43 out of 464). Genetic

mutations observed indicated that 63% of the clinical isolates resistant to INH

had mutations in the katG gene, while 37% had mutations in the inhA gene.

Conclusion. The increasing prevalence of Mycobacterium tuberculosis complex

strains resistant to one or more first-line anti-TB drugs highlights the urgent

need for targeted and ongoing epidemiological surveillance. In this study, we

found that INH resistance affected 9% of TB cases over the 3-year period,

underscoring a significant yet under-recognized threat to TB control efforts in

Morocco. Molecular analysis revealed that the majority of resistant strains

carried mutations in the katG gene, with a smaller proportion exhibiting

mutations in the inhA promoter region. These findings emphasize the importance

of incorporating molecular diagnostics capable of detecting INH resistance even

in the absence of RIF resistance into routine TB surveillance programmes.

Strengthening diagnostic capacity and updating treatment protocols accordingly

will be essential to curb the spread of INH-resistant TB and prevent the

emergence of MDR forms.

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PMCID: PMC12451310

PMID: 40988883

**7. Pediatr Pulmonol. 2025 Sep;60(9):e71305. doi: 10.1002/ppul.71305.**

Co-Occurrence of Pulmonary Tuberculosis and Hydatid Disease in a Single Patient:

Highlighting the Dual Burden in Resource-Limited Settings.

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DOI: 10.1002/ppul.71305

PMID: 40988430

**8. J Public Health Res. 2025 Sep 20;14(3):22799036251376872. doi:**

**10.1177/22799036251376872. eCollection 2025 Jul.**

Community-driven strategies and policies for drug-resistant tuberculosis control

in Banyumas Regency, Indonesia: A comprehensive 2023 analysis.

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**BACKGROUND:** Central Java, Indonesia, struggles with low drug-resistant

tuberculosis (DR-TB) case detection (33%) and treatment rates (25%), far below

the 60% target. Despite policies, including Minister of Health Regulation No.

67/2016 and Presidential Regulation No. 67/2021, along with the National TB

Strategy for Tuberculosis Control 2020-2024 have been implemented, targets

remain unmet due to weak community involvement. This study analyzed TB policy

implementation in high-prevalence Banyumas Regency, focusing on cadres and

community organizations.

**DESIGN AND METHODS:** This qualitative study employed the Van Meter and Van Horn

framework to assess policy implementation. Key stakeholders involved informants

from Puskesmas (community health centers), TB cadres, TB program holders at the

Regency Health Office, and the Mentari Sehat Indonesia Foundation. Data

collection involved in-depth interviews with these informants, as well as policy

documents, guidelines, and reports from agencies or institutions. Triangulation

methods were used to enhance the validity of the findings.

**RESULTS:** Implementers understood policy standards, supported by consistent

communication among Health Offices, community health workers, local

organizations, and village leaders. Positive attitudes were reflected in joint

commitments and Regional Action Plans. Cadres and communities actively supported

case-finding, treatment, education, socioeconomic aid, and stigma reduction.

**CONCLUSIONS:** Policies lack sufficient local budget allocation. Weak motivation

of TB cadres, lack of commitment among regional organizations, and persistent

stigma in the community are evident. The Global Fund aids DR-TB control through

grants and patient support to ensure treatment adherence. However, sustained

impact requires government attention to policy, human resources, infrastructure,

and complementary resources to achieve synergy.

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**9. Indian J Thorac Cardiovasc Surg. 2025 Oct;41(10):1425-1431. doi:**

**10.1007/s12055-025-01978-9. Epub 2025 Jun 30.**

Quantitative C-reactive protein for differentiating tuberculous and malignant

pleural effusion: A cross-sectional study.

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**PURPOSE:** Pulmonary or pleural tuberculosis and malignancy are the most common

causes of lymphocyte-rich pleural effusion. In resource-limited settings,

establishing a definitive diagnosis for patients with pleural effusion (PEs) may

be challenging, emphasizing the need for a simple diagnostic test. This study

aimed to investigate the diagnostic value of quantitative C-reactive protein

(qCRP) for differentiating between tuberculous pleural effusion (TPE) and

malignant pleural effusion (MPE).

**METHODS:** A cross-sectional study was performed on 81 patients admitted for

lymphocyte-rich exudative pleural effusion at a tertiary care center.

Comprehensive biochemical analyses, including qCRP levels in the pleural fluid

and pathological examinations of blood, pleural fluid, and/or tissue, were

performed. The t-test was used for continuous variables, and the chi-square test

was used for categorical variables. To assess the independent associations

between variables, multivariate logistic regression analysis was performed. The

diagnostic performance of pleural fluid qCRP levels was evaluated using a

receiver operating characteristic (ROC) curve.

**RESULTS:** Forty-four (54.3%) patients were diagnosed with TPE and 34 (42.0%) with

MPE. The qCRP levels in the pleural fluid were significantly greater in the TPE

group than in the MPE group (55.5 ± 45.9 mg/L vs. 18.6 ± 19.1 mg/L, P < 0.001). The cutoff value for pleural fluid CRP levels (≥ 24.1 mg/L) yielded a

sensitivity of 65.9% and a specificity of 73.5% in predicting TPE.

**CONCLUSIONS:** Pleural fluid qCRP is a simple, rapid, cost-effective diagnostic

tool for differentiating tuberculous from malignant etiology in patients with

lymphocyte-rich exudative pleural effusion.

SUPPLEMENTARY INFORMATION: The online version contains supplementary material

available at 10.1007/s12055-025-01978-9.

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**10. Prog Mol Biol Transl Sci. 2025;217:355-406. doi: 10.1016/bs.pmbts.2025.06.020.**

**Epub 2025 Jul 8.**

Cell death mechanisms during Mycobacterium tuberculosis infection: A perspective

from a host-pathogen interface.

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Tuberculosis, caused by Mycobacterium tuberculosis (Mtb), is a life threatening

disease, which accounts for millions of lives annually. Mtb is an intracellular

bacterium, has coevolved with humans to premeditate its machinery to surpass the

immunity mounted against it in order to persist for long durations in the

system. Cell death is a fundamental process required not only for tissue

homeostasis but also for providing protection against intracellular pathogens.

Various forms of cell death processes are known including apoptosis, pyroptosis,

necroptosis, autophagy etc., that have been shown to play important roles in

anti-TB immunity against Mtb. Moreover, inhibition of these pathways by Mtb is

considered as one of the virulence mechanisms by which the pathogen is able to

survive and replicate inside the host. Apart from identification of newer drug

targets and development of anti-TB drugs that solely target the pathogen, recent

advancements have been made in developing host-directed therapies against TB,

which are aimed at modulating the host responses to reduce excessive

inflammation and tissue damage. Thus, understanding the proteins and signaling

cascades associated with cell death modalities and their relation with Mtb

infection will give us new insights into the area of host-pathogen interactions

and help us design better host-directed therapies.

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**11. BMJ Case Rep. 2025 Sep 21;18(9):e266068. doi: 10.1136/bcr-2025-266068.**

Tuberculous epididymo-orchitis mimicking testicular cancer: a diagnostic

challenge.

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Thiruvananthapuram, Kerala, India.

A patient in his early 60s with a long-standing history of scrotal swelling and

recent onset of pain underwent high inguinal orchidectomy due to a suspected

testicular malignancy. Tumour markers were normal, but histopathological

examination revealed caseating granulomas, confirming tuberculous

epididymo-orchitis. He was diagnosed with genitourinary tuberculosis and

initiated on anti-tubercular therapy. The patient responded well to treatment

with no recurrence. This case highlights the importance of considering

tuberculosis in the differential diagnosis of testicular lesions and the

critical role of histopathology in confirming the diagnosis.

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**12. BMC Public Health. 2025 Oct 3;25(1):3336. doi: 10.1186/s12889-025-24715-8.**

Burden of pulmonary tuberculosis among Ethiopians seeking jobs in the Middle

East: a retrospective study.

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**BACKGROUND:** Globally, pre-and post-migration TB screening are integral to

controlling TB among migrants. Annually, approximately 300,000 Ethiopians

migrate to the Middle East in search of job opportunities. But prior to their

trip the migrants are randomly distributed by Wafid to 12 authorized clinics in

Addis Ababa, for pre-migration medical screening for communicable diseases

including Tuberculosis (TB), which is one of the main concerns and screened

using chest X-ray (CXR). Based on the screening results, the job seekers are

classified as Fit or Unfit to travel to the Middle East. This study aimed to

estimate the prevalence of presumptive TB among Ethiopian Migrant Workers upon

screening and identify the possible associated risk factors.

**METHOD:** A retrospective cross-sectional study was conducted using data between

June,2023 and June, 2025 collected from three clinics utilizing Sefed Software

Systems database. Ethiopian Migrant Domestic Workers (MDWs) are randomly placed

for pre-migration screening to these health facilities by the Ministry of Labor

and Skills. The prevalence of presumptive TB was estimated using STATA software

version 14. Logistic regression model was applied to determine associations

between X-ray TB diagnosis and with socio-demographic and clinical variables.

**RESULTS:** Among 233,941 individuals screened during the study period, 10, 342

(4.42%) were deemed Unfit to travel due to abnormal CXR findings. Significant

associations were observed between TB-suspects based on X-rays and several

variables. Using multivariable logistic regression analysis, religion

(OR = 1.24; 95% CI: 1.19-1.28); marital status (OR = 0.88; 95% CI: 0.84-0.93),

age (OR = 3.35; 95% CI: 2.70-4.15), hepatitis B (OR = 1.71; 95% CI: 1.48-1.97),

syphilis (VDRL) (OR = 1.97; 95% CI: 1.63-2.37) and pregnancy (OR = 1.56, 95%

CI = 1.34-1.81) showed statistically significant association with potential TB

status with P < 0.05. HIV status showed marginal association (OR = 1.40; 95% CI:

0.91-2.14).

**CONCLUSION:** This study revealed a relatively high prevalence of presumptive TB

among Ethiopian (MDWs) seeking jobs in the Middle East. The X-ray results may

not be confirmatory diagnosis for TB. Therefore, further investigation is

required using other confirmatory methods such as Gene Xpert or TB culture.

Linking medically unfit individuals to TB care is crucial to mitigate

transmission risks based on the WHO recommendations.

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DOI: 10.1186/s12889-025-24715-8

PMID: 41044689 [Indexed for MEDLINE]

**13. Res Involv Engagem. 2025 Oct 3;11(1):112. doi: 10.1186/s40900-025-00787-z.**

Amplifying every echo; public partnerships in ongoing CONTROL (COgNitive Therapy

for depRessiOn in tubercuLosis treatment) research study.

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F(2), Milner A(3), Haq IU(2), Ullah A(2), Zarkaish R(2), Khan Z(2), Haq HU(2),

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With the health and social care research trends shifting towards conception,

development, delivery, and implementation of more evidence-based interventions,

public partnerships have emerged as key foundational moral components to tailor

best practices to conduct research with the patient, public, and community. This

paper reflects on how public partnerships were established in the ongoing

CONTROL research study to open, trustworthy, and mutually beneficial

relationships with public partners. This paper presents a reflective case study

that exemplifies collaborative research in action using the Public Involvement

Impact Assessment Framework and the UK standard of Public Involvement. We

reflected on our approaches to public involvement and engagement, establishing a

public advisory group, its capacity development, and contribution to the main

study and multilevel impact of relational community engagement. Our strategies

can inform future public partnerships in funded projects, especially in lower-

and middle-income countries.

Plain Language Summary: People affected by Tuberculosis and depression face

stigma, poor treatment outcomes, and lack of access to healthcare, especially in

low-income communities and refugee groups. The VoICE of CONTROL initiative was

launched as part of the CONTROL research program to establish and strengthen the

public partnership regarding tuberculosis and depression and shape the research

from the start. We held community engagement sessions to learn about people’s

experiences with TB, stigma, myths, mental health, and challenges they face in

accessing health care. From these sessions, we invited individuals to join the

advisory group and contribute regularly to the CONTROL study’s design,

intervention development and refinement, materials, and outreach activities. To

enhance capacity development, training sessions were arranged for team and

advisory group members regarding patient and public involvement in research. The

feedback from the community and advisory group helped shape a culturally

sensitive mental health intervention and awareness campaign. This paper presents

how meaningful public partnerships can lead to more relevant, respectful, and

inclusive research with underserved communities.

© 2025. The Author(s).

DOI: 10.1186/s40900-025-00787-z

PMID: 41044686

**14. Trop Dis Travel Med Vaccines. 2025 Oct 3;11(1):33. doi:**

**10.1186/s40794-025-00269-w.**

Global research trends in BPaL and BPaLM regimens for drug-resistant

tuberculosis: a bibliometric analysis.

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**BACKGROUND:** The introduction of BPaL and BPaLM regimens has revolutionized

drug-resistant tuberculosis treatment, offering superior efficacy, shorter

duration, and better tolerability than conventional therapies. Despite their

rapid WHO guideline incorporation, no prior bibliometric analysis has been

conducted on this topic. This study addresses this gap by mapping global

knowledge production, collaborations, and thematic trends to inform future

research and implementation strategies.

**METHODS:** We analyzed Scopus-indexed publications using controlled vocabulary for

BPaL/BPaLM regimens. From 551 initial records, 120 met inclusion criteria after

screening. Bibliometrix and VOS Viewer software evaluated publication trends,

authorship, institutional/geographical contributions, citations, and keyword

networks. Visualization tools mapped collaborations and thematic clusters, while

statistical methods assessed growth rates and citation impacts.

**RESULTS:** The study identified 1,081 authors, with publications growing at 11.61%

annually and peaking in 2024 (n = 56). International collaborations featured in

53.33% of studies, led by the US (n = 56), UK (n = 25), and South Africa

(n = 20). Johns Hopkins University was the top institution (n = 56), and

Antimicrobial Agents and Chemotherapy the leading journal (n = 15). Landmark

2019 publications had the highest citation rate (13.05/year). Thematic analysis

revealed categorization into three domains: pathogen and drug resistance,

treatment regimens and efficacy, and demographics and clinical studies. Strong

collaborations linked high-income and high-burden countries, notably the US and

South Africa.

**CONCLUSION:** This first bibliometric assessment of BPaL/BPaLM research highlights

progress in evidence generation but reveals gaps in implementation science and

equitable knowledge production. Future work should address operational

challenges, special populations, and resistance monitoring. These insights can

guide researchers, policymakers, and funders to optimize TB control programs and

advance global elimination goals.

© 2025. The Author(s).

DOI: 10.1186/s40794-025-00269-w

PMID: 41044664

**15. BMC Pulm Med. 2025 Oct 3;25(1):448. doi: 10.1186/s12890-025-03756-0.**

Serum metabolic disparity between patients with lymph node tuberculosis and

patients with sarcoidosis: towards differential diagnosis.

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**BACKGROUND AND HYPOTHESIS:** Sarcoidosis (SAR) and lymph-node tuberculosis (LNTB)

are granulomatous diseases that present diagnostic challenges, especially in

TB-endemic regions. We hypothesized that serum-metabolic profiles would help in

differentiating SARs from LNTBs.

**OBJECTIVE:** This study aimed to identify serum metabolic biomarkers to

distinguish SAR from LNTB using NMR-based metabolomics analysis.

**METHODS:** Serum samples were collected from 26 SAR and 22 LNTB patients. The

serum metabolic profiles were measured using 800 MHz NMR spectroscopy and

quantified using the commercial software CHENOMX. The serum metabolic profiles

were compared using multivariate partial least squares discriminant analysis

(PLS-DA), and potential discriminatory metabolites were identified using

variable importance in projection (VIP) scores and subsequently evaluated for

statistical significance using a volcano plot. The diagnostic potential of the

discriminatory metabolites was evaluated using receiver operating characteristic

(ROC) curve analysis.

**RESULTS:** PLS-DA demonstrated significant metabolic disparity between the SAR and

LNTB groups. The key metabolic features identified included elevated levels of

glutamate, pyroglutamate, acetate, and leucine and a decreased

glutamate-to-glutamine ratio (EQR) and decreased levels of glutamine, pyruvate,

and myo-inositol in TB patients. These metabolic changes suggest that

TB-infection involves activated glutaminolysis and elevated host lipid

metabolism. ROC curve analysis revealed several metabolites with high diagnostic

potential (AUC > 0.8), including glutamate, pyroglutamate, and glutamine

(AUC > 0.98).

**CONCLUSION:** In conclusion, this study underscores the potential of serum

metabolic profiling as a noninvasive tool for distinguishing SARs from LNTBs.

However, further studies are imperative to validate these findings on

independent patient cohorts and to facilitate their integration into routine

clinical practice.

© 2025. The Author(s).

DOI: 10.1186/s12890-025-03756-0

PMID: 41044523 [Indexed for MEDLINE]

**16. BMC Pulm Med. 2025 Oct 3;25(1):450. doi: 10.1186/s12890-025-03931-3.**

Trends in tuberculosis-related mortality among adults 35-85 years old in the

United States, 1999 to 2022: a nationwide analysis.

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**BACKGROUND:** Tuberculosis (TB) is a significant cause of mortality in the United

States (US), impairing individual health and causing national financial burden.

Although TB-related mortality has declined in recent years, a variety of factors

still make TB difficult to prevent, necessitating further analysis of which

demographic groups are most impacted by TB.

**METHODS:** Trends in TB-related mortality in individuals aged 35 to 85 + years in

the US from 1999 to 2022 were analyzed utilizing the Centers for Disease Control

and Prevention Wide-ranging Online Data for Epidemiologic Research (CDC WONDER)

database. Following data collection, age-adjusted mortality rate (AAMR) and

average annual percent change (AAPC) in TB-related mortality were examined. Data

was further stratified by sex, race, age, region, and locality.

**RESULTS:** Between 1999 and 2022, there were 26,600 deaths related to TB in the

US. Overall TB-related mortality significantly declined between 1999 and 2022

(AAPC, -3.95%). Males had consistently higher AAMR than females, with 16,741

deaths among males and 9,859 deaths among females. All racial groups, including

Asian or Pacific Islander, Black or African American, White, and Hispanic or

Latino individuals experienced significant declines in mortality (AAPC, -3.24%,

-5.75%, -3.83%, -4.70%, respectively). Asian or Pacific Islander, Black or

African American, and Hispanic or Latino patients had consistently higher AAMR

than White patients between 1999 and 2022, however. Individuals older than 65

experienced significantly higher AAMR than younger individuals. South and West

regions had higher AAMR than Northeast and Midwest regions, with the West and

South experiencing the smallest and largest declines in mortality that were

statistically significant, respectively (AAPC, -3.04%, -4.66%). TB-related

mortality was higher in urban areas, with 20,680 deaths compared to 3,707 deaths

in rural areas.

**CONCLUSION:** Although TB-related mortality has declined in the US overall, this

improvement has not been experienced equally by all demographic groups.

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DOI: 10.1186/s12890-025-03931-3

PMID: 41044485 [Indexed for MEDLINE]

**17. Microb Pathog. 2025 Oct 1:108087. doi: 10.1016/j.micpath.2025.108087. Online**

**ahead of print.**

The Gut-Lung Axis in Tuberculosis: A New Frontier in Immunomodulation and

Microbiota-Directed Therapeutic Strategies.

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Tuberculosis (TB) is a transmissible disease that contributes to the global

health burden due to drug resistance. The gut-lung axis is an emerging and

promising frontier for understanding Mycobacterium tuberculosis (MTB)

pathogenesis and disease progression via gut and lung bidirectional

communication. Increasing evidence highlights that regulation in gut and lung

microbial communities, termed dysbiosis, influences homeostatic conditions,

innate and adaptive responses, and susceptibility to TB. Growing research has

witnessed a paradigm shift toward the immunological interplay between gut

microbiota and lung microbiota, and modulation in TB. This review deals with the

interplay of immune cells and gut microbiota in TB, highlighting the importance

of innate and adaptive responses in stabilizing the dysbiosis and inflammation.

Host-directed therapies such as probiotics, prebiotics, synbiotics, short-chain

fatty acids (SCFAs), and fecal microbiota transplantation support the

stabilization of gut microbiota and maintain the disease severity. Moreover,

personalized microbiota therapies, such as bacteriophage therapy, diagnostic

agents, and biomarkers, are explored for their several roles in maintaining the

eubiosis condition. We also highlight the future perspective of addressing the

knowledge gap to develop a personalized and combined approach to novel drug

delivery systems and host-directed therapies. This review provides an in-depth

outline of the gut-lung axis as a potential therapeutic intervention, offering a

conceptual framework for developing next-generation, microbiota-directed

therapies to suppress and combat MTB infection.

Copyright © 2025. Published by Elsevier Ltd.

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PMID: 41043596

**18. Expert Rev Respir Med. 2025 Oct 3. doi: 10.1080/17476348.2025.2569845. Online**

**ahead of print.**

High burden of severe and very severe undernutrition among adults with

tuberculosis: findings from a state wide operational research in Chhattisgarh,

India.

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**BACKGROUND:** Undernutritiondrives the TB epidemic in India with 4-5 times higher

mortality among adultswith severe/very severe undernutrition. We assessed

proportion of severe/verysevere undernutrition among adults with TB and

timeliness in receiving monetarysupport for nutrition (Direct benefit

transfer-DBT) and food baskets.

**RESEARCH DESIGN AND METHODS:** Thisanalytical cross-sectional study conducted in

Chhattisgarh-tribal Indian state,utilized program data of adults with TB

notified in public facilities under theNational TB Elimination Program from

April-June 2024. Body Mass Index (BMI) wascategorized for nutritional status and

equity in distribution of DBT and foodbaskets was evaluated using frequency,

proportions, and Chi-square for trend.

**RESULTS:** Of 6568adults with TB, BMI was calculated for 6397 (97%). Proportion of

severe andvery severe undernutrition was 22% and 13% respectively. First DBT

instalmentwas received by 81%, with 29% receiving it within two months; 21%

received foodbaskets, with similar coverage across all undernutrition

categories(p > 0.05), reflecting inequity.

**CONCLUSIONS:** There ishigh burden of severe/very severe undernutrition among TB

patients. Similar DBTand food basket coverage among those with severe/very

severe undernutrition andother TB patients indicates inequity in distribution.

Undernutrition-basedindicators and linkage of DBT and food baskets should be

prioritized.

DOI: 10.1080/17476348.2025.2569845

PMID: 41042600

**19. FEMS Microbiol Lett. 2025 Oct 3:fnaf106. doi: 10.1093/femsle/fnaf106. Online**

**ahead of print.**

Advances in our understanding of the lung-gut axis in tuberculosis.

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Human and animal studies have supported the existence of the gut-lung axis,

where gastrointestinal commensals and their products can modulate lung immune

function. The role of a balanced healthy gut microbiota, and its restoration may

impact the microbiota in the lung. Yet the robustness of this evidence varies

considerably, with many studies having considerable limitations. Intestinal

microbiota diversity is decreased in pulmonary TB patients, and changes in the

intestinal microbiota after M. tuberculosis. infection have been reported,

underscoring the bidirectionality of the lung-gut axis. These changes may be

associated with the progression of TB, influencing the microbiota and immunity

homeostasis in those receiving anti-TB treatment. The crosstalk between the gut

and the lung is increasingly recognized as a key modulator in the development,

progression, and treatment outcomes of tuberculosis (TB). A protective role of

the intestinal microbiota against lung infections through its role in macrophage

activation, makes it a promising approach as anti-TB adjunct therapy. This mini

review synthesizes current understanding of gut-lung interactions in TB

pathogenesis, appraising strengths and limitations of the literature, clarifying

areas of consensus versus speculation, highlighting where findings remain

preliminary, summarizing the impact of anti-TB treatment on microbial

communities, and discussing future directions for microbiota-informed

interventions to improve patient outcomes.

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PMID: 41042232

**20. Clin Infect Dis. 2025 Oct 3:ciaf559. doi: 10.1093/cid/ciaf559. Online ahead of print.**

Precision Prevention of Tuberculosis in Biologic Therapy: Lessons Beyond

Screening Strategies.

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DOI: 10.1093/cid/ciaf559

PMID: 41042105

**21. RSC Adv. 2025 Oct 1;15(43):36331-36343. doi: 10.1039/d5ra04418a. eCollection**

**2025 Sep 26.**

Identification of potential inhibitors of dihydrofolate reductase (DHFR) through

blocking the folate biosynthetic pathway of Mycobacterium tuberculosis utilizing

structure-based virtual screening.

Halder SK(1)(2), Sultana A(1), Ahmad I(3), Rafi MO(4), Sultana I(2)(5), Elma

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Tuberculosis (TB) has emerged as a leading cause of death due to a single

infectious agent-Mycobacterium tuberculosis (Mt). This situation is exacerbated

by delayed diagnosis, inadequate administration of effective TB medications,

prolonged duration of treatment, shortage of toxin-free TB drugs, and frequent

increases in resistance to most TB drugs. In an urge to find potential drug

candidates for the treatment of fatal infectious TB disease, we targeted the

folate biosynthetic pathway that involves the ubiquitous enzyme dihydrofolate

reductase (DHFR), which catalyzes the NADPH-dependent reduction of dihydrofolate

with the generation of tetrahydrofolate (THF). Blocking the enzymatic activity

of DHFR exhausts the cellular pool of THF, which results in cessation of DNA

synthesis in rapidly proliferating cells and ultimately cell death. Herein, a

total of 1026 drug-like molecules with antibacterial activities were tested

using several in silico tools for determining drug-likeness features, ADMET

(absorption, distribution, metabolism, excretion, and toxicity) profiling,

binding affinity, and conformation analysis using Autodock Vina and Schrodinger

Suite. This exhaustive investigation identified CHEMBL577, CHEMBL161702, and

CHEMBL1770248 as potential drug candidates for the inhibition of M. tuberculosis

DHFR protein. Root mean square deviation, root mean square fluctuation, hydrogen

bond, and MMGBSA evaluation by 100 ns molecular dynamics simulation (MDS)

confirmed their molecular stability with the target protein. All of these

drug-like compounds outperformed the control drugs trimethoprim and methotrexate

in molecular docking and molecular dynamics simulation tests. Therefore, our

study suggests these M. tuberculosis DHFR inhibitors as promising drug

candidates. However, additional wet-lab experiments are required to verify their

potential therapeutic potency as novel drugs against M. tuberculosis.

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DOI: 10.1039/d5ra04418a

PMCID: PMC12486253

PMID: 41041286

**22. Euro Surveill. 2025 Oct;30(39). doi: 10.2807/1560-7917.ES.2025.30.39.2500096.**

Tuberculosis contact investigation: an evaluation of yield and guideline

adherence, Upper Bavaria, Germany, 2018 to 2022.

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**BACKGROUND** Contact investigation of index cases is important for tuberculosis

(TB) control in low-incidence countries, yet key performance metrics have not

been evaluated in Germany.AIMWe aimed to assess the yield of TB contact

investigations, compliance with national guidelines and risk factors for

infection among contacts.**METHODS** We analysed anonymised data of TB patients and

their contacts collected between 2018 and 2022 in Upper Bavaria, Germany. We

assessed testing coverage, latent TB infection (LTBI), TB yield, primary

prophylaxis and preventive treatment coverage. Risk factors for M. tuberculosis

infection (positive tuberculin skin test (TST) / interferon-gamma release assay

(IGRA) and/or TB diagnosis) among contacts were identified using multivariable

logistic regression and classification tree.**RESULTS** Of the 2,186 contacts of 174

TB patients, 2,022 (92.5%) had a valid TST/IGRA result and/or a TB diagnosis. Of

these, 308 (15.2%) had M. tuberculosis infection, including 10 (0.5%) with TB.

Of 241 contacts with LTBI, 66 (28.2%) completed preventive treatment. Among 124

children < 5 years, testing coverage was 75.8%, 16.9% received an immediate

chest X-ray and 72.7% primary prophylaxis. Key predictors of infection were born

outside Germany (odds ratio (OR) = 2.85; 95% confidence interval

(CI): 1.94-4.21) and exposure in community housing (OR = 2.65; 95% CI: 1.65-4.30; reference: exposure at work) or household/family (OR = 2.62; 95% CI: 1.74-4.00)**.CONCLUSION** We observed high screening coverage of contacts and yield and risk factors comparable to other low-incidence settings. There is room for improvement regarding preventive treatment and screening of children < 5 years.

DOI: 10.2807/1560-7917.ES.2025.30.39.2500096

PMID: 41040068 [Indexed for MEDLINE]

**23. Trop Med Int Health. 2025 Oct 3. doi: 10.1111/tmi.70043. Online ahead of print.**

Rates and Risk Factors for On-Treatment Mortality Among a Cohort of Adults

Treated for Drug-Sensitive Tuberculosis: Analysis of Data From the Adherence

Support Coalition to End Tuberculosis Consortium in Five Countries.

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Africa.

**BACKGROUND**: Tuberculosis remains a leading cause of death globally, particularly

in countries with high tuberculosis and HIV burdens. Disruptions caused by the

COVID-19 pandemic may have further impacted tuberculosis outcomes. This study

examines on-treatment mortality and associated risk factors in five countries.

**METHOD:** We conducted a secondary analysis of data from ASCENT cluster-randomised

trials of digital adherence tools for improved adherence involving 23,799 adults

with drug-sensitive tuberculosis in South Africa, Tanzania, Ethiopia, the

Philippines, and Ukraine. Analyses were conducted separately by country.

Mortality rates were measured from treatment initiation to the earliest of

6 months, death, or loss to follow-up. Cox regression models (with random

effects or robust standard errors for clustering) assessed the associations

between mortality and HIV status, ART use, tuberculosis diagnosis type, and

calendar periods (COVID-19 pandemic and conflict in Ukraine).

**RESULTS:** Mortality rates ranged from 7.6 (Ethiopia) to 23.2 (Tanzania) and 23.3

(Ukraine) per 100 person-years. Higher mortality was associated with: older age

in all countries (age < 30 versus ≥ 60 years, adjusted rate ratio [aRR] ranging

from 2.38 to 6.57 by country); HIV status (positive versus negative, aRR ranging

from 1.44 to 2.98 by country); tuberculosis diagnosis type (clinical vs.

bacteriological, aRR 1.5-1.6 in Ethiopia, Tanzania and South Africa);

extrapulmonary tuberculosis (aRR 1.44 to 1.60 in Ukraine and Tanzania). ART

versus HIV-positive not on ART was linked to lower mortality in South Africa and

Ukraine but not in Tanzania. Analyses suggested possible mortality variations by

calendar period.

**CONCLUSION:** Our findings suggest variability in tuberculosis mortality across

settings, influenced by HIV/ART and diagnosis type. The high mortality rates

across countries may reflect underlying causes or potential misdiagnoses.

Further investigation into these factors may be needed to improve tuberculosis

outcomes globally.

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Wiley & Sons Ltd.

DOI: 10.1111/tmi.70043

PMID: 41039891

**24. BMC Infect Dis. 2025 Oct 2;25(1):1224. doi: 10.1186/s12879-025-11620-z.**

Use of interferon-gamma release assay (IGRA) and CXCL-10/IP-10 for latent

tuberculosis infection (LTBI) screening in chronic kidney disease and

hemodialysis patients.

da Silva JCB(1), Vieira NB(1), Ribeiro-Alves M(2), de Almeida Ribeiro RS(1), da

Silva Lemos CC(3), Mendes R(3), Gomes CLR(3), Santos AP(4), Suassuna JH(3),

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DOI: 10.1186/s12879-025-11620-z

PMID: 41039242

**25. J Infect Dis. 2025 Oct 1:jiaf510. doi: 10.1093/infdis/jiaf510. Online ahead of print.**

Targeting Tryptophan Metabolism for Tuberculosis Biomarkers and Host Directed

Therapy.

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Epidemiology, Atlanta, Georgia, USA.

Greater understanding of the role of tryptophan metabolism in the immune

response to tuberculosis (TB) has provided promising avenues to explore new

diagnostic and therapeutic modalities. Animal and human studies have

demonstrated that host indoleamine 2,3-dioxygenase-1 (IDO1) is upregulated in

response to infection with Mycobacterium tuberculosis resulting in increased

tryptophan metabolism to kynurenine. In TB disease, this is evidenced by

elevation of the plasma kynurenine to tryptophan ratio, which is reversed with

effective TB treatment thus showing utility as a potential diagnostic and

therapeutic biomarker. Kynurenine and downstream metabolites promote an

immunosuppressive microenvironment in TB granulomas, which may facilitate immune

evasion. IDO inhibition in non-human primates has highlighted its potential role

as host-directed therapy by demonstrating increased T cell trafficking to the

granuloma core, reduced bacterial burden, and decreased immunopathology. To

realize the potential of exploiting the tryptophan to kynurenine metabolic

pathway, innovative biomarker and host-directed therapy trials are needed.

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DOI: 10.1093/infdis/jiaf510

PMID: 41037490

**26. J Infect Dis. 2025 Oct 1:jiaf511. doi: 10.1093/infdis/jiaf511. Online ahead of print.**

NAT2 polymorphisms and Antituberculosis-Induced Hepatotoxicity in Thai People

Living with HIV: Insights from a Pharmacogenetic-Pharmacokinetic Cohort Study.

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Torvorapanit P(5), Suwanpimolkul G(6), Phaisal W(7), Chariyavilaskul P(8), Cho

YS(9), Shin JG(10), Mahasirimongkol S(11), Avihingsanon A(1).

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 Thailand.

**BACKGROUND:** The N-Acetyltransferase (NAT2) slow acetylator phenotype has been

associated with a higher risk of isoniazid (INH)-induced hepatotoxicity. We

investigated the association between NAT2 genotypes with inferred acetylator

status, hepatotoxicity and INH pharmacokinetics in Thai people living with HIV

(PLWH) receiving INH-based Tuberculosis (TB) preventive or treatment regimens.

**METHODS:** In this prospective cohort study of Thai PLWH initiating INH-based

regimens; NAT2 genotyping classified participants as slow (SA), intermediate

(IA), or rapid acetylators (RA). Hepatotoxicity was defined as transaminase

elevations more than 2.5 times the upper limit of normal (ULN). Multivariable

logistic regression identified genotypes and factors associated with

hepatotoxicity. A pharmacokinetic (PK) substudy assessed INH exposure across

phenotypes.

**RESULTS:** Of 894 participants, 32.4% were SA, 41.2% IA, and 26.4% RA.

Hepatotoxicity occurred in 10.9% overall and was highest in SA (15.2%). SA had

increased hepatotoxicity risk vs RA (adjusted odds ratio [aOR] 2.43; 95%CI:

1.32-4.48). Genotypes NAT2\*6A/\*6A (aOR 1.84) and NAT2\*7B/\*7B (aOR 4.46) were

associated with increased risk; NAT2\*4/\*4 was protective (aOR 0.33). Other

independent risk factors included high baseline alanine aminotransferase (ALT),

HCV co-infection, 2HRZE/4HR regimen (vs. 1HP), and efavirenz-based antiviral

therapy (vs. dolutegravir). In the PK substudy (n=93), INH exposure assessed by

the area under the concentration time curve from 0-24 hours, was significantly

increased by approximately 2-fold in SA, regardless of anti-TB regimen.

**CONCLUSIONS:** NAT2 SA phenotype, particularly \*6A/\*6A and \*7B/\*7B genotypes, is

associated with an increased risk of antituberculosis-induced hepatotoxicity and

higher INH exposure in Thai PLWH. Incorporating NAT2-guided dosing may enhance

safety of INH-containing regimens in PLWH.

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DOI: 10.1093/infdis/jiaf511

PMID: 41037485

**27. Elife. 2025 Oct 2;14:RP106814. doi: 10.7554/eLife.106814.**

Lipid peroxidation and type I interferon coupling fuels pathogenic macrophage

activation causing tuberculosis susceptibility.

Yabaji SM(1), Zhernovkov V(2), Araveti PB(1), Lata S(1), Rukhlenko OS(2),

Abdullatif SA(3), Vanvalkenburg A(4)(5), Alekseyev YO(6), Ma Q(7), Dayama G(7),

Lau NC(1)(7), Johnson WE(4)(5), Bishai WR(8), Crossland NA(1)(6), Campbell

JD(3), Kholodenko BN(2)(9)(10), Gimelbrant AA(11), Kobzik L(12), Kramnik

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Update of

 doi: 10.1101/2024.03.05.583602.

 doi: 10.7554/eLife.106814.1.

A quarter of the human population is infected with Mycobacterium tuberculosis,

but less than 10% of those infected develop pulmonary TB. We developed a

genetically defined sst1-susceptible mouse model that uniquely reproduces a

defining feature of human TB: the development of necrotic lung granulomas and

determined that the sst1-susceptible phenotype was driven by the aberrant

macrophage activation. This study demonstrates that the aberrant response of the

sst1-susceptible macrophages to prolonged stimulation with TNF is primarily

driven by conflicting Myc and antioxidant response pathways leading to a

coordinated failure (1) to properly sequester intracellular iron and (2) to

activate ferroptosis inhibitor enzymes. Consequently, iron-mediated lipid

peroxidation fueled superinduction of Ifnβ and sustained the type I interferon

(IFN-I) pathway hyperactivity that locked the sst1-susceptible macrophages in a

state of unresolving stress and compromised their resistance to Mtb. The

accumulation of the aberrantly activated, stressed, macrophages within the

granuloma microenvironment led to the local failure of anti-tuberculosis

immunity and tissue necrosis. The upregulation of the Myc pathway in peripheral

blood cells of human TB patients was significantly associated with poor outcomes

of TB treatment. Thus, Myc dysregulation in activated macrophages results in an

aberrant macrophage activation and represents a novel target for host-directed

TB therapies.

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**28. Rev Soc Bras Med Trop. 2025 Sep 29;58:e02292025. doi:**

**10.1590/0037-8682-0229-2025. eCollection 2025.**

A case of tuberculosis in the cavitary lesion suggestive of neoplasm.

Altınkaya C(1), Karaman A(1).

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Turkey.

DOI: 10.1590/0037-8682-0229-2025

PMID: 41036901

**29. Microbiol Spectr. 2025 Oct 2:e0076525. doi: 10.1128/spectrum.00765-25. Online**

**ahead of print.**

A universal, high-quality, and high-yield DNA purification method for

mycobacteria, including Mycobacterium tuberculosis: large-scale assessment of

the chloroform-bead method.

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A(2), Takaki A(1), Mitarai S(1)(3); Japan Tuberculosis Genotyping Group (2023);

Japan Tuberculosis Genotyping Group.

Collaborators: Takahashi Y, Kamitaka N, Yodotani Y, Yajima M, Tani F, Shibata S,

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Genomic analysis of mycobacteria has become increasingly crucial for

understanding drug-resistance mechanisms, molecular epidemiology, and

pathogenesis. However, efficient extraction of high-molecular-weight genomic DNA

from these organisms remains challenging because of their thick mycolic

acid-rich cell walls. In this study, we report the chloroform-bead method, a

universal DNA extraction protocol that combines chemical and mechanical

disruptions to overcome these challenges. Multi-laboratory evaluation (16 sites)

demonstrated the chloroform-bead method's superiority over conventional methods

for Mycobacterium tuberculosis (DNA yield: 17.9 vs 1.9 µg, purity A260/A230:

1.86 vs 1.22, both P < 0.001). Single-facility assessment extended these

findings to >32 nontuberculous mycobacterial species (n = 1,058), showing

performance comparable to M. tuberculosis (n = 1,000), with both achieving

median yields of 22.2 µg DNA and consistent quality metrics. The chloroform-bead

method significantly reduced the processing time from 2 to 3 days to 2 h while

ensuring complete sample sterilization, eliminating the need for

species-specific optimization. This streamlined and universally applicable

protocol represents a practical advancement in mycobacterial DNA extraction

methodology, ideal for high-throughput genomic studies and routine clinical

diagnostics.

**IMPORTANCE:** Mycobacterial genomics is crucial for understanding pathogenesis and

drug resistance; however, DNA extraction remains a significant challenge because

of its unique cell wall. Traditional methods rely on enzymatic treatments,

resulting in complex and time-consuming protocols with variable results. The

chloroform-bead method introduces a paradigm shift by chemically and

mechanically disrupting the mycolic acid layer and eliminating the need for

enzymatic treatment. This standardized approach ensures consistent, high-quality

DNA extraction across diverse mycobacterial species, thereby enhancing research

capabilities and clinical applications.

DOI: 10.1128/spectrum.00765-25

PMID: 41036864

**30. BMJ Public Health. 2025 Sep 29;3(2):e001861. doi: 10.1136/bmjph-2024-001861.**

**eCollection 2025.**

Stakeholders' perspectives on funding malaria, HIV/AIDS and tuberculosis

services in Tanzania through domestic resources mobilisation: a qualitative

study.

Ngadaya FD(#)(1)(2), Isangula K(#)(3), Kimambo H(2), Soka G(2), Kitinya C(2),

Philbert D(2), Mwenda L(2), Kagaruki GB(2), Kimaro G(2)(4), Ngadaya E(2)(4),

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**BACKGROUND:** Low-income and middle-income countries continue to face challenges

in financing health programmes due to budgetary constraints and decreased donor

funding. Off-budget financing has become crucial for controlling diseases like

malaria, HIV/AIDS and tuberculosis (TB). However, there is limited evidence on

alternative domestic funding approaches to support implementation of healthcare

programmes in Tanzania.

**OBJECTIVE:** The study explored stakeholder perspectives on alternative domestic

funding approaches to support malaria, HIV/AIDS and TB services in Tanzania.

**METHODS:** A qualitative descriptive design was employed to gather insights from

76 purposely selected stakeholders, including policymakers, programme managers,

regional health managers, district health managers and healthcare workers. Data

were managed and analysed thematically.

**RESULTS:** Four major themes emerged: current sources of funds, financial

resources needed, proposed alternative domestic funding mobilisation strategies

to support implementation of malaria, HIV/AIDS and TB and challenges of

implementing the proposed strategies. Current major sources of funds included

multilateral donors, development partners, the central government and internal

sources. There was a consensus on a decrease in donor funding due to the

COVID-19 pandemic. The proposed alternative domestic funding strategies included

establishing universal health insurance, reducing beneficiaries of service

exemptions, establishment of disease-specific funds and taxation of certain

products. Implementation challenges for the proposed strategies included poor

awareness, conflicting political promises and accountability issues.

**CONCLUSIONS:** The financing gap for malaria, HIV/AIDS and TB services is

significant due to decreasing donor funding. Strategies such as strengthening

insurance schemes, reducing exemption groups and taxation could help, but

community sensitisation and improved fund accountability are crucial.

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BY-NC. Published by BMJ Group.

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PMCID: PMC12481267

PMID: 41035768

**31. Physiother Res Int. 2025 Oct;30(4):e70115. doi: 10.1002/pri.70115.**

Peripheral Muscle Strength and Pulmonary Function Negatively Impact Functional

Capacity in Patients With Post-Tuberculosis Lung Disease: A Cross-Sectional

Study.

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University of Rio de Janeiro (UERJ), Rio de Janeiro, Brazil.

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State University of Rio de Janeiro (UERJ), Rio de Janeiro, Brazil.

**BACKGROUND AND PURPOSE:** Tuberculosis primarily affects the lungs, and many

patients experience sequelae, including loss of lung function and a decline in

health-related quality of life (HRQoL), despite bacteriological cure. Although

post-tuberculosis lung disease (PTLD) is a growing concern worldwide due to poor

physical functioning, little is known about peripheral muscle dysfunction.

Therefore, the objective of this study was to evaluate patient performance

during the Glittre Activities of Daily Living Test (TGlittre) and assess its

association with muscle function, lung function, and HRQoL.

**METHODS:** This cross-sectional study included 47 patients with PTLD who underwent

the TGlittre. We also assessed patients for respiratory muscle strength,

handgrip strength (HGS), quadriceps muscle strength (QMS), and HRQoL using the

Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36).

**RESULTS:** HGS and QMS were reduced in 34% and 25.5% of participants,

respectively. Spirometry showed an obstructive pattern, a restrictive pattern,

and a normal pattern in 46.8%, 31.9% and 21.3% of participants, respectively,

while 42.6% of them had reduced diffusion capacity of lung for carbon monoxide

(DLCO). The median TGlittre time was 4.43 (3.48-4.96) minutes, about 15% longer

than the expected time to complete it. There was a significant correlation

between TGlittre time and DLCO (rs = -0.532, p < 0.0002), maximum inspiratory

pressure (rs = -0.407, p = 0.005), maximum expiratory pressure (rs = -0.382,

p = 0.008), HGS (rs = -0.327, p = 0.024), QMS (rs = -0.314, p = 0.031), and various SF-36 domains. In the regression analysis, DLCO, QMS, and HGS explained

39% of the variability in TGlittre time.

**DISCUSSION:** PTLD significantly impacts functional capacity, as determined by

TGlittre. These patients have muscle dysfunction, deteriorated HRQoL, and

impaired lung function. Impaired lung diffusion and reduced peripheral muscle

strength (PMS) are independently associated with lower functional capacity.

Therefore, rehabilitative strategies are crucial for improving care for this

group of patients. This is the first study using the TGlittre to explore PMS in

PTLD.

**TRIAL REGISTRATION:** The protocol was registered on ClinicalTrials.gov with the

identifier NCT06127641.

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DOI: 10.1002/pri.70115

PMID: 41035122 [Indexed for MEDLINE]

**32. Nat Rev Genet. 2025 Oct 1. doi: 10.1038/s41576-025-00901-7. Online ahead of**

**print.**

The evolution of Mycobacterium tuberculosis as humans migrated out of Africa.

Suliman S(1).

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California, San Francisco, San Francisco, CA, USA. sara.suliman@ucsf.edu.

DOI: 10.1038/s41576-025-00901-7

PMID: 41034572

**33. Intern Med. 2025 Oct 2. doi: 10.2169/internalmedicine.6076-25. Online ahead of print.**

A Case Report of Smear-positive Pulmonary Tuberculosis with False-negative

Loop-mediated Isothermal Amplification and T-SPOT.TB Assays.

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(3)Department of Clinical Laboratory, Kindai University Nara Hospital, Japan.

Rapid molecular and immunological assays for tuberculosis, including

loop-mediated isothermal amplification (LAMP) and T-SPOT. TB assays, may yield

false-negative results. We herein report a 62-year-old immunocompetent man with

a productive cough, elevated C-reactive protein (22.8 mg/dL) and procalcitonin

(2.7 ng/mL) levels, and computed tomography findings suggestive of

nontuberculous mycobacterial infection. Despite the acid-fast bacilli-positive

smears, two separate Mycobacterium tuberculosis LAMP assays and a T-SPOT. TB

assay were negative. Empirical treatment with ampicillin/sulbactam and

erythromycin improved the patient's condition. Four-week cultures confirmed

pulmonary tuberculosis. This case underscores the importance of interpreting

rapid assays within the clinical context and supports the use of reflex

polymerase chain reaction for a definitive diagnosis.

DOI: 10.2169/internalmedicine.6076-25

PMID: 41033997

**34. Cell. 2025 Sep 30:S0092-8674(25)01036-0. doi: 10.1016/j.cell.2025.09.005. Online ahead of print.**

Evolution of Mycobacterium tuberculosis transcription regulation is associated

with increased transmission and drug resistance.

Culviner PH(1), Frey AM(1), Liu Q(2), Ha DTM(3), Thai PVK(3), Thu DDA(4), Quang

NL(4), Calderon R(5), Lecca L(6), Caws M(7), Dunstan SJ(8), Murray MB(9), Thuong

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Mycobacterium tuberculosis (Mtb) has co-evolved with humans for thousands of

years and is characterized by variation in virulence, transmissibility, and

disease phenotypes. To identify bacterial contributors to phenotypic diversity,

we developed new RNA sequencing (RNA-seq) and phylogenomic tools to capture

hundreds of Mtb isolate transcriptomes, link transcriptional and genetic

variation, and find associations between variants and epidemiologic traits.

Across 274 Mtb clinical isolates, we uncovered unexpected diversity in virulence

gene expression, which we linked to known and unknown regulators. Surprisingly,

we found that many isolates harbor variants associated with decreased expression

of EsxA (Esat6) and EsxB (Cfp10), which are virulence effectors, dominant T cell

antigens, and immunodiagnostic targets. Across >55,000 isolates, these variants

associate with increased transmissibility, especially in drug-resistant Mtb

strains. Our data suggest expression of Mtb virulence genes is evolving in

response to drug-linked pressure, raising concerns about use of these targets in

immunodiagnostics and next-generation vaccines.

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DOI: 10.1016/j.cell.2025.09.005

PMID: 41033311

**35. BMC Pulm Med. 2025 Sep 30;25(1):430. doi: 10.1186/s12890-025-03906-4.**

Missed opportunity for tuberculosis screening and prevention and the associated

factors among child contacts in rural southwestern Uganda.

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**BACKGROUND:** Tuberculosis (TB) treatment and control guidelines recommend

screening of contacts of bacteriologically confirmed TB cases and prompt

initiation of preventive therapy. However, many children exposed to TB in

high-burden settings like Uganda remain unscreened. The extent of the missed

opportunity for screening TB-exposed children in Ugandan rural settings remains

largely unknown. We determined the burden and associated factors of missed

opportunity for TB screening and prevention in rural southwestern Uganda.

**METHODS:** We conducted a cross-sectional study in four high-volume TB treatment

centers in Kanungu District, southwestern Uganda. Using consecutive sampling, we

included children aged 0-14 years who were household contacts of

bacteriologically-confirmed persons with TB. We defined a missed opportunity as

not being screened for TB or not receiving preventive TB treatment despite being

eligible. We used modified Poisson regression to identify factors associated

with the missed opportunities.

**RESULTS:** Among 279 children enrolled from 79 households, 119 (42.7%) were

aged < 5 years, 103 (36.9%) were 5-10 years, and 57 (20.4%) were 11-14 years.

Overall, 140 (50.2%) were never screened. Of the 139 screened, 25 (18.0%)

reported TB symptoms and 6 (24.0%) of these received TB treatment; among the 19

symptomatic but untreated, 3 (15.8%) missed isoniazid preventive therapy (IPT)

initiation. Of 114 asymptomatic contacts, 60 were IPT-eligible, yet 34 (56.7%)

were not initiated on IPT. Overall, 177/279 (63.4%; 95% CI: 67.6-68.9%)

experienced a missed screening or prevention opportunity. Factors independently

associated with missed opportunity were living in a household below the poverty

line (adjusted prevalence ratio [aPR] = 1.62, 95% CI: 1.19-2.21), lack of formal

education among index patients (aPR = 1.41, 95% CI: 1.09-1.83), and being a

contact aged < 5 years (aPR = 1.45, 95% CI: 1.12-1.88).

**CONCLUSION:** Our study revealed a high burden of missed opportunity for TB

screening and prevention among child contacts in this rural setting, driven by

socio-economic disadvantages, including household poverty, lack of formal

education, and younger age for household TB contacts (< 5 years). Interventions

should target socio-economically disadvantaged households to improve access to

TB screening and preventive care.

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**36. Implement Sci Commun. 2025 Sep 30;6(1):95. doi: 10.1186/s43058-025-00776-z.**

Between Process Gaps, Knowledge, and Patient Trust: Healthcare Workers' Insights

on Implementing Tuberculosis Preventive Therapy for People with HIV in the

Philippines and Indonesia.

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**BACKGROUND:** Tuberculosis (TB) poses a considerable challenge for people with HIV

(PWH), especially in low- and middle-income countries. Even with the

availability of effective preventive strategies such as tuberculosis preventive

therapy (TPT), the implementation of these measures continues to fall short. Our

study explores the perceptions of healthcare workers (HCWs) regarding the

barriers and facilitators to TPT implementation in the Philippines and

Indonesia.

**METHODS:** We performed 10 focus group discussions and four in-depth interviews

with HCWs from June to December 2023. Each discussion and interview lasted

between 45 and 120 min. Discussions explored HCWs' perspectives on the policies,

logistics, and prescribing practices related to TPT, as well as their personal

experiences, concerns, and suggested improvements. Data were coded using

MAXQDA24 qualitative software informed by the tenets of constructivist grounded

theory. We organized themes using the Consolidated Framework for Implementation

Research (CFIR), while contextualizing implementation determinants most

pertinent to the local contexts.

**RESULTS:** Our findings revealed nuanced barriers and facilitators-marked by

paradoxes-organized across three CFIR domains: the outer, inner, and individual

domains of HIV-TB care. In the outer setting, barriers include limited patient

knowledge and drug shortages, while facilitators involved national policies and

external pressures from mass media and peer imitation. The inner setting was

shaped by structural gaps-such as poor documentation, staff turnover, and

procedural challenges in ruling out active TB-that affected patient trust,

whereas open communication and role clarity supported TPT implementation. At the

individual level, HCWs expressed high motivation but cited limited capacity due

to lack of training and information to deliver effective TPT care.

**CONCLUSIONS:** Our findings highlight implementation determinants to TPT

implementation across outer, inner, and individual domains of HIV-TB care.

Understanding how structural gaps, provider capacity, and patient trust

intersect with supportive policies, and peer and mass media influences offer

insights into the complex dynamics shaping TPT uptake and integration. Our study

insights may inform policy adjustments and guide strategies to better integrate

TPT into national health frameworks.

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PMID: 41029364

**37. Sci Rep. 2025 Sep 30;15(1):33737. doi: 10.1038/s41598-025-95096-6.**

Risk of tuberculosis and hepatitis B reactivation during adalimumab use in the

treatment of hidradenitis suppurativa.

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Recently, adalimumab has become an important drug frequently used by

dermatologists in the treatment of Hidradenitis suppurativa. While there are

many publications by rheumatologists about the risk of hepatitis B and

tuberculosis reactivation, the literature on reactivation in the treatment of

hidradenitis is not extensive. With this study, we wanted to emphasize that

adalimumab is a safe drug despite the risk of hepatitis B and tuberculosis

reactivation and the importance of porphylaxis during the treatment of

hidradenitis suppurativa. In this study, data from 462 HS patients followed up

at the Dicle University Dermatology Clinic between 1 January 2017 and 30 June

2024 were retrospectively analyzed. Adalimumab use was detected in 56 of the 462

patients. Patients over 18 years of age and used adalimumab for at least 6

months were selected for this study. Two of these patients were not included in

the study because they did not meet the criteria for age and duration of

adalimumab use. All the participants were divided into 5 subgroups according to

their HBV serological test results: natural immunity, chronic HBV infection,

isolated anti-HBcIgG positivity, vaccinated and susceptible. Hepatitis B

reactivation was detected only in those with positive anti-HBc IgG (chronic HBV

infection, isolated anti-HBcIgG positivity, and natural immunity) tests who were

at risk of reactivation. To investigate reactivation, HBV DNA test results

before and after biological treatment and ALT-AST levels during the continuation

of biological treatment were examined. Patients with a positive HBV DNA test

before biological therapy and an increase of > 1 log10İU/ml in the HBV DNA titer

during biological therapy and patients with a negative HBV DNA test before

biological therapy and a positive HBV DNA test during the biological therapy use

period were considered reactivation positive. Patients for whom no HBV DNA test

was performed during the study period, those who had one positive HBV DNA test

result before or after biological treatment and the other test result was not

investigated, and those who had never been checked after starting biological

treatment were not included in the reactivation investigation. For tuberculosis

reactivation, those who had a latent tuberculosis test (quantitative test), did

not report any symptoms and were chronic carriers were included. Among the

patients with a positive latent TB test and suspicious clinical and radiological

evaluation during biological treatment, those with a positive culture were

considered reactivation positive. Of the 12 patients at risk of hepatitis B

reactivation during adalimumab treatment, 8 received entecavir, and 4 received

tenofovir prophylaxis. No hepatitis B reactivation was observed in any of the 12

patients during adalimumab treatment. Among the 54 patients, 4 were at risk of

TB reactivation, and 4 received isoniazid as preophylactic treatment. None of

the 4 patients were observed to have TB reactivation. Adalimumab has become a

frequently preferred drug in the treatment of hidradenitis, and it is known that

there is a risk of hepatitis b and TBc reactivation, which should be prevented.

Despite these risks, we found that adalimumab can be safely used to treat

hidradenitis suppurativa, especially with the use of prophylaxis.

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**38. Sci Rep. 2025 Sep 30;15(1):33941. doi: 10.1038/s41598-025-09171-z.**

Quantifying undetected tuberculosis in Ethiopia using a novel geospatial

modelling approach.

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Tuberculosis (TB) is the leading infectious cause of death globally, with

approximately three million cases remaining undetected, thereby contributing to

community transmission. Understanding the spatial distribution of undetected TB

in high-burden settings is critical for designing and implementing

geographically targeted interventions for early detection and control. This

study presents the first estimates of numbers of undetected TB cases in Ethiopia

at national and local levels using novel geospatial method. We employed a

Bayesian geostatistical modelling framework, incorporating national TB

prevalence survey and TB notification data together with climatic and

environmental variables, to estimate the number of undetected TB cases at

district and national levels. Spatial clustering of undetected TB cases was

assessed using Moran's Index statistic and Local Indicator of Spatial

Autocorrelation (LISA). A Bayesian Poisson regression model with conditional

autoregressive (CAR) prior structure was developed to identify drivers of the

clustering. We estimated a total of 51,041 undetected TB cases (95% CI: 50,599,

51,486) in Ethiopia, with the majority of these cases predicted in the Oromia

region (20,440), Amhara region (9614), and South Ethiopia region (6061). Spatial

clustering of undetected TB cases was observed in districts near the

international borders, including the Ethiopia-Somalia and Ethiopia-Kenya border

regions, as well as in several districts of Southern Ethiopia. The number of

undetected TB cases was negatively associated with the proportion of the

population with good mass media exposure (Incidence rate ratio (IRR): 0.67 95%

CI: 0.56, 0.80) and the proportion of the population with high wealth index

(IRR: 0.73, 95% CI: 0.60, 0.90). Our findings revealed a high burden of

undetected TB in Ethiopia, with spatial clustering in border regions and areas

with limited healthcare access. Targeted TB screening interventions to

communities with low socioeconomic status along with improving mass media

exposure in these regions, could significantly reduce the burden of undetected

TB in Ethiopia.

© 2025. The Author(s).

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**39. Lancet Digit Health. 2025 Sep 29:100895. doi: 10.1016/j.landig.2025.100895.**

**Online ahead of print.**

Digital adherence technology interventions to reduce poor end-of-treatment

outcomes and recurrence among adults with drug-sensitive tuberculosis in

Ethiopia: a three-arm, pragmatic, cluster-randomised, controlled trial.

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**BACKGROUND:** The effect of digital adherence technologies (DATs) on long-term

tuberculosis treatment outcomes remains unclear. We aimed to assess the

effectiveness of DATs in improving tuberculosis treatment outcomes and

recurrence.

**METHODS:** We did a pragmatic cluster-randomised trial in Ethiopia. 78 health

facilities (clusters) were randomised (1:1:1) to smart pillbox, medication

labels, or standard of care. Adults aged 18 years or older with drug-sensitive

pulmonary tuberculosis on a fixed-dose combination tuberculosis treatment

regimen were enrolled and followed up for 12 months after treatment initiation.

Those in the smart pillbox group received a pillbox with customisable

audio-visual reminders, whereas participants in the medications label group

received their tuberculosis medication with a weekly unique code label. Opening

the box or texting the code prompted real-time dose logging on the adherence

platform, facilitating differentiated response to an individual's adherence by a

health-care worker. The primary composite outcome comprised death, loss to

follow-up, treatment failure, switch to drug-resistant tuberculosis treatment,

or recurrence. Secondary outcomes were poor end-of-treatment outcome and loss to

follow-up. Analysis accounted for clustered design with multiple imputation for

the primary composite outcome. The trial is registered with Pan African Clinical

Trials Registry (PACTR202008776694999) and is complete.

**FINDINGS:** From May 24, 2021, to Aug 8, 2022, 8477 individuals undergoing

tuberculosis treatment were assessed for eligibility. Of the 3885 participants

enrolled, 3858 were included in the intention-to-treat population. 1567 (40·6%)

of 3858 participants were women and the median age of all participants was 30

years (IQR 24-40). At 12 months, using multiple imputation, neither the smart

pillbox group (adjusted odds ratio [OR] 1·04 [95% CI 0·74 to 1·45]; adjusted

risk difference: 0·96 percentage points [95% CI -1·19 to 3·11]) nor the

medication labels group (adjusted OR 1·14 [0·83 to 1·61]; adjusted risk

difference: 0·42 percentage points [-1·75 to 2·59]) reduced the risk of the

primary composite outcome. There was no evidence of effect on poor

end-of-treatment outcomes or loss to follow-up in either intervention group,

although the label intervention showed weak evidence of reduced loss to

follow-up. Results were similar in complete case and per-protocol analyses.

**INTERPRETATION:** The DAT interventions showed no reduction in unfavourable

outcomes. This emphasises the necessity to optimise DATs to enhance tuberculosis

management strategies and treatment outcomes.

FUNDING: Unitaid.

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PMID: 41027822

**40. Am J Respir Crit Care Med. 2025 Sep 30. doi: 10.1164/rccm.202506-1489OC. Online ahead of print.**

Transmission of Bedaquiline-resistant Mycobacterium tuberculosis in

KwaZulu-Natal, South Africa.

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**RATIONALE:** Bedaquiline is a critical component of new drug-resistant

tuberculosis (DR-TB) treatment regimens. Emergence of bedaquiline-resistant

Mycobacterium tuberculosis (Mtb) threatens to undermine already limited

treatment options. Understanding the evolution and transmission of

bedaquiline-resistant strains is a high priority for TB control.

**OBJECTIVES:** We evaluated the prevalence, strain genetic diversity, and

transmission of bedaquiline resistance among people with DR-TB.

**METHODS:** We conducted a prospective study of all patients diagnosed with TB

resistant to a fluoroquinolone or a second-line injectable drug in KwaZulu-Natal

province, South Africa, between 2018 and 2022. We utilized whole genome

sequencing (WGS), SNP-based clustering, and Bayesian reconstruction of

transmission trees to examine the genomic characteristics and transmission

networks of bedaquiline-resistant Mtb strains.

**MEASUREMENTS AND MAIN RESULTS:** We enrolled 843 of 1070 eligible individuals and

obtained WGS for 632 participants. Of the sequenced isolates, 14% (n=89) were

genotypically bedaquiline-resistant, 67% (n=60) of which were in clusters of

recently transmitted infections. Resistance was present across all Mtb lineages

and across strains with different resistance profiles to other TB drugs. We

observed no differences in lineage distribution, bedaquiline

resistance-associated mutations, or drug resistance profiles between clustered

and non-clustered isolates. Transmission inference and geographic reconstruction

of transmission networks indicate considerable unsampled cases within

transmission networks.

**CONCLUSIONS:** Bedaquiline resistance was common in this cohort of individuals

with highly DR-TB. Most bedaquiline-resistant infections were attributable to

recent transmission, involving Mtb strains with diverse genetic backgrounds and

a variety of causative mutations. The diversity and transmissibility of

bedaquiline-resistant Mtb signal a growing public health threat.

DOI: 10.1164/rccm.202506-1489OC

PMID: 41026808

**41. J Aerosol Med Pulm Drug Deliv. 2025 Sep 30. doi: 10.1177/19412711251383716.**

**Online ahead of print.**

Development of Exclusive and Efficient Intranasal or Pulmonary Dosing Methods

for a Dry Powder Tuberculosis Vaccine for Use in Nonhuman Primates.

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**Background:** In spite of efforts to eradicate tuberculosis (TB), TB remains the

deadliest infectious disease in the world; there is an urgent need for a

thermostable, noninvasive TB vaccine suitable for distribution in the developing

world. Spray-dried versions of a clinical-stage TB vaccine, ID93 + GLA-SE, are

currently undergoing testing in baboons in both pulmonary and intranasal

versions. We developed manufacturing processes and delivery systems to achieve

delivery of each version to its intended site of action while avoiding

off-target deposition**. Methods:** Pulmonary ID93 + GLA-SE was manufactured in a

custom research-scale spray dryer. Delivery efficiency using a custom

intratracheal insufflator was measured gravimetrically, and aerodynamic

performance was evaluated via cascade impaction. Intranasal ID93 + GLA-SE was

manufactured in a pilot-scale spray dryer. In vitro regional deposition in the

Alberta Idealized Nasal Inlet, measured by LC-MS/MS, was used as a surrogate for

aerodynamic performance; total deposition was used to calculate a total

delivered dose. For both powders, ID93 antigen content was assessed using sodium

dodecyl sulfate-polyacrylamide gel electrophoresis, and GLA-SE adjuvant content

was assessed via HPLC. **Results:** No substantial processing losses of the antigen

or adjuvant were observed after spray drying in either formulation. For the

pulmonary powder, the emitted dose exiting the endotracheal tube across three

tube sizes ranged from 15.9% to 21.4% of the nominal dose; for the 8 mm tube

size, the emitted dose mass median aerodynamic diameter was 5.3 µm, which was

deemed suitable for pulmonary administration. For the intranasal powder, the

delivered dose was 88% ± 2% of nominal, and in vitro deposition in the posterior

nasal cavity was 63% ± 10% of the emitted dose, with minimal anticipated lung

deposition. **Conclusions:** Pulmonary and intranasal spray-dried ID93 + GLA-SE

powders were successfully manufactured. The proposed dosing systems are expected

to achieve exclusive pulmonary or intranasal delivery to nonhuman primates while

requiring only a moderate amount of powder.

DOI: 10.1177/19412711251383716

PMID: 41026578

**42. Antimicrob Agents Chemother. 2025 Sep 30:e0118325. doi: 10.1128/aac.01183-25. Online ahead of print.**

Sterilizing activity of spectinamide MBX-4888A when replacing linezolid in the

Nix-TB regimen in the relapsing BALB/c mouse model of tuberculosis.

Peroutka-Bigus N(1), Scherman MS(1), Kaya F(2), Waidyarachchi SL(3), Liu J(4),

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Spectinamides have garnered interest as experimental tuberculosis therapeutics

owing to their safety profile and efficacy as partner agents when used in

conjunction with established regimens in mice. The Nix-TB regimen of

bedaquiline, pretomanid, and linezolid represents a short, effective regimen

recommended for treatment of pre-extensively drug-resistant tuberculosis.

However, linezolid administration is associated with severe adverse events that

limit its use. Here we present preclinical data comparing Nix-TB regimens

anchored by either linezolid or spectinamide MBX-4888A.

DOI: 10.1128/aac.01183-25

PMID: 41025648

**43. BMC Infect Dis. 2025 Sep 29;25(1):1183. doi: 10.1186/s12879-025-11637-4.**

Mortality and associated factors among children with the double burden of human

immunodeficiency virus and tuberculosis in African countries: a systematic

review and meta-analysis.

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**INTRODUCTION:** The dual burden of Human Immunodeficiency Virus (HIV) and

Tuberculosis (TB) in children is leading to significant mortality. Although

primary studies have reported wide ranges of mortality rates among HIV-TB

co-infected children in various African countries, a comprehensive estimate of

mortality and associated factors is lacking. Therefore, this study aims to

assess mortality and associated factors among HIV-TB co-infected children in

Africa, which will address existing inconsistencies and assist the development

of preventive strategies.

**METHODS:** A systematic search was conducted to retrieve studies from PubMed,

Scopus, Embase, Google Scholar, ScienceDirect, HINARI, and other relevant

sources. All studies conducted in Africa on mortality among HIV-TB co-infected

children were included. The study was reported using the Preferred Reporting

Items for Systematic Reviews and Meta-Analysis (PRISMA) guideline. A

random-effects model was used to estimate the mortality rate, and the Higgins

heterogeneity statistic (I²) was applied to assess variation between studies.

Sub-group analysis and meta-regression were conducted to detect the source of

heterogeneity, while the quality of the studies was assessed using the Newcastle

Ottawa Scale (NOS). Publication bias was checked with the funnel plots and

regression tests. The summary estimates were presented with forest plots and

tables.

**RESULTS:** A total of 30 studies with 13,406 HIV-TB co-infected children between

2007 and 2023 in 11 African countries were included. The pooled estimate of the

mortality rate was 15.89% (95%CI:13.62, 18.17) heterogeneity (I2 = 92.1%,

p < 0.001). The highest mortality was observed in the Central African region

(41.00%, 95% CI: 27.62, 54.37), followed by Western (16.89%, 95% CI: 8.47,

25.32), Southern (14.57%, 95% CI: 10.86, 18.29), and Eastern Africa region

11.33% (95% CI:9.63, 13.04). Factors like being rural residents (Pooled Odds

Ratio (POR) = 1.5, 95% CI: 1.12, 1.90), low hemoglobin (POR = 7.41, 95% CI:

2.20, 12.61), extrapulmonary tuberculosis (EPTB) (POR = 5.67, 95% CI:1.68,

9.66), severe immunosuppression (POR = 5.82, 95% CI: 1.55, 10.08), and poor

antiretroviral therapy (ART) adherence (POR = 10.17, 95% CI: 3.52, 16.82) were

found to increase the odds of mortality. Conversely, Cotrimoxazole Preventive

Therapy (CPT) (POR = 0.38, 95% CI: 0.02, 0.73) was observed as a protective

factor of mortality.

**CONCLUSION:** This study demonstrates that HIV-TB co-infected children in Africa

have a high burden of mortality, underscoring the implementation of dual

infection testing and prompt treatment to achieve the 2030 Sustainable

Development Goal (SDG) target of mortality reduction. To reduce mortality,

strengthening care and treatment are needed with a special focus on rural

residents and regular screening of hemoglobin status, CD4 counts, ART adherence,

and EPTB infection. Besides, CPT provision should be enforced via integrated

HIV-TB health services in the continent.

REVIEW REGISTRATION: It was registered in the International Prospective Registry

of Systematic Reviews (PROSPERO) with registration number CRD42024542095.

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DOI: 10.1186/s12879-025-11637-4

PMCID: PMC12482352

PMID: 41023920 [Indexed for MEDLINE]

**44. BMC Infect Dis. 2025 Sep 29;25(1):1177. doi: 10.1186/s12879-025-11603-0.**

Co-infection of active pulmonary tuberculosis and invasive pulmonary

aspergillosis following a liver transplant: a case report.

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Hospital, Tehran, Iran.

**BACKGROUND:** We report a rare case of co-infection involving pulmonary

tuberculosis and invasive aspergillosis following a liver transplant.

**CASE PRESENTATION:** A 25-year-old female housewife immigrant from Afghanistan,

who had autoimmune hepatitis and underwent a liver transplant, presented with a

history of fever and cough for over a month. Probable diagnosis of pulmonary

tuberculosis and invasive aspergillosis was made by chest CT, as evidenced by a

positive AFB and aspergillosis smear, and MTB PCR, along with the presence of

galactomannan antigen in the BAL fluid. The patient improved after 9 months of

treatment with anti-tuberculosis and anti-fungal.

**CONCLUSIONS:** In an endemic setting, the probability of pulmonary tuberculosis is

elevated, and co-infection with invasive pulmonary aspergillosis, though rare,

is significantly more complex. Early detection and targeted management are

crucial for improving outcomes.

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DOI: 10.1186/s12879-025-11603-0

PMCID: PMC12482388

PMID: 41023837 [Indexed for MEDLINE]

**45. J Med Case Rep. 2025 Sep 29;19(1):460. doi: 10.1186/s13256-025-05376-y.**

Atypical subacute thyroiditis mimicking tuberculosis: a case report and review

of literature.

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**INTRODUCTION:** Subacute thyroiditis is a self-limiting condition caused by

thyroid inflammation. It usually presents with fever, neck pain and symptoms of

thyrotoxicosis. Atypical presentations without neck pain are rare and often lead

to misdiagnosis, especially in low-resource settings.

**CASE REPORT:** We report a case of atypical subacute thyroiditis in a man of

Middle Eastern descent that was initially misdiagnosed as tuberculosis, with

lymphoma, painless sporadic thyroiditis, and laryngeal malignancy being

differentials. The patient, a 41-year-old male, presented with progressively

worsening fevers, night sweats, and weight loss, with thyroid cartilage

thickening and tenderness on physical exam. He was diagnosed with subacute

thyroiditis through Doppler ultrasound scanning of the thyroid gland, elevated

inflammatory markers, and the presence of antibody-negative hyperthyroidism on

his biochemical thyroid screen. Symptomatic relief was provided with salicylate

and prednisolone. The patient experienced transient asymptomatic hypothyroidism

4 months after disease onset, which was not treated. Euthyroidism was achieved

6 months after symptom onset.

**CONCLUSION:** Subacute thyroiditis is a rare disease thought to be postviral in

origin. It generally presents with fever, neck pain, and signs of thyrotoxicosis

and evolves in three phases-a hyperthyroid, hypothyroid, and euthyroid phase.

Atypical subacute thyroiditis without neck pain is even rarer; therefore,

clinicians should maintain a high index of suspicion for thyroid disorders

whenever symptoms suggestive of thyrotoxicosis are encountered, and should

always consider thyroid abnormalities when investigating weight loss or

persistent fevers in an African setting.

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DOI: 10.1186/s13256-025-05376-y

PMCID: PMC12481771

PMID: 41023757 [Indexed for MEDLINE]

**46. J Med Case Rep. 2025 Sep 29;19(1):466. doi: 10.1186/s13256-025-05558-8.**

Fatal acute miliary tuberculosis complicated by obstructive jaundice, acute

pancreatitis, and hemophagocytic lymphohistiocytosis in a 57-year-old

immunocompetent female: a case report.

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**BACKGROUND:** Miliary tuberculosis occurs in 2% of all patients with tuberculosis

when Mycobacterium tuberculosis circulates in the bloodstream, leading to

various nonspecific features. Delayed diagnosis and treatment are associated

with poor prognosis and outcomes, with complications becoming life-threatening,

making management very challenging for clinicians.

**CASE PRESENTATION:** A 57-year-old immunocompetent Pakistani female presented with

nonspecific features, and further investigations yielded a diagnosis of miliary

tuberculosis, accompanied by several rare complications, including pancreatitis,

obstructive jaundice, acute respiratory distress syndrome, disseminated

intravascular coagulation, hemophagocytic lymphohistiocytosis syndrome, and

liver failure. Management was challenging, and the patient subsequently died

owing to further derangement in liver function.

**CONCLUSION:** Miliary tuberculosis may present with nonspecific features and

symptoms, and a thorough correlation between clinical examination, radiological

findings, and laboratory tests is required to establish the diagnosis. The

delayed diagnosis and treatment of miliary tuberculosis majorly affect patient

outcomes. The progression of the disease is unpredictable, and several

complications, although rare, may occur all at once, emphasizing the importance

of multidisciplinary collaboration between specialists. Hemophagocytic

lymphohistiocytosis symptoms may overlap with miliary tuberculosis symptoms, and

antituberculosis therapy medications are irreplaceable in the treatment of

tuberculosis-related hemophagocytic lymphohistiocytosis. Immunocompetence is not

a basis for excluding miliary tuberculosis.

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DOI: 10.1186/s13256-025-05558-8

PMCID: PMC12482558

PMID: 41023720 [Indexed for MEDLINE]

**47. Sci Rep. 2025 Sep 29;15(1):33454. doi: 10.1038/s41598-025-99053-1.**

In vitro investigation of Datura innoxia phytocompounds against Mycobacterium

tuberculosis H37Ra strain in association with in silico studies.

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Tuberculosis (TB) is a recurrent and progressive bacterial disease caused by

Mycobacterium tuberculosis (Mtb), posing a significant challenge globally due to

its drug resistance. This study focuses on identifying natural phytocompounds

from the plant Datura innoxia (leaves), which is well known for its biologically

active metabolites. Initially, the current study employed in vitro analysis of

20 phytocompounds, revealing that the natural compound 9, o-vanillin, exhibited

the best minimal inhibitory concentration (MIC) which was 12.5 µg/mL, and

minimal bactericidal concentration (MBC) was 50 µg/mL, all other phytocompounds

showing remarkable antitubercular activity against the Mtb H37Ra strain. The

molecular docking and simulation also validated the strong affinity and stable

binding interactions between compound 9 and target protein kinase. The

pharmacokinetic analysis highlighted the suitable oral bioavailability and no

significant CYP450 inhibition for the lead compound 9, reducing the risk for

drug-drug interactions. Moreover, the density functional theory analysis of lead

compound 9 demonstrated optimal molecular properties, further contributing to

the chemical stability and reactivity. Therefore, these results suggest that D.

innoxia contains the potent phytocompound o-vanillin, which possesses

antitubercular activity and can potentially be used as a drug against TB.

However, future studies will focus on in vivo validation and formulation

development for clinical applications.

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DOI: 10.1038/s41598-025-99053-1

PMCID: PMC12479965

PMID: 41023414 [Indexed for MEDLINE]

**48. NPJ Prim Care Respir Med. 2025 Sep 29;35(1):40. doi: 10.1038/s41533-025-00449-3.**

Psychosocial interventions to improve tuberculosis preventive treatment uptake

and psychosocial outcomes: a systematic review.

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Despite its importance in global TB elimination, tuberculosis preventive

treatment (TPT) remains underutilized. Psychosocial barriers significantly

contribute to this issue. This systematic review aims primarily to synthesize

psychosocial interventions to improve the initiation of TPT. We analyzed

psychosocial outcomes as secondary objectives when relevant data were available.

This review included studies indexed in PubMed, Scopus, and PsycInfo until

August 25, 2025. Original studies addressing psychosocial interventions for

people with latent tuberculosis infection (LTBI) indicated for TPT were included

in this review. The risk of bias was assessed via the Crowe Critical Appraisal

Tool (CCAT). A narrative synthesis summarized the characteristics of

interventions, including the format of delivery, settings, intervention

providers, psychosocial content, duration, and outcomes. Among the 1725

identified studies, nine (14,428 participants) met the inclusion criteria. The

CCAT classification was moderate to high quality, with strengths in clearly

articulated study rationales but weaknesses in study design. Most studies were

from upper-middle-income countries with a high burden of TB; none were from

Asia. Health education is a core component, often incorporating culturally

adapted survivor testimonials to reduce stigma and increase motivation.

Interventions were mostly community-based and led by multidisciplinary

healthcare professionals and community workers. TPT initiation improved in all

included studies, with risk differences ranging from 10-52%. This review

emphasizes the potential of psychosocial interventions in supporting behavior

change and increasing TPT initiation. Methodological limitations and a lack of

research in high-burden Asian contexts restrict the current evidence. Future

studies should focus on developing rigorous, contextually appropriate strategies

for scalable psychosocial interventions that are effective and sustainable.

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DOI: 10.1038/s41533-025-00449-3

PMCID: PMC12480859

PMID: 41022732 [Indexed for MEDLINE]

**49. BMJ Case Rep. 2025 Sep 28;18(9):e267999. doi: 10.1136/bcr-2025-267999.**

Tuberculous monoarthritis in a rituximab-treated patient with rheumatoid

arthritis: diagnostic and therapeutic challenges in a tuberculosis-endemic

region.

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A woman in her 60s with seropositive rheumatoid arthritis developed tuberculous

arthritis of the wrist following rituximab therapy, despite negative latent

tuberculosis (TB) screening. Although rituximab is considered safer than

anti-TNF agents in terms of TB risk, this case highlights a rare yet serious

complication. Diagnosis was confirmed via synovial fluid analysis after

persistent monarthritis unresponsive to standard RA therapy. Management was

complicated by drug-induced liver injury and ototoxicity, leading to multiple

modifications of anti-tubercular therapy. The therapeutic dilemma centred on

balancing effective TB treatment with drug tolerability, necessitating a

cautious, stepwise reintroduction of first-line agents. Despite these

challenges, the patient achieved full recovery and later resumed low-dose

methotrexate for RA. This case underscores the importance of considering TB even

with negative screening and demonstrates that individualised therapy can

overcome complex treatment barriers in immunosuppressed patients in TB-endemic

settings.

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PMID: 41022420 [Indexed for MEDLINE]

**50. Chembiochem. 2025 Sep 29:e202500529. doi: 10.1002/cbic.202500529. Online ahead of print.**

Five-In-One Antibacterial Strategy: A Mn(I) Complex Lights Up the Fight Against

Tuberculosis.

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Tuberculosis, which the WHO describes as the "world's top infectious killer,"

demands novel combating strategies rather than conventional ones, as the

situation of Mycobacterium tuberculosis (Mtb) resistance to therapeutic drugs is

continuous, leading to millions of deaths each year. In a recent study, Lai et

al. report a manganese(I)-based photoactivatable carbon monoxide-releasing

molecule (Mn-PTP) that unifies photodynamic therapy, transition metal

reactivity, and carbon monoxide (CO) delivery into a single light-activated

therapeutic platform. Upon white-light irradiation, Mn-PTP releases CO,

generates both type I and type II reactive oxygen species (ROS), liberates a

toxic antibacterial ligand (PTP), and forms catalytically active manganese

oxides (MnOx) species that decompose intracellular hydrogen peroxide (H2O2),

thereby alleviating hypoxia and amplifying ROS generation. Mn-PTP demonstrates

high selectivity for Mycobacterium smegmatis with, potent in vitro antibacterial

activity (MIC90 = 3.11 μM), robust biofilm disruption of M. smegmatis, and

minimal cytotoxicity to normal cells. In in vivo, the compound significantly

accelerates wound healing in infected mice, outperforming isoniazid. This

highlight discusses Mn-PTP as a powerful "one-for-all" agent which, upon

irradiation, releases five key components that, much like the five fingers

through coordinated action, form a fist that effectively combats and eliminates

bacterial infections, offering a powerful blueprint for next-generation

metal-based therapeutics against persistent mycobacterial infections.

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DOI: 10.1002/cbic.202500529

PMID: 41021835

**51. PLoS One. 2025 Sep 29;20(9):e0333662. doi: 10.1371/journal.pone.0333662.**

**eCollection 2025.**

Active case finding for tuberculosis in tea gardens of Bangladesh: A

cross-sectional survey.

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Tea garden populations with poor socio-economic status are at risk of developing

TB. The active case finding (ACF) approach is effective in finding TB among the

people at risk. We have conducted ACF for TB to find people with presumptive TB

in the tea gardens of Sylhet division to identify TB disease. It was a

cross-sectional survey conducted at the household level, in the randomly

selected three tea gardens of Sylhet division. The selected population was

20,215 and was screened for TB presumptive symptoms between July and Oct 2022.

Each presumptive had required TB testing, which includes GeneXpert MTB/RIF

(Xpert) or Sputum microscopy, X-ray, and Fine Needle Aspiration Cytology (FNAC)

if there was gland swelling. Around 99.6% (20,127/20,215) of the surveyed

population were screened for TB. Among the screened population, gender

distribution was almost equal, and 34% had no education. And people with

presumptive TB were 0.8%; among them, most (91%) were pulmonary TB presumptive

with male predominance. Among all presumptive, 87.4% had a cough for ≥ 14 days

and 78% had a fever. We identified a total of 17 pulmonary TB; among them,

bacteriologically confirmed TB were only 6 (35.3%). The estimated proportion of

TB among the surveyed population was 0.10%. The findings suggest a need for

sustained TB screening activities integrated with community involvement.

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PMCID: PMC12478949

PMID: 41021625 [Indexed for MEDLINE]

**52. Vet Res Commun. 2025 Sep 29;49(6):336. doi: 10.1007/s11259-025-10906-6.**

Mycobacterial infections in cats and a dog: A case series from Southern Brazil

and one health implications.

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Lopes BC(2), Cerva C(3), Lerner DD(4), Bianchi MV(5), Rodrigues ACB(6),

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Infections by M. avium and M. tuberculosis in companion animals are little

reported. This case series describes four instances of mycobacterial infections

in companion animals (three cats and one dog) in southern Brazil. We detail the

diagnostic challenges and emphasize their epidemiological relevance in a One

Health context. Histopathology, acid-fast bacilli staining, mycobacterial

culture and PCR were used to confirm the infections. Clinical presentations,

diagnostic workups, and therapeutic outcomes were reviewed. One case involved

disseminated infection by M. avium in a cat with partial therapeutic success,

representing the first such case reported in Rio Grande do Sul. Two cats were

diagnosed with disseminated M. tuberculosis var bovis infection, all with a

fatal outcome. A final case of M. tuberculosis var tuberculosis in a dog showed

multisystemic dissemination and was linked to an owner previously treated for

TB. These findings highlight the underrecognized role of companion animals in

the epidemiology of mycobacterial infections in Brazil. Increased awareness and

surveillance are needed, particularly in rural settings. A One Health approach

is crucial for mitigating risks to both animal and human health.

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PMID: 41021062 [Indexed for MEDLINE]

**53. Clin Case Rep. 2025 Sep 24;13(10):e71013. doi: 10.1002/ccr3.71013. eCollection 2025 Oct.**

Frontal Tuberculoma Presenting With Atypical Foster Kennedy Syndrome in a

Pregnant Patient.

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Foster Kennedy syndrome (FKS), accounting for 1%-2.5% of intracranial masses,

typically arises in the frontal lobe and may result from various etiologies,

including rare causes such as tuberculoma. Although the incidence of central

nervous system (CNS) tuberculosis is increasing, published reports in this

setting remain scarce. We report the case of a 32-year-old pregnant woman with a

history of childhood asthma who presented with progressive headaches and

neurological symptoms. Initially treated for eclampsia, she was later referred

for neurological assessment. Clinical evaluation and neuroimaging revealed a

supratentorial, intra-axial lesion in the left frontal lobe. Surgical resection

and histopathology confirmed a cortico-subcortical lesion, prompting further

investigations, including GeneXpert testing, lumbar puncture (LP), and chest

imaging. Antituberculous therapy was initiated upon confirmation of tuberculoma

and identification of a probable pulmonary focus. This case illustrates an

atypical form of FKS secondary to frontal tuberculoma with cerebrospinal fluid

(CSF) disruption in the absence of meningitis-an exceptionally rare

presentation. It highlights the importance of considering tuberculoma in the

differential diagnosis of intracranial masses, particularly in endemic regions.

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**54. EClinicalMedicine. 2025 Sep 17;88:103511. doi: 10.1016/j.eclinm.2025.103511.**

**eCollection 2025 Oct.**

Antitubercular therapy for uveitis of undetermined cause with positive

interferon-gamma release assay: a single-blind, single-centre, phase 2

randomised controlled trial.

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Edwar L(1), Susiyanti M(1), Aziza Y(1), Waliyuddin MZ(1), Widodo E(1), Sifyana

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**BACKGROUND:** No randomised controlled trial (RCT) has previously evaluated the

effect of antitubercular therapy (ATT) in patients with uveitis of undetermined

cause who tested positive on interferon-gamma release assays (IGRA), despite the

absence of other identifiable causes of uveitis. We aimed to assess the efficacy

and safety of treatment involving ATT compared to treatment without ATT in these

patients, with respect to uveitis resolution and reduction in the risk of

relapse.

**METHODS:** We conducted a single-blind, single-centre, phase 2 RCT at the uveitis

clinic of Cipto Mangunkusumo Hospital in Jakarta, Indonesia, from August 16,

2021, to February 5, 2024. Seventy-six adults with newly diagnosed, active

uveitis of undetermined cause and a positive IGRA were randomised 1:1 using

block randomisation (block size 4) into two groups. Participants in the ATT

group received an additional full course of ATT in addition to systemic

corticosteroids. The control group received systemic corticosteroids without

ATT. Investigators were masked to group assignment. The primary endpoint was the

complete resolution of uveitis six months after randomisation. The trial is

registered at ClinicalTrials.gov (NCT05005637).

**FINDINGS:** Seventy-six participants were randomly assigned to either ATT (n = 37)

or control (n = 39) group. At primary end point, more participants assigned to

the ATT group achieved the primary outcome of complete uveitis resolution

compared to the control group (30/37, 81.1% vs. 20/39 participants; 51.3%,

relative risk [RR] 1.58, 95% CI 1.12-2.23, p = 0.0060). Over the subsequent

follow-up period, complete uveitis resolution was observed in 34 and 24

participants assigned to the ATT and the control groups, respectively.

Additionally, uveitis relapse occurred in fewer participants assigned to the ATT

group compared to those assigned to the control group (2/34 participants, 5.9%

vs. 7/24 participants, 29.2%; HR 0.20, 95% CI 0.05-0.89, p = 0.0210). The

findings regarding uveitis resolution and relapse rates were consistent in the

per-protocol analysis.

**INTERPRETATION: I**n IGRA-positive patients with uveitis of undetermined cause,

initial treatment with ATT resulted in a significant benefit over those not

receiving ATT.

FUNDING: This work was supported by RISPRO-LPDP (Riset Inovatif

Produktif-Lembaga Pengelola Dana Pendidikan).

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**55. Infect Dis (Lond). 2025 Sep 29:1-10. doi: 10.1080/23744235.2025.2563642. Online ahead of print.**

Comparison between osteoarticular tuberculosis and nontuberculous mycobacterial

infection: a retrospective observational cohort study.

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**BACKGROUND**: Osteoarticular mycobacterial infections significantly impact patient

health by causing severe joint and bone diseases. However, clinical experience

in diagnosis and treatment remains limited.

**OBJECTIVES:** We investigated the clinical characteristics and prognosis of

patients with osteoarticular mycobacterial infection.

**METHODS:** We retrospectively enrolled 74 adult patients diagnosed with

osteoarticular mycobacterial infection, including 57 (77%) with tuberculosis

(TB) and 17 (23%) with non-tuberculous mycobacteria (NTM) infection, between

January 2009 and January 2023 from a tertiary hospital in Korea. Osteoarticular

mycobacterial infection was defined as the presence of osteoarticular infection,

including prosthetic joint infection, diagnosed using clinical and radiological

findings, and aspirate or tissue culture positive or polymerase chain reaction

positive for Mycobacterium tuberculosis complex or NTM.

**RESULTS:** Several differences were observed in the predisposing factors, affected

sites and multifocal infections between the osteoarticular TB and NTM infection

groups. The proportion of disseminated infection in patients with TB was higher

than that in those with NTM infection (40% vs. 6%, p = .008). The positivity

rate of acid-fast bacilli stain, mycobacterial culture, molecular testing and

histological examination in all patients was 34%, 89%, 79% and 51%,

respectively. Culture-positive or PCR-positive specimens from another site

(respiratory specimens, pleural fluid, urine or blood) were collected from 22

patients (30%). Anti-mycobacterial therapy combined with surgical treatment was

performed in 77% of all follow-up patients, and clinical failure occurred in

19%.

**CONCLUSIONS:** These findings suggest that, given the differences in optimal

treatments, using multiple diagnostic modalities to detect microbiological

evidence for discriminating NTM infection from TB is essential.

DOI: 10.1080/23744235.2025.2563642

PMID: 41017732

**56. Can J Neurol Sci. 2025 Sep 29:1-49. doi: 10.1017/cjn.2025.10436. Online ahead of print.**

Movement Disorders in Central Nervous System Tuberculosis: A Systematic Review.

Garg RK, Pandey S, Mahdi RA, Singhal S.

DOI: 10.1017/cjn.2025.10436

PMID: 41017616

**57. Econ Hum Biol. 2025 Sep 23;59:101537. doi: 10.1016/j.ehb.2025.101537. Online**

**ahead of print.**

Maternal mortality, tuberculosis and social deprivation in Madrid during the

second and third decades of the 20th century.

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In this paper we jointly study maternal mortality and tuberculosis during the

second and third decades of the 20th century in Madrid. Nicknamed the "city of

death", the Spanish capital was marked by a high mortality where tuberculosis

accounted for approximately 26/28 % of all deaths of women of reproductive age.

Using a large longitudinal individual-level database including causes of death,

we discuss the definitions of maternal mortality, then highlight its high level

in the Spanish capital. However, the risk of dying was significantly lower for

migrant women than for native. In the context studied, an evident example of the

"healthy migrant" paradox with selection at origin is outlined. At the same

time, there are clear links between tuberculosis as a cause of death during the

60 days following a delivery and the socio-spatial inequalities characteristic

of a city that saw wealthy areas side by side with disadvantaged areas,

characterized by low standards of living conditions and insufficient hygiene.

The results of the statistical models analyzed are controlled for geographic,

social and biological variables in addition to individual demographic

characteristics. The robustness of the results is ensured by the size of the

sample used, which allowed us to study an event - a death following delivery -

that, even at the time of this study, was rare.

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DOI: 10.1016/j.ehb.2025.101537

PMID: 41043215

**58. Front Immunol. 2025 Sep 17;16:1662454. doi: 10.3389/fimmu.2025.1662454.**

**eCollection 2025.**

Clinical laboratory analytes and platelet-associated parameters as surrogate

markers of subclinical inflammation in latent tuberculosis infection.

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Frederick A(5), Rajeshkumar M(6), Kumar MS(1), Sampath P(1), Sankar G(6), Roy

CL(2), Karishma SJ(7), Murugesan A(8), Balakrishnan P(9), Govindaraj S(10),

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(#)Contributed equally

**BACKGROUND**: The global burden of latent tuberculosis infection (LTBI), with

one-third of the population, poses a significant challenge in the diagnosis and

treatment of TB. Household contacts (HHCs) of active TB-infected individuals are

one of the major high-risk groups for whom early screening and timely

intervention are highly critical to interrupt TB transmission. The subclinical

latent infection transitions into active TB disease due to multiple factors.

Laboratory diagnostic markers inherent to interferon-gamma release assay (IGRA)

positive and negative HHCs may help predict the risk of LTBI and subsequent

reactivation. The study aims to identify biochemical and hematological

diagnostic markers associated with HHCs and their IGRA status, and to explore

the likelihood of clinical laboratory analytes and platelet-associated

parameters for use as surrogate markers of subclinical inflammation in LTBI.

**METHODS:** A cross-sectional study was carried out on the HHCs of active

TB-infected individuals and healthy controls to determine the association of

biochemical and hematological markers with their IGRA status. Blood samples

collected from the participants were tested for different laboratory parameters

and analyzed by binary regression analysis to determine their efficacy in

predicting the development of LTBI.

**RESULTS:** Erythrocyte sedimentation rate (ESR), mean platelet volume (MPV),

D-dimer, platelet-large cell ratio (P-LCR), and platelet distribution width

(PDW) were significantly high among LTBI-positive individuals. Among different

markers, significant association with LTBI was observed with ESR, PDW, and

P-LCR, with their AUC and p values reported as 0.6950 (p=0.0095\*\*), 0.7333

(p=0.0469\*), 0.7150 (p=0.0042\*\*), respectively. Binary regression analysis

revealed significantly higher odds of LTBI in individuals with elevated ESR (OR

= 3.05), PDW (OR = 4.67), MPV (OR = 3.5), and P-LCR (OR = 7.67).

**CONCLUSION:** Our study demonstrated clinical laboratory parameters and platelet

indices as useful surrogate markers of subclinical inflammation associated with

LTBI.

Copyright © 2025 Selvavinayagam, Anusree, Yong, Sankar, Frederick, Rajeshkumar,

Kumar, Sampath, Sankar, Roy, Karishma, Murugesan, Balakrishnan, Govindaraj,

Byrareddy, Velu, Shankar, Larsson, Kannan and Raju.

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PMCID: PMC12484228

PMID: 41041335 [Indexed for MEDLINE]

**59. J Family Med Prim Care. 2025 Aug;14(8):3556-3559. doi:**

**10.4103/jfmpc.jfmpc\_1279\_24. Epub 2025 Sep 24.**

Tuberculosis-related vasculitis presenting as multisystem organ infarcts: A case

report.

Saini K(1), Kampani G(1), Rawat R(1), Jain S(1).

Author information:

(1)Department of Medicine, ABVIMS and Dr Ram Manohar Lohia Hospital, New Delhi,

India.

Tuberculosis (TB) continues to be a major global health concern, particularly in

regions where it is endemic. While TB commonly affects the lungs and

extrapulmonary sites, its presentation as vasculitis leading to multiple organ

infarcts is an extremely rare phenomenon. This case report describes a

34-year-old female who developed simultaneous infarctions in the spleen, kidney,

and lungs due to TB-related vasculitis. The diagnosis was established through

clinical presentation, imaging studies, and confirmation of Mycobacterium

tuberculosis via sputum CBNAAT. The patient was successfully managed with

antitubercular therapy (ATT) and corticosteroids, demonstrating significant

clinical improvement. The rarity of multisystem infarcts caused by TB

underscores the importance of considering tuberculous vasculitis in the

differential diagnosis of unexplained infarcts, particularly in endemic regions.

Early detection and timely intervention are crucial in preventing severe

complications and improving patient outcomes.

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DOI: 10.4103/jfmpc.jfmpc\_1279\_24

PMCID: PMC12488083

PMID: 41041245

**60. J Family Med Prim Care. 2025 Aug;14(8):3586-3588. doi:**

**10.4103/jfmpc.jfmpc\_171\_25. Epub 2025 Sep 24.**

Kikuchi-Fujimoto disease misdiagnosed as tubercular lymphadenitis: A puzzle in

cervical lymph nodes.

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Kikuchi-Fujimoto disease (KFD) is a rare and benign condition characterized by

regional necrotizing lymphadenopathy. Acute or subacute painful cervical

lymphadenopathy is the most common clinical presentation. The characteristic

morphology in histopathologic examination of the lymph node specimen is

diagnostic of KFD. Fine needle aspiration cytology (FNAC), often employed as the

initial diagnostic method, gives inconclusive results due to inadequate

specimens. Our patient was a 36-year-old woman who presented with cervical

lymphadenopathy for six weeks. Despite an inconclusive FNAC result, she was

treated with empirical antituberculosis therapy (ATT). Later, she was diagnosed

with KFD in our facility on excisional lung biopsy in view of non-improvement

with ATT. Ambiguous cytological findings may usually lead to the initiation of

empirical ATT since tuberculosis (TB) is a major cause of cervical

lymphadenitis, particularly in TB-endemic areas. As a result, there is not only

a delay in the management of the actual disease, but also a chance of developing

adverse reactions to ATT.

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PMCID: PMC12488096

PMID: 41041201

**61. J Family Med Prim Care. 2025 Aug;14(8):3451-3455. doi:**

**10.4103/jfmpc.jfmpc\_16\_25. Epub 2025 Sep 24.**

Evaluation of intensified case finding of tuberculosis using four symptom

complex screening through reach, effectiveness, adoption, implementation,

maintenance (RE-AIM) framework in Puducherry.

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**INTRODUCTION:** Tuberculosis (TB) remains the leading infectious cause of death

worldwide, with co-morbidities such as diabetes mellitus (DM) significantly

increasing the risk of developing TB and leading to poor treatment outcomes. The

End TB Strategy and Sustainable Development Goals emphasize addressing TB

co-morbidities to achieve TB elimination. We have assessed the impact of

implementing joint TB-DM collaborative activities using the Reach,

Effectiveness, Adoption, Implementation, Maintenance (RE-AIM) framework in a

tertiary care setting.

**OBJECTIVES:** This study aimed at evaluating the impact of the execution of the

TB-DM collaborative activity, using the RE-AIM framework.

**MATERIAL AND METHODS:** This study was undertaken by the Department of Community

Medicine, in outpatient departments (OPDs) at Sri Manakula Vinayagar Medical

College and Hospital (SMVMCH), Puducherry from March 2021 to September 2022. The

study involved three phases: qualitative design of intervention strategies,

quantitative pre- and post-intervention evaluation, and post-intervention

qualitative assessment. Interventions included sensitization programs for

healthcare professionals, the use of Institutional Ethics Committee (IEC)

materials, and systematic screening of DM patients using the 4s complex (cough

>2 weeks, fever >2 weeks, night sweats, weight loss). The outcome of the

implementation of TB-DM collaborative activity was evaluated using the RE-AIM

framework.

**RESULTS:** The application of the RE-AIM framework for joint TB-DM collaborative

activities emphasized healthcare professional sensitization, IEC material

development, and effective inter-departmental collaboration. Key outcomes

included enhanced TB case detection through 4s screening, improved knowledge

among healthcare professionals, and sustainable integration of interventions

into routine practices for long-term impact.

**CONCLUSION:** Implementation of the 4s complex screening activity improved TB

detection among DM patients and demonstrated the feasibility and effectiveness

of joint TB-DM collaborative strategies. The RE-AIM framework provided a

structured evaluation, highlighting the intervention's strengths and areas for

improvement. Sustaining these efforts and expanding to other high-risk groups is

critical to achieving TB elimination targets.

Copyright: © 2025 Journal of Family Medicine and Primary Care.

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PMID: 41041191

**62. bioRxiv [Preprint]. 2025 Sep 27:2025.09.26.678883. doi:**

**10.1101/2025.09.26.678883.**

Pyrazinamide kills Mycobacterium tuberculosis via pH-driven weak-acid permeation

and cytosolic acidification.

Laudouze J, Rokitskaya TI, Abolet A, Point V, Firsov AM, Khailova LS, Cavalier

JF, Canaan S, Baulard AR, Antonenko YN, Gouzy A, Santucci P.

Pyrazinamide (PZA) is a cornerstone drug in tuberculosis (TB) treatment with a

strong bactericidal activity in vivo on both actively and non-replicating

bacterial subpopulations. Yet the precise mode of action of its active form,

pyrazinoic acid (HPOA), remains unclear. In this study, we comprehensively

explore and challenge the two major and conflicted models of PZA mode of action.

The pH-dependent model, where the drug is mostly effective at acidic pH by

acidifying Mycobacterium tuberculosis ( Mtb ) cytosol, and the PanD-dependent

model where PZA's active form targets the aspartate decarboxylase PanD,

therefore depleting pantothenate and subsequently coenzyme A (CoA) levels

regardless of the surrounding pH. By combining standard antimicrobial

susceptibility testing at various pH with fluorescence-based live recording of

Mtb intrabacterial pH, we demonstrate that PZA kills Mtb by decreasing

intrabacterial pH, independently of pantothenate levels. Comparative studies

between a prototrophic Mtb strain and a pantothenate auxotrophic mutant lacking

the panCD locus confirmed that PZA bactericidal activity is primarily driven by

pH and its ability to acidify Mtb cytosol, independently of the aspartate

decarboxylase PanD. Bio-electrophysiology experiments revealed that acidic pH

promotes the conversion of the pyrazinoate anion POA⁻ into HPOA which in turn

acts as conventional weak acid that facilitates membrane permeation and

cytosolic acidification. Finally, using custom-based culture media, we

demonstrate that PZA displays heterogeneous efficacy according to the media

composition, therefore proposing a revisited biological model that might explain

the discrepancies around PZA's unique mode of action. Overall, this work

constitutes the first comprehensive side-by-side investigation of the two models

and univocally supports a pH-dependent mechanism of action underlying PZA

sterilizing activity, providing new insights for the development of more

effective PZA-like drugs.

DOI: 10.1101/2025.09.26.678883

PMCID: PMC12486132

PMID: 41040375

**63. bioRxiv [Preprint]. 2025 Sep 25:2025.09.23.678181. doi:**

**10.1101/2025.09.23.678181.**

Direct nanopore sequencing of M. tuberculosis on sputa and rescue of suboptimal

results to enhance transmission surveillance.

Saleeb SM, Marcos-Abellán A, Fernández MTC, Vallejo-Godoy S, Martínez-Lirola M,

Ramirez GB, Herranz-Martín M, Buenestado-Serrano S, Pardo-Diaz A, Serrano MJR,

Muñoz P, Pérez-Lago L, García de Viedma D.

Whole-genome sequencing (WGS) enhances precision in predicting antimicrobial

resistance and tracking Mycobacterium tuberculosis (MTB) transmission. Due to

MTB's slow-growing nature, genomic results are delayed; however, few efforts

have sought to accelerate them by performing WGS directly on respiratory

specimens. Most culture-free efforts have focused on accelerating resistance

prediction. The present study provides further evidence to the only preceding

study aiming to accelerate precise delineation of transmission, coupling

culture-free WGS to a surveillance programme. Our study is distinguished from

its predecessor by being the first to apply flexible nanopore sequencing to

further accelerate the process. A total of 71 sputa were selected, in which we

applied only a procedure to deplete human DNA, thus avoiding costly and

cumbersome capture-bait alternatives. Optimal results (>90% genome covered, mean

coverage >45× and >70% genome covered >20×) were obtained from 33.8% of cases,

allowing the assignment to transmission clusters close to diagnosis of every new

case. A further 12.6% of samples yielded suboptimal results (15.5%-90.92% at

>10×), which were exploited through a rescue pipeline. This approach was based

on identifying informative SNPs acting as markers for relevant transmission

clusters in our population. The pipeline enabled pre-allocation of new cases to

pre-existing clusters and, in some cases, precise genomic relationships with the

preceding cases in the cluster. In summary, this study demonstrates that

epidemiologically valuable information can be obtained directly from sputum in

approximately half the samples analysed. It represents a new advancement in the

pursuit of faster comparative genomics, with epidemiological purposes, at

diagnosis.

DOI: 10.1101/2025.09.23.678181

PMCID: PMC12485859

PMID: 41040363

**64. bioRxiv [Preprint]. 2025 Sep 24:2025.09.24.678100. doi:**

**10.1101/2025.09.24.678100.**

Mycobacterium tuberculosis growth arrest on propionate at acidic pH is

suppressed by mutations in phoPR and pyrazinamide treatment.

Murdoch H, Dechow SJ, Abdalla BJ, Abramovitch RB.

Mycobacterium tuberculosis (Mtb) arrests its growth at acidic pH, when grown on

specific single carbon sources, including propionate. To understand the basis of

the propionate-driven growth arrest at acidic pH, we conducted a genetic

selection for mutants enabling growth on propionate at pH 5.7. All the selected

mutants had insertions in the two-component regulatory genes phoR or phoP . We

hypothesized that growth arrest at acidic pH is caused by PhoPR diverting carbon

from central carbon metabolism towards lipid anabolism and that when PhoPR is

inactivated, growth is promoted through metabolizing propionate by the methyl

citrate cycle (MCC) into pyruvate, a permissive carbon source for growth at

acidic pH. Using chemical inhibition and mutants of the MCC pathway, we

demonstrate that the enhanced growth is dependent on the MCC. Furthermore,

stimulating lipid synthesis via the methylmalonyl-CoA pathway by adding Vitamin

B12 restricts growth in the ΔphoPR mutant and, conversely, restricting lipid

anabolism by inhibiting the triacylglycerol (TAG) synthase tgs1 enhances growth

of the ΔphoPR mutant. Notably, CoA pools increased in the ΔphoPR mutant grown on propionate, directly supporting our model. Given the role of CoA metabolism in

pyrazinamide sensitivity, Mtb sensitivity to pyrazinamide was examined on

propionate at acidic pH. Surprisingly, pyrazinamide treatment of WT Mtb

suppresses growth arrest on propionate at acidic pH. In contrast, the phoPR

mutant has enhanced sensitivity to pyrazinamide. Together, these findings

support that propionate-driven growth arrest at acidic pH is caused by metabolic

remodeling that is regulated by PhoPR and is associated with pyrazinamide

sensitivity.

**IMPORTANCE:** When grown on certain single carbon sources, such as propionate, Mtb

arrests its growth at acidic pH and establishes a state of non-replicating

persistence (NRP). To understand the genetic basis of this growth restriction, a

genetic selection was performed to identify mutants unable to arrest growth at

acidic pH with propionate as a sole carbon source. The selection exclusively

identified mutants in the PhoPR two-component regulatory system, which functions

to modulate cell envelope lipids and redox homeostasis through the upregulation

of lipid synthesis at acidic pH. We demonstrate that PhoPR arrests growth at

acidic pH by diverting carbon away from the methyl citrate cycle towards lipid

anabolism. Surprisingly, treatment of Mtb with pyrazinamide at acidic pH on

propionate also enabled growth. These data suggest that drug susceptibility may

be impacted by enhanced growth and metabolic capacity of Mtb in acidic and

propionate-rich environments, such as within the macrophage or the granuloma.

DOI: 10.1101/2025.09.24.678100

PMCID: PMC12485784

PMID: 41040295

**65. bioRxiv [Preprint]. 2025 Sep 24:2025.09.24.678246. doi:**

**10.1101/2025.09.24.678246.**

Structure-Guided Development of a Potent BioA Inhibitor Validates Biotin

Synthesis Inhibition as a Therapeutic Strategy for Tuberculosis.

Liu Q, Wallach JB, Jayasinghe YP, Sullivan MR, Proietto J, Rodriguez S, Vo S,

Boshoff HIM, Jia Z, Ostrer L, Mehdiratta K, Shi R, Dartois V, Baughn AD, Rubin

EJ, Ronning DR, Zimmerman MD, Schnappinger D, Aldrich CC.

Structure-guided optimization was applied to develop a potent and selective

inhibitor of the aminotransferase BioA, a key enzyme in bacterial biotin

biosynthesis. Strategic modifications of a screening hit enhanced potency and

pharmacokinetics, yielding C48 , which binds BioA with a K i of 200 pM and

displays sub-micromolar MICs against Mycobacterium tuberculosis (Mtb) and

nontuberculous mycobacteria. Biochemical, structural, and genetic studies

confirmed C48 's mechanism of action. In vitro, C48 induced cell envelope stress

and membrane remodeling, mimicking biotin starvation. Pharmacokinetic profiling

revealed excellent oral bioavailability resulting in over 39,000-fold improved

exposure versus the parent compound. To address the discrepancy in biotin levels

between humans and mice, we developed a low-biotin mouse model that

recapitulates human biotin physiology. In this model C48 reduced Mtb burden in

lungs and spleen, providing the first in vivo proof-of-concept for targeting

biotin biosynthesis as a therapeutic strategy against tuberculosis.

DOI: 10.1101/2025.09.24.678246

PMCID: PMC12485673

PMID: 41040207

**66. bioRxiv [Preprint]. 2025 Sep 24:2025.09.24.678375. doi:**

**10.1101/2025.09.24.678375.**

PE/PPE proteins contribute to Mycobacterium tuberculosis drug resistance.

Boradia V, Chen J, Frando A, Clark LV, Grundner C.

The outer membrane (OM) of mycobacteria is a formidable permeability barrier

that confers drug tolerance, and whether drugs traverse the OM by mechanisms

beyond passive diffusion remains unclear. The proline-glutamic acid (PE) and

proline-proline-glutamic acid (PPE) proteins of pathogenic mycobacteria include

several OM transporters. Here, we tested the role of PE/PPE proteins in

Mycobacterium tuberculosis ( Mtb ) drug transport and resistance. Mutations in

multiple pe/ppe genes were strongly associated with drug resistance in a genetic

association study, and mutations in ppe42 and ppe51 also conferred increased

resistance in vitro . Deletion of a pe/ppe pair transcriptionally responsive to

drug exposure, pe25/ppe41 , led to elevated resistance to isoniazid (INH) across

all major Mtb lineages and accelerated INH resistance emergence in vitro . These

data identify a role for Mtb PE/PPE proteins in drug resistance consistent with

the PE/PPE transporter paradigm, suggest a broader contribution of this large

protein family, and a new factor of Mtb clinical drug resistance.

DOI: 10.1101/2025.09.24.678375

PMCID: PMC12485710

PMID: 41040171

**67. bioRxiv [Preprint]. 2025 Sep 25:2025.09.23.676583. doi:**

**10.1101/2025.09.23.676583.**

The structural context of mutations in proteins predicts their effect on

antibiotic resistance.

Green AG, Tasmin M, Vargas R, Farhat MR.

In Mycobacterium tuberculosis , a prevalent and deadly pathogen, resistance to

antibiotics evolves primarily through non-synonymous mutations in proteins.

Sequence-based analyses are currently used to understand the genetic basis of

antibiotic resistance, either via genotype-phenotype association, or via signals

of convergent evolution. These methods focus on primary sequence and usually

neglect other biological signals such as protein structural information. We

hypothesize that integrating the structural context of mutations improves the

prediction of effects on function and phenotype. We curate high confidence

structural annotations for the M. tuberculosis proteome from 1,371

crystallography and 2,316 AlphaFold predictions, and combine the structures with

mutations from over 31,000 clinical M. tuberculosis isolates. We demonstrate

that mutations in proteins known to cause resistance are clustered in 3D space,

even in proteins where inactivating mutations at any position are thought to

cause resistance. We develop a statistic to search the M. tuberculosis proteome

for signal of clustered non-synonymous mutations, finding over 450 proteins that

display this signal, many of which have a known relationship with antibiotic

resistance. Innovatively, we show that a supervised classifier trained on

structure features alone has an F1 score of 94.6% at classifying mutations as

resistance-conferring. This work demonstrates that protein structure provides

useful information for categorizing which variants may cause antibiotic

resistance, even when the majority of structures are AI-predicted.

DOI: 10.1101/2025.09.23.676583

PMCID: PMC12485870

PMID: 41040149

**68. Acta Med Philipp. 2025 Aug 29;59(12):92-98. doi: 10.47895/amp.vi0.9832.**

**eCollection 2025.**

Cecal Perforation in an Adolescent as a Paradoxical Response to

Anti-tuberculosis Treatment: A Case Report.

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of the Philippines Manila.

Paradoxical response to anti-tuberculosis treatment, defined as clinical or

radiologic worsening of pre-existing lesions or the development of new lesions

while ongoing treatment, poses diagnostic dilemma. Intestinal perforation as a

paradoxical response is rare. We report a 10-year-old female who presented with

recurrent abdominal pain, anorexia, and bloody diarrhea, and was diagnosed with

disseminated tuberculosis. She had marked improvement after one month of

anti-tuberculosis treatment but developed a recurrence of initial symptoms on

the third month of therapy and was treated for cecal perforation. Histopathology

of cecum revealed chronic granulomatous inflammation. The patient improved after

the surgery and the resumption of anti-tuberculosis medications. Recognition of

paradoxical reactions and differentiating it from drug resistance of other

pathology is important as these necessitates different management strategies.

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PMCID: PMC12487434

PMID: 41040076

**69. Front Microbiol. 2025 Sep 16;16:1649137. doi: 10.3389/fmicb.2025.1649137.**

**eCollection 2025.**

Genetic diversity, drug resistance, and transmission patterns of tuberculosis

based on whole-genome sequencing in Almaty, Kazakhstan.

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Tuberculosis, particularly multidrug-resistant TB (MDR-TB), remains a major

public health concern in Kazakhstan, where 26% of new TB cases are MDR, far

exceeding the global average. To better understand the genetic diversity, drug

resistance, and transmission dynamics of Mycobacterium tuberculosis in

Kazakhstan, we conducted a retrospective study at the National Scientific Center

of Phthisiopulmonology in Almaty from 2023 to 2024. Whole-genome sequencing

(WGS) was performed on 272 culture-confirmed TB isolates collected from patients

across the country. Phylogenetic analysis revealed the predominance of Lineage 2

(East Asian genotype, 72.4%) and Lineage 4 (Euro-American genotype, 26.8%). Drug

resistance profiling identified 29.0% of isolates as MDR-TB, of which 3.3% were

classified as pre-XDR and 0.7% as XDR. The most frequently observed

resistance-associated mutations were katG S315T (99.2%) and rpoB S450L (91.1%).

Cluster analysis using a ≤ 12 SNP threshold identified 22 genomic clusters

involving 80 isolates (29.4%), indicating recent and possibly ongoing

transmission. Spatial mapping showed that nearly 60% of clusters spanned

multiple regions, while others were highly localized, suggesting household or

close-contact transmission. A Mantel correlogram test revealed a statistically

significant correlation between geographic and genomic SNP distances in Almaty

and Almaty Region (r = 0.0634, p = 0.041) within the first distance class

(average 5 km, range 0-8 km). These findings suggest that patients living in

close proximity are more likely to carry genetically similar strains. As

distance increases, geographic proximity becomes less predictive of

transmission, with other factors-such as mobility, shared environments, or

healthcare contact-likely playing a greater role. Our findings underscore the

need to integrate WGS into national TB control programs to guide targeted

interventions, enhance surveillance, and curb the spread of drug-resistant TB

strains across Kazakhstan.

Copyright © 2025 Takenov, Kaziyev, Mukhamadi, Chingissova, Toxanbayeva,

Bismilda, Adenov, Eralieva, Nakisbekov and Zhunussova.

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PMCID: PMC12479430

PMID: 41035895

**70. Arch Bronconeumol. 2025 Sep 22:S0300-2896(25)00332-1. doi:**

**10.1016/j.arbres.2025.09.005. Online ahead of print.**

Addressing Neglected 'Hot Spots' of Tuberculosis Persistent Transmission:

Prisons and Jails.

[Article in English, Spanish]

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DOI: 10.1016/j.arbres.2025.09.005

PMID: 41033912

**71. Diagn Microbiol Infect Dis. 2025 Sep 26;114(2):117127. doi:**

**10.1016/j.diagmicrobio.2025.117127. Online ahead of print.**

The invisible burden of pediatric tuberculosis in sub-Saharan Africa: An urgent

call for child-centered diagnostic strategies.

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DOI: 10.1016/j.diagmicrobio.2025.117127

PMID: 41033164

**72. Tuberculosis (Edinb). 2025 Sep 11;155:102690. doi: 10.1016/j.tube.2025.102690.**

**Online ahead of print.**

Evaluating selection at intermediate scales within genes provides robust

identification of genes under positive selection in M. tuberculosis clinical

isolates.

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Multiple studies have reported genes in the M. tuberculosis (Mtb) genome that

are under diversifying selection, based on genetic variants among Mtb clinical

isolates. These might reflect adaptions to selection pressures associated with

modern clinical treatment of TB. Many, but not all, of these genes under

selection are related to drug resistance. Most of these studies have evaluated

selection at the gene-level. However, positive selection can be evaluated on

different scales, including individual sites (codons) and local regions within

an ORF. In this paper, we use GenomegaMap, a Bayesian method for calculating

selection, to evaluate selection of genes in the Mtb genome at all three levels.

We present evidence that the intermediate analysis (windows of codons) yields

the most credible list of candidate genes under selection (excluding PPE and

PE\_PGRS genes, which are predicted less reliably due to frequent sequencing

errors). A further advantage of this approach is that it identifies specific

regions within proteins that are under selective pressure, which is useful for

structural and functional interpretation. In an analysis of two separate

collections of Mtb clinical isolates (from Moldova; and a

globally-representative set), we observed 53 and 173 significant genes under

selection, with 36 % overlap. The lists of genes under selection include many

drug-resistance genes, as well as other genes that have previously been reported

to be under selection (resR, phoR). The specific regions under selection

identified within drug-resistance genes are shown to correspond to protein

structural features known to be involved in resistance, supporting accuracy of

the method. Positive selection in several ESX-1-related genes was also observed,

suggesting adaptation to immune pressure.

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PMID: 41033137

**73. J Clin Tuberc Other Mycobact Dis. 2025 Sep 12;41:100562. doi:**

**10.1016/j.jctube.2025.100562. eCollection 2025 Dec.**

Retreatment TB is a risk factor for multidrug-resistant TB among people with HIV

in rural eastern Uganda: A nested case-control study.

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**RATIONALE:** People with human immunodeficiency virus (PWH) have an increased risk

of multidrug-resistant TB (MDR-TB) compared to those without HIV.

**OBJECTIVE:** To investigate the risk factors for MDR-TB among PWH in rural eastern

Uganda.

**METHODS:** We conducted a nested case-control study at Soroti Regional Referral

Hospital in rural eastern Uganda. TB records from January 2017 to May 2024 were

retrospectively reviewed to identify all PWH. MDR-TB was defined as resistance

to at least both Isoniazid and Rifampicin following GeneXpert Mycobacterium TB

and Rifampicin assay and culture-based drug-susceptible testing. Cases were PWH

with MDR-TB, while controls were a random sample of PWH without MDR-TB, in a 1:3

ratio. Multivariable binary logistic regression was used to identify factors

independently associated with being a case rather than a control. Adjusted odds

ratios (aORs) and 95% confidence intervals (CIs) were reported.

**RESULTS:** We included 37 cases and 111 controls, and found retreatment TB was

associated with being a case rather than a control (aOR 6.97; 95% CI

2.65-19.46). Male sex (aOR: 1.59; 95% CI: 0.67-3.93), clinically diagnosed

pulmonary TB (aOR: 0.38; 95% CI: 0.10-1.23) or extrapulmonary TB (aOR: 0.37; 95%

CI: 0.05-1.62), and recent anti-retroviral therapy initiation (aOR: 2.07; 95%

CI: 0.83-5.28) were insignificantly associated with being a case.

**CONCLUSION:** This study showed that retreatment TB is associated with a higher

likelihood of MDR-TB among PWH in a referral hospital in rural eastern Uganda.

These findings underscore the need for intensified drug resistance surveillance

and adherence support among PWH with prior TB treatment.

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PMID: 41031316

**74. Front Pharmacol. 2025 Sep 15;16:1667592. doi: 10.3389/fphar.2025.1667592.**

**eCollection 2025.**

Evaluating the efficacy of HRZE-based regimens in a high-burden murine model: a

back-translational assessment of rifamycins and moxifloxacin substitutions in

tuberculosis treatment.

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(#)Contributed equally

**INTRODUCTION:** The standard treatment for tuberculosis is the isoniazid,

rifampicin, pyrazinamide, and ethambutol (HRZE) regimen. Despite its efficacy,

this regimen has limitations, including prolonged treatment duration and poor

clinical outcomes in drug-resistant cases. This back translational study

assessed the efficacy of alternative drug combinations, focusing on high-dose

rifamycins (rifampicin and rifapentine) and substituting moxifloxacin for

ethambutol in the HRZE regimen.

**METHODS:** Using a preclinical high-burden aerosol model of tuberculosis in BALB/c

mice, we tested seven treatment combinations, including high-dose rifampicin

(HD-RIF), high-dose rifapentine (HD-RPT), and moxifloxacin.

**RESULTS:** By day 12, the HD-RIF+HZM and HD-RPT+HZM regimens reduced lung

bacterial burdens from 6.59 ± 0.08 log10 CFU in untreated controls to 3.70 ±

0.19 and 3.91 ± 0.43 log10 CFU, respectively. By day 54, bacterial loads were

undetectable (<1 log10 CFU) in all groups except for HRZE (1.48 ± 0.32 log10

CFU). RS ratio analysis showed lower ratios for HD-RIF+HZM and HD-RPT+HZM

compared to HRZE by day 26, indicating a superior ability of both regimens to

interrupt rRNA synthesis. Histopathological analysis revealed similar

granulomatous changes across all treatment groups. Mass spectrometry confirmed

higher systemic exposure for HD-RIF and HD-RPT groups than RIF used in HRZE.

**DISCUSSION:** The findings indicate that higher doses of rifamycins and the

substitution of moxifloxacin offer improved bactericidal activity and could

shorten TB treatment duration.

Copyright © 2025 Cummings, Woolhiser, Guglielmi, Wernsman, Romano, Pauly,

Belisle, Walter, Robertson and Slayden.

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PMID: 41031156

**75. bioRxiv [Preprint]. 2024 Oct 3:2024.10.02.616386. doi:**

**10.1101/2024.10.02.616386.**

Immunopeptidomics informs discovery and delivery of Mycobacterium tuberculosis

MHC-II antigens for vaccine design.

Leddy O, Ogongo P, Huffaker J, Gan M, Milligan R, Mahmud S, Yuki Y, Bobosha K,

Wassie L, Carrington M, Liu Q, Ernst JD, White FM, Bryson BD.

No currently licensed vaccine reliably prevents pulmonary tuberculosis (TB), a

leading cause of infectious disease mortality. Developing effective new vaccines

will require identifying which of the roughly 4000 proteins in the Mycobacterium

tuberculosis ( Mtb ) proteome are presented on MHC class II (MHC-II) by infected

human phagocytes and can be recognized by CD4+ T cells to mediate protective

immunity. Vaccines must also elicit T cell responses recognizing the same

peptide-MHC complexes presented by infected cells, and successful presentation

of target human MHC-II peptides is currently challenging to evaluate and

optimize. Here, we define antigenic targets for TB vaccine development by using

mass spectrometry (MS) for proteome-wide discovery of Mtb epitopes presented on

MHC-II by infected human cells. We next iteratively design and evaluate

candidate mRNA vaccine immunogens, revealing design principles that enhance

presentation of target MHC-II peptides. Our results will inform the development

of new TB vaccine candidates.

DOI: 10.1101/2024.10.02.616386

PMCID: PMC12478359

PMID: 41031036

**76. bioRxiv [Preprint]. 2025 Jun 9:2025.06.06.658135. doi:**

**10.1101/2025.06.06.658135.**

Inflammasome activation differences underpin different Mycobacterium

tuberculosis infection outcomes.

Kumar R, Kolloli A, Bhargavi G, Husain S, Ghanny S, Soteropoulos P, Subbian S.

The clinical outcome of Mycobacterium tuberculosis (Mtb) infection ranges from

latent/non-progressive disease to active/progressive tuberculosis (TB), but the

cellular events contributing to these variable outcomes remain unknown. Here, we

report that progressive Mtb infection is associated with upregulation of

guanylate-binding protein-1 (GBP1), hypoxia-inducible factor 1α (HIF-1α) and

elevated NLR family pyrin domain-containing (NLRP3) inflammasome activation

pathways. Using rabbit lungs and in primary rabbit and human macrophages as well

as human THP-1 cell line-derived macrophages for infection with laboratory

(H37Rv) or clinical Mtb strains (HN878 or CDC1551) that differ in virulence, we

show that NLRP3 inflammasome activation by HIF-1α and GBP1 leads to elevated

mitochondrial stress, apoptosis and necrosis during progressive infection by

HN878. These biological functions and pathways are dampened in rabbit lungs,

primary rabbit and human macrophages during non-progressive infection by

CDC1551. These findings are consistent with and confirmed by Mtb infection

studies of macrophages knocked-down for HIF-1α or GBP1 expression. Our study

indicates that differences in HIF-1α- and GBP1-mediated NLRP3 inflammasome

activation influence the outcome of Mtb infection to active or latent TB.

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PMCID: PMC12478344

PMID: 41031010

**77. Ann Agric Environ Med. 2025 Sep 18;32(3):437-438. doi: 10.26444/aaem/197249.**

**Epub 2025 Jan 7.**

Chronic neck lymphadenitis - challenges in the diagnosis of extrapulmonary

tuberculosis.

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Neck lymph node involvement is common in infections caused by various

microorganisms, but determining the causative agent can be challenging. The case

study details a 58-year-old male with left-sided cervical lymphadenopathy,

fever, and weight loss persisting for two years. Despite extensive testing and

empirical treatments, the cause remained unidentified. A CT scan revealed

numerous enlarged lymph nodes with central necrosis. Histopathological

examination suggested granulomatous lymphadenitis, although no bacteria were

initially detected. Eventually, acid-fast bacilli were found via Ziehl-Neelsen

staining, and Mycobacterium tuberculosis was confirmed through molecular tests.

The patient was diagnosed with tuberculosis (TB) and successfully treated with

anti-tuberculous therapy. The case highlights the diagnostic challenges of

extrapulmonary TB, and underscores the importance of considering TB in atypical

presentations, especially given the rise in multidrug-resistant strains.

DOI: 10.26444/aaem/197249

PMID: 41025194 [Indexed for MEDLINE]

**78. Ann Agric Environ Med. 2025 Sep 18;32(3):421-423. doi: 10.26444/aaem/207808.**

**Epub 2025 Jul 14.**

Occupational tuberculosis at a healthcare laboratory - case report.

Spanovic M(1)(2), Mikov I(1)(3), Pericevic Medic S(1)(2), Maric N(4)(5),

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Tuberculosis (TB) is a complex health problem, which occurs more frequently in

healthcare workers. However, TB is rarely recognized as an occupational disease.

The report presents a case of occupational tuberculosis in a medical

microbiologist, initially misinterpreted as lung cancer. A 59-year-old

microbiologist at healthcare laboratory, smoker, underwent lung lobectomy.

Histopathological analysis suggested tuberculosis. Follow-up revealed positive

mycobacterium tuberculosis culture. Occupational exposure was confirmed and

criteria for occupational disease were met. This case highlights the importance

of vigilance, accurate tuberculosis diagnosis, and implementation of preventive

measures for healthcare workers at increased risk. Tuberculosis remains a global

health concern, sometimes mimicking malignancies. Comprehensive diagnostic

approaches, protective measures, and collaboration between occupational health

services and pulmonologists are essential to reduce risks at the workplace, and

ensure early detection.

DOI: 10.26444/aaem/207808

PMID: 41025190 [Indexed for MEDLINE]

**79. Osong Public Health Res Perspect. 2025 Sep 19. doi: 10.24171/j.phrp.2025.0153.**

**Online ahead of print.**

Factors influencing adherence to anti-tuberculosis treatment in Morocco: a

cross-sectional study from the Béni Mellal-Khénifra region.

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**OBJECTIVES:** Adherence to anti-tuberculosis treatment is essential for achieving

successful outcomes and preventing the emergence of drug-resistant strains. This

study aimed to evaluate adherence levels and identify factors associated with

non-adherence among tuberculosis patients in the Béni Mellal-Khénifra region of

Morocco. We hypothesized that sociodemographic, clinical, and behavioral factors

influence adherence.

**METHODS:** A facility-based cross-sectional study was conducted from January 2023

to December 2024 in 2 Tuberculosis and Respiratory Disease Diagnostic Centers in

the Béni Mellal-Khénifra region. A total of 481 patients who had been on

treatment for at least 2 months were recruited using convenience sampling. Data

were collected through structured, pre-tested questionnaires administered in

face-to-face interviews and verified against treatment cards and medical

records. Adherence was defined as taking ≥90% of prescribed doses. Multivariable

logistic regression was used to identify independent predictors of

non-adherence.

**RESULTS:** Among the 481 participants, 8.1% were non-adherent. Significant

predictors of non-adherence included forgetfulness (adjusted odds ratio [AOR],

38.84; 95% confidence interval [CI], 11.35-132.88), adverse effects (AOR, 14.26;

95% CI, 3.17-64.13), male sex (AOR, 6.77; 95% CI, 1.45-31.60), rural residence

(AOR, 4.42; 95% CI, 1.37-14.25), self-adjusted dosing (AOR, 5.83; 95% CI,

1.20-28.34), stopping treatment after symptom improvement (AOR, 6.56; 95% CI,

1.34-32.14), and missed follow-up visits (AOR, 6.74; 95% CI, 1.56-29.19).

**CONCLUSION:** Although overall adherence was high, 8.1% of patients were

non-adherent. Strategies to improve adherence should focus on addressing

forgetfulness, managing side effects, enhancing access in rural areas, and

reinforcing patient education and follow-up systems to improve treatment

outcomes in this and similar settings.

DOI: 10.24171/j.phrp.2025.0153

PMID: 41025160

**80. World J Virol. 2025 Sep 25;14(3):107214. doi: 10.5501/wjv.v14.i3.107214.**

Uptake and disparities in tuberculosis screening using urine-lipoarabinomannan

among patients with advanced human immunodeficiency virus-disease in Africa: A

systematic review.

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Musoke R(7), Salim SM(8), Karia MF(9), Karia LF(10), Fussi HF(4), Mustafa

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**BACKGROUND:** Due to low bacteria count and high likelihood of having

extrapulmonary tuberculosis (TB) among patients with advanced human

immunodeficiency virus (HIV) disease, the World Health Organization (WHO)

recommended the use of urine lateral flow urine lipoarabinomannan (LF-LAM) or

sputum-Xpert to screen for TB.

**AIM:** To estimate pooled prevalence of TB screening uptake, TB diagnosis, TB

treatment initiation and mortality among patients with advanced HIV disease in

Africa.

**METHODS:** PubMed, Cochrane Library and EMBASE were searched for articles

published between January 2011 and December 2024. TB screening uptake was

defined as percentage of patients with advanced HIV disease (CD4 ≤ 200 cells/mm3

or WHO stage III/IV) who tested for TB. Using random effects models, we computed

the pooled estimate of TB screening uptake, TB prevalence, TB treatment

initiation and mortality and their corresponding 95%CIs. Stratified analysis to

compare uptake of TB testing and TB prevalence between children vs adults and

multisite vs single site studies was performed.

**RESULTS:** A total of nineteen studies with 16065 people with advanced HIV disease

were analyzed. The pooled prevalence of TB screening uptake was 64.6% (95%CI:

49.2-80.1). The pooled prevalence of TB was 29.4% (95%CI: 22.0-36.8), and TB

treatment initiation was 77.9% (95%CI: 63.9-91.8), and mortality was 19.5%

(95%CI: 8.9-30.0). The pooled prevalence of TB testing uptake was significantly

lower among children compared to adults (28.2% vs 66.4%, P = 0.003) and lower

for multi-sites compared to single site studies (58.8% vs 82.9%, P = 0.002). The

pooled prevalence of TB was significantly lower among children compared to

adults (24.2% vs 27.6%, P = 0.012) and higher among studies that involved multi

vs single sites (30.0% vs 21.9%, P = 0.001).

**CONCLUSION:** Four in ten people with advanced HIV disease were not screened for

TB as recommended by the WHO, indicating significant gaps in identifying

patients with TB. Excluding patients with evidence of TB is critical to avoid

exposing them to subtherapeutic levels of anti TB treatment.

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PMID: 41025091

**81. Math Biosci Eng. 2025 Aug 27;22(10):2720-2760. doi: 10.3934/mbe.2025100.**

Backward bifurcation and periodic dynamics in a tuberculosis model with

integrated control strategies.

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In this study, we present a unified mathematical model for tuberculosis (TB)

that integrates key interventions: Mask use and media campaigns to raise

community awareness and promote vaccine booster uptake. The model also

incorporates slow-fast disease progression and limited treatment capacity. A

mathematical analysis was conducted to determine the existence and stability of

equilibrium points. From the mathematical analysis on the stability criteria of

the TB-free equilibrium point, we show that TB can be eradicated if the basic

reproduction number is below one. However, due to insufficient treatment

capacity, a backward bifurcation may occur when the reproduction number equals

one, enabling the coexistence of endemic and disease-free equilibria even when

the reproduction number is below one. The parameter estimation is based on TB

incidence data per 100,000 individuals in Indonesia. Sensitivity analysis

reveald that although both interventions are effective, media campaigns combined

with vaccine boosters are more impactful in reducing TB transmission than the

use of masks. Numerical simulations further suggest the possibility of periodic

outbreaks, indicating potential seasonal TB patterns. To explore adaptive

intervention strategies, we extended the model using an optimal control

framework. Our findings suggested that combined implementation of face masks and

media campaigns is more effective than using either alone, particularly when the

likelihood of rapid disease progression increases.

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**82. Int J Biol Macromol. 2025 Sep 27;330(Pt 1):147950. doi:**

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Crystal structure of dihydrodipicolinate synthase from Mycobacterium

tuberculosis in complex with pyruvate and insights into allosteric regulation.

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

and is one of the leading causes of death worldwide. This disease is typically

treated by combining several antimicrobials for extended periods, which can lead

to treatment interruptions by patients and promote the emergence of

multidrug-resistant strains, necessitating the use of alternative or second-line

drugs. In this perspective, dihydrodipicolinate synthase (DapA) from M.

tuberculosis (MtDapA), which catalyzes the aldol condensation between pyruvate

and aspartate-semialdehyde (ASA) to produce dihydrodipicolinate, is an essential

enzyme in Mtb for the production of l-lysine and meso-diaminopimelate (mDAP).

Through crystallographic assays, we have determined the structure of MtDapA in

complex with its substrate, pyruvate, covalently bonded through a Schiff base to

the catalytic l-lysine at a resolution of 1.5 Å. Through structural analysis, we

describe the arrangement of interactions between the active site amino acid

residues and pyruvate, providing insight into the binding mode of this molecule.

In addition, we performed further biophysical assays, including differential

scanning fluorimetry (DSF) and isothermal titration calorimetry (ITC), to obtain

insights into the pyruvate affinity and the potential role of l-lysine and mDAP

as allosteric regulators of MtDapA. However, in contrast to those observed in

other orthologous enzymes, particularly those from Gram-negative bacteria,

MtDapA does not have an affinity for l-lysine or mDAP. Consequently, this enzyme

is not allosterically regulated by the products of this pathway. The results

shown here provide evidence regarding the functioning of the enzyme regulatory

mechanism and valuable structural features to aid in the future development of

MtDapA inhibitors, which may be further explored in drug discovery campaigns

against tuberculosis.

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Mapping Bacillus Calmette-Guérin vaccination coverage in Africa from 1990 to

2022: a novel spatiotemporal modelling study.

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**BACKGROUND:** Bacillus Calmette-Guérin (BCG) protects children from severe

tuberculosis and remains the only licensed vaccine for tuberculosis. Subnational

estimates of BCG coverage are essential for identifying underserved populations

across Africa. This study aimed to map BCG vaccination coverage in Africa from

1990 to 2022.

**METHODS:** We conducted an advanced Bayesian geostatistical analysis, integrating

spatial covariates through stacked ensemble modelling and adjusting for spatial

and residual effects to estimate BCG coverage. The analysis included 110

demographic and health surveys, and multiple indicator household surveys,

comprising data on 180 449 children from 35 countries in Africa. BCG vaccination

coverage among children aged 12-23 months was estimated at a 5 × 5 km spatial

resolution. These estimates were then aggregated to second administrative and

national levels over the study period weighting by the same age child

population. Coverage changes were estimated by comparing coverage metrics in

1990 and 2022. The population-weighted number of unvaccinated children was also

estimated at first administrative level. The likelihood of second

administrative-level areas achieving the Global Vaccine Action Plan target of

80% coverage threshold in 2020 was quantified using posterior exceedance

probabilities.

**FINDINGS:** Between 1990 and 2022, BCG vaccination coverage increased by at least

25% in 85·32% (95% uncertainty interval 84·11-86·50) of second administrative

level areas, with an average increase of 40·52%. Despite this progress,

significant geographical disparities remain within and between countries. In

2022, many local areas still had low BCG coverage, including countries with high

national BCG vaccination rates. Some countries showed notable improvements, but

only a few (such as Burundi, Rwanda, Uganda, Gambia, and Togo) have achieved the

Global Vaccine Action Plan target of 80% coverage in all second administrative

level areas by 2020.

**INTERPRETATION:** Despite significant progress in BCG vaccination across Africa

over the last three decades, notable geographical disparities persist. These

findings suggest a need to prioritise resources and boost BCG coverage,

especially in underserved areas.

**FUNDING:** Curtin University Strategic Scholarship and Australian National Health

and Medical Research Council.

**TRANSLATIONS:** For the Amharic, Icibemba and Swahili translations of the abstract

see Supplementary Materials section.

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18 F-PSMA-1007 and 18 F-FDG PET/CT Findings of Pulmonary Tuberculosis Mimicking

Malignancy.

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A 78-year-old man with hormone-sensitive metastatic prostate cancer underwent

chest CT, which revealed a gradually enlarging pulmonary nodule in the left

upper lobe, suggestive of lymphangitic metastasis. To further evaluate the

lesion, both 18 F-FDG and 18 F-PSMA-1007 PET/CT were performed. The lesion

showed intense FDG uptake but relatively low PSMA uptake, raising the suspicion

of a primary lung malignancy. Histopathologic examination after wedge resection

confirmed pulmonary tuberculosis.

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PMID: 41021885

**85. Curr Issues Mol Biol. 2025 Sep 19;47(9):776. doi: 10.3390/cimb47090776.**

Anti-TB Drugs for Drug-Sensitive and Drug-Resistant Mycobacterium tuberculosis:

A Review.

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Tuberculosis (TB) is a global health challenge caused by Mycobacterium

tuberculosis, with drug resistance, treatment toxicity, and treatment adherence

challenges continuing to impede control efforts. The objective of this review is

to explore current advancements in TB treatment, for both drug-sensitive and

drug-resistant TB, focusing on pharmacologic regimens, diagnostics, and

adjunctive therapies. For drug-sensitive TB, a 4-month rifapentine-moxifloxacin

regimen has been proven to be non-inferior to the traditional 6-month standard,

while optimized pyrazinamide dosing or faropenem substitution may improve

culture conversion and reduce adverse events. In drug-resistant TB, regimens

such as the bedaquiline, pretomanid, linezolid, and moxifloxacin have

demonstrated efficacy with substantially shorter treatment duration; however,

incidents of hepatotoxicity and linezolid-related neuropathy require careful

monitoring. Adjunctive therapies, such as metformin, N-Acetylcysteine, aspirin,

and statins, show promising effects in modulating host immunity and reducing

long-term lung damage. Advances in diagnostics, including whole genome

sequencing and CRISPR-based methods, are enabling rapid detection of resistance

mutations and directed therapy. Vaccine development has advanced beyond the BCG

vaccine to explore vaccines with enhanced immunogenicity or ones that are safe

for immunocompromised patients. Implementation strategies such as video directly

observed therapy are improving adherence; additionally, community-based,

technology-supported interventions significantly improve TB knowledge and

compliance. An integrated approach that combines optimized pharmacologic

regimens, host-directed therapies, advanced diagnostics, and patient-centered

public health strategies is essential to reduce TB incidence, long-term

morbidity, and mortality.

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PMID: 41020898

**86. Infect Med (Beijing). 2025 Sep 6;4(3):100203. doi: 10.1016/j.imj.2025.100203.**

**eCollection 2025 Sep.**

The growing impact of nontuberculous mycobacteria: A multidisciplinary review of

ecology, pathogenesis, diagnosis, and treatment.

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Nontuberculous mycobacteria (NTM) are emerging pathogens responsible for a

growing spectrum of diseases, particularly in individuals with underlying lung

disorders or immune suppression. Once considered primarily environmental

saprophytes, NTM are now recognized as important causes of pulmonary, cutaneous,

lymphatic, and disseminated infections. With more than 200 species identified

and regional variations in prevalence, their diagnosis and management present

significant clinical and microbiological challenges. The lack of standardized

reporting systems and overlapping features with tuberculosis complicate

epidemiological understanding and case identification. This review provides an

updated and integrated overview of NTM-associated diseases, emphasizing

diagnostic advancements, environmental sources, mechanisms of transmission, host

immunity, genetic susceptibility, and therapeutic options. Special attention is

given to molecular diagnostic techniques, species-level identification

strategies, and the role of gene sequencing in differentiating NTM species. We

also highlight the limitations of conventional methods, discuss antimicrobial

resistance mechanisms, and summarize current treatment guidelines. By

synthesizing current knowledge across microbiology, clinical medicine, and

public health, this review aims to support a multidisciplinary approach to NTM

diagnosis and management and address the pressing need for increased awareness,

better surveillance, and targeted research on this under-recognized group of

pathogens.

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**87. Front Epidemiol. 2025 Sep 11;5:1571065. doi: 10.3389/fepid.2025.1571065.**

**eCollection 2025.**

Geographic mapping and spatiotemporal patterns of tuberculosis in Libya within

ten years' period (2015 to 2024).

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Grebi A(5), Dhu AM(5), Alkarghali AF(6), Mohammed SH(6), Miftah RK(6),

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**INTRODUCTION**: Tuberculosis(TB) is still a serious problem with a remarkable

global impacts particularly within developing countries such as Libya. According

to World Health Organization (WHO) global report, the country is considered a

moderate TB burden with incidence of 40 per 100,000 in 2011. Geographic

epidemiology has been considered an important tool in preventing TB in large

countries. In this study, we intended to identify the geographic and

spatiotemporal patterns of the TB incidence rate in Libya between 2015 and 2024.

**METHODS:** A cross-sectional retrospective analytical study was conducted within

ten years on the data reported through the National TB surveillance system. The

data on all TB cases reported from 2015 to 2024 by municipality and region was

abstracted. Choropleth maps were drawn showing the TB case notification rates

(CNR) per 100,000. Local Moran's I was performed to identify the spatial

variations of the disease and temporal and Spatiotemporal analyses were employed

in all instances.

**RESULTS:** During the entire study period, 26,478 TB cases were reported from all

22 municipalities in Libya with an annual rate of 40.29/100,000 (95% CI:

(40.229 ± 9.01). The highest incidence was reported in 2015 and the lowest one

in 2024. Males were significantly reported more than females among notified TB

cases, (P < 0.001). The highest CNR was reported in the Eastern region followed

by Western and Southern regions. The geospatial distribution of reported cases

of TB varied greatly within the provinces and during the study period. There was

evident variability throughout the country and over time. High-rate and low-rate

clusters were predominantly distributed in the periods. High clusters were

concentrated northeast and northwest, though low-level clusters were mainly

located in the middle and the southern region of the country.

**CONCLUSION:** The results of this study provided clear insights into the

geographic and spatiotemporal mapping of TB in Libya. There was an overall

decreasing trend in TB CNR from 2015 to 2024 parallel with high-risk and

low-risk areas. This information should allow the decision-making personnel to

implement proper policies to combat TB at national and regional levels.

© 2025 Daw, El-Bouzedi, Abumahara, Najjar, Ben Ashur, Grebi, Dhu, Alkarghali,

Mohammed, Miftah, abdulsamad, Elbasha, Doukali, Elmhidwi, Albouzaidi, Wareg and

Ahmed.

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**88. Radiol Case Rep. 2025 Sep 16;20(12):6042-6047. doi: 10.1016/j.radcr.2025.08.024. eCollection 2025 Dec.**

Thyroid tuberculosis: Rare case report.

Abourak C(1), Oukassem S(1), Zouita W(1), Bentalha K(1), Boubekri M(2),

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Tuberculosis remains a major public health issue, particularly in developing

countries where it is endemic, such as Morocco. While pulmonary tuberculosis is

the most common form, extrapulmonary involvement can affect various organs,

including the thyroid gland, although this localization is exceptionally rare.

We report the case of a middle-aged Moroccan man diagnosed with a tuberculous

thyroid abscess, an uncommon and misleading presentation. The diagnosis was

confirmed by cytobacteriological and histopathological analysis of a thyroid

specimen. This case underscores the need to consider tuberculosis in the

differential diagnosis of atypical cervical masses, especially in endemic

regions.

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**eCollection 2025 Jul-Sep.**

Role of Diagnostic Laparoscopy and Hysteroscopy in Predicting Genital

Tuberculosis - A Systematic Review.

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Genital tuberculosis (female genital tuberculosis [FGTB]) continues to be an

essential underdiagnosed cause of infertility and reproductive morbidity, most

significantly in resource-limited settings. Diagnostic laparoscopy and

hysteroscopy have become crucial for assessing suspected FGTB cases, mainly when

supported by molecular and histopathological tests. This systematic review has

evaluated these modalities' diagnostic utility, sensitivity, specificity, and

clinical outcomes for predicting FGTB. A comprehensive systematic review was

performed with the help of the PECOS framework and PRISMA guidelines. Studies

were identified by running Boolean operators and MeSH terms on seven databases:

PubMed, Embase, Scopus, Web of Science, Cochrane Library, CINAHL, and Google

Scholar. Cohort and cross-sectional designs were considered, focusing on

clinically relevant outcomes such as sensitivity, specificity, prevalence, and

procedural findings obtained from diagnostic laparoscopy and hysteroscopy. Data

extraction was done using a standardized template, and bias was assessed using

ROBINS-I and AXIS tools. The certainty of evidence was evaluated using the GRADE

framework, and sensitivity analyses were performed to assess the robustness of

the findings. Thirteen studies involving 2201 participants were included in the

review. Tubal beading, adhesions, and hydrosalpinx were the constant findings of

diagnostic laparoscopy, with sensitivities and specificities varying between 33%

and 85.71% and 22.8% and 100%, respectively. Hysteroscopy revealed intrauterine

fibrosis in up to 48.48% of cases. Adhesions and synechiae were seen in 46% and

18%, respectively. Molecular diagnostics GeneXpert and tuberculosis-polymerase

chain reaction (TB-PCR) showed high sensitivity (up to 100%) and varied

specificity (33% to 100%). The prevalence of FGTB ranged from 6.73% to 45%, with

conception rates improved by 39% postantitubercular therapy. Sensitivity

analyses revealed lower heterogeneity (I² <40%) in studies applying combined

diagnostic modalities compared to single-method approaches. This systematic

review showed that integrating diagnostic laparoscopy and hysteroscopy with

molecular tools such as GeneXpert and TB-PCR improves the predictive and

therapeutic approach to FGTB. These modalities effectively identify structural

abnormalities and correlate the findings with molecular and histopathological

results. Standardized protocols and more extensive multicenter studies will be

required to reduce heterogeneity and further refine diagnostic accuracy.

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**90. J Med Ultrasound. 2025 Mar 21;33(3):216-221. doi: 10.4103/jmu.jmu\_52\_24.**

**eCollection 2025 Jul-Sep.**

Comparison of Lung Ultrasound Findings in Patients with Pulmonary Tuberculosis

and Lobar Pneumonia: A Case-control Study.

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**BACKGROUND:** The utility of lung ultrasound (LUS) in diagnosing respiratory

disorders is being studied only in recent times. We aimed to describe the

ultrasound (USG) features of pulmonary tuberculosis (TB) and compare them with

those of lobar pneumonia. In addition, the LUS findings of both diseases were

corroborated with chest X-ray findings.

**METHODS:** The study subjects consisted of adult subjects recently diagnosed with

pulmonary TB and those diagnosed with lobar pneumonia. Both subsets of patients

underwent LUS evaluation.

**RESULTS:** Ninety-six subjects with 64 microbiologically confirmed TB and 32 lobar

pneumonia patients were included. The study subjects' mean age was 46.78 ± 15.75

years and the majority were males (n = 62; 64.6%). LUS showed focal interstitial

pattern, cavity, and irregular pleura in TB patients which were significantly

different (P ≤ 0.001) from the findings of air bronchogram and/or shred sign

seen in patients with lobar pneumonia. The overall sensitivity of LUS compared

to X-ray, to identify abnormalities in TB and lobar pneumonia patients, was

88.6%. The LUS and CXR findings were concordant in 93.75% of TB patients and

90.6%) of lobar pneumonia patients. Additional USG abnormalities other than that

seen on CXR were demonstrated in 13 (20.3%) TB patients.

**CONCLUSION:** LUS is a valuable tool to detect TB and lobar pneumonia and can

discriminate between the two conditions. LUS performance was on par with CXR in

the detection of abnormalities. The lack of radiation exposure and portability

of LUS makes it an attractive tool for bedside use as well as in field

conditions where radiography may not be readily available.

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PMID: 41018829

**91. J Med Ultrasound. 2025 Mar 21;33(3):282-284. doi: 10.4103/jmu.jmu\_28\_24.**

**eCollection 2025 Jul-Sep.**

Epididymo-orchitis with Epididymal Abscess in a Patient with Disseminated

Tuberculosis: A Case Report.

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Tuberculosis (TB) remains a global health concern, and while primarily affecting

the lungs, extrapulmonary manifestations such as genitourinary tubercular

epididymitis are rare and diagnostically challenging. Accurate differentiation

is crucial for appropriate treatment. This case study presents a 34-year-old man

with left scrotal swelling, backache, and fever, highlighting the importance of

considering TB in genitourinary conditions. High-resolution sonography revealed

an edematous left testis with increased vascularity and hypoechoic nodules.

Further imaging, including high-resolution computed tomography thorax and CEMRI

dorso-lumbar spine, confirmed disseminated TB. Despite negative urine culture,

aspiration cytology from the epididymal collection indicated tubercular

etiology. Urogenital TB, especially isolated epididymal involvement without

renal effects, presents diagnostic challenges, often occurring in

immunocompromised patients. The case underscores the role of clinical,

biochemical, and radiological evidence in establishing a correct diagnosis.

High-resolution ultrasonography plays a crucial role in diagnosing scrotal

pathologies, and when accompanied by an epididymal collection, further

diagnostic steps involving biochemical parameters and aspiration followed by

cytoanalysis and culture are essential. The diagnosis of TB epididymitis can be

confirmed through acid-fast bacilli (AFB) identification, positive AFB culture,

or granulomas seen in a biopsy specimen in the right clinical context.

Radiological imaging aids in detecting local and disseminated disease forms,

including complications such as hydrocele, testicular calcifications, scrotal

abscesses, sinus tracks, and fistulous communications.

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**eCollection 2025.**

Determinants of the lost to follow-up status among patients with tuberculosis

who emigrated to the Republic of Korea: a mixed-method study.

Jeon S(1)(2), Lee JY(2), Jeong I(2), Sin S(2), Lee I(2), Kim Y(2), Han AY(2),

Lee SE(3), Seo S(3), Kim H(3), Kwon Y(3), Song C(3), Joh JS(2), Kim SH(1)(4).

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**INTRODUCTION:** Tuberculosis (TB) remains a significant global health concern,

with foreign migrants in the Republic of Korea (ROK) representing a particularly

vulnerable group; despite comprising only 3.5% of the population, they account

for over 5% of annual TB cases and exhibit disproportionately high rates of lost

to follow up (LTFU) from treatment compared to native Koreans. This

mixed-methods study aimed to identify key factors influencing non-adherence to

treatment and LTFU among migrants.

**METHODS:** Utilizing national TB surveillance data from 2016 to 2018 for 4,011

migrant and 64,620 native patients, quantitative analysis were employed to

identify factors associated with LTFU for migrants. Complementary in-depth

qualitative interviews with Public-Private Mix (PPM) nurses provided deeper

insights into barriers to adherence.

**RESULTS:** The study revealed a significantly higher LTFU rate (21.5%) among

migrant patients compared to domestic patients (2.3%). Key contributing factors

included nationality (highest crude odds for migrants from Thailand, Central,

and North Asia), living arrangements (increased risk for those not with family

or living alone), and male gender. Drug-resistant TB made patients over four

times more likely to discontinue treatment and systemic issues such as frequent

care transfers and the presence of comorbidities. Qualitative findings

highlighted inadequate patient education and misconceptions about TB severity

(often seen as a "mild cold"), leading to premature discontinuation. Poor

medical interpretation services and low awareness among migrants of free TB

treatment under the PPM program were also critical barriers.

**DISCUSSION:** These findings imply that high LTFU among migrant patients is

multifactorial, stemming from personal, clinical, and systemic issues.

Addressing this disparity requires targeted interventions, including culturally

tailored multilingual educational campaigns, improved medical interpretation,

and increased awareness of PPM program eligibility and free treatment.

Streamlining interfacility care transfer processes (such as the "Tuberculosis

Relief Belt" initiative), expanding PPM coverage, and ensuring access to

specialized care for comorbid conditions are also essential. Addressing these

multifaceted challenges is critical to reducing LTFU rates and enhancing

treatment continuity and outcomes, thereby advancing TB control efforts in ROK's

shifting migration context.

Copyright © 2025 Jeon, Lee, Jeong, Sin, Lee, Kim, Han, Lee, Seo, Kim, Kwon,

Song, Joh and Kim.

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**eCollection 2025.**

Empowering tuberculosis genomic surveillance in Limpopo, South Africa through

capacity building.

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**INTRODUCTION:** Limpopo, a predominantly rural province in South Africa, faces

significant challenges in the management of tuberculosis (TB) due to its high

mobility and limited healthcare infrastructure. This study aims to improve the

genomic surveillance of TB in Limpopo through capacity building initiatives.

**METHODS:** A comprehensive training program was implemented that focuses on both

theoretical and practical aspects of TB research, including whole genome

sequencing (WGS) and bioinformatics. Sputum samples from 232 patients diagnosed

with pulmonary TB were collected, with 30 isolates selected for WGS analysis.

The MAGMA bioinformatics pipeline was used for genomic analysis, identifying

drug resistance mutations and phylogenetic relationships.

**RESULTS:** Of the 28 Mycobacterium tuberculosis (Mtb) isolates analyzed, 53.6%

were females, with a median age of 39 years. The isolates predominantly belonged

to Lineage 4 (53.6%) and Lineage 2 (35.7%). High levels of drug resistance were

observed, with 100% of isolates resistant to rifampicin and 61% resistant to

isoniazid. In particular, 54% of the isolates were resistant to fluoroquinolones

(FLQs) and 18% showed resistance to bedaquiline (BDQ). Phylogenetic analysis

revealed two distinct clusters, indicating localized and interdistrict

transmission.

**CONCLUSION:** The study highlights the genetic diversity and drug resistance

patterns of Mtb in Limpopo, highlighting the need for continued genomic

surveillance and tailored public health interventions. Capacity building efforts

have laid the groundwork for improved TB diagnosis and surveillance in this

strategic region.

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Unusual Manifestation of Extrapulmonary Tuberculosis: A Soft Tissue Mass in an

Immunocompetent Patient.

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We report a case of disseminated tuberculosis (TB) manifesting as a soft tissue

mass of the back associated with pain and difficulty walking. Its clinical

presentation poses diagnostic challenges and can sometimes mimic neoplasms. The

first imaging study with computed tomography was suggestive of metastatic bone

disease or locally advanced malignancy. Advanced imaging studies, such as

magnetic resonance imaging (MRI) or computed tomography (CT), are required to

evaluate the extent of organ involvement. A definitive diagnosis necessitates

histopathological analysis and microbiological confirmation through acid-fast

Bacilli staining and polymerase chain reaction (PCR) testing for Mycobacterium

tuberculosis (MTB). Disseminated TB is rare in immunocompetent patients, which

accounts for <2% of all TB cases. It usually occurs from progressive primary

infection or the reactivation of latent infection focus through

lymphohematogenous spread. The risk of communicable diseases has increased due

to recent migration, so it is important to investigate MTB in patients with

unusual presentations, especially for people from endemic areas.

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Ethambutol optic neuropathy.

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Ethambutol is an antitubercular drug that is commonly used in the areas of the

world that is endemic to tuberculosis. It is used in infections caused by

Mycobacterium tuberculosis and some non-tuberculous infections caused by

Mycobacterium species. Ethambutol related toxic optic neuropathy remains one of

the most concerning adverse effects of the medication in addition to other

non-specific side effects like peripheral neuropathy, nausea, vomiting, joint

pain and rash. Recently the guidelines for treatment of tuberculosis in some

countries where tuberculosis (TB) is endemic have been revised to allow for

fixed dose combinations (wherein a single tablet contains a fixed strength of

isoniazid, rifampicin, pyrazinamide, and ethambutol) and longer duration of

treatment with ethambutol. Thus, it is anticipated that there will be an

increase in ethambutol toxic optic neuropathy. In this minireview we plan to

discuss the clinical features, neuro-ophthalmic evaluation, screening and

diagnosis of ethambutol toxic optic neuropathy. We will also discuss the

available treatment options for this condition.

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Apparent prevalence, lesion distribution and risk factors of bovine tuberculosis

in cattle slaughtered at the Shashemene and Arsi Negelle municipal abattoirs,

Ethiopia.

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Bovine tuberculosis (bTB) is a chronic infectious disease caused by

Mycobacterium bovis, primarily affecting cattle and presenting a zoonotic risk

to humans. It adversely impacts milk and meat production, ultimately

jeopardizing food security and livelihoods, particularly in developing countries

like Ethiopia, where the disease is endemic. This cross-sectional study,

conducted from January to December 2023, aimed to estimate the apparent

prevalence of bTB, assess the distribution of lesions, and identify associated

risk factors among cattle slaughtered at two municipal abattoirs. The study

systematically examined the carcasses of 648 cattle. The results revealed an

overall apparent prevalence of bTB of 6.2 % (95 % CI: 4.4 % - 8.3 %), with no

significant difference observed between the two abattoirs (p > 0.05). The

highest proportion of TB lesions (48.8 %) was identified in the lungs and

associated lymph nodes, followed by the mesenteric lymph nodes and livers

(29.3 %), and the lymph nodes of the head (21.9 %). Multivariable logistic

regression model identified breed and body condition scores as significant risk

factors for the apparent prevalence of bTB. Specifically, crossbred cattle were

found to be 2.8 times more likely to exhibit TB lesions than Zebus.

Additionally, cattle in poor body condition were 8.4 times more likely to show

TB lesions compared with those in good condition. These findings highlight the

widespread occurrence of bTB among cattle, particularly in crossbred and poorly

conditioned animals, with both respiratory and gastrointestinal tract

involvement in the disease's spread. The study underscores the urgent need for

enhanced control and prevention strategies against bTB in the region.

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