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**境外学者发表的结核病英文文章摘要**

**（135篇）**

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

**1. Infect Disord Drug Targets. 2025 Jul 3. doi:**

**10.2174/0118715265361578250504110100. Online ahead of print.**

Flavonoids: Potential Novel Inhibitors of Mycobacterium tuberculosis.

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Tuberculosis (TB) is a major global health concern and a leading cause of death

world-wide. The emergence of drug-resistant TB strains poses a significant

threat to public health and is contributing to the growing rate of TB infections

globally. Therefore, it is crucial to explore new and safe drugs for TB

treatment. Despite significant progress in developing new drugs, many ex-isting

treatments and prevention strategies for TB do not achieve the desired positive

health out-comes for various reasons. Small-molecule treatments can potentially

address drug resistance and provide opportunities for multimodal therapy. This

review focuses on recent advancements in un-derstanding the pathogenesis of

Mycobacterium tuberculosis and the mechanisms of flavonoids in antimycobacterial

properties. Given the urgent need for new antimycobacterial agents to enhance

the effectiveness of current drugs, investigating flavonoids as potential

candidates is promising. Evidence suggests that specific structural

characteristics in flavonoids play a significant role in their antimycobacterial

effects, among other pharmacological activities. Flavonoids can act through

various mechanisms, such as disrupting bacterial cell membranes or inhibiting

the produc-tion of essential cellular components like DNA. These findings may

prompt further research to enhance our understanding of how flavonoids combat

tuberculosis, potentially establishing their importance as key compounds in

treating the disease.

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epub@benthamscience.net.

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PMID: 40619653

**2. Lancet Respir Med. 2025 Jul 3:S2213-2600(25)00164-X. doi:**

**10.1016/S2213-2600(25)00164-X. Online ahead of print.**

Evidence required to evaluate the use of bacteriologically confirmed

asymptomatic tuberculosis disease as a primary endpoint in prevention of

tuberculosis disease vaccine licensure trials.

White RG(1), Churchyard GJ(2), Horton KC(3), Fiore-Gartland A(4), Behr MA(5),

Clark RA(3), Cobelens F(6), Ernst JD(7), Esmail H(8), Garcia-Basteiro AL(9),

Hadinegoro SR(10), Hanekom WA(11), Hatherill M(12), Hill PC(13), Muloiwa R(14),

Pelzer PT(15), Rangaka L(8), Rees H(16), Schrager L(15), Stanley M(17), Tufet

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Birmingham, Birmingham, AL, USA.

Current licensure trials of new vaccines to prevent tuberculosis disease use

bacteriologically confirmed symptomatic tuberculosis disease as the primary

endpoint. Globally, the incidence of symptomatic tuberculosis disease is low,

making licensure trials large, long, and expensive. New data suggest that

bacteriologically confirmed asymptomatic tuberculosis disease might occur more

frequently than symptomatic tuberculosis disease. Therefore, if vaccines have

efficacy against asymptomatic disease, tuberculosis vaccine licensure trials

could include it in the primary endpoint, potentially leading to smaller or

shorter trials. We describe the potential benefits and risks of this inclusion

in the primary endpoint of tuberculosis vaccine licensure trials. We also

simulate licensure trial endpoint accrual and summarise feedback from anonymous

regulators and policy makers on the knowledge needed to consider this proposal

and research studies needed to fill these evidence gaps. If bacteriologically

confirmed asymptomatic tuberculosis disease could be included in the primary

endpoint of tuberculosis disease licensure trials, it could lead to cheaper and

more rapid tuberculosis vaccine development.

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data mining, AI training, and similar technologies.

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**3. Lancet. 2025 Jul 3:S0140-6736(25)01328-5. doi: 10.1016/S0140-6736(25)01328-5.**

**Online ahead of print.**

Undoing progress through sudden tuberculosis funding cuts.

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PMID: 40618769

**4. Lancet. 2025 Jul 3:S0140-6736(25)00831-1. doi: 10.1016/S0140-6736(25)00831-1. Online ahead of print.**

The case for optimal investment in combating HIV, tuberculosis, and malaria: a

global modelling study.

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and Malaria, Geneva, Switzerland.

**BACKGROUND:** The Sustainable Development Goals (SDGs) include ending the

epidemics of HIV, tuberculosis, and malaria by 2030. With 5 years remaining to

meet this goal, and with the Global Fund to Fight AIDS, Tuberculosis and Malaria

seeking funding for programmes in 2027-29, establishing what can be achieved

through continued investment in combatting these diseases is crucial. We aimed

to estimate the potential for impact by analysing the funding landscape and

epidemiological situations of these three diseases, the costs of key programmes,

and the extent of possible future progress in the countries eligible for Global

Fund support.

**METHOD:** In this modelling study, we developed estimates of the financial

resources needed in Global Fund-supported countries to combat HIV, tuberculosis,

and malaria from the global plans produced by UNAIDS, the Stop TB Partnership,

and WHO. Estimates of available resources in the coming years were obtained by

assuming that national expenditure on the three diseases would grow in line with

general governmental expenditures, that the Global Fund would contribute an

additional $18·0 billion, and that other developmental assistance would be at

the same level in real terms as the average in the period 2020-22.

Epidemiological and costing models for each of the three diseases were used to

quantify the possible impact in Global Fund-eligible countries (including on

aggregated mortality and incidence rates). The return on investment (ROI) was

computed considering both the intrinsic value of health and the direct economic

benefits of the reduced risk of morbidity and premature mortality. The analysis

was completed at the end of 2024 with the latest available data, which pertained

to the year 2023. The focus of the projection period was 2027-29, a period for

which scale-up plans and funding have not yet been committed and the period when

most of the resources raised by the eighth replenishment of the Global Fund

would be used.

**FINDINGS:** The total resource needs for the three diseases were estimated to be

US$140·6 billion in 2027-29. We calculated that $111·3 billion (79%) of this

need could be met from domestic financing ($69·7 billion), the Global Fund

($18·0 billion), and other external donors ($23·6 billion). Optimal use of these

available resources could save 23 million lives and avert 400 million cases and

new infections during 2027-29. The trajectory of the combined mortality rate for

all diseases was projected to approach that needed to reach the SDG for 2030

(with a difference between the target in 2030 and the projection at the end of

2029 of between 1·5% and 15·5% of the normalised aggregated mortality rate),

inequality in life expectancy between countries would be 7% lower by 2029, and

189 million fewer hospital days and 572 million fewer outpatient visits would be

needed in 2027-29, saving $1·1 billion. For every $1·00 invested, there could be up to $19·00 in intrinsic health value created or $3·50 in direct economic

benefits.

**INTERPRETATION:** Continued investments to combat HIV, tuberculosis, and malaria

could yield enormous health gains and a high return on investment. Realising

these benefits will require continued growth in national expenditure and a broad

maintenance of external financing for these diseases, including a successful

replenishment of the Global Fund in 2025.

FUNDING: The Global Fund.

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**5. Respiration. 2025 Jul 5:1-16. doi: 10.1159/000547109. Online ahead of print.**

Increased Risk of Tuberculosis Disease in Lung Cancer Patients Undergoing Immune

Checkpoint Inhibitor Therapy: A Retrospective Multicenter Study.

Park Y, Min J, Lim JU, Yeo CD, Kang HS, Choi JY, Kim KY, Kim SH, Park JW.

**INTRODUCTION:** The introduction of immune checkpoint inhibitor (ICI) therapy in

lung cancer has improved survival rates, leading to its widespread use. However,

there has been a recent increase in case reports of tuberculosis (TB) disease

occurrence following ICI treatment. The objective of this study was to ascertain

whether the incidence of TB disease is elevated in the ICI group compared to the

group receiving platinum-based chemotherapy among all lung cancer patients.

**METHODS:** To compare the risk of TB disease occurrence between the ICI group and

the Platinum group in lung cancer patients, a retrospective study was conducted

using the clinical data warehouse platform of eight university hospitals

affiliated with the Catholic Medical Center in South Korea.

**RESULTS:** Out of a total of 7,980 patients, those meeting the exclusion criteria

were excluded, 991 were categorized into the ICI group, and 3,646 were

classified into the Platinum group. The TB disease incidence rate was

significantly higher in the ICI group (4.46 per 1,000 person-years) than in the

platinum group (1.12 per 1,000 person-years), with a rate ratio (RR) of 3.98

(95% CI: 1.58-10.00; p = 0.003). Multivariable analysis confirmed ICI therapy as

the sole factor significantly associated with TB disease occurrence (adjusted

HR: 3.701 95% CI: 1.467-9.333; p = 0.006).

**CONCLUSION:** Treatment with ICI in lung cancer patients was associated with a

statistically significant increase in the risk of TB disease occurrence compared

to conventional platinum-based chemotherapy. Therefore, particularly in patients

treated with ICI therapy, prompt respiratory sample tests should be performed

for early TB disease diagnosis when new lung lesions are identified.

The Author(s). Published by S. Karger AG, Basel.

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PMID: 40618751

**6. Biomed Pharmacother. 2025 Jul 5;189:118314. doi: 10.1016/j.biopha.2025.118314.**

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Metformin induces iron deprivation and enhances mitochondrial ROS in macrophages

creating a hostile environment for survival of intracellular Mycobacterium

tuberculosis.

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Diabetes, especially type 2 diabetic mellitus (T2DM) is associated with

increased risk of contracting tuberculosis (TB). Though several factors,

including immune system dysfunction, have been linked to this sensitivity the

exact reasons have yet to be fully elucidated. Although metformin, a diabetic

medication, has been suggested as a potential supplementary for host-directed

therapy of tuberculosis, the mechanisms of its anti-TB effects remain unclear.

Extremely virulent pathogens including M. tb require copious supplies of iron

for their survival within host. Macrophages are a key player of innate immunity,

and a target for invading mycobacteria to colonize. Upon infection macrophages

attempt to withhold this strategic mineral from the pathogen and clear it. We

sought to ascertain as to how anti-hyperglycemic medications like metformin

affect the regulation of iron metabolism and oxidative stress. Our findings

demonstrate that metformin decreases intracellular iron levels by decreasing the

endocytosis of iron carrier protein transferrin. Studying macrophages in a cell

culture model (in-vitro and ex-vivo) as well as from an in-vivo rodent model we

observed that the recruitment of both classical and non-classical transferrin

receptors (CD71 and GAPDH) to their surface was decreased. Metformin was also

found to induce mitochondrial ROS production though cellular ROS was inhibited.

Since iron and mitochondrial reactive oxygen species (mitoROS) are essential for

regulating intra cellular Mycobacterium tuberculosis growth, our current

findings indicate that metformin could be the first choice in the treatment for

T2DM2 in individuals from tuberculosis-endemic areas and also as an adjunct

therapeutic for TB patients in general.

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**7. Syst Rev. 2025 Jul 5;14(1):139. doi: 10.1186/s13643-025-02888-y.**

Impact of alcohol consumption, substance use, and smoking on treatment outcomes

in tuberculosis: a systematic review and meta-analysis.

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**BACKGROUND:** This study aimed to elucidate the influence of alcohol, smoking, and

substance use on tuberculosis (TB) treatment failure using a meta-analysis

approach.

**METHOD:** A comprehensive search strategy was developed and applied to three major

databases: MEDLINE, Web of Science, and Scopus. Additionally, Google Scholar,

and Google were used to locate grey literature. Studies were identified through

title and abstract screening, followed by a full-text review for eligibility.

The Newcastle-Ottawa Scale checklist was employed to assess the quality of

included studies. Pooled odds ratios (OR) with 95% confidence intervals (CI)

were calculated for each factor.

**RESULTS:** The initial database search and other sources yielded 10,518 articles.

After applying inclusion criteria, 19 studies with a total of 180,119

participants were selected for the meta-analysis. The results revealed

significant associations between all three factors and treatment failure. Pooled

ORs indicated that alcohol consumption (OR 2.05; 95% CI 1.65 to 2.55), smoking

(OR = 1.85; 95% CI 1.44 to 2.37), and substance use (OR 2.04; 95% CI 1.63 to

2.55) were each associated with an increased risk of TB treatment failure.

Additionally, the majority of included studies demonstrated high methodological

quality.

**CONCLUSION:** Our findings suggest that alcohol, smoking, and substance use are

significant risk factors for unsuccessful TB treatment. To enhance TB treatment

efficacy, preventive interventions aimed at reducing these behaviors before

treatment initiation are recommended.

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PMID: 40618124 [Indexed for MEDLINE]

**8. Tuberculosis (Edinb). 2025 Jul 1;154:102669. doi: 10.1016/j.tube.2025.102669.**

**Online ahead of print.**

Exploring novel salivary host biomarkers for immunological diagnosis of

tuberculosis: A preliminary biomarker discovery study.

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Tuberculosis is a serious public health concern on a global scale, which

emphasises the critical need for quick and precise diagnostic and treatment

response monitoring techniques. In this study, Luminex multiplex immunoassay was

used to detect the concentrations of 37 host biomarkers in saliva samples from

46 patients newly diagnosed with active pulmonary tuberculosis (PTB) and 46

patients with other respiratory diseases (ORD). Multiple logistic regression and

the area under the receiver operator characteristics curve (AUC) were used to

evaluate the diagnostic accuracy of biomarkers, which showed significant

differences between the 2 groups. This study reported that Fractalkine exhibited

the highest diagnostic accuracy and excellent discriminatory power, with

statistically significant results (p ≤ 0.05), an AUC of 0.91, 89.1 % sensitivity and 76.1 % specificity, highlighting its strong potential to distinguish PTB cases from ORD cases. Additionally, our study found that the median levels of IL-17A, IL-23, and VEGF were statistically significant (p ≤ 0.05). General discriminant analysis further identified Fractalkine, VEGF, GM-CSF, IL-23, and IL-1α as the top five most effective biomarkers for combinations. The backward elimination approach demonstrated the potential usefulness of a four-marker combination (Fractalkine + GM-CSF + IL-23 + IL-1α) as a confirmatory diagnostic tool by achieving the greatest overall diagnostic accuracy with an AUC of 0.94 and 91.3 % specificity. Thus, combining multiple markers with high discriminating power may improve diagnostic performance and subsequently provide a more accurate, non-invasive saliva-based PTB diagnostic tool.

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PMID: 40617182

**9. ACS Infect Dis. 2025 Jul 5. doi: 10.1021/acsinfecdis.5c00311. Online ahead of print.**

Design, Synthesis, and Antibacterial Evaluation of Rifampicin-Siderophore

Conjugates.

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The growing concern over antibiotic resistance has sparked increased attention

toward developing alternative antibiotic strategies. One promising approach,

known as the "Trojan horse" strategy, involves the use of siderophores to hijack

bacteria's iron transport systems as a way of delivering antibiotics inside the

bacterial cell. This method is particularly promising in tackling Gram-negative

bacteria, which have an outer membrane that many antibiotics cannot penetrate.

One such antibiotic is rifampicin, a drug used to treat tuberculosis and

infections caused by Gram-positive bacteria. Although rifampicin binds to a

highly conserved bacterial RNA subunit, its activity is generally poor against

Gram-negative bacteria due to their outer membrane. Aiming to expand

rifampicin's efficacy, we here report the design and synthesis of several

rifampicin-siderophore conjugates that exhibit enhanced activity against

Gram-negative pathogens. Our findings indicate that the structural features of

both the linker and catechol are crucial for the activity of conjugates with

compound 33, wherein rifampicin is connected to chlorocatechol via a short ester

linker, showing an up to 32-fold improvement in activity.

DOI: 10.1021/acsinfecdis.5c00311

PMID: 40616779

**10. Int J Equity Health. 2025 Jul 4;24(1):195. doi: 10.1186/s12939-025-02516-0.**

Public-private partnership to end tuberculosis: challenges and opportunities.

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DOI: 10.1186/s12939-025-02516-0

PMCID: PMC12228387

PMID: 40616075

**11. BMC Complement Med Ther. 2025 Jul 4;25(1):240. doi: 10.1186/s12906-025-04987-8.**

CRISPRi knockdown of mycobacterial tkt gene potentiates the anti-mycobacterial

activity of phyto-compounds from selected medicinal plants.

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**BACKGROUND:** Mycobacterium tuberculosis (Mtb) infection is well known to be

challenging to treat. Treatment effectiveness is restricted by the pathogen's

inherent drug resistance. A deeper understanding of essential bacterial pathways

that influence Mtb growth and survival can expediate the development of more

effective therapies from various sources. Here, using mycobacterial tkt gene as

a model target, we report on the use of CRISPR interference gene knockdown to

potentiate the antimycobacterial activity of selected medicinal plant extracts.

**METHODS:** The growth phenotypes were investigated on solid and liquid media.

Broth micro-dilution assay was used to determine minimum inhibitory

concentrations. Potential cytotoxicity of the extracts was investigated using

Vero cell lines. LC-MS was used for phytochemical analysis. In silico docking

was performed on transketolase (Rv1449c), NADH-dependent

enoyl-[acyl-carrier-protein] reductase (Rv1484), catalase-peroxidase (Rv1908c).

**RESULTS:** Phenotypic characterisation of the CRISPRi mutants showed that gradual

tkt knockdown fully, led to growth disruption. Chemical-genetic interactions

showed that tkt knockdown increased the antimycobacterial activity of acetone

extracts from Peltophorum africanum and Croton gratissimus by twofold in CRISPRi

hypomoprhs. Molecular docking data revealed that Phlorizin from C. gratissimus

(-8.1 kcal/mol), Ficus sur tritepernoid (-9.6 kcal/mol) and P. africanum

(6-hydroxydelphinidin 3-glucoside) (-8.9 kcal/mol) had the best binding

affinities to the TKT active site pocket. Moreover, these compounds had better

binding affinities to both NADH-dependent reductase and catalase-peroxidase than

Isoniazid.

**CONCLUSION:** The research demonstrated that the mycobacterial tkt gene is crucial

for bacterial growth, and CRISPRi-mediated knockdown of this gene enhanced the

anti-mycobacterial activity of phyto-compounds, which showed multiple binding

affinities to established anti-Mtb targets.

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**12. Indian J Med Microbiol. 2025 Jul 2:100912. doi: 10.1016/j.ijmmb.2025.100912.**

**Online ahead of print.**

Defining drug resistance beyond rifampicin: use of Xpert® MTB/XDR assay in

Tuberculous meningitis.

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**PURPOSE:** - The emerging drug resistance in Tuberculous meningitis (TBM) worsens

the prognosis and hamper elimination efforts. The need of the hour is a

relatively simple, rapid, near point-of-care test that could allow universal

drug susceptibility testing, beyond rifampicin (RIF). The current study

evaluated performance of Xpert MTB/XDR in defining drug resistant TBM.

**METHODS:** - A total of 45 cerebrospinal fluid samples (29 culture-positive, 16

culture-negative) reported TBM by Xpert MTB/Ultra were subjected to Xpert

MTB/XDR to determine susceptibility towards isoniazid (INH), fluoroquinolones

(FLQ), second-line injectables (SLID) and ethambutol (ETM). The performance of

Xpert MTB/XDR was evaluated against genotypic drug susceptibility testing (line

probe assay (LPA) and phenotypic drug susceptibility testing (culture)).

**RESULTS:** - There was 100% concordance between Xpert MTB/XDR and drug

susceptibility using both culture and LPA for INH and SLIDs. For FLQ, the

sensitivity and specificity of Xpert MTB/XDR was 93% and 100%, respectively

against both culture and LPA, as there was one case each reported

false-susceptible by Xpert MTB/XDR. The sensitivity and specificity of Xpert

MTB/XDR for ETM was 93% and 100%, respectively against culture and one case of

false-resistance was reported.

**CONCLUSION:** - Xpert MTB/XDR can serve as a useful tool to rapidly identify

resistance to INH, FLQ, SLID and ETM, thus offering targeted therapy to the

patients of TBM.

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Elsevier B.V. All rights reserved.

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**13. Lancet HIV. 2025 Jul 1:S2352-3018(25)00124-9. doi:**

**10.1016/S2352-3018(25)00124-9. Online ahead of print.**

Safety and immunogenicity of investigational tuberculosis vaccine M72/AS01(E-4)

in people living with HIV in South Africa: an observer-blinded, randomised,

controlled, phase 2 trial.

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K(6), Tameris M(7), Wilkinson RJ(8), Ananworanich J(2), Bower D(2), Schlehuber

L(2), Frahm N(2), Cinar A(2), Dunne M(2), Schmidt AC(2).

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Africa; Francis Crick Institute, London, UK; Department of Infectious Diseases,

Imperial College London, London, UK.

**BACKGROUND:** M72/AS01E-4 is a recombinant fusion protein vaccine candidate

derived from two Mycobacterium tuberculosis antigens (Mtb32A and Mtb39A) and

AS01E-4 adjuvant. We evaluated safety and immunogenicity of M72/AS01E-4 in

people living with HIV in South Africa.

**METHODS:** In this observer-blinded, randomised, controlled, phase 2 trial,

participants aged 16-35 years with well controlled HIV were enrolled from urban,

semi-urban, and semi-rural settings in South Africa, including sites with high

tuberculosis and HIV prevalence, as well as agricultural and mining communities.

Participants were randomly assigned (1:1), stratified by site and

interferon-gamma release assay (IGRA) status, to receive two intramuscular doses

of M72/AS01E-4 or placebo. Eligibility criteria included antiretroviral therapy

for at least 3 months, HIV viral load of less than 200 copies per mL, CD4 counts

of 200 cells per μL or higher, and previous completion of tuberculosis

preventive therapy and no tuberculosis history. The sponsor and its delegates,

the laboratory team, investigators, site staff, and participants were blinded to

randomisation, whereas an unblinded pharmacist who was not involved in trial

procedures prepared placebo and reconstituted M72/AS01E-4 in unit-dose syringes

covered with a blinding label. All participants who received at least one dose

of either M72/AS01E-4 or placebo were included in the safety population for

safety analyses. Immunogenicity analyses were conducted using the per-protocol

population, which included participants who received the intervention as planned

and did not substantially deviate from the protocol procedures. Safety

assessments included solicited adverse events in the first 7 days after each

dose, unsolicited adverse events in the first 28 days after each dose, and

serious adverse events. Humoral responses were measured with ELISA and cellular

responses were assessed using multiparameter flow cytometry, in the per-protocol

population. This study is complete and is registered with ClinicalTrials.gov,

NCT04556981.

**FINDINGS:** Between Nov 17, 2020, and Aug 12, 2022, 402 eligible participants were

assigned treatment, of whom 401 participants received at least one dose of

M72/AS01E-4 (n=201; 175 [87%] were female and 26 [13%] were male; 196 [98%] were

Black) or placebo (n=200; [176 [88%] were female and 24 [12%] were male; 196

[98%] were Black) and followed for a median duration of 372 days (IQR 364-389).

Among M72/AS01E-4 recipients, solicited adverse events were more frequent,

ranging from 17% (33 of 199) for gastrointestinal symptoms to 77% (140 of 183)

for injection-site pain. Most events were mild to moderate, with severe events

ranging from 0% (0 of 197) for swelling and (0 of 198) redness to 13% (24 of

183) for injection-site pain, resolving within 3 days. Unsolicited adverse

events related to vaccine were mainly injection-site reactions in the

M72/AS01E-4 group (8% [15 of 201] vs 1% [two of 200] in the placebo group),

including erythema, pruritis, swelling, bruising, induration, and pain. No

vaccine-related serious adverse events were reported. Among M72/AS01E-4

recipients at day 57 (1 month after dose two), M72-specific antibody geometric

mean concentration (GMC) was 479·70 EU/mL (95% CI 421·79-545·56) with median

magnitude of CD4 cells of 0·383% (IQR 0·177%-0·663). Among M72/AS01E-4

recipients, at day 57 GMCs were 559·49 EU/mL (95% CI 461·75-677·93) in with

baseline IGRA positivity and 424·95 EU/mL (357·74-504·80) in those without;

median magnitudes of CD4 cells were 0·447% (IQR 0·287-0·819) and 0·321%

(0·147-0·581).

**INTERPRETATION:** The two-dose regimen of the M72/AS01E-4 tuberculosis vaccine was

immunogenic, with an acceptable safety profile. These outcomes led to the

inclusion of people living with HIV in the ongoing global registration phase 3

trial.

FUNDING: Gates Foundation and the Wellcome Trust.

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PMID: 40614747

**14. Tuberculosis (Edinb). 2025 Jul 1;154:102672. doi: 10.1016/j.tube.2025.102672.**

**Online ahead of print.**

Efficient cell model for assessing inflammatory responsive genes in

Mycobacterium tuberculosis and SARS-CoV-2 co-infection.

de Lucena TMC(1), Miranda DEO(1), Arcoverde JVB(1), Cavalcanti MSB(1), Dantas

WM(2), Pena LJ(2), Barros de Lorena VM(3), Rabello MCDS(3), de Azevedo Silva

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Mycobacterium tuberculosis (Mtb) and severe acute respiratory syndrome

coronavirus-2 (SARS-CoV-2) may induce immunopathology with extensive lung damage

in hosts. To elucidate the dynamics of co-infection Mtb and SARS-CoV-2 and its

impact on inflammatory mediators' expression, we conducted a study to evaluate

A549, lung epithelial cells, as a potential model for hosting both pathogens

simultaneously. Cell infection initiated with Mtb H37Rv and following a 24-h

incubation period, the cells were then infected with SARS-CoV-2. After a 72 h

incubation period, a precision test was conducted for both pathogens, and total

RNA was extracted for subsequent analysis of gene expression by RT-qPCR of the

target genes: IFN-γ, TNF-α, IL-6, and IL-1β. Additionally, the levels of IL-1β, IL-2, IL-4, IL-6, IL-10, IFN-γ, and TNF-α in the culture supernatants were

measured. A549 cells are a stable and reliable cellular model for co-infection

between Mycobacterium tuberculosis and SARS-CoV-2. Co-infection with both

pathogens led to downregulation of IFN-γ, TNF-α, and IL-10, and upregulation of

IL-6 and IL-1β compared to uninfected cells. A549 cells function as a cellular

model for co-infection and seems a good model for elucidating host inflammatory

responses in the initial site of infection.

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DOI: 10.1016/j.tube.2025.102672

PMID: 40614291

**15. Sci Immunol. 2025 Jul 4;10(109):eaea0953. doi: 10.1126/sciimmunol.aea0953. Epub 2025 Jul 4.**

TB or not TB: That depends on the antibody Fc.

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Fc-swapped variant monoclonal antibodies reveal new mechanisms underlying

Mycobacterium tuberculosis restriction.

DOI: 10.1126/sciimmunol.aea0953

PMID: 40614213 [Indexed for MEDLINE]

**16. FEMS Microbiol Ecol. 2025 Jul 4:fiaf072. doi: 10.1093/femsec/fiaf072. Online**

**ahead of print.**

Genomic Survey Reveals no Detectable Bacteriophage Activity in Mycobacterium

bovis Across a Large Population.

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Universidade de Lisboa, Lisboa, Portugal.

Phages are major drivers of bacterial evolution, yet their ecological and

evolutionary interactions with Mycobacterium bovis, a key member of the

Mycobacterium tuberculosis complex (MTBC), remain understudied. In this work, we

investigate the elusive phage-bacterium interface in M. bovis by integrating

comparative genomics of 200 isolates from infected animals with molecular

analyses of M. bovis-positive environmental samples. Despite employing diverse

and complementary approaches, we found no evidence of active or recent phage

infections: no novel prophages beyond the conserved phiRv1, no expansion of

CRISPR arrays, and no co-occurrence of M. bovis and mycobacteriophages in host

tissues or environmental matrices. Intriguingly, we identified multiple

independent excision events of phiRv1 across closely related lineages,

suggesting recent prophage mobilization driven by unidentified ecological or

genomic triggers. These findings echo previous observations in M. tuberculosis

and point toward a stable, phage-scarce landscape across MTBC members. Our

results raise compelling questions about the barriers to phage predation in M.

bovis, the functionality of its CRISPR-Cas system, and the selective pressures

underlying prophage retention and loss. By shedding light on these underexplored

dynamics, our study reveals critical gaps in the ecological understanding of M.

bovis and highlights opportunities for phage-based innovation in TB control.

© The Author(s) 2025. Published by Oxford University Press on behalf of FEMS.

DOI: 10.1093/femsec/fiaf072

PMID: 40613815

**17. J Dtsch Dermatol Ges. 2025 Jul 4. doi: 10.1111/ddg.15674. Online ahead of print.**

Recognising cutaneous tuberculosis.

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Author information:

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Technical University of Munich, Munich, Germany.

Tuberculosis (TB) continues to be a leading cause of death in many countries,

and also remains a significant concern in Germany, particularly due to

migration. The diagnosis of rare cutaneous tuberculosis is challenging as it

manifests in various clinical forms that resemble more common dermatological

conditions. Especially in paucibacillary forms, gold-standard diagnostic tests

may yield negative results, complicating the identification of the disease.

Therefore, a strong clinical suspicion based on the clinical presentation is

essential for guiding further or repeated diagnostic evaluations. In this

article, we present various forms of cutaneous tuberculosis, using excerpts from

the image collection of the Department of Dermatology and Allergy at

Biederstein, Technical University of Munich, to improve clinical recognition of

cutaneous TB and raise awareness of this condition also as a potential

differential diagnosis.

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Gesellschaft.

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**18. Future Med Chem. 2025 Jul 4:1-15. doi: 10.1080/17568919.2025.2525069. Online**

**ahead of print.**

Exploration of pyrazole-based pyridine-4-carbohydrazide derivatives as

drug-resistant Mtb agents: design, synthesis, biological evaluation, and

in-silico studies.

Kumar P(1), Malik P(2), Ali J(2), Saxena D(2), Singampalli A(1), Bandela R(1),

Bellapukonda SM(1), Rajyalakshmi SI(1), Bhale NA(3), Dikundwar AG(3), Nanduri

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India.

**BACKGROUND:** Development of new effective drugs against multidrug resistant

Mycobacterium tuberculosis is the need of the hour to combat tuberculosis (TB)

disease.

**MATERIALS AND METHODS:** Pyridine-4-carbohydrazide and substituted pyrazole

aldehydes were used to synthesize target molecules (6a-r) which were evaluated

against H37Rv and drug-resistant TB strains. Time kill kinetics assay was

performed to check bactericidal/bacteriostatic effect, molecular docking,

dynamics simulation over 100 ns was performed against enoyl acyl carrier protein

reductase (InhA) along with QSAR, ADMET profile prediction.

**RESULTS:** All compounds displayed excellent MICs in the range of 0.125-16 µg/mL.

The most potent compound, 6q, with an MIC of 0.125 µg/mL showed bactericidal

effect and was effective on ethambutol and streptomycin resistant Mtb strains

with an MIC of 0.03 µg/mL and rifampicin resistant Mtb strain with an MIC of

0.25 µg/mL.

**CONCLUSION:** The pyrazole clubbed with pyridine-4-carbohydrazide is a potential

scaffold for further exploration as anti-TB agent.

DOI: 10.1080/17568919.2025.2525069

PMID: 40613379

**19. J Brown Hosp Med. 2025 Jul 1;4(3):140744. doi: 10.56305/001c.140744. eCollection 2025.**

Peritoneal Tuberculosis in a Patient on Tumor Necrosis Factor inhibitors: A Case

Report and Review of the Literature.

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Peritoneal tuberculosis (PTB) is a diagnostic challenge due to its nonspecific

presentation, low sensitivity of ascitic fluid microbiologic tests, and possible

resemblance to peritoneal carcinomatosis. We describe a case of 51-year-old

woman with long-term tumor necrosis factor alpha (TNF-α) inhibitor exposure

presented with fever and abdominal distension after returning from the

Philippines. Initial tests, including microbiological studies, were

inconclusive, despite imaging findings suggestive of carcinomatosis with

elevated CA-125. Diagnostic laparoscopy revealed miliary white nodules; however,

omental biopsy showed non-necrotizing granulomas without AFB. High clinical

suspicion prompted excision of an enlarged axillary lymph node, which

demonstrated necrotizing granulomas with rare AFB-positivity and ultimately grew

Mycobacterium tuberculosis. The patient experienced rapid symptomatic relief and

near-complete radiological resolution within four months of tuberculosis (TB)

treatment. PTB should remain on the differential for unexplained ascites or

peritoneal nodularity - particularly in immunosuppressed travelers from endemic

regions - even when early microbiologic tests are negative. Timely invasive

sampling and, when warranted, empirical anti-TB therapy is critical. Clinicians

must recognize that patients on TNF-α inhibitors remain at heightened risk for

extrapulmonary TB despite negative baseline screening.

DOI: 10.56305/001c.140744

PMCID: PMC12224322

PMID: 40612084

**20. BMC Infect Dis. 2025 Jul 3;25(1):891. doi: 10.1186/s12879-025-11284-9.**

Genotyping and transmission analysis of Mycobacterium tuberculosis in a

pediatric population in Czech Republic and Slovakia.

Mäsiarová S(1), Dvořáková V(2), Hromádková M(2), Norman A(3), Kunč P(4)(5),

Fábry J(4)(5), Hnilicová J(6), Porvazník I(7)(8), Solovič I(7)(8), Rasmussen

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**BACKGROUND:** Tuberculosis remains a global health concern, with rising pediatric

and adolescent cases. The advancement of diagnostic strategies is crucial for

effective control, with whole-genome sequencing emerging as a promising tool.

This study explores using whole-genome sequencing in pediatric Tuberculosis.

**METHODS:** Mycobacterium tuberculosis isolates from pediatric patients and their

contacts were collected between January 2023 and June 2024 in Slovakia and the

Czech Republic. The isolates were subjected to WGS to characterize the

resistance patterns and transmission.

**RESULTS:** The study included 37 patients in total-30 pediatric cases and 7 adult

index cases-with a single M. tuberculosis isolate collected per patient. The

phylogenetic analysis results revealed that 32 out of 37 (86.5%) isolates

belonged to the Euro-American lineage. Five isolates (13.5%) belonged to the

East-Asian lineage. Genotypic resistance to at least one drug was confirmed in 6

patients (16%). 24 patients were divided into 9 clusters (65%), leaving 13

unclustered (35%). Moreover, the concordance between the identification of

source case by WGS and epidemiological anamnesis was confirmed in 60% of

patients.

**CONCLUSIONS:** Epidemiological data may not always provide accurate insights into

the transmission of TB. Consequently, integrating molecular methods, such as

WGS, is essential to enhance the reliability and precision of epidemiological

analyses.

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DOI: 10.1186/s12879-025-11284-9

PMCID: PMC12225057

PMID: 40610922 [Indexed for MEDLINE]

**21. Eur J Intern Med. 2025 Jul 2:S0953-6205(25)00269-9. doi:**

**10.1016/j.ejim.2025.06.031. Online ahead of print.**

Constrictive pericarditis and tuberculosis: A second look.

Beun AJ(1), Gabrovska M(2), Nasreddine R(3).

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DOI: 10.1016/j.ejim.2025.06.031

PMID: 40610345

**22. Eur Respir J. 2025 Jul 3:2500902. doi: 10.1183/13993003.00902-2025. Online ahead of print.**

Risk of rifampin resistance emergence after incomplete first-line tuberculosis

treatment.

Dupuis GN(1), Dolynska M(2), Chiang SS(3)(4), Horsburgh CR Jr(1)(5), Stagg

HR(6), Rybak NR(7), Petrenko V(8), Jenkins HE(1).

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DOI: 10.1183/13993003.00902-2025

PMID: 40610055

**23. Eur Respir J. 2025 Jul 3:2500992. doi: 10.1183/13993003.00992-2025. Online ahead of print.**

Post Tuberculosis Lung Disease: questions and answers.

Migliori GB(1), Centis R(2), D'Ambrosio L(3), Rossato Silva D(4), Podlekareva

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Africa.

DOI: 10.1183/13993003.00992-2025

PMID: 40610051

**24. Hum Vaccin Immunother. 2025 Dec;21(1):2521190. doi:**

**10.1080/21645515.2025.2521190. Epub 2025 Jul 3.**

Unleashing the power of the BCG vaccine in modulating viral immunity through

heterologous protection: A scoping review.

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The Bacillus Calmette-Guérin (BCG) vaccine, used against tuberculosis for a

century, shows promise in protecting against viral infections through

trained/innate immunity. This review maps clinical and preclinical studies on

both parental (WT) and recombinant BCG (rBCG) against 17 common viruses. From 68

studies, BCG strains were found to enhance innate immune responses by

reprogramming myeloid cells, leading to stronger responses to related

infections. Sixteen rBCG candidates expressed viral antigens, activating CD4+

and CD8+ T cells, and stimulating antibody production specific to the viral

antigens. However, challenges like genetic stability and varied efficacy among

BCG strains remain. The review highlights the potential of BCG, especially rBCG,

as a multivalent vaccine platform for immunization campaigns, with significant

public health implications. More translational studies and clinical trials are

needed to confirm these findings.

DOI: 10.1080/21645515.2025.2521190

PMID: 40610004 [Indexed for MEDLINE]

**25. PLoS One. 2025 Jul 3;20(7):e0326324. doi: 10.1371/journal.pone.0326324.**

**eCollection 2025.**

Breaking barriers for TB elimination: A novel community-led strategy

revolutionizing tuberculosis case finding and treatment support in Senapati

District Manipur-A quasi-experimental pre-post study protocol.

S A(1), S S(2), K N(1), M M(1), B W(1), L M(3), Sk M(4), V E(5), Ws S(3), D

N(1), A N(1), Kt L(1), T S(3), P P(6), D N(1), Anand S V(1), Rk E(7), Ps M(8),

Rn H(9), P Y(8), S P(6), C PP(1), H K(2).

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**INTRODUCTION**: Despite being the world's highest tuberculosis (TB) burden

country, India still misses millions of TB cases annually. To address this

issue, the India National Strategic Plan, following WHO strategy, promotes

combining active case finding (ACF) with passive case finding (PCF) activities.

National TB Elimination Programme (NTEP) began ACF campaigns thrice a year,

targeting vulnerable populations. However, states like Manipur faced challenges

in implementing and sustaining ACF activities due to resource constraints.

**OBJECTIVE:** To assess the impact of engaging student and women organizations

(SAWOs) in improving TB case notifications, treatment adherence, and completion

rate in NTEP, as well as to estimate the cost-effectiveness of the ACF

intervention.

**METHOD:** A quasi-experimental pre-post study is being conducted among individuals

≥15 years residing in Senapati District, Manipur, having two phases: preparatory

and enhanced case finding and implementation of the ACF. Data is being collected

and compared on TB case notification, treatment adherence, and outcomes

beforeand after the intervention. Chi-square test will be used to test the

statistical significance and logistic regression to identify the factors

independently associated with the impact of intervention. Potential confounders

at both patient and facility levels will be identified based on expert opinion

and bivariate analysis. A multi-level logistic regression model will be used to

control the confounding, with sensitivity analysis to ensure result

robustness.Cost analysis will cover direct, indirect, medical, and non-medical

costs for patients and health system. Incremental cost-effectiveness ratio per

quality-adjusted life years gained will be evaluated.

**DISCUSSION:** This study introduces a novel community-led model involving SAWOsto

improve TB case detection and treatment support, comprehensively addressing

allfour pillars of 'END TB' strategy. The intervention is a community-based

participatory research, emphasizing collaboration between researchers

andcommunity to address TB control. The main activities of this intervention

include community TB sensitization, ECF, ACF, treatment support and monitoring.

This model could significantly impact TB control efforts, especially in

resource-constrained settings like Manipur, offering valuable insights into ACF

implementation and its economic implications.

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and source are credited.

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PMID: 40608799 [Indexed for MEDLINE]

**26. Rev Saude Publica. 2025 Jun 30;59:e11. doi: 10.11606/s1518-8787.2025059006489.**

**eCollection 2025.**

Spatial clusters of risk and cartography of care for drug-resistant

tuberculosis.

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IZ(1), Palha PF(1), Monroe AA(1), Ferreira QR(1), Leal GDC(1), Teixeira LO(1),

Costa YBD(1), Pinto IC(1), Andrade RLP(1), Arcêncio RA(1).

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Preto, SP, Brasil.

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**OBJECTIVE:** To identify spatial clusters of risk and map the care network for

people with drug-resistant tuberculosis in the state of São Paulo.

**METHODS:** This is an ecological study, carried out by collecting data from the

Special Tuberculosis Treatment Information System (Site-TB) of people treated

for drug-resistant tuberculosis from 2013 to 2020, in the state of São Paulo.

Mapping was carried out using Kernel and scan statistic techniques.

**RESULTS:** 1,084 cases were reported in the period analyzed. São Paulo, Ribeirão

Preto, Santos, Guarulhos, and Campinas were the municipalities with the highest

number of cases. The spatial pattern of agglomeration of cases and referral

centers for treatment were similar, with gaps in coverage in the southwest and

northwest of the state. Six spatial clusters were identified: four low-risk and

two high-risk, located in São Paulo, Diadema, Santos, and Guarujá.

**CONCLUSIONS:** The concentration of cases and tertiary referral centers in

metropolitan areas highlights inequalities in access to treatment for

drug-resistant tuberculosis. These findings indicate the need for health

policies to expand diagnosis and treatment, improving the control of

drug-resistant tuberculosis in the state of São Paulo.

DOI: 10.11606/s1518-8787.2025059006489

PMCID: PMC12211794

PMID: 40608609 [Indexed for MEDLINE]

**27. Acta Pharm. 2025 Jul 3;75(2):185-218. doi: 10.2478/acph-2025-0016. Print 2025**

**Jun 1.**

Development and evaluation of novel InhA inhibitors inspired by thiadiazole and

tetrahydropyran series of inhibitors.

Rambaher MH(1), Gradišek N(1), Frlan R(1), Sosič I(1), Bolje A(1), Kljun J(2),

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Tuberculosis (TB), caused by Mycobacterium tuberculosis, remains a leading

global health challenge, exacerbated by the emergence of multidrug-resistant

(MDR) and extensively drug-resistant (XDR) strains. One promising therapeutic

target is the enzyme enoyl-acyl carrier protein reductase (InhA), which plays a

vital role in the biosynthesis of mycolic acids, essential components of the

bacterial cell wall. Direct inhibition of InhA offers a potential strategy for

overcoming resistance mechanisms, particularly in cases where the activation of

conventional drugs like isoniazid is compromised. This study investigates two

novel series of InhA inhibitors based on thiadiazole and tetrahydropyran lead

compounds, originally identified through high-throughput screening by GSK.

Analogues were synthesised using the copper-catalysed azide-alkyne cycloaddition

(CuAAC) click reaction, and their inhibitory activity was tested against InhA.

Among the tested compounds, only one exhibited modest inhibitory activity, with

an IC 50 of 11 µmol L-1, while others were inactive. Interestingly, during the

synthetic efforts, a novel reaction was discovered between aryl methyl ketones

and ethynylmagnesium bromide, yielding 1,3-diols, as confirmed by X-ray

diffraction analysis. These findings underscore the challenges of optimising

InhA inhibitors and highlight the potential of synthetic innovations in

exploring new synthetic pathways.

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DOI: 10.2478/acph-2025-0016

PMID: 40608557 [Indexed for MEDLINE]

**28. Appl Biochem Biotechnol. 2025 Jul 3. doi: 10.1007/s12010-025-05299-w. Online**

**ahead of print.**

Molecular Cloning, Optimization of Expression and Functional Characterization of

the Global Transcriptional Regulator MosR (Rv0348) of Mycobacterium

tuberculosis.

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In-vivo microarray analysis on murine model of Tuberculosis had identified a

novel transcriptional regulator MosR, which regulates the expression of ~ 163

genes, many of which are important for intracellular persistence of dormant

Mycobacterium tuberculosis. MosR therefore, may be considered as potential

target for anti-tuberculosis drug discovery. In this work, this important

regulator has been cloned, expressed, purified to homogeneity, and characterized

to some extent. MosR is found to cooperatively bind within the ORF of the

previous gene rv0347. The environmental conditions for most favorable

interaction between MosR and its cognate DNA are determined to be 8.0 pH, 25 mM

NaCl, and 25 ℃ temperature. The equilibrium dissociation constant (Kd) for

MosR-DNA interaction is determined to be 0.23 ± 0.02 µM under the optimized

conditions. MosR is composed of mostly α-helices with minor β-sheets and β-turns as major secondary structural elements. Interestingly, MosR is found to harbor a highly conserved homeodomain and a long N-terminal arm which might be involved in binding to specific DNA, supported by the predicted three-dimensional

structure. The tertiary structure of MosR is found to be stable under different

pH and salt concentrations while secondary structure undergoes distinct

conformational changes. MosR is unable to maintain its structure and DNA-binding

activity at a temperature more than 35 ℃ and forms microaggregate in solution

which suggests that it is a moderately thermosensitive protein. These

information would be useful for in-vitro screening and validations of inhibitors

against MosR in a high throughput manner.

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Media, LLC, part of Springer Nature.

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PMID: 40608257

**29. Clin Pharmacokinet. 2025 Jul 3. doi: 10.1007/s40262-025-01537-w. Online ahead of print.**

Rifampicin Exposure in Tuberculosis Patients with Comorbidities in Sub-Saharan

Africa: Prioritising Populations for Treatment-A Systematic Review and

Meta-analysis.

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**BACKGROUND AND OBJECTIVES:** Emerging evidence suggests that comorbidities like

human immunodeficiency virus (HIV) infection, diabetes mellitus (DM), and

malnutrition in tuberculosis (TB) patients can alter drug concentrations,

thereby affecting the treatment outcomes. For these populations, personalised

strategies such as therapeutic drug monitoring (TDM) may be essential. We

investigated the variations of drug levels within comorbid populations and

analysed the differences in patterns observed between sub-Saharan Africa (SSA)

and non-SSA regions.

**METHODS:** We performed a systematic review and meta-analysis of rifampicin drug

pharmacokinetics (PK) through searches of major databases from 1980 to December

2023. A random-effects meta-analysis model using R-studio version 4.3.2 was

conducted to estimate pooled serum rifampicin exposure (area under the

concentration-time curve [AUC], and peak maximum concentration [Cmax]) between

patients with TB-HIV infection, and TB-DM.

**RESULTS:** From 3300 articles screened, 24 studies met inclusion criteria,

contributing 33 comorbidity subgroups for meta-analysis. In SSA, 14 subgroups

assessed rifampicin PK in TB-HIV, 1 in TB-DM, and none in TB-malnutrition. The

pooled mean Cmax was below the recommended range (8-24 mg/L) for all subgroups.

For TB-HIV, the pooled Cmax was 5.59 mg/L, 95% CI (4.59-6.59), I2 = 97% for SSA

populations and 5.59 mg/L, 95% CI (3.65; 6.59) for non-SSA populations. The Cmax

for TB-DM in SSA (9.60 ± 4.4 mg/L) exceeded non-SSA (4.27 mg/L, 95% CI

[2.77-5.76]). The lowest AUC was in TB-HIV (SSA, 29.09 mg/L h, 95% CI [21.06;

37.13, I2 = 91%]). High variability and heterogeneity (I2 >90%) were observed,

with most studies (20/23) showing low bias.

**CONCLUSION:** Our results emphasise the need for individualised dosing and

targeted TDM implementation among TB-HIV and TB-DM populations on rifampicin in

SSA. Although all populations exhibited low Cmax levels, TB-HIV populations may

be prioritised as AUC levels were lowest. In clinical settings in SSA,

Cmax-based TDM is more practical, but AUC can be used in treatment where

feasible.

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DOI: 10.1007/s40262-025-01537-w

PMID: 40608197

**30. Curr Microbiol. 2025 Jul 3;82(8):361. doi: 10.1007/s00284-025-04341-8.**

Proteomic Analysis of Drug-Resistant Mycobacterium tuberculosis Clinical

Isolates Under Aminoglycoside Drug Pressure.

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Pharmacoproteomics enables the actual status of the drug-induced conditions at

the protein level. Aminoglycosides have been a major component of second-line

anti-TB therapy and with a well-known mechanism to inhibit protein synthesis in

bacteria by interacting with several steps of the translational process.

Researchers suggested the benefit of treating antibiotic-resistant M.

tuberculosis strains with the same antibiotics at an effective and safe level.

In this study, we analyzed the pharmaco-proteomic effects of aminoglycosides on

eight drug-resistant clinical isolates by 2DE coupled with MALDI-TOF MS.

Further, bioinformatics tools have been employed to characterize the

protein-antibiotic interactions. This study revealed that nine proteins showed

consistently increased intensities under drug pressure. 60 kDa chaperonin1

(Rv3417c) is a heat shock protein (Hsp) that plays a key role in the survival of

bacilli under stress conditions. Elongation factor Tu (Rv0685) promotes

GTP-dependent binding of aminoacyl-tRNA to the A-site of the ribosome during

protein biosynthesis. Dihydrolipoyl dehydrogenase (Rv0462) is involved in energy

metabolism. Ribosome recycling factor Rv2882c is responsible for increasing the

efficiency of translation by recycling ribosomes from one round of translation

to another. Proteasome subunit beta (Rv2110c) is involved in protein

degradation. Antigen 85-A precursor (Rv3804c) is involved in cell-wall

mycoloylation. Three proteins (Rv2623, Rv3389c, and Rv2744c) were identified

with unknown functions. Overexpressed proteins and pathways could be

directly/indirectly involved in aminoglycoside resistance. Bioinformatics

revealed that three proteins of unknown functions showed good binding with

aminoglycosides, suggesting their direct/indirect role in resistance, and need

further exploration.

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Media, LLC, part of Springer Nature.

DOI: 10.1007/s00284-025-04341-8

PMID: 40608075 [Indexed for MEDLINE]

**31. IJU Case Rep. 2025 May 28;8(4):419-422. doi: 10.1002/iju5.70057. eCollection**

**2025 Jul.**

Combination of Neoadjuvant Gemcitabine-Cisplatin and Anti-Tuberculosis Therapy

for a Patient With Muscle-Invasive Bladder Cancer and Renal Granulomatosis That

Progressed After Intravesical Bacillus Calmette-Guérin Therapy.

Tsumori T(1), Hoshi S(1), Yaginuma K(1), Meguro S(1), Matsuoka K(1), Hata J(1),

Sato Y(1), Akaihata H(1), Ogawa S(1), Kojima Y(1).

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**INTRODUCTION:** A case of muscle-invasive bladder cancer and renal granulomatosis

that developed after intravesical Bacillus Calmette-Guérin therapy, in which a

combination of neoadjuvant gemcitabine-cisplatin and anti-tuberculosis therapy

was safely administered, and radical cystectomy was ultimately performed, is

reported.

**CASE PRESENTATION: A** 64-year-old man with non-muscle-invasive bladder cancer

underwent transurethral resection and intravesical Bacillus Calmette-Guérin

therapy every time bladder cancer recurred. However, the patient developed left

renal granulomatosis during treatment. Anti-tuberculosis therapy was prioritized

since there was no bladder cancer progression. However, local bladder cancer

progression was observed during the anti-tuberculosis therapy. To successfully

cure the renal granulomatosis and suppress tumor progression, neoadjuvant

gemcitabine-cisplatin was combined with anti-tuberculosis therapy for 2 months,

followed by radical cystectomy. There were no gemcitabine-cisplatin

complications and no renal granulomatosis recurrence during combination therapy.

**CONCLUSION:** Combination of gemcitabine-cisplatin and anti-tuberculosis therapy

was possible for a patient with bladder cancer when Bacillus Calmette-Guérin

infection was under control.

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Ltd on behalf of Japanese Urological Association.

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PMCID: PMC12212942

PMID: 40607477

**32. Open Forum Infect Dis. 2025 Jun 11;12(7):ofaf347. doi: 10.1093/ofid/ofaf347.**

**eCollection 2025 Jul.**

Social Vulnerability Modifies the Effects of Geographic Proximity on Engagement

in Latent Tuberculosis Infection Care in a United States Safety Net Healthcare

Network.

Campbell JI(1), Garing A(1), Lavache D(1), Bahad S(2), Hofman M(3), Haberer

JE(4)(5), Brooks MB(6), Sinha P(7), White LF(8), Sabharwal V(1), Tschampl CA(9),

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Chobanian and Avedisian School of Medicine, Boston, Massachusetts, USA.

**BACKGROUND:** Latent tuberculosis (TB) infection care often requires engagement

with multiple teams in several locations throughout the diagnostic and treatment

steps of the TB infection care cascade. The intersecting effects of geographic

proximity and social drivers on care cascade retention have not been well

examined.

**METHODS:** We conducted a retrospective cohort study of patients with a positive

TB infection test between 2018-2019 within a health system in Boston,

Massachusetts. The primary outcome was attendance at a TB clinic after a

referral was placed. The primary exposure was geographic proximity, as measured

by travel time by car. We assessed effect modification of proximity by Social

Vulnerability Index (SVI), a composite measure of census tract social drivers.

**RESULTS:** We identified 1677 patients with positive TB infection tests; 1208

(72%) were referred to a TB clinic, of whom 748 (62%) completed referral. Longer

travel times were associated with lower odds of referral completion (furthest vs

nearest quartiles: adjusted odds ratio, 0.76 [95% confidence interval,

.71-.82]). SVI significantly modified the effects of proximity: Increasing

travel time was associated with decreasing probability of clinic attendance for

patients in lower-vulnerability census tracts but had minimal effect on clinic

attendance among patients in higher vulnerability census tracts.

**CONCLUSIONS:** Additional support is needed for individuals referred to TB clinics

that require long travel times to attend. Support should also account for other

social drivers affecting care access for those living near TB clinics.

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Infectious Diseases Society of America.

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PMID: 40606058

**33. J Infect Dis. 2025 Jul 3:jiaf354. doi: 10.1093/infdis/jiaf354. Online ahead of print.**

Single-cell transcriptomics reveals depletion and dysregulation of Mycobacterium

tuberculosis-specific Th1 and Th17 cells early after acquisition of HIV.

Pearson RA(1)(2), Krish KN(1)(2), Whatney WE(1)(2), Jaoko W(3), Mandaliya K(4),

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HIV significantly increases the risk of developing tuberculosis (TB) and is

associated with impaired CD4 T cell responses to Mycobacterium tuberculosis

(Mtb). We evaluated the frequency and functional capacity of Mtb-specific CD4 T

cells in individuals with and without HIV using flow cytometry and performed

single-cell RNA sequencing on these cells longitudinally in a subset of

individuals before and after acquisition of HIV. Our findings reveal

preferential depletion and functional impairment of Mtb-specific CD4 T cells

early after acquisition of HIV, characterized by reduced cytokine production,

loss of effector functions, and transcriptional dysregulation. Mtb-specific Th1

and Th17 cells decreased, whereas TCF7+ stem-like cells were enriched following

acquisition of HIV. Pathway analysis revealed upregulation of hypoxia and WNT

signaling, and downregulation of cell adhesion, migration, antigen processing,

and cytokine signaling pathways. These findings provide novel insights into

HIV-mediated dysregulation of CD4 T cell responses to Mtb.

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PMID: 40605619

**34. BMC Public Health. 2025 Jul 2;25(1):2260. doi: 10.1186/s12889-025-23491-9.**

Impact of the COVID-19 pandemic on unfavorable tuberculosis outcomes: a

comparative analysis of unhoused and general populations.

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**INTRODUCTION:** Tuberculosis care has been seriously affected by the COVID-19

pandemic. Few studies have assessed the impact of the pandemic on tuberculosis

outcomes in vulnerable populations. We aimed to evaluate tuberculosis outcomes

before and during the pandemic in general and in unhoused populations in São

Paulo, Brazil.

**METHODS:** We performed a retrospective cohort study that compared tuberculosis

outcomes between the unhoused and general populations using data from 2017 to

2019 and 2020 to 2022. Unfavorable outcomes were defined as loss to follow-up,

treatment failure, death, toxicity, and resistance to drugs. Cox regression

models and Kaplan‒Meier curves were used to evaluate the data.

**RESULTS**: Among 47,293 patients diagnosed with tuberculosis using the National

Notifiable Diseases Information System (SINAN) between January 1, 2017, and

December 31, 2021, 29,247 patients were included in our study. Patients

diagnosed with TB during the pandemic were more likely to have unfavorable

outcomes in the general population (hazard ratio [HR], 1.45, [95% confidence

interval (CI), 1.37 to 1.55], p < 0.001), but not in the unhoused population.

Patients with lost to follow-up (HR, 1.42, 95% CI 1.21-1.66, p < 0.001) or

hospitalized (HR, 1.50, 95%CI 1.29-1.74, p < 0.001) were more likely to

experience unfavorable outcomes in the unhoused population.

**CONCLUSIONS:** In conclusion, during the pandemic of COVID-19 period the

tuberculosis care was not affected in the specific unhoused population but

rather affected the general population in the largest city of São Paulo, Brazil.

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PMID: 40604738 [Indexed for MEDLINE]

**35. Lancet Public Health. 2025 Jul;10(7):e588-e598. doi:**

**10.1016/S2468-2667(25)00120-3.**

Sex differences in the risk of Mycobacterium tuberculosis infection: a

systematic review and meta-analysis of population-based immunoreactivity

surveys.

Rickman HM(1), Phiri MD(2), Feasey HRA(3), Krutikov M(4), Shao H(5), Horton

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**BACKGROUND:** Tuberculosis killed 1·25 million people globally in 2023. Men have a 1·7 times higher tuberculosis incidence than women, but it is not known to what extent this discrepancy is driven by greater exposure to Mycobacterium

tuberculosis. We aimed to analyse the effect of age and sex on M tuberculosis

immunoreactivity.

**METHODS:** In this systematic review and meta-analysis, we reviewed Embase, Global

Health databases, Science Citation Index Expanded, and Global Index Medicus for

population-based M tuberculosis immunoreactivity (with interferon-γ release

assay or skin test) surveys done in high tuberculosis incidence settings from

Jan 1, 1993, to Dec 31, 2022, with a sample size of at least 150 people. We

included cross-sectional surveys, baseline surveys for interventional or cohort

studies, and control groups of case-control studies with

population-representative groups. We extracted data on M tuberculosis

immunoreactivity prevalence, disaggregated by sex and age group. We constructed

Bayesian hierarchical models, first of immunoreactivity prevalence by age and

sex and second of the male-to-female (M:F) prevalence ratio by age. We analysed

the effect of covariables including region, tuberculosis incidence, and study

year. This study was registered on PROSPERO (CRD42022360483).

**FINDINGS:** We screened 26 517 studies, of which 167 met our inclusion criteria.

Sex-disaggregated results were available from 80 studies (81 surveys), from 38

different countries, comprising data from 478 968 participants. We found little

sex difference in M tuberculosis immunoreactivity in childhood (M:F prevalence

ratio for children younger than 10 years was 0·95; 95% credible interval

0·90-1·01). However, from adolescence onwards, men experienced higher

immunoreactivity conversion than women (1·4 times higher by age 30 years). This

higher conversion rate cumulatively drove a higher immunoreactivity prevalence

in men, with a prevalence ratio of 1·07 (95% credible interval 1·01-1·13) in

those aged 10-19 years, 1·13 (1·06-1·20) in those aged 20-39 years, and 1·28

(1·19-1·37) for those aged 40 years and older. Adult men had consistently higher

M tuberculosis prevalence across different settings, with low between-study

heterogeneity in M:F prevalence ratio.

**INTERPRETATION:** Men have higher M tuberculosis immunoreactivity risk than women,

which is likely to be a key driver of the sex differences in global tuberculosis

morbidity and mortality. This difference could be due to higher exposure through

social and behavioural differences in time spent in congregate indoor spaces

where tuberculosis transmission occurs, further amplified by longer duration of

infectiousness in men, and age-assortative and sex-assortative mixing. Public

health interventions addressing men's determinants of M tuberculosis exposure

will be crucial to ending the tuberculosis epidemic.

FUNDING: Wellcome Trust and UK Foreign, Commonwealth & Development Office.

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PMID: 40602858 [Indexed for MEDLINE]

**36. Sci Adv. 2025 Jul 4;11(27):eadw5194. doi: 10.1126/sciadv.adw5194. Epub 2025 Jul 2.**

Loss of the PPE71-esxX-esxY-PPE38 locus drives adaptive transcriptional

responses and hypervirulence of Mycobacterium tuberculosis lineage 2.

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Mycobacterium tuberculosis (M.tb) is remarkable for its immense global disease

burden and low mutation rate. Despite strong selective pressure, M.tb shows

frequent deletions at the PPE71-38 locus, most notably in hypervirulent L2

Beijing strains. Here, we show that loss of the PPE71-38 locus causes increased

stress response gene expression and increased triglyceride levels. In addition,

we demonstrate that reintroduction of PPE71 into the L2 strain HN878 suppresses

the baseline elevation of these transcripts, while overexpression of PPE71

increases the localization of PE\_PGRS proteins and lipoproteins to the M.tb

outer mycomembrane. Mouse infection confirmed the hypervirulence of the PPE71-38

deletion strain and conversely showed that PPE71 overexpression attenuates M.tb.

Our results indicate that loss of PPE71-38 is sufficient to drive an adaptive

transcriptional response seen in M.tb L2 strains that likely contributes to the

hypervirulence of this lineage.

DOI: 10.1126/sciadv.adw5194

PMCID: PMC12219505

PMID: 40601738 [Indexed for MEDLINE]

**37. PLoS Negl Trop Dis. 2025 Jul 2;19(7):e0013204. doi:**

**10.1371/journal.pntd.0013204. eCollection 2025 Jul.**

Treatment outcomes of multi-drug-resistant and rifampicin-resistant tuberculosis

with and without isolation of nontuberculous mycobacteria between 2018-2021: A

retrospective cohort study in Ghana.

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Multi-drug-resistant and rifampicin-resistant tuberculosis (MDR/RR-TB) pose an

urgent health threat in Ghana. Despite ongoing interventions, the outcomes for

MDR/RR-TB in Ghana have remained suboptimal over recent years. During this

period, there has been an increasing detection of nontuberculous mycobacteria

(NTM) in mycobacterial cultures. We sought to examine if the isolation of NTM

could be a factor contributing to unfavourable MDR/RR-TB treatment outcomes. We

also estimated predictors of NTM isolation, including using the short-course

injectable-containing regimen (SCI) versus the all-oral bedaquiline (SCO)

regimen and other covariates. This retrospective cohort study analysed MDR/RR-TB

patients in Ghana from 2018 to 2021 across four regions. Demographic, clinical,

and diagnostic data were collected under the National Tuberculosis Control

Program framework. Mycobacterial smears and cultures were used to monitor

treatment response, with further identification of NTM using line probe assays

and Sanger sequencing. Multivariable logistic regression models evaluated

predictors of NTM isolation and having an unfavourable outcome. Of 427

identified MDR/RR-TB patients, 380 were included for analysis: 76.3% were male,

the mean age was 43.9 years, and 18.9% were people living with HIV. NTM were

isolated in 7.1% of cases, primarily Mycobacterium intracellulare and M.

fortuitum, with higher odds of isolation in individuals from the Eastern Region

(aOR:14.18, 95% CI: 3.95-50.92). Overall, 67.9% achieved favourable outcomes:

71.4% (185/259) in those on the SCO versus 60.3% (73/121) on the SCI regimen.

People living with HIV (aOR 14.18, 95% CI: 3.95-50.92) had an increased odds of

having an unfavourable outcome. NTM isolation was not associated with

unfavourable outcomes. Our study results suggest that although NTM isolation may

occur during the course of MDR/RR-TB treatment, it does not affect MDR/RR-TB

treatment outcome. Future research should further explore the implications of

NTM co-infection on longer-term MDR/RR-TB outcomes, such as post-TB lung

disease, to refine management strategies tailored to the reality of

low-resource, high-burden settings.

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PMCID: PMC12221066

PMID: 40601698 [Indexed for MEDLINE]

**38. Proc Natl Acad Sci U S A. 2025 Jul 8;122(27):e2423349122. doi:**

**10.1073/pnas.2423349122. Epub 2025 Jul 2.**

A Mycobacterium tuberculosis secreted virulence factor Rv1435c/hsr1 disrupts

host snRNP biogenesis.

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Arora N(1), Das M(1), Rao K(1), Singh L(1), Gautam A(1), Sharma RD(1), Sarkar

B(4), Yadav M(4), Malakar B(4), Kalam H(1), Saini P(5), Mehra L(6), Das P(6),

Ahuja V(7), Singhal A(8)(9), Nandicoori V(2)(4), Kumar D(1).

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Transcriptional adaptation drives the host responses to Mycobacterium

tuberculosis (Mtb) infection. However, Mtb alters host RNA splicing to quench

host antibacterial responses, the mechanism for which remains unknown. Here, we

report a mechanism whereby a secreted Mtb protein interferes with the biogenesis

of key spliceosomal components. A high-throughput yeast-2-hybrid screen

identified several Mtb-secreted proteins interacting with the host RNA splicing

factors (SFs). Through custom-designed in-cell assays, we show that one of those

proteins, Rv1435c/hsr1 (host splicing regulator 1), targets specific

exon-skipping events. The Mtb Rv14345c/hsr1 facilitates direct interaction

between Mtb phagosomes and U5 snRNA and SNRPF, key components of the snRNPs.

Genetic deletion of Rv1435c/hsr1 reverses the specific exon-skipping events

caused by WT Mtb infection. The Δhsr1 strain shows compromised growth during ex

vivo infection in macrophages and in vivo infection in mice. Tissue sections

from the WT Mtb or Δhsr1-infected mice showed significant hsr1-dependent SNRPF

staining, a phenomenon also noted in the human intestinal tuberculosis (ITB)

biopsies. Thus, hsr1 is a virulence factor that disrupts host snRNP biogenesis

for pathogenesis. The splicing regulators from the host and pathogen are novel

targets for antituberculosis therapy.

DOI: 10.1073/pnas.2423349122

PMID: 40601628 [Indexed for MEDLINE]

**39. PLoS One. 2025 Jul 2;20(7):e0326444. doi: 10.1371/journal.pone.0326444.**

**eCollection 2025.**

Spatiotemporal hotspot analysis of tuberculosis lost to follow-up cases in

Ghana: A district-level study from 2019-2023.

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**INTRODUCTION:** Despite existing measures to control Tuberculosis (TB), the burden

of TB remains a serious challenge in Ghana, with declining treatment success

rates over recent years. Lost to Follow-Up (LTFU) has been attributed to this

decline. This cross-sectional study aims to employed spatiotemporal analysis, an

underutilized approach in this context, to explore areas with high prevalence of

LTFUs in order to improve TB treatment success rates.

**METHODS:** A spatiotemporal analysis was conducted in Ghana using TB LTFU data

from 2019-2023 extracted from the District Health Information Management System

2 (DHIMS2). Proportions of LTFU were used for spatial mapping. We adopted the

Global Moran's I, LISA and Getis-Ord G\* techniques to determine spatial

autocorrelation, optimized clusters or outliers and identify hotspot areas

respectively.

**RESULTS:** A total of 2,887 TB LTFU cases were recorded out of 75,604 TB cases. We

observed an initial increase of TB LTFU from 2019 (4.12%) to 2020, and a

diminishing trend (5.28% to 3.11%) from 2020 to 2023. The Global Moran's I

estimations showed significant spatial clustering of TB LTFU cases from 2019 to

2021, shifting to a more random distribution in 2022 and 2023. High spatial

clustering of LTFU were primarily reported in districts within Eastern, Central,

and Greater Accra regions across 2019-2023, with clusters in Volta and Ashanti

regions in 2021. We identified significant hotspot areas in districts within

Greater Accra, Central, and Eastern regions.

**CONCLUSIONS:** Hotspot areas of TB LTFU were primarily identified in densely

populated regions. Strategic plans such as intensive education programs should

be implemented to address pertinent issues regarding LTFU in the affected

districts. Priorities should be directed towards populated regions, particularly

Greater Accra, Central and Eastern regions, to improve TB treatment adherence

and outcomes.

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original author and source are credited.

DOI: 10.1371/journal.pone.0326444

PMCID: PMC12221003

PMID: 40601620 [Indexed for MEDLINE]

**40. Eur J Clin Pharmacol. 2025 Jul 2. doi: 10.1007/s00228-025-03871-1. Online ahead of print.**

Pretomanid can significantly increase plasma rivaroxaban concentrations-a case

report.

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**BACKGROUND: R**ivaroxaban, a direct factor Xa inhibitor, is an oral anticoagulant

used in the prevention and treatment of thromboembolic disease. The clearance of

rivaroxaban involves excretion unchanged via the kidneys where it is subject to

active secretion into the renal tubules, involving P-glycoprotein (P-gp) and

organic anion transporter 3 (OAT3). Pretomanid, a nitroimidazole antibiotic used

for multidrug-resistant tuberculosis (MDR-TB), is an OAT3 inhibitor based on in

vitro data. This case report describes a "natural experiment" involving

rivaroxaban concentration monitoring. It entails a novel pharmacokinetic

interaction between rivaroxaban and pretomanid in a 61-year-old male undergoing

MDR-TB treatment.

**RESULT:** Following pretomanid initiation, rivaroxaban trough plasma concentration

increased more than two-fold, prompting a halving of rivaroxaban dose, and

subsequent restoration of trough concentration to pre-pretomanid value.

**DISCUSSION:** This interaction appears to be mediated by pretomanid inhibition of

OAT3, which reduces renal clearance of rivaroxaban. Other components of MDR-TB

regimen and pre-existing medications are unlikely to be contributory based on

their pharmacokinetic profiles.

**CONCLUSION:** This case highlights the potential impact of drug interactions

involving pretomanid and known OAT3 perpetrators on the pharmacokinetics of

rivaroxaban and other OAT3 substrates, particularly those of low therapeutic

index, such as methotrexate. Given the global rise in MDR-TB, further research

into pretomanid as a perpetrator of drug interactions is warranted.

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part of Springer Nature.

DOI: 10.1007/s00228-025-03871-1

PMID: 40601036

**41. AJR Am J Roentgenol. 2025 Jul 2. doi: 10.2214/AJR.25.33059. Online ahead of**

**print.**

Multimodal Generative Artificial Intelligence Model for Creating Radiology

Reports for Chest Radiographs in Patients Undergoing Tuberculosis Screening.

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**Background:** Chest radiographs play a crucial role in tuberculosis screening in

high-prevalence regions, although widespread radiographic screening requires

expertise that may be unavailable in settings with limited medical resources.

Objectives: To evaluate a multimodal generative artificial intelligence (AI)

model for detecting tuberculosis-associated abnormalities on chest radiography

in patients undergoing tuberculosis screening. **Methods:** This retrospective study

evaluated 800 chest radiographs obtained from two public datasets originating

from tuberculosis screening programs. A generative AI model was used to create

free-text reports for the radiographs. AI-generated reports were classified in

terms of presence versus absence and laterality of tuberculosis-related

abnormalities. Two radiologists independently reviewed the radiographs for

tuberculosis presence and laterality in separate sessions, without and with use

of AI-generated reports and recorded if they would accept the report without

modification. Two additional radiologists reviewed radiographs and clinical

readings from the datasets to determine the reference standard. **Results:** By the

reference standard, 422/800 radiographs were positive for tuberculosis-related

abnormalities. For detection of tuberculosis-related abnormalities, sensitivity,

specificity, and accuracy were 95.2%, 86.7%, and 90.8% for AI-generated reports;

93.1%, 93.6%, and 93.4% for reader 1 without AI-generated reports; 93.1%, 95.0%,

and 94.1% for reader 1 with AI-generated reports; 95.8%, 87.2%, and 91.3% for

reader 2 without AI-generated reports; and 95.8%, 91.5%, and 93.5% for reader 2

with AI-generated reports. Accuracy was significantly lower for AI-generated

reports than for both readers alone (p<.001), but significantly higher with than

without AI-generated reports for one reader (reader 1: p=.47; reader 2: p=.47).

Localization performance was significantly lower (p<.001) for AI-generated

reports (63.3%) than for reader 1 (79.9%) and reader 2 (77.9%) without

AI-generated reports and did not significantly change for either reader with

AI-generated reports (reader 1: 78.7%, p=.71; reader 2: 81.5%, p=.23). Among

normal and abnormal radiographs, reader 1 accepted 91.7% and 52.4%, while reader

2 accepted 83.2% and 37.0%, respectively, of AI-generated reports. Conclusion:

While AI-generated reports may augment radiologists' diagnostic assessments, the

current model requires human oversight given inferior standalone performance.

**Clinical Impact:** The generative AI model could have potential application to aid

tuberculosis screening programs in medically underserved regions, although

technical improvements remain required.

DOI: 10.2214/AJR.25.33059

PMID: 40600508

**42. Open Forum Infect Dis. 2025 Jun 25;12(7):ofaf344. doi: 10.1093/ofid/ofaf344.**

**eCollection 2025 Jul.**

High Rates of Mortality During Drug-Resistant Tuberculosis Treatment Among

Individuals With Diabetes Mellitus and Low Body Mass Index.

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**BACKGROUND:** Diabetes is a risk factor for mortality during rifampicin-resistant

tuberculosis (RR-TB) treatment, but whether its impact differs by nutritional

status is unknown. We estimated the effect of diabetes and its interaction with

low body mass index (BMI) (ie, <18.5 kg/m2) on all-cause mortality during

treatment of RR-TB.

**METHODS:** We used medical record data of adults treated for RR-TB in Indonesia

between March 2020 and May 2022. Diabetes was defined as glycated hemoglobin

≥6.5% or prior diabetes diagnosis by healthcare providers. Cox proportional

hazards regression was used to estimate the hazard rates of mortality during

treatment comparing those with and without diabetes. Multiplicative and additive

interactions were evaluated to determine if the effect of diabetes on mortality

during treatment was moderated by BMI status.

**RESULTS**: Among 345 individuals (57% male, 1.7% with human immunodeficiency

virus, 59% with BMI <18.5 kg/m2), 96 (28%) had diabetes and 62 (18%) died.

Adjusting for confounders, the hazard rates of mortality during treatment were

higher among those with diabetes (adjusted hazard rate ratio [aHR], 2.05 [95%

CI, 1.17-3.58]) or those with BMI <18.5 kg/m2 (aHR, 2.33 [95% CI, 1.28-4.21]).

No significant multiplicative nor additive interaction was detected, but the

hazard rates of mortality were highest among those with diabetes and BMI

<18.5 kg/m2 (aHR, 7.14 [95% CI, 2.71-18.82]) compared to those without diabetes

and BMI ≥18.5 kg/m2.

**CONCLUSIONS:** Having diabetes doubled the risk of mortality during RR-TB

treatment. Highest mortality rates were observed among individuals with combined

diabetes and low BMI.

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Infectious Diseases Society of America.

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PMCID: PMC12207741

PMID: 40599491

**43. J Proteome Res. 2025 Jul 1. doi: 10.1021/acs.jproteome.4c00989. Online ahead of print.**

Multiomics and Machine Learning Identify Immunometabolic Biomarkers for Active

Tuberculosis Diagnosis Against Nontuberculous Mycobacteria and Latent

Tuberculosis Infection.

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This study utilized multiomics combined with a comprehensive machine

learning-based predictive modeling approach to identify, validate, and

prioritize circulating immunometabolic biomarkers in distinguishing tuberculosis

(TB) from nontuberculous mycobacteria (NTM) infections, latent tuberculosis

infection (LTBI), and other lung diseases (ODx). Functional omics data were

collected from two discovery cohorts (76 patients in the TB-NTM cohort and 72

patients in the TB-LTBI-ODx cohort) and one validation cohort (68 TB patients

and 30 LTBI patients). Mutiomics integrative analysis identified three plasma

multiome biosignatures that could distinguish active TB from non-TB with

promising performance, achieving area under the receiver operating

characteristic curve (AUC) values of 0.70-0.90 across groups in both the

discovery and validation cohorts. The lipid PC(14:0\_22:6) emerged as the most

important predictor for differentiating active TB from non-TB controls,

consistently presenting at lower levels in the active TB group compared with its

counterparts. Further validation using two independent external data sets

demonstrated AUCs of 0.77-1.00, confirming the biomarkers' efficacy in

distinguishing active TB from other non-TB groups. Our investigation highlights

lipids as promising biomarkers for classifying TB, NTM, LTBI, and ODx. Rigorous

validation further indicates PC(14:0\_22:6) as a TB differential diagnostic

biomarker candidate.

DOI: 10.1021/acs.jproteome.4c00989

PMID: 40598791

**44. Adv Rheumatol. 2025 Jul 1;65(1):29. doi: 10.1186/s42358-025-00462-7.**

Brazilian guidelines for the management of tuberculosis infection in

immune-mediated inflammatory diseases: is retesting in latent tuberculosis

screening appropriate and Safe?

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The article "Brazilian Recommendations for the Management of Tuberculosis

Infection in Immune-Mediated Inflammatory Diseases" by Viviane de Souza et al.

presents important discussions on the subject; however, the recommendation for

annual repetition of the TST/IGRA test for three years and after medication

changes raises considerable concerns. This approach may lead to overdiagnosis

and overtreatment of latent tuberculosis infection (LTBI). Frequent

false-positive results in retests can result in unnecessary antibiotic use,

contributing to bacterial resistance, a problem of global significance. The

recommendation, considered to have a moderate level of evidence, is subject to

criticism. Arguments used to support retesting, such as high conversion rates of

tests after one year, reports of tuberculosis cases despite negative screenings

being attributed to false negatives, and reliance on other sources with lower

levels of evidence, do not constitute sufficient evidence to confirm

tuberculosis infection or justify the recommendation. On the other hand, there

is evidence that has not been considered in the discussion against the

recommendation for retesting, indicating that this practice may increase the

risk of diagnosing false-positive infections, leading to overtreatment without

clinically proven benefits. Potentially harmful interventions should not be

implemented without solid evidence to support them. In this letter to the

editor, we briefly discuss this recommendation and the arguments against its

implementation, highlighting its associated risks.

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DOI: 10.1186/s42358-025-00462-7

PMID: 40598706 [Indexed for MEDLINE]

**45. BMC Health Serv Res. 2025 Jul 1;25(1):858. doi: 10.1186/s12913-025-12967-4.**

Review: missed tuberculosis cases in India: a systematic analysis of diagnostic,

treatment, and reporting gaps.

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**BACKGROUND:** India aims to eliminate tuberculosis (TB) by 2025. Despite ongoing

efforts to transform TB care, numerous factors contribute to the persistence of

missing cases in India. To gain insight into this issue, we performed a

comprehensive review to identify the factors responsible for these missing

cases, segregating them into patient- and provider-related factors, with

reference to the layers of the onion model.

**METHODS:** We conducted a comprehensive literature review using relevant search

strings in the MEDLINE, Scopus, and Web of Science databases from 2000 to 2024.

Given the heterogeneity of the included studies, a qualitative rather than

quantitative data analysis approach was considered. For the quality evaluation

of studies, we employed a modified version of the Critical Appraisal Skills

Program (CASP) checklist.

**RESULTS:** Of the 253 articles identified, 25 studies that met the criteria for

“missing cases” were selected for analysis. Based on the objectives of this

review, we identified patient-related factors contributing to missing cases,

including geographical displacement due to migration or occupational reasons,

alcoholism, illiteracy, personal commitments, side effects to Anti-Tubercular

Treatment (ATT), depressive symptoms, perceived social stigma, reluctance to

reveal prior treatment history, and no record keeping. Provider-related factors

highlighted were inadequate communication and sputum sample collection,

exhaustion of pharmaceutical supplies, patient loss to follow-up, ACF versus

PCF, inadequacy of diagnostic tests, lack of history taking, misclassification,

and issues related to Ni-KSHAY notification. Based on this layer-wise model of

missing factors, we discuss pertinent challenges along with plausible strategies

and recommendations to stem the rise in missing cases within the Indian context.

**CONCLUSION:** Our novel findings with reference to the onion model allow for

systematic highlighting and addressing of the key patient and provider factors

that are fuelling missing cases. The results revealed that provider factors

predominantly contributed to the missing case TB scenario. Improved

accessibility to services, provider training, and competency building (i.e.,

handling samples, co-morbid patients, and case notifications), along with

improving diagnostic infrastructure, would serve to strengthen the cause of TB

elimination.

SUPPLEMENTARY INFORMATION: The online version contains supplementary material

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**46. Int J Equity Health. 2025 Jul 1;24(1):185. doi: 10.1186/s12939-025-02566-4.**

Stigmatization and discrimination of female tuberculosis patients in Kyrgyzstan

- a phenomenological study.

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A(2), Kalmambetova G(2), Chen M(1), Unterkircher SC(3)(5), Moidunova N(2),

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**INTRODUCTION:** The Republic of Kyrgyzstan is among the 30 countries with the

highest burden of multidrug-resistant Tuberculosis worldwide. One of the reasons

is widespread stigmatization and discrimination. As previous research has shown,

particularly women experience stigma while its impact on their life and (mental)

health is even greater than for men. This is the first phenomenological study to

explore women's lived experiences of TB-related stigmatization in Kyrgyzstan.

This study aims to raise awareness about the gender-specific impact of

stigmatization and discrimination.

**METHODOLOGY:** Descriptive phenomenology was used. 15 semi-structured in-depth

interviews with female TB-patients were conducted between 28th May and 14th June

2024. Themes were stigma experiences, their consequences and coping strategies.

Participants were recruited from two TB Hospitals and two Family Medical Centers

(primary health care units) in Bishkek through purposive sampling. The data

analysis followed a thematic approach based on a combination of deductive and

inductive coding.

**RESULTS:** 14 of 15 participants experienced stigmatization and discrimination in

one way or another. Anticipated stigma was very prominent, manifesting in

non-disclosure of the diagnosis apart from close family. Enacted stigma mostly

occurred within society or non-TB-specialized healthcare facilities.

Self-stigmatization often followed anticipated and enacted stigma. Stigma

experiences impacted daily and social life, marital prospects and access to

educational and work opportunities but mainly led to mental health issues, which

12 of 15 participants reported.

**DISCUSSION:** and Conclusion. In contrast to previous research, this study did not

find diagnostic delay nor non-adherence to treatment because of stigmatization

and discrimination. However, experiences within the healthcare facilities

impacted the perceived quality of care. Stigmatization within the family, mostly

by in-laws, was anchored in the patriarchal and conservative attitudes of Kyrgyz

society. Overall, key findings of this study were widespread lack of knowledge

about the disease and its transmission as a reason for and mental health issues

because of stigmatization and discrimination. The findings imply the need for

intervention strategies and policies focusing on education about TB, integration

of psychosocial support into treatment and improvements in quality of care.

Altogether, this could contribute to the reduction of TB-related stigmatization

and discrimination which would reduce the individual burden of TB.

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**47. Trop Med Health. 2025 Jul 1;53(1):89. doi: 10.1186/s41182-025-00771-z.**

Evaluation of the PATHFAST TB LAM Ag assay as a treatment monitoring tool for

pulmonary tuberculosis in Nairobi, Kenya.

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**BACKGROUND:** Treatment monitoring is important in pulmonary tuberculosis (PTB)

management, since prolonged treatment necessitates regular assessments to

prevent treatment failure and the emergence of drug-resistant strains. However,

the lack of a simple, rapid, and reliable treatment monitoring tool (TMT)

remains a major challenge. We evaluated the utility of measuring sputum

lipoarabinomannan (LAM) concentration by the PATHFAST TB LAM Ag assay (PHC

Corporation, Tokyo, Japan) as a TMT in patients with PTB in Nairobi, Kenya.

**METHODS**: We retrospectively analyzed sputum LAM levels via the PATHFAST TB LAM

Ag assay from a Nairobi cohort of patients with PTB and compared these results

with conventional microbiological tests (acid-fast bacilli [AFB] smear

microscopy; mycobacterial growth indicator tube [MGIT] culture). Stored sputum

pellets processed with N-acetyl-L-cysteine (NALC)-NaOH were used for LAM

measurement. Serial LAM concentrations measured every 2 weeks over an 8-week

period were compared across bacterial load categories to assess correlations

with AFB smear grades and culture results using the Kruskal-Wallis and

Mann-Whitney U tests.

**RESULTS: T**he 98 patients included here had a median age of 37 years

(Interquartile Range: 27-44). The majority were men (74/98, 75.5%) and the MGIT

culture was positive for 89 (90.8%) of them. Patients with elevated baseline LAM

concentrations showed a significant reduction in LAM levels with treatment (90%

median reduction by week 8), whereas those with low baseline LAM concentrations

did not show a declining trend. Sputum LAM levels were significantly higher in

culture-positive samples compared to culture-negative samples (23.8 pg/mL vs.

10.8 pg/mL, P < 0.001). Sputum LAM levels showed a significant correlation with

AFB smear grades, with median concentrations increasing progressively from

11.3 pg/mL in smear-negative samples to 19.7 pg/mL in scanty/1 + samples, and

46.7 pg/mL in 2 + /3 + samples (P = 0.0001). LAM levels were significantly

higher in culture-positive/AFB-positive sputum samples (viable bacilli) than in

culture-negative/AFB-positive samples (non-viable bacilli) (P < 0.0001).

**CONCLUSION:** Our findings revealed that sputum LAM concentration declined during

TB treatment, particularly among patients with high baseline levels, and

correlated with AFB smear grades and culture results. Additionally, LAM

concentrations differed between culture-positive and culture-negative samples

among AFB smear-positive samples. Further prospective studies are needed to

assess LAM levels as a TMT.

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**48. BMC Infect Dis. 2025 Jul 1;25(1):821. doi: 10.1186/s12879-025-11218-5.**

Delayed culture conversion predicts poor outcomes for isoniazid mono-resistant

TB in Uganda: a retrospective cross-sectional study from 2017- 2022.

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**BACKGROUND:** Isoniazid-resistant, Rifampicin-susceptible Tuberculosis (TB) is

estimated to occur in 13% of new cases and 17% of previously treated cases.

Current WHO guidelines recommend treatment with Rifampicin (RFP), ethambutol

(EMB, E), pyrazinamide (PZA, Z), and levofloxacin (LFX, Q) for 6 months in

patients with isoniazid mono-resistant TB (Hr-TB) but the effectiveness and use

of other regimens in managing Hr-TB has not been established. There is a need to

pay increased attention to the timely identification of Hr-TB patients to

improve treatment success along with the reduction of the risk for further drug

resistance development. This study was performed to determine the treatment

outcomes and their associated factors among isoniazid mono-resistant TB patients

in Uganda.

**METHODS:** This was a cross-sectional study performed among newly diagnosed and

retreatment TB patients whose sputum samples were referred to the National TB

Reference Laboratory (NTRL)-Uganda from March 2017 to March 2022. Patient

samples exhibiting Isoniazid mono-resistance as determined by phenotypic drug

resistance testing (DST) were included in this study. Samples with data

incompleteness and those whose treatment centers could not be traced were

excluded from the study. Selected samples were tested for mutations associated

with Isoniazid resistance using line probe. Patient demographic data was

obtained from the National TB Reference Laboratory (NTRL) electronic data system

and request forms with additional data, such as treatment regimen, adverse

effects, and treatment start dates obtained from treatment registers. The

independent variables available (age, sex, regimen used, M. tuberculosis

mutation genes for isoniazid, specifically InhA and KatG, history of TB, HIV

status, and reporting year) were assessed as possible factors in the

relationship between Hr-TB and treatment success.

**RESULTS:** A total of 85 isoniazid monoresistant isolates from different patients

were analyzed in this study. In this study, most of the participants belonged to

the category of newly diagnosed 35/85 (41.2%). Most of the participants 36/85,

42.3%) turned culture negative at month one upon initiation of treatment. The

findings from this study show that the most dominant Mycobacterium tuberculosis

mutation occurred in the KatG MUT1 region with a nucleotide change of S315T1.

There was no significant treatment outcome difference among the different age

groups in this study when compared (unsuccessful Vs successful treatment, median

age 35.4 years and 35.86 years, p = 0.078). However, the study found that most

deaths were among people aged above 36 years 71.4%, (5/7 participants).

**CONCLUSION:** This study revealed Isoniazid mono-resistant TB as a significant

factor associated with delayed culture conversion of beyond two (2) months. This

emphasizes the need for prompt detection using routine point-of-care testing

molecular diagnostic platforms to test for Isoniazid and Rifampicin resistance

to improve TB treatment outcomes and reduce failures.

CLINICAL TRIAL NUMBER: Not applicable.

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**49. BMC Infect Dis. 2025 Jul 1;25(1):870. doi: 10.1186/s12879-025-11228-3.**

Forecasting tuberculosis in Ethiopia using deep learning: progress toward

sustainable development goal evidence from global burden of disease 1990-2021.

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**BACKGROUND:** Tuberculosis (TB) is a preventable and treatable disease caused by

Mycobacterium tuberculosis, which most often affects lungs and remains the

second leading cause of death from infectious diseases worldwide. The National

End TB Strategy aims to eliminate the TB epidemic by reducing TB-related deaths

by 95% and decreasing incident TB cases by 90% by 2030, using 2015 as the

baseline. Tuberculosis is the primary cause of morbidity, ranks third in

hospital admissions, and is the second leading cause of death in Ethiopia,

following malaria. Hence, this analysis aims to forecast and provide evidence

that supports the combined intervention to monitor TB incidence in Ethiopia's

progress toward the Sustainable Development Goals.

**METHOD:** Study employed secondary data analysis from the Global Burden of Disease

database (1990-2021) to forecast tuberculosis incidence in Ethiopia. LSTM-based

models, including multistep LSTM and hybrid ARIMA + LSTM, were implemented for

prediction in TensorFlow frameworks while ARIMA model was built using the

statsmodels and pmdarima libraries using the Python programming language. The

statistical significance level was set at 0.05 to check data stationarity. Model

performance was evaluated using Root Mean Squared Error, Mean Absolute Error,

Mean Absolute Percentage Error, and Symmetric Mean Absolute Percentage Error.

Finally, the best model was used to forecast the next 9 years from 2021 to 2030.

**RESULT:** According to GBD data, the incidence of TB in Ethiopia shows a long-term

downward trend, decreasing from 466.93 cases per 100,000 in 1990 to 185.53 by

2021. The analysis result revealed that multistep LSTM model outperformed all

achieving MAE: 5.53, RMSE: 6.74, MAPE: 2.72% and sMAPE:2.76%. The incidence of

tuberculosis in Ethiopia is projected to decline slightly through 2030,

according to a multi-step LSTM model. The forecast estimates that the TB

incidence will be 189 cases per 100,000 people by 2025, decreasing further to

179 by 2030.

**CONCLUSION:** Overall, the analysis indicates that Ethiopia is still falling short

of the national "END TB strategy" goal of 90% reduction in TB incidence cases

per 100,000 population by 2030. It highlights the necessity for Ethiopia's TB

control strategies to improve access to prevention, early diagnosis, and

treatment, focusing on high-risk groups and vulnerable populations.

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**50. BMC Infect Dis. 2025 Jul 1;25(1):878. doi: 10.1186/s12879-025-11249-y.**

The delivery of new tuberculosis vaccines to people living with HIV - when to

vaccinate?

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**BACKGROUND:** Tuberculosis (TB) remains a major cause of morbidity and mortality

in people living with HIV (PLHIV). New TB vaccines may help reduce this burden.

There is limited data on the response to new TB vaccines in PLHIV and how this

may vary with levels of immunosuppression and anti-retroviral therapy (ART). The

potential interaction between vaccine efficacy and ART raises questions about

the optimum timing of vaccination against TB in PLHIV.

**METHODS:** Using a simple cumulative risk model, we compared the impact of

different TB vaccination strategies for PLHIV. We compared the impact of

vaccinating at linkage to HIV care, to the impact of vaccinating at ART

initiation. We explored how the optimum timing of vaccination depends on

characteristics of the vaccine and the ART program at an individual and

population level.

**RESULTS:** For an individual, the optimum timing of vaccination against TB is at

ART initiation unless the time to ART initiation is more than 6 months or if the

reduction in vaccine efficacy when given prior to ART is small. At a population

level, the proportion of PLHIV who initiate ART is a key determinate of the

optimum strategy. If ART uptake is low, it would be better to vaccinate at

linkage to HIV care, even if vaccine efficacy in ART naïve individuals is less

than 50% of efficacy in individuals on ART.

**CONCLUSIONS:** Our results suggest that the optimum timing of new TB vaccination

for PLHIV will depend on the relative efficacy of vaccination in ART-naïve

individuals vs. individuals on ART, and the uptake and timing of ART initiation.

If vaccine efficacy is lower among ART-naïve individuals, improvements in HIV

programs may help maximize the impact of new TB vaccines.

SUPPLEMENTARY INFORMATION: The online version contains supplementary material

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**51. BMC Infect Dis. 2025 Jul 1;25(1):856. doi: 10.1186/s12879-025-11224-7.**

Time to a tuberculosis treatment cure and its predictors among tuberculosis

patients at public health facilities in Arba minch town, South Ethiopia: A

retrospective cohort study.

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**INTRODUCTION:** The WHO’s 2024 Global tuberculosis (TB) Report shows that TB

causes 1.25 million deaths annually, including 161,000 TB-Human Immunodeficiency Virus (HIV) infections. It affects 10.6 million people, mainly in Asia and Africa, 75% of whom are in the economically active age group of 15–54 years. Treatment interruptions hinder efforts to eliminate TB by 2030. According to a recent systematic review conducted using Ethiopian studies indicated that the pooled prevalence of TB treatment cure rate was 33.9%. There is a lack of evidence on time to TB treatment cure in Ethiopia using survival analysis.

**OBJECTIVE:** This study aimed to determine the time to TB treatment cure and its

predictors among TB patients from January 2021 to December 2023 at public health

facilities in Arba Minch town. South Ethiopia.

**METHOD:** An institution-based retrospective cohort study was conducted among 628

selected TB patients who were admitted to the TB care unit at Arba Minch General

Hospital, Dilfana Primary Hospital, and both health centers from 2021 to 2023. A

Kaplan Meier survival curve was fitted to test the survival time. The Cox

proportional hazards model was used to identify predictors with TB treatment

cure. Significance was considered at a p value ≤ 0.05 with an adjusted hazard

ratio (AHR) 95% CI in the multivariate analysis.

**RESULTS:** Out of the 628 patients whose records were analyzed, the median time to

cure was 162 days. The significant predictors of time to TB cure included being

male (AHR 0.3, 95% CI: 0.35–0.95), history of TB treatment (AHR 0.56, 95% CI:

0.35–0.95), normal BMI (AHR 1.04, 95% CI: 1.32–1.49) and attending at secondary

heath facility (AHR 1.69, 95% CI: 1.40–2.00).

**CONCLUSIONS:** Socio-demographic and clinical related factors were found to be

independent predictors of time to cure. TB control programs should adopt

gender-sensitive approaches to address delayed cure in male patients, integrate

nutritional assessment into care and strengthen primary health facilities.

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PMID: 40597695

**52. Sci Rep. 2025 Jul 1;15(1):22264. doi: 10.1038/s41598-025-06532-6.**

MIP-3α-antigen fusion DNA vaccine enhances sex differences in tuberculosis model

and alters dendritic cell activity early post vaccination.

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Tuberculosis disease (TB) caused by Mycobacterium tuberculosis (Mtb) bacteria

remains a major cause of global morbidity and mortality. Efforts to control TB

are hampered by the lengthy and cumbersome treatment required to eradicate the

Mtb infection. Bacterial persistence during exposure to bactericidal antibiotics

is at least partially mediated by the bacterial stringent response enzyme,

RelMtb. A therapeutic DNA vaccine targeting RelMtb has been shown to increase

the efficacy of antitubercular drugs, and fusing macrophage-inflammatory protein

3α (MIP-3α), which interacts with CCR6 on immature dendritic cells (iDCs), to

RelMtb further increases the vaccine's therapeutic efficacy. A secondary

analysis of these prior studies elucidated prominent sex-based differences in

vaccine therapeutic efficacy, with female mice showing improved microbial

outcomes compared to males as a result of the Rel and MIP-3α-Rel vaccine

constructs, with a more pronounced sex-associated difference in the MIP-3α-Rel

group. In the current study, we addressed the hypothesis that these sex-related

differences are at least in part due to differential DC activation/function soon

after vaccination. An EαGFP reporter vaccine model was used to track vaccine

antigen presentation in the draining node with flow cytometry panels by an

antibody Y-Ae which binds the Eα peptide tag in complex with I-Ab MHC-II

molecules. Additionally, a qRT-PCR panel assessing DC-related genes compared

sexes receiving the MIP-3α-Rel vaccine. MIP-3α-EαGFP groups had more DCs

presenting vaccine antigen infiltrating from the periphery, with more abundant

Langerhans cells in males and greater CD8+ CD103+ cross-presenting dermal DCs in

females. This model also shows there is greater DC activation, as measured by

CD80 and MHC II MFI, by MIP-3α compared to EαGFP alone, especially in female

mice. The genetic panel showed females more enriched for chemokines and genes

related to cell movement and cross-presentation. Our findings are consistent

with the sex- and MIP-3α-related differences seen in the therapeutic model and

supports the hypothesis that in both sexes MIP-3α enhances vaccine uptake and

cell activation by peripheral iDCs. Additionally, female mice showed greater

levels of antigen presentation, especially in DCs able to cross-present antigen,

likely explaining why they had the best outcomes. Further studies are required

to understand underlying mechanisms and to link APC results directly to T-cell

responses.

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**53. Sci Rep. 2025 Jul 1;15(1):21383. doi: 10.1038/s41598-025-05644-3.**

Development and optimization of an injectable in-situ gel system for sustained

release of anti-tuberculosis drugs.

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Addressing the challenges of drug-resistant Mycobacterium tuberculosis requires

regular drug intake and consistent therapeutic drug concentrations, for which

in-situ gel systems offer a promising solution by enabling sustained drug

release. This study aims to develop an injectable system for chronic

tuberculosis treatment, focusing on an in-situ gel formulation created using

Poloxamer 407, Carbopol 940, and Hydroxy Propyl Methyl Cellulose (HPMC). The

experiments involved a combination of two FDA-approved first-line anti-TB

molecules, namely Rifampicin (RIF) and Isoniazid (INZ), by loading in the

in-situ gel (IGS) formulations prepared by cold process. The gelling polymers

were varied at three levels of concentration and optimized through the molecular

docking method, wherein the blend of polymers with drugs showed the docking

score of - 3.085. The physicochemical properties and analytical

characterization, including gelation temperature, drug content, FT-IR, SEM,

TG-DSC, in-vitro drug release, ex-vivo permeation, and cytotoxicity, were

performed. According to the study results, the optimized gelation temperature

was 26 °C, the viscosity of the sol and gel was 238 cP and 1700 cP,

respectively, with the maximum drug content (RIF 100 ± 2.17% and INZ

97 ± 1.31%). The FTIR analysis confirmed the stability of drugs, the

morphological study using SEM showed the formation of a network structure, and

thermal analysis by TG-DSC confirmed the solid-state transition of drugs. The

in-vitro drug release studies in phosphate buffer pH 7.4 showed sustained

release of Rifampicin and Isoniazid for up to 10 days and 6 days, respectively.

The selected formulation exhibited non-toxic effects in the L929 cell line.

Based on the results, in-situ gel administration could be recommended for

intramuscular administration for sustained release of the drugs, which is

expected to reduce the dosing frequency and improve patient compliance for

chronic tuberculosis therapy.

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DOI: 10.1038/s41598-025-05644-3

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PMID: 40595921 [Indexed for MEDLINE]

**54. Sci Rep. 2025 Jul 1;15(1):21746. doi: 10.1038/s41598-025-04038-9.**

The identification Mycobacterium tuberculosis genes that modulate long term

survival in the presence of rifampicin and streptomycin.

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In 2023, Mycobacterium tuberculosis (Mtb) caused 10.6 million new tuberculosis

cases and 1.3 million deaths. The WHO proscribed treatment is not always

successful, even when strains were sensitive to the antibiotics.as clinical Mtb

populations contain phenotypically tolerant subpopulations, termed persisters.

Here a Mtb transposon library was challenged with rifampicin (RIF) and

streptomycin (STM) under conditions designed to identify genes that modulate

persister frequency. Mutants with reduced survival in RIF were predominantly in

genes associated with membrane integrity e.g. arabinogalactan assembly genes

cpsA/lytR/Psr, whilst for STM, reduced survival was associated with

toxin/antitoxin genes. Some mutations enhanced survival. For RIF these included

the methyl citrate cycle genes prpC, prpD and prpR, and the trkA-C K+ uptake

system genes ceoB and Rv2690, and for STM, the resistance associated gene, gidB,

and anion-transport genes Rv3679c and Rv3680c. Few genes overlapped the RIF and

STM selections, demonstrating that survival mechanisms were antibiotic-specific.

Directed deletions of ΔprpD and ΔfadE5 confirmed their predicted enhanced and

reduced RIF fitness respectively. The study identified genes that modulate not

only persister frequency but also resistance and tolerance, and demonstrates

that the mechanisms that produce these phenotypes are diverse and

antibiotic-specific.

© 2025. The Author(s).

DOI: 10.1038/s41598-025-04038-9

PMCID: PMC12216072

PMID: 40595703 [Indexed for MEDLINE]

**55. Sci Rep. 2025 Jul 2;15(1):22687. doi: 10.1038/s41598-024-81558-w.**

Quantification of tuberculosis exposure in a high-burdened setting.

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Recent studies using sensitive aerosol sampling and detection methodologies,

have enumerated aerosolized Mycobacterium tuberculosis (Mtb) across a spectrum

of tuberculosis states in a high-burdened setting. To estimate the Mtb exposure

rate we used a Bayesian inference approach to fit a reversible catalytic model

to age-specific, respiratory bioaerosol Mtb prevalence data. Longitudinal

monitoring of symptomatic sputum-negative, untreated clinic attendees informed a

prior for the Mtb bioaerosol clearance rate. Based on an observed bioaerosol Mtb

population prevalence of 62.6% and a clearance half-life of 83 days, the

estimated exposure rate was 5.1/year. This result was extremely sensitive to

bioaerosol Mtb population prevalence but including a simulated rate of exposure

of zero until the age of 10-years did not influence the overall estimate for

rate of exposure. A catalytic model without reversion was a poorer fit to the

prevalence data than the primary reverse catalytic model. Mtb bioaerosol

sampling findings imply an extremely high rate of Mtb exposure within

tuberculosis endemic communities with rapid cycling between bioaerosol carriage

and clearance. Even assuming a much lower bioaerosol Mtb population prevalence,

the estimated exposure rate is an order of magnitude greater than published

annual rates of Mtb infection.

© 2024. The Author(s).

DOI: 10.1038/s41598-024-81558-w

PMCID: PMC12218470

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**56. J Antibiot (Tokyo). 2025 Jul 1. doi: 10.1038/s41429-025-00839-2. Online ahead of print.**

Tuberculosis drug development; fluoroquinolone structural tailoring.

Gutiérrez-Mauricio AM(#)(1)(2), Trujillo-Paez JV(#)(3), Trejo-Martinez LA(4),

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Tuberculosis (TB) is a contagious infectious disease caused by the bacillus

Mycobacterium tuberculosis (Mtb). It is transmitted through small particles in

the air (<5 µm) expelled by active tuberculosis patients; when inhaled by a new

host, they can potentially cause infection. Nowadays, TB is still the major

cause of morbidity and mortality by a single infectious agent, this is further

exacerbated by the worldwide emergence of multidrug-resistant strains of Mtb.

Thus, effective methods of diagnosis, prophylaxis, and new pharmacological

therapies must be carried out in order to control this disease. Fluoroquinolones

(FQ) are synthetic antibiotics with a broad spectrum against Gram-negative and

Gram-positive bacteria, including M. tuberculosis. The treatment with FQ plays

an important role in managing drug-resistant tuberculosis. Modifications on FQ

structure have been extensively studied, thereby, four generations of FQ have

emerged having a broad spectrum of antibacterial properties. These modifications

improve the overall efficiency of FQ by increasing tissue penetration, reducing

side effects, and addressing emerging bacterial resistance. In this scenario,

current trends on FQ research have focused on new synthetic approaches that

allow fluoroquinolones to address the worldwide issue of multidrug-resistant

tuberculosis. The aim of this review is to highlight the overall effects of

newly synthesized FQ molecules having antitubercular activity.

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Association.

DOI: 10.1038/s41429-025-00839-2

PMID: 40595331

**57. Sci Rep. 2025 Jul 2;15(1):22540. doi: 10.1038/s41598-025-06164-w.**

Comparing the accuracy of computer-aided detection (CAD) software and

radiologists from multiple countries for tuberculosis detection in chest X-Rays.

Qin ZZ(1)(2)(3), Van der Walt M(4), Moyo S(5), Ismail F(6), Maribe P(5),

Denkinger CM(7), Zaidi S(8), Barrett R(8)(9), Mvusi L(10), Tsibolane Y(10),

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Nearly a third of TB cases go undetected annually. WHO recommends computer-aided

detection (CAD) to enhance TB screening, with studies showing comparable

performance to local radiologists. Using 774 chest X-rays from the South African

National TB Prevalence Survey, we compared 12 CAD software with 11 radiologists

from Nigeria, India, the UK, and the US, against a composite microbiological

reference standard. Sensitivity, specificity and Cohen's kappa were calculated.

Receiver-operating characteristic curves were developed for CAD and Euclidean

distance assessed radiologists' alignment with the best-performing software.

Binomial regression tested the impact of radiologists' characteristics on

accuracy. Radiologist performance varied. On the restricted read, British

radiologists had the highest sensitivity (78.7% [73.2-83.5%]) and Indian

radiologists the lowest (67.1% [61.0-72.8%]). Specificity ranged from 75.8%

(71.8-79.4%, Nigeria) to 84.3% (80.9-87.3%, the US). Radiologist performance was

significantly impacted by HIV, prior TB, and age. The top CAD outperformed all

except Indian radiologists when matching specificity. CAD with Conformité

Européenne generally matched or surpassed radiologists. British radiologists'

sensitivity was closest to the top CAD, while American radiologists were closest

in specificity and overall. Experience, TB reads, and country had no significant

impact on accuracy. CAD performed well against radiologists globally,

highlighting potential to enhance access to care.

© 2025. The Author(s).

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PMID: 40594615 [Indexed for MEDLINE]

**58. Nat Commun. 2025 Jul 1;16(1):5993. doi: 10.1038/s41467-025-60847-6.**

Evolutionarily divergent Mycobacterium tuberculosis CTP synthase filaments are

under selective pressure.

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The final and rate-limiting enzyme in pyrimidine biosynthesis, cytidine

triphosphate synthase (CTPS), is essential for the viability of Mycobacterium

tuberculosis and other mycobacteria. Its product, cytidine triphosphate (CTP),

is critical for RNA, DNA, lipid and cell wall synthesis, and is involved in

chromosome segregation. In various organisms across the tree of life, CTPS

assembles into higher-order filaments, leading us to hypothesize that M.

tuberculosis CTPS (mtCTPS) also forms higher-order structures. Here, we show

that mtCTPS does assemble into filaments but with an unusual architecture not

seen in other organisms. Through a combination of structural, biochemical, and

cellular techniques, we show that polymerization stabilizes the active

conformation of the enzyme and resists product inhibition, potentially allowing

for the highly localized production of CTP within the cell. Indeed, CTPS

filaments localize near the CTP-dependent complex needed for chromosome

segregation, and cells expressing mutant enzymes unable to polymerize are

altered in their ability to robustly form this complex. Intriguingly, mutants

that inhibit filament formation are under positive selection in clinical

isolates of M. tuberculosis, pointing to a critical role needed to withstand

pressures imposed by the host and/or antibiotics. Taken together, our data

reveal an unexpected mechanism for the spatially organized production of a

critical nucleotide in M. tuberculosis, which may represent a vulnerability of

the pathogen that can be exploited with chemotherapy.

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**59. PLoS Pathog. 2025 Jul 1;21(7):e1012632. doi: 10.1371/journal.ppat.1012632.**

**Online ahead of print.**

Disruption of riboflavin biosynthesis in mycobacteria establishes riboflavin

pathway intermediates as key precursors of MAIT cell agonists.

Chengalroyen MD(1), Oketade N(2), Worley A(3), Lucas M(2), Ramirez LMN(2),

Raphela ML(1), Swarbrick GM(3), Soma PS(2), Zuma M(1), Warner DF(1)(4),

Lewinsohn DA(5), Mehaffy C(2), Adams EJ(6), Hildebrand W(7), Dobos KM(2),

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Mucosal-associated invariant T (MAIT) cells exhibit an intrinsic ability to

recognize and respond to microbial infections. The semi-invariant antigen

recognition receptor of MAIT cells specifically detects the non-polymorphic

antigen-presenting molecule, major histocompatibility complex class I-related

protein 1 (MR1), which primarily binds riboflavin-derived metabolites of

microbial origin. To further interrogate the dependence of these antigens on

riboflavin biosynthesis in mycobacteria, we deleted individual genes in the

riboflavin biosynthesis pathways in Mycobacterium smegmatis (Msm) and

Mycobacterium tuberculosis (Mtb) and evaluated the impact thereof on MAIT cell

activation. Blocking the early steps of the pathway by deletion of RibA2 or RibG

profoundly reduced, but did not completely ablate, MAIT cell activation by Msm

or Mtb, whereas deletion of RibC, which catalyzes the last step in the pathway,

had no significant effect. Interestingly, deletion of the lumazine synthase

(RibH) specifically enhanced MAIT cell recognition of Mtb whereas loss of

lumazine synthase activity had no impact on MAIT cell activation by Msm. MAIT

cell activation by Msm was likewise unaffected by blocking the production of the

MAIT cell antagonist, Fo (by inhibiting its conversion from the riboflavin

pathway intermediate, 5-amino-6-D-ribitylaminouracil (5-A-RU), through the

deletion of fbiC). Together, these results confirm a central role for 5-A-RU in

generating mycobacterial MR1 ligands and reveal similarities and differences

between Msm and Mtb in terms of the impact of riboflavin pathway disruption on

MAIT cell activation.

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PMID: 40591719

**60. PLoS One. 2025 Jul 1;20(7):e0327348. doi: 10.1371/journal.pone.0327348.**

**eCollection 2025.**

Mixed-methods study to assess delay among patients with tuberculosis in an urban

setting of Bangladesh.

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**BACKGROUND:** Tuberculosis (TB) regained its position as the leading cause of

death globally from a single infectious disease agent in 2024. Delayed diagnosis

and treatment hamper effective TB control. We investigated the duration of

diagnostic and treatment delay along with the associated factors among people

with pulmonary TB in Bangladesh.

**METHODS:** A mixed-method study was conducted between December'19 and March'21, at

icddr,b TB Screening and Treatment Centres (TBSTCs), Dhaka. We interviewed

people with TB (PWTB) seeking care at these TBSTCs using a structured

questionnaire to collect data on socio-demographic, clinical and healthcare

seeking behaviors. We used established frameworks to define stages of delay and

associated factors. Qualitative interviews were conducted among a subset of

participants to gain further insight into the factors associated with delay.

**RESULTS:** We enrolled 895 PWTB with mean (±SD) age 36.6 (±16.1) years; majority

of participants were males (69.9%) and living in urban areas (82.3%). The median

(IQR) patient delay estimated was 47 (29-72) days, with diagnostic delay 45

(30-70) days and treatment delay 2 (2-4) days. The predictors of delay were

those with diabetes (OR 2.0, 95% CI - 1.11, 3.42), who initially self-treated

(OR 2.1, 95% CI - 1.09, 3.88), and were bacteriologically diagnosed (OR 3.7, 95%

CI - 1.31, 10.46). Qualitative approach supported the quantitative findings and

revealed the practice of visiting formal physicians during worsening illness,

neglecting to acknowledge signs or symptoms consistent with TB, lack of TB

related knowledge, and financial insolvency as major reasons for delay.

**CONCLUSION:** Our findings showed that improper health-seeking behavior is one of

the major drivers of patient delay. Thus, targeted programmatic intervention to

raise community awareness on TB and its care services with a special focus on

informal providers can help reduce this delay.

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PMCID: PMC12212489

PMID: 40591627 [Indexed for MEDLINE]

**61. Chem Biol Drug Des. 2025 Jul;106(1):e70152. doi: 10.1111/cbdd.70152.**

In Vitro and In Silico Evaluation of Isatin-Derived Spirooxindoles as

Antituberculosis Drug Candidates.

de Lima FR(1), de Oliveira Viana J(1)(2), de Castro AC(1), Cristiano R(1)(2),

Perelló MA(3), Czeczot AM(3)(4), Bizarro CV(3)(4), Machado P(3)(4)(5), Basso

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Tuberculosis (TB) remains a major global health threat, exacerbated by

multidrug-resistant Mycobacterium tuberculosis (MTB) strains. The development of

new anti-TB agents is crucial. In this study, 17 isatin derivatives synthesized

by our research group were evaluated for their in vitro activity against MTB

strains and the two most potent compounds were assessed for cytotoxicity.

Additionally, molecular docking was performed against 22 MTB protein targets to

explore possible mechanisms of action, and ADMET predictions were used to

determine pharmacokinetic and pharmacodynamic suitability. Also, we investigated

the activity of A15, A16, and A17 against two genetically characterized

multidrug-resistant clinical isolates (PT-12 and PT-20). As a result, the

compounds A16 and A17 exhibited the highest anti-TB activity (MIC = 10 μM for

both). Inverse molecular docking indicated the enzyme

enoyl-[acyl-carrier-protein] reductase as a potential biological target.

Cytotoxicity assays confirmed that A16 and A17 were non-toxic, and ADMET

predictions indicated suitable drug-like properties for anti-TB therapy.

Notably, A16 and A17 showed inhibitory effects against drug-resistant MTB

isolates, with minimum inhibitory concentrations (MICs) ranging from 10 to

20 μM, suggesting their potential to overcome resistance mechanisms linked to

mutations in katG and rpoB. These findings highlight A16 and A17 as promising

candidates for anti-TB agents, particularly against multidrug-resistant strains.

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Sons Ltd.

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**62. JMIRx Med. 2025 Jul 1;6:e66029. doi: 10.2196/66029.**

Improving Tuberculosis Detection in Chest X-Ray Images Through Transfer Learning

and Deep Learning: Comparative Study of Convolutional Neural Network

Architectures.

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**BACKGROUND:** Tuberculosis (TB) remains a significant global health challenge, as

current diagnostic methods are often resource-intensive, time-consuming, and

inaccessible in many high-burden communities, necessitating more efficient and

accurate diagnostic methods to improve early detection and treatment outcomes.

**OBJECTIVE:** This study aimed to evaluate the performance of 6 convolutional

neural network architectures-Visual Geometry Group-16 (VGG16), VGG19, Residual

Network-50 (ResNet50), ResNet101, ResNet152, and Inception-ResNet-V2-in

classifying chest x-ray (CXR) images as either normal or TB-positive. The impact

of data augmentation on model performance, training times, and parameter counts

was also assessed.

**METHODS:** The dataset of 4200 CXR images, comprising 700 labeled as TB-positive

and 3500 as normal cases, was used to train and test the models. Evaluation

metrics included accuracy, precision, recall, F1-score, and area under the

receiver operating characteristic curve. The computational efficiency of each

model was analyzed by comparing training times and parameter counts.

**RESULTS:** VGG16 outperformed the other architectures, achieving an accuracy of

99.4%, precision of 97.9%, recall of 98.6%, F1-score of 98.3%, and area under

the receiver operating characteristic curve of 98.25%. This superior performance

is significant because it demonstrates that a simpler model can deliver

exceptional diagnostic accuracy while requiring fewer computational resources.

Surprisingly, data augmentation did not improve performance, suggesting that the

original dataset's diversity was sufficient. Models with large numbers of

parameters, such as ResNet152 and Inception-ResNet-V2, required longer training

times without yielding proportionally better performance.

**CONCLUSIONS:** Simpler models like VGG16 offer a favorable balance between

diagnostic accuracy and computational efficiency for TB detection in CXR images.

These findings highlight the need to tailor model selection to task-specific

requirements, providing valuable insights for future research and clinical

implementations in medical image classification.

© Alex Mirugwe, Lillian Tamale, Juwa Nyirenda. Originally published in JMIRx Med

(https://med.jmirx.org).

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**63. Antimicrob Agents Chemother. 2025 Jul 1:e0009925. doi: 10.1128/aac.00099-25.**

**Online ahead of print.**

Population pharmacokinetics of pyrazinamide and isoniazid in plasma and

cerebrospinal fluid from South African adults with tuberculous meningitis.

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Pyrazinamide and isoniazid are first-line drugs for tuberculous meningitis

(TBM), but limited information is available on their plasma pharmacokinetics,

and particularly cerebrospinal fluid (CSF) penetration, in patients with TBM.

Any potential effect of co-administration with high-dose rifampicin, also being

evaluated in trials for TBM, is unknown. Understanding this is important for

dose optimisation. We characterized pyrazinamide and isoniazid plasma and CSF

pharmacokinetics among adults enrolled in a phase 2 clinical trial of

intensified antibiotic therapy for HIV-associated TBM. Participants were

randomized to receive either standard TBM treatment (including rifampicin 10

mg/kg) or high-dose rifampicin (35 mg/kg) plus linezolid, with or without

aspirin. Plasma and lumbar CSF samples were collected on days 3 and 28 after

study enrollment, and drug concentrations were measured using liquid

chromatography-tandem mass spectrometry. Data were analysed using nonlinear

mixed-effects modeling. Forty-nine participants provided 414 plasma and 44 CSF

concentrations. Pyrazinamide CSF concentrations equilibrated with plasma with a

half-life of 0.66 h and a pseudo-partition coefficient of 1.05. Isoniazid

concentrations equilibrated with a half-life of 3.87 h and a pseudo-partition

coefficient of 1.04. Pyrazinamide clearance increased by 30% from day 3 to day

28. NAT2 phenotype determined multi-modal isoniazid clearance. High-dose

rifampicin did not affect pyrazinamide or isoniazid plasma pharmacokinetics or

CSF penetration. Both drugs achieved exposure in CSF similar to plasma,

supporting their crucial role in TBM treatment. Plasma pharmacokinetics of

pyrazinamide and isoniazid in TBM were consistent with previously reported

values in pulmonary tuberculosis, even when co-administered with high-dose

rifampicin.

DOI: 10.1128/aac.00099-25

PMID: 40590723

**64. Monaldi Arch Chest Dis. 2025 Jun 30. doi: 10.4081/monaldi.2025.3442. Online**

**ahead of print.**

Prevalence of tuberculosis infection among patients undergoing regular

hemodialysis: a multicenter study in Egypt.

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EL-Arab, Alexandria.

Dear Editor, About one-third of the human population is presently infected by

Mycobacterium tuberculosis, and about 10% during their life develop active

tuberculosis (TB) (5% during the first 2 years following infection)...

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PMID: 40590577

**65. J Clin Microbiol. 2025 Jul 1:e0058025. doi: 10.1128/jcm.00580-25. Online ahead of print.**

Waste to worth: diagnostic accuracy of Xpert MTB/XDR on contaminated liquid

cultures to salvage the detection of drug-resistant tuberculosis.

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Mycobacterium Growth Indicator Tube (MGIT) 960 culture is critical for

tuberculosis (TB) drug susceptibility testing (DST) but is vulnerable to

contamination. We evaluated the accuracy of Xpert MTB/XDR, a molecular DST for

isoniazid, fluoroquinolone, amikacin, and ethionamide, on to-be-discarded

contaminated growth. Xpert MTB/XDR was applied to acid-fast-bacilli-negative,

contaminated cultures from sputum from people with rifampicin-resistant TB when

Xpert MTB/XDR on sputum was unsuccessful (not resistant or susceptible for all

drugs), either at diagnosis (Cohort A) or during treatment monitoring (Cohort

B). Future DSTs within 3 months served as a reference standard. We determined

potential care cascade improvements. In Cohort A, 10% (66/650) of people had a

contaminated culture; 89% (59/66) of contaminated growths were Xpert MTB/XDR

TB-positive. Sensitivity and specificity for isoniazid, fluoroquinolone,

amikacin, and ethionamide resistance were 100% (95% confidence interval [CI] 85,

100) and 100% (79, 100); 100% (59, 100) and 100% (89, 100); 100% (16, 100) and

100% (91, 100); and 100% (72, 100) and 96% (78, 100), respectively. In Cohort B,

22% (28/129) of people with a contaminated culture were Xpert MTB/XDR

TB-positive. Of these, 57% (16/28), 7% (2/28), and 43% (12/28) were isoniazid-,

fluoroquinolone-, and ethionamide-resistant (in two, one, and four people,

respectively, this would be the first resistant result). In both cohorts,

time-to-DST could improve by a median (IQR) of 22 (12-42) days. Xpert MTB/XDR on

contaminated MGIT960 cultures had high sensitivity and specificity for DST. This

approach could mitigate culture contamination's negative effects and improve

gaps in the drug-resistant TB diagnostic cascade.

**IMPORTANCE:** Culture contamination is a common impediment to drug susceptibility

testing for tuberculosis, the single biggest infectious cause of death globally.

Xpert MTB/XDR is a World Health Organization-recommended rapid molecular test

for second-line drug resistance. We evaluated Xpert MTB/XDR on contaminated

liquid culture growth that would otherwise be discarded, with the people who

provided these specimens potentially lost from care cascades. By applying Xpert

MTB/XDR to contaminated growth in a high-volume programmatic laboratory, we

found the number of people who had second-line DST improved, as did the number

of resistant cases diagnosed and time to diagnosis. Furthermore, DST information

was generated in people who otherwise would have had none. This approach can

therefore reduce the effect of culture contamination on tuberculosis DST,

permitting earlier diagnosis and effective treatment initiation and potentially

ultimately contributing to improving clinical outcomes and reducing transmission

of drug-resistant TB.

DOI: 10.1128/jcm.00580-25

PMID: 40590556

**66. Exp Dermatol. 2025 Jul;34(7):e70134. doi: 10.1111/exd.70134.**

Incidence and Clinical Characteristics of Active Tuberculosis in Psoriasis

Patients From a High-Burden Setting: An 18-Year Retrospective Study of 86

Patients.

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Real-world data on concurrent psoriasis and active tuberculosis (TB) remain

limited, particularly in high TB-burden settings. This retrospective study

evaluated the incidence, prevalence, and clinical characteristics of psoriasis

patients with active TB who had received topical or systemic treatments. Medical

records from 13 066 psoriasis patients who presented at Siriraj Hospital over

18 years were reviewed. Among these, 86 (0.66%) developed active TB, yielding an

incidence range of 135-1332 per 100 000 psoriasis patients. The mean patient age

was 50.4 ± 15.7 years; 63 were men and 23 were women. Pulmonary TB occurred in

55 patients (64.0%), whereas 31 (36.0%) developed extrapulmonary TB. Male sex

and smoking were associated with pulmonary TB. The most common pulmonary

symptoms were chronic cough (65.5%) and dyspnoea (60.0%), although 7.3% were

asymptomatic. Time to TB onset was shorter for extrapulmonary cases

(5.7 ± 5.1 years) than for pulmonary cases (7.4 ± 6.5 years), but this

difference was not statistically significant. Extrapulmonary disease most

frequently involved the lymph node and pleura (25.8%) or the gastrointestinal

tract (16.1%). Notably, all four patients who received infliximab within 1 year

before TB diagnosis developed extrapulmonary TB. In conclusion, the incidence of

TB in psoriasis patients in endemic regions may be high. Geographic factors,

sex, smoking, and treatment history appear to influence TB risk. Close

monitoring is critical, particularly in high-burden settings.

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**67. ERJ Open Res. 2025 Jun 30;11(3):00952-2024. doi: 10.1183/23120541.00952-2024.**

**eCollection 2025 May.**

Predicting rifampicin resistance in Mycobacterium tuberculosis using machine

learning informed by protein structural and chemical features.

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**BACKGROUND:** Rifampicin remains a key antibiotic in the treatment of

tuberculosis. Despite advances in cataloguing resistance-associated variants

(RAVs), novel and rare mutations in the relevant gene, rpoB, will be encountered

in clinical samples, complicating the task of using genetics to predict whether

a sample is resistant or not to rifampicin. We have trained a series of machine

learning models with the aim of complementing genetics-based drug susceptibility

testing.

**METHODS:** We built a Test+Train dataset comprising 219 susceptible mutations and

46 RAVs. Features derived from the structure of the RNA polymerase or the change

in chemistry introduced by the mutation were considered; however, only a few,

notably the distance from the rifampicin binding site, were found to be

predictive on their own. Owing to the paucity of RAVs we used Monte Carlo

cross-validation with 50 repeats to train four different machine learning

models.

**RESULTS:** All four models behaved similarly with sensitivities and specificities

in the range 0.84-0.88 and 0.94-0.97, although we preferred the ensemble of

decision tree models as they are easy to inspect and understand. We showed that

measuring distances from molecular dynamics simulations did not improve

performance.

**CONCLUSIONS:** It is possible to predict whether a mutation in rpoB confers

resistance to rifampicin using a machine learning model trained on a combination

of structural, chemical and evolutionary features; however, performance is

moderate and training is complicated by the lack of data.

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PMID: 40589903

**68. Nat Rev Microbiol. 2025 Jun 30. doi: 10.1038/s41579-025-01201-x. Online ahead of print.**

Mycobacterium tuberculosis biology, pathogenicity and interaction with the host.

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Since the release of the first Mycobacterium tuberculosis genome in 1998, major

advances have been made in understanding the biology of this pathogen, the

leading infectious cause of death in modern human history. In this Review, we

outline the physiological and metabolic features thought to underpin the

survival, evasion and subversion strategies employed by M. tuberculosis as it

drives a cycle of transmission, infection and disease in its obligate human

host. We also consider adaptations to key host innate immune effectors,

including the roles of granulocytes, phagosomal damage and repair, autophagy and

cell death in determining host-mycobacterium outcomes. Given the increasing

awareness of the importance of asymptomatic M. tuberculosis infection and

transmission, we advocate for the need to ensure greater intersection between

laboratory and clinical research, taking into account the environmental context

in which natural infection and disease occur. We identify knowledge gaps in the

field and reflect on the opportunities and challenges for integrating host,

bacterium and environment into future investigations to inform intervention

strategies to control tuberculosis disease.

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PMID: 40588584

**69. Ann Am Thorac Soc. 2025 Jun 30. doi: 10.1513/AnnalsATS.202404-422OC. Online**

**ahead of print.**

Effectiveness and Implementation of A Clinical Risk Score for Early Diagnosis of

Tuberculosis in Uganda: A Pragmatic, Clustered Randomization Clinical Trial.

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**Background** Undertreatment of tuberculosis (TB) is common in resource-limited

settings where same-day microbiological diagnosis is unavailable. We evaluated

if a simple clinical risk score for predicting active TB could facilitate

treatment initiation among individuals at high risk for TB. **Methods** We conducted

a pragmatic, implementation-effectiveness study in peri-urban primary health

clinics in Uganda. Four intervention clinics were paired with standard-of-care

comparison clinics. Providers in intervention clinics were trained to use the

score and set a threshold score for considering same-day treatment initiation;

treatment decisions were at the providers' discretion. Our primary effectiveness

outcome was the change in the proportion of individuals with confirmed TB who

started on treatment within seven days of presentation, comparing

pre-intervention and post-intervention periods. **Results** Among intervention

clinics, 594/720 (83%) people diagnosed with TB started treatment within seven

days during the pre-intervention period, versus 264/316 (84%) after

implementation (pre-post difference 1%; 95% confidence interval [95%CI]: -6,

8%). In comparison clinics, seven-day treatment initiation changed from 312/363

(86%) pre-intervention to 153/211 (73%) post-intervention (pre-post difference

-13%; 95%CI: -22, -5%). A difference-in-differences estimate was 14% (95%CI: 10,

19%). In intervention clinics, 1,206 of 1,826 (66%) people presenting with TB

symptoms were administered the risk score. 229 (19%) had a score above the

treatment threshold and 105 (46%) initiated treatment on the same day.

**Conclusions** An easy-to-use clinical risk score did not increase seven-day

empiric treatment initiation in intervention clinics. However, it improved rapid

treatment initiation relative to clinics using the prevailing standard-of-care.

The score was also highly acceptable to clinical providers. Clinical trial

registration available at www.clinicaltrials.gov, ID: \_\_NCT05122624 \_\_\_\_\_\_\_\_\_\_.

DOI: 10.1513/AnnalsATS.202404-422OC

PMID: 40587503

**70. PLoS One. 2025 Jun 30;20(6):e0326500. doi: 10.1371/journal.pone.0326500.**

**eCollection 2025.**

Crystal structures of Mycobacterium tuberculosis and Mycobacterium

thermoresistibile glycyl-tRNA synthetases in various liganded states.

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S(1)(4), Liu L(1)(4), Battaile KP(5), Barrett LK(1)(3), Van Voorhis WC(1)(3),

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Glycyl tRNA synthetases (GlyRSs) are prospective drug targets for combating

Mycobacterium tuberculosis (Mtb) and cancer in humans. These synthetases are of

the α2-subtype, with the ortholog in humans being dual targeted to the cytosol

and mitochondria. Whereas the human enzyme has been structurally characterized

previously in several liganded states, no structures of MtbGlyRS have thus far

been reported. Here, we describe our recent work with MtbGlyRS and the

closely-related Mycobacterium thermoresitibile GlyRS (MtrGlyRS), which

progressed through all phases of the structural genomics pipeline, for the

purpose of facilitating structure-based drug discovery. MtbGlyRS was expressed

in Mycobacterium smegmatis and MtrGlyRS in Escherichia coli. Crystal structures

are described for complexes of the two enzymes with adenosine monophosphate

(AMP) and glycyl-sulfamoyl-adenylate (glycyl-AMS) at resolutions of 1.65/2.90

and 2.25/1.95 Å, respectively, and for MtrGlyRS in its apo state at 2.85 Å.

Despite crystallizing in the dimeric state characteristic of many class II

synthetases, the two enzymes elute predominantly as monomers during size

exclusion chromatography. Strikingly, significant portions of the dimer

interface and active site are unstructured in the MtrGlyRS apoenzyme crystal.

AMP orders two tRNA recognition loops and a section of the insertion domain, and

glycyl-AMS further stabilizes the structure, including the closure of a lid

motif. Both the active and anticodon binding sites display structural

differences with the human GlyRS and thus the collection of crystal structures

should be useful for guiding drug development efforts targeting the various

characterized structural states.

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PMID: 40587479 [Indexed for MEDLINE]

**71. Indian J Dermatol Venereol Leprol. 2025 Jul-Aug;91(4):567. doi:**

**10.25259/IJDVL\_63\_2023\_ER.**

Primary drug resistant cutaneous tuberculosis: A retrospective case series of

seven patients.

[No authors listed]

DOI: 10.25259/IJDVL\_63\_2023\_ER

PMID: 40587374

**72. mSystems. 2025 Jun 30:e0042025. doi: 10.1128/msystems.00420-25. Online ahead of print.**

Phosphoglucomutase A-mediated metabolic adaptation is essential for antibiotic

and disease persistence in Mycobacterium tuberculosis.

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The long-term survival of Mycobacterium tuberculosis (Mtb) requires efficient

use of host resources and uninterrupted access to host-derived nutrients. This

is done by utilization of a highly flexible and integrated network of metabolic

pathways. Phosphoglucomutase A (pgmA) is essential for glycogen biosynthesis,

which acts as a nutrient reservoir and is known to modulate carbon flux in

various pathogens. We, for the first time, investigated the role of pgmA in Mtb

by creating a strain lacking this gene. The absence of pgmA hinders the survival

of pathogens under nutrient-limiting and reactivation conditions. Our study

shows that the lack of cell membrane-associated glycolipids in ΔpgmA compromises

cell wall integrity and increases susceptibility to stress. Interestingly, ΔpgmA

exhibits an enhanced growth phenotype on cholesterol compared to the wild type

due to low cyclic adenosine monophosphate (cAMP) levels. Differential gene

expression and 13C3 carbon dilution analyses indicate that stored carbon as

glycogen is crucial for Mtb survival under nutrient-limiting conditions. We

demonstrate that pgmA is vital for Mtb growth within the host. This study

highlights the critical role of pgmA in metabolic adaptation during nutrient

starvation and reactivation and its implication on antibiotic and disease

persistence. These insights are crucial for developing novel, shorter, and more

effective anti-tuberculosis strategies.IMPORTANCEThis study for the first time

investigated the role of metabolic enzyme phosphoglucomutase A (pgmA) in

Mycobacterium tuberculosis (Mtb), revealing its crucial functions as a toggle

switch between biosynthesis and growth. This work highlights the importance of

pgmA in maintaining the metabolic flexibility of Mtb during the nutritional

switch. The presence of pgmA is critical for the production of

membrane-associated glycolipid, which helps maintain the cell wall integrity

under various growth and stress conditions. This adaptability is pivotal for

generating starvation-induced antibiotic tolerance in Mtb. In addition to the

clinical context, these findings provide a mechanistic foundation for

understanding adaptive strategies by Mtb to harsh environments and the

development of drug-tolerant bacilli.

DOI: 10.1128/msystems.00420-25

PMID: 40586596

**73. Animal Model Exp Med. 2025 Jun 30. doi: 10.1002/ame2.70055. Online ahead of**

**print.**

Diosgenin ameliorates silica-induced tuberculosis in rats.

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**BACKGROUND:** Silicosis is an occupational lung disease that is caused by chronic

exposure to silica dust. Silica-exposed workers are at higher risk of developing

TB, resulting in lung fibrosis and significant respiratory dysfunction.

Diosgenin is a steroidal saponin that has been shown to exert a therapeutic

effect on lung injury. Therefore, we investigated the potential efficacy of

diosgenin in treating silicotuberculosis by evaluating its effectiveness against

Mycobacterium smegmatis, as well as its antifibrotic and antioxidant effects in

silica-induced TB in rats.

**METHODS:** Silicosis was induced by intratracheal instillation of 50 mg/kg

crystalline silica in Sprague-Dawley rats. Rats were grouped into 7 (10 per

group). Different doses of diosgenin (1, 10, and 20 mg/kg) and saline were

administered for 30 days. Afterwards, five rats from each group were sacrificed,

and the five remaining rats in each group, except the control, received

Mycobacterium smegmatis. Treatment continued until the 50th day, and the animals

were sacrificed at the end of the experiment. The result was analyzed using a

one-way analysis of variance (ANOVA) with GraphPad Prism.

**RESULTS:** At a half-maximal inhibition concentration of 0.006043 μg/mL, diosgenin

inhibited the growth of Mycobacterium smegmatis. Oxidative stress markers such

as malondialdehyde were significantly reduced. The health-enhancing effects of

catalase and superoxide dismutase were elevated. Additionally, histological

findings demonstrated a significant improvement in respiratory function

following diosgenin treatment.

**CONCLUSION:** Diosgenin treatment inhibited the growth of Mycobacterium smegmatis,

leading to a reduction in the susceptibility of rats to infection and improved

pulmonary function through its antioxidant effect.

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Wiley & Sons Australia, Ltd on behalf of The Chinese Association for Laboratory

Animal Sciences.

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**74. Lancet Glob Health. 2025 Jul;13(7):e1240-e1249. doi:**

**10.1016/S2214-109X(25)00114-7.**

Implications of progressive lung damage and post-tuberculosis sequelae for the

health benefits of prompt tuberculosis treatment in high HIV prevalence

settings: a mathematical modelling analysis.

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H Chan School of Public Health, Boston, MA, USA.

**BACKGROUND:** Untreated pulmonary tuberculosis causes ongoing lung damage, which

can persist after treatment. Conventional modelling approaches for assessing

tuberculosis health effects might not fully capture these mechanisms. We

evaluated how tuberculosis-associated lung damage and post-tuberculosis sequelae

affect the lifetime health consequences of tuberculosis in high HIV prevalence

settings.

**METHODS:** We developed a microsimulation model (computer simulations that

reproduce disease natural history and intervention effects for sampled

individuals) representing dynamic changes in lung function for individuals

evaluated for tuberculosis in routine clinical settings. We parametrised the

model with data (from a previously published study) for three African countries

with a high burden of tuberculosis and HIV: Uganda, Kenya, and South Africa, and

estimated lifetime health outcomes under prompt, delayed, and no tuberculosis

treatment scenarios. We compared results to earlier modelling approaches that

omit progressive lung damage and post-tuberculosis sequelae.

**FINDINGS:** We estimated a 5·1 years (95% uncertainty interval 3·8-6·4) reduction

in life expectancy due to tuberculosis with prompt treatment, 7·7 years

(5·5-10·1) with delayed treatment, and 18·5 years (15·5-20·6) with no treatment. Estimated per-person disability-adjusted life-years (DALYs) from tuberculosis were 11·4 years (8·9-14·2) with prompt treatment, 17·1 years (13·1-22·1) with delayed treatment, and 37·7 years (34·3-40·3) with no treatment. Compared with individuals without HIV, individuals with HIV had a greater proportion of tuberculosis-attributable deaths, but fewer life-years lost to tuberculosis. Post-tuberculosis DALYs represented 52·5% of total DALYs with prompt treatment, 42·7% with delayed treatment, and 9·1% with no treatment. Modelling approaches that omit progressive lung damage and post-tuberculosis sequelae underestimated lifetime health losses of tuberculosis by 48-57% and underestimated the benefits of prompt treatment by 45-64%.

**INTERPRETATION:** Delayed initiation of tuberculosis treatment causes greater lung

damage and higher mortality risks during and after the disease episode than

prompt treatment. In settings with coprevalent tuberculosis and HIV, accounting

for these factors substantially increased estimates of the lifetime disease

burden and life expectancy loss caused by tuberculosis. These findings imply

greater health effects and cost-effectiveness for interventions to prevent

tuberculosis and achieve earlier treatment initiation than indicated in previous

analytical approaches.

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**75. Emerg Infect Dis. 2025 Jul;31(7):1344-1352. doi: 10.3201/eid3107.250031.**

Spatiotemporal Distribution and Clinical Characteristics of Zoonotic

Tuberculosis, Spain, 2018-2022.

Roy Á, Gómez-Barroso D, Cruz-Ferro E, Fernández A, Martínez-Pino I, Del Henar

Marcos M, Ursúa-Díaz I, Miras S, Echave N, Ounarou E, Romero B, Herrera-León L,

Herrador Z; Study Group on Zoonotic Tuberculosis.

Zoonotic tuberculosis (zTB) is a communicable disease that has major effects on

both human and animal health. Spain reports the highest number of zTB cases in

humans annually in the European Union. We describe the epidemiology of human

cases of zTB caused by Mycobacterium bovis and M. caprae in Spain during

2018-2022. The incidence of M. bovis infection compared with M. tuberculosis

infection was higher in patients who were native-born (adjusted odds ratio

[aOR) 2.32, 95% CI 1.44-3.82), HIV-negative (aOR 3.39, 95% CI 1.24-14.0), or had extrapulmonary forms of TB (aOR 2.20, 95% CI 1.46-3.28). The spatial pattern

differed by M. tuberculosis complex species; we identified 3 significant

clusters of M. bovis and 1 of M. caprae in bovine TB-free regions. Our results

show the importance of including animal and human data on circulating zoonotic

pathogens under the One Health umbrella.

DOI: 10.3201/eid3107.250031

PMCID: PMC12205449

PMID: 40562720 [Indexed for MEDLINE]

**76. Emerg Infect Dis. 2025 Jul;31(7):1284-1293. doi: 10.3201/eid3107.241827.**

Systematic Review of Contact Investigation Costs for Tuberculosis, United

States.

Asay GRB, Young KH, Hill TD, Njie GJ.

Contact investigation is a fundamental component of tuberculosis (TB) programs

that drives prompt diagnosis and treatment of Mycobacterium tuberculosis

infection among those exposed. Few studies have examined contact investigation

costs for TB. We conducted a systematic review of TB contact investigation costs

in the United States by searching English-language articles published during

January 1990-August 2024 in electronic databases, including MEDLINE, Embase,

CINAHL, and Scopus. We identified 2,920 titles and abstracts; 10 studies met our

inclusion criteria. We abstracted costs for labor, diagnostic tests, and chest

radiographs. Labor cost per contact was estimated at $175.94 (range

$79.97-$293.51); total cost, including diagnostic testing and chest radiography,

was $228.93 (range $132.95-$346.49).The overall cost of contact investigation in

the United States was $9.94 (range $5.77-$15.04) million in 2022; total cost

during 2013-2022 was $137.35 million. Contact investigations are essential to

prevent TB and avert TB-related labor and diagnostic costs.

DOI: 10.3201/eid3107.241827

PMCID: PMC12205448

PMID: 40562712 [Indexed for MEDLINE]

**77. Trop Biomed. 2025 Jun 1;42(2):213-219. doi: 10.47665/tb.42.2.014.**

Discovery of alcohol dehydrogenase (ADH) as a potential vaccine target from

Mycolicibacterium smegmatis extracellular vesicles via immunoproteomics.

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Kelantan, Malaysia.

Mycobacterium tuberculosis (MTB), the causative agent of tuberculosis, releases

extracellular vesicles (EVs) that impair macrophage functions and circulate

bacterial components to modulate the host immune response. While EVs are

increasingly investigated as new vaccines and biomarkers, studying MTB EVs is

challenging due to the slow growth rate and pathogenic properties of MTB.

Mycolicibacterium smegmatis (MSMEG), a non-pathogenic surrogate with a faster

growth rate, offers a safer and more convenient option for laboratory studies

due to its similarities to MTB. In this study, we explore the antigenic

properties of MSMEG EVs to assess their potential use in developing safer

tuberculosis vaccine strategies. Through an immunoproteomics approach that

combines comprehensive protein separation by OFFGELTM fractionation, Western

blot analysis and mass spectrometry, we identified alcohol dehydrogenase (ADH) -

a 46 kDa protein involved in mycobacterial cell wall synthesis - as an antigenic

protein from MSMEG EVs. Our findings suggest that MSMEG EVs-derived ADH could

improve tuberculosis vaccine formulations and potentially be used for

coimmunization with the BCG vaccine, offering new and safer strategies to combat

tuberculosis.

DOI: 10.47665/tb.42.2.014

PMID: 40618367 [Indexed for MEDLINE]

**78. Tuberculosis (Edinb). 2025 Jun 28;154:102668. doi: 10.1016/j.tube.2025.102668.**

**Online ahead of print.**

Hereditary and antimicrobial factor shaping extracellular bacteria dynamics in

an in-host mathematical model of tuberculosis for disease control.

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Tuberculosis (TB) remains a global health challenge, necessitating deeper

insights into the dynamics of extracellular bacterial populations within

infected hosts. This study presents an in-host mathematical model that

incorporates hereditary and antimicrobial factors influencing TB progression.

The biological feasibility of the model is established by analyzing the

boundedness of solutions within a realistic parameter space. The equilibrium

states, including the disease-free and endemic equilibria, are examined,

revealing conditions under which the system remains locally asymptotically

stable. Sensitivity analysis is conducted to determine the key parameters

driving infection dynamics, providing insights into potential control

strategies. Notably, the model exhibits a backward bifurcation, indicating the

possibility of multiple stable states and suggesting that reducing the basic

reproduction number R0 below unity may not be sufficient for disease

eradication. These findings highlight the importance of targeted interventions

to effectively control extracellular bacterial populations and mitigate TB

infection.

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DOI: 10.1016/j.tube.2025.102668

PMID: 40617181

**79. Diagn Microbiol Infect Dis. 2025 Jun 25;113(3):116978. doi:**

**10.1016/j.diagmicrobio.2025.116978. Online ahead of print.**

Novel heterocycles as antitubercular drugs: A review.

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Tuberculosis (TB) treatments rely on novel compounds, improved delivery, and

combination therapies, but challenges like toxicities, drug resistance, HIV

incompatibility, and lack of knowledge about drug processes persist. TB remains

one of the most prevalent infectious diseases globally, impacting millions

annually. It has led to the spread of multidrug-resistant strains and

extensively drug-resistant Mycobacterium tuberculosis. New drugs are urgently

needed to improve treatment for drug-resistant TB, reduce new infections, and

eliminate death rates. Fortunately, some novel heterocyclic ring-containing

potential antitubercular candidate drugs have entered clinical trials in recent

years. These drugs are most likely to be successful against resistant strains.

An overview of new anti-TB agents with diverse molecular structures highlights

efforts to develop new drug molecules as lead anti-TB agents. Recent

developments in the study of new heterocyclic compounds are highlighted in this

review, emphasizing the compounds' antimycobacterial activity, modes of action,

toxicity, and structure-activity relationships (SARs).

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DOI: 10.1016/j.diagmicrobio.2025.116978

PMID: 40614507

**80. Health Educ Res. 2025 Jun 26;40(4):cyaf028. doi: 10.1093/her/cyaf028.**

Exploring diabetes self-management practices among people with TB in Eswatini: a

qualitative analysis.

Senthilvelan S(1), Mantell JE(2), Palmo L(3), Howard AA(4)(5), Vambe D(6)(7),

Ginindza N(8), Dlamini N(9), Hirsch-Moverman Y(4)(5).

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Diabetes mellitus (DM), prevalent globally among individuals with tuberculosis

(TB) and associated with suboptimal TB treatment outcomes, is a major concern in

Eswatini, where high TB incidence and care gaps in screening for and managing

pre-DM and DM exist. Understanding the feasibility and acceptability of DM

self-management practices among individuals with TB and pre-DM/DM is key to

improving both TB treatment success and glycaemic control in Eswatini and other

resource-limited settings. To explore barriers and facilitators to adopting DM

self-management practices, we conducted 26 in-depth interviews with individuals

diagnosed with both TB and pre-DM/DM in Manzini, Eswatini. Our analyses were

guided by the situated Information Motivation and Behavioural Skills model.

While participants demonstrated substantial knowledge about the dietary and

exercise changes needed to manage pre-DM/DM, many were unaware of the link

between TB and DM. Some attributed their pre-DM/DM diagnosis to dietary habits

or family history. Despite being well-informed and motivated to engage in

self-management practices, structural barriers, especially financial

constraints, frequently hindered their efforts. Participants suggested

addressing these challenges by enhancing community education on DM, promoting

home gardening initiatives, and offering financial assistance for transportation

to clinics.

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PMID: 40614336 [Indexed for MEDLINE]

**81. J Clin Tuberc Other Mycobact Dis. 2025 Jun 20;40:100541. doi:**

**10.1016/j.jctube.2025.100541. eCollection 2025 Aug.**

Multi-month dispensing of tuberculosis medications in sub-Saharan Africa: A

feasible, person-centered care model.

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California Irvine, Irvine, CA, USA.

The treatment success rate among people with tuberculosis in sub-Saharan Africa

is suboptimal despite the availability of shortened and efficacious TB regimens.

Barriers such as long travel distances and frequent clinic visits for medication

refills hinder access to care and compromise treatment adherence and completion.

Multi-month dispensing of anti-retroviral drugs has proved successful in

improving treatment adherence and viral load suppression among people living

with human immunodeficiency virus. The strategy could be adapted for

tuberculosis care to address treatment access and adherence barriers to optimize

treatment success. In this perspective, we discuss the key considerations for

the multi-month dispensing of tuberculosis drugs in sub-Saharan Africa. In

particular, we highlight treatment monitoring, strengthening of logistics and

supply chain systems, multi-month dispensing protocols, healthcare provider

capacity building, community engagement, and monitoring and evaluation

framework. We call for research, policy reforms, and pilot programs to evaluate

and scale up multi-month dispensing of tuberculosis medications to end the

epidemic by 2035.

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PMCID: PMC12221744

PMID: 40613038

**82. Iran J Microbiol. 2025 Jun;17(3):358-365. doi: 10.18502/ijm.v17i3.18817.**

Genotypic diversity of Mycobacterium tuberculosis strains collected from

immigrant patients in Mashhad, Iran using MIRU-VNTR method.

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University of Medical Sciences, Mashhad, Iran.

**BACKGROUND AND OBJECTIVES:** This research aimed to explore the genetic diversity

and phylogenetic relationships of Mycobacterium tuberculosis (Mtb) strains, as

well as to assess their drug susceptibility, specifically in strains isolated

from immigrant patients attending the Referral Tuberculosis Laboratory in

Mashhad.

**MATERIALS AND METHODS:** A total of 52 sputum samples isolated from patients were

examined utilizing the Mycobacterial Interspersed Repetitive-Unit Variable

Number of Tandem Repeats (MIRU-VNTR). Drug-susceptibility testing against

rifampin (RIF) and isoniazid (INH) was measured utilizing the proportional

strategy. Thereafter, for more examination, Xpert MTB/RIF and multiplex

allele-specific PCR (MAS-PCR) was performed to determine RIF and INH-resistance

within the Mtb strains.

**RESULTS:** Among 52 Mtb isolates, 2 (3.8%) were resistant to rifampin and one

isolate was resistant to both INH and RIF and considered as multidrug-resistance

(MDR) isolate. According to MIRU-VNTR, the most prominent genetic-variation

patterns of these samples, were related to NEW-1 (n=18, 34.6%), followed by

CAS/Delhi (n=17, 32.7%), Haarlem (n=12, 23%), Uganda I (n=2, 3.8%), S (n=1,

1.9%), Beijing (n=1, 1.9%), and unknown (n=1, 1.9%) genotypes. The statistical

analysis showed that the estimated percentage of the recent TB-transmission in

this study was 0.21%.

**CONCLUSION:** The result of this study indicated a great diversity of MTBC

circulating among Afghan-immigrants which might be one of the reasons for the

infection to become active. The relatively high percentage of resistant isolates

in the studied population shows the importance of screening the immigrants

especially at the entry borders and treatment and follow up of patients, to

control TB-incidence in country.

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DOI: 10.18502/ijm.v17i3.18817

PMCID: PMC12218889

PMID: 40612727

**83. South Afr J HIV Med. 2025 Jun 17;26(1):1705. doi: 10.4102/sajhivmed.v26i1.1705. eCollection 2025.**

Urine-based assays for inpatients with HIV-associated tuberculosis in rural

South Africa.

Mntonintshi M(1), Sossen B(2), Bookholane H(2), Lifson A(2), Africa L(3),

Goliath R(4), Wearne N(5), Parrish A(6), Meintjes G(2)(4)(7).

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of London, London, United Kingdom.

**BACKGROUND:** Accurate non-sputum-based tuberculosis (TB) diagnostics are urgently

needed to improve diagnostic yield and patient outcomes.

**OBJECTIVES:** To compare the diagnostic accuracy and diagnostic yield of Urine

Xpert Ultra (Urine-XPU) and Urine DetermineTM TB Lipoarabinomannan (LAM) antigen

test (AlereLAM) against both a microbiological and composite reference standard

(MRS and CRS) in a rural, routine care setting in South Africa.

**METHOD:** Adults (≥ 18 years) with HIV had sputum, urine and blood collected for

comprehensive TB testing shortly after admission. Additionally, focused

assessment with sonography for HIV-associated TB (FASH) was performed. The MRS

was defined by Xpert Ultra or culture-based tests for Mycobacterium

tuberculosis. The CRS incorporated these mycobacterial tests, FASH findings, and

clinical response to empiric TB treatment. Follow-up was conducted at 3 months.

**RESULTS:** A total of 206 participants were enrolled, with a median age of 39

years and 63% were female. Using the MRS the sensitivity of AlereLAM was 45.2%

(95% confidence interval [CI]: 31.2-60.1) and Urine-XPU, 59.5% (95%CI:

44.5-73.0); and the specificity of AlereLAM was 93.6% (95%CI: 88.2-96.6) and

Urine-XPU 95.0% (95%CI: 90.0% - 97.6%). Urine-XPU and AlereLAM performed better

than sputum Xpert Ultra (Sputum-XPU) in patients with more severe illness.

Additionally, Urine-XPU showed potential for accurately detecting rifampicin

resistance.

**CONCLUSION:** Urine-XPU and AlereLAM demonstrated comparable diagnostic accuracy

for TB in hospitalised adults with HIV. Integrating Urine-XPU alongside AlereLAM

and Sputum-XPU may improve timely and accurate diagnosis of TB and rifampicin

resistance. Further research is required to optimise the diagnosis-to-treatment

pathway.

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DOI: 10.4102/sajhivmed.v26i1.1705

PMCID: PMC12224061

PMID: 40612624

**84. iScience. 2025 Jun 7;28(7):112839. doi: 10.1016/j.isci.2025.112839. eCollection 2025 Jul 18.**

Protection of infant mice against pertussis, tuberculosis and influenza by

co-administration of nasal pertussis vaccine candidate BPZE1 and BCG.

Rouanet C(1), Debrie AS(1), Cauchi S(1), Mielcarek N(1).

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U1019-UMR 9017-CIIL-Center for Infection and Immunity of Lille, 59000 Lille,

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Protecting neonates at risk of serious pertussis disease or death represents a

global emergency. BPZE1 is the most advanced, next-generation pertussis vaccine

undergoing clinical evaluation in children and adults. We investigated the

feasibility of co-administering BPZE1 and Bacillus Calmette-Guerin (BCG), the

most widely used tuberculosis vaccine worldwide. We showed that BPZE1 can be

co-administered with BCG without altering its immunogenicity and protective

efficacy against B. pertussis in infant mice. Conversely, BCG immunogenicity and

protective efficacy against M. tuberculosis are not affected by BPZE1. Both

vaccines induce off-target protection against heterologous infections. In this

study, we showed that BPZE1 and BCG alone or in combination induced high levels

of protection against influenza challenge in infant mice. In contrast to BCG,

the off-target properties of BPZE1 were independent of the age of vaccination.

Vaccination with BPZE1 might be considered at the same time as BCG, facilitating

its effective implementation in the childhood immunization schedule.

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DOI: 10.1016/j.isci.2025.112839

PMCID: PMC12221715

PMID: 40612502

**85. SA J Radiol. 2025 Jun 20;29(1):3139. doi: 10.4102/sajr.v29i1.3139. eCollection 2025.**

A rare case of intercostal-to-pulmonary artery fistula and its endovascular

treatment in the setting of post pulmonary tuberculosis bronchiectasis and

haemoptysis.

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Intercostal artery-to-pulmonary artery fistula is an extremely rare variant of

systemic artery-to-pulmonary artery fistulas (SA-PAFs). A case of a 38-year-old

man presenting with clinically significant haemoptysis secondary to an

intercostal artery-to-pulmonary artery fistula in the setting of post-pulmonary

tuberculosis (TB) bronchiectasis is described. The fistulae were successfully

treated with endovascular coils.

**CONTRIBUTION:** This case report illustrates an intercostal artery-to-pulmonary

artery fistula associated with post-primary tuberculosis bronchiectasis,

highlighting its multimodal radiological features and successful endovascular

treatment.

© 2025. The Authors.

DOI: 10.4102/sajr.v29i1.3139

PMCID: PMC12223871

PMID: 40612284

**86. Sage Open Pediatr. 2025 Mar 21;12:30502225251319895. doi:**

**10.1177/30502225251319895. eCollection 2025 Jan-Dec.**

Isolated Tuberculous Brain Abscess in a 7-Year-Old Child: A Rare Presentation of

CNS Tuberculosis: A Case Report.

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(2)Haramaya University College of Health and Medical Sciences, Harar, Ethiopia.

**Background.** Tuberculous brain abscess (TBA) is a rare and often overlooked

manifestation of central nervous system tuberculosis (CNS TB), particularly in

children. The occurrence of isolated TBAs, where there is no clinical or

radiological evidence of tuberculosis elsewhere in the body, is exceedingly

uncommon in pediatric patients. **Case presentation.** A 7-year-old girl presented

with a two-week history of persistent headaches and progressive left-sided

weakness. Initially diagnosed and treated for pyogenic brain abscesses. However,

microbiological and histopathological analysis of the drained abscess revealed

the presence of acid-fast bacilli (AFB) and a positive CBNAAT for Mycobacterium

tuberculosis, confirming TBA. The patient was successfully treated with surgical

drainage and a course of anti-tubercular therapy (ATT). **Conclusion.** Isolated

TBA, though rare, is a critical diagnostic consideration in pediatric CNS TB,

especially in tuberculosis-endemic regions. This case emphasizes the need to

consider Mycobacterium tuberculosis in the differential diagnosis of pediatric

brain abscesses, particularly in regions with a high tuberculosis burden. It

also highlights the need for routine tuberculosis testing, including CBNAAT, on

all pus samples from intracranial abscesses to ensure timely and accurate

diagnosis.

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DOI: 10.1177/30502225251319895

PMCID: PMC12220871

PMID: 40612180

**87. IJID Reg. 2025 Apr 11;15:100649. doi: 10.1016/j.ijregi.2025.100649. eCollection 2025 Jun.**

Tuberculosis preventive treatment in India: Is budget allocation for

tuberculosis elimination sufficient?

Singh S(1).

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Foundation (Deemed University), Pondicherry, India.

DOI: 10.1016/j.ijregi.2025.100649

PMCID: PMC12225025

PMID: 40611933

**88. IJID Reg. 2025 Apr 15;15:100647. doi: 10.1016/j.ijregi.2025.100647. eCollection 2025 Jun.**

Tuberculosis treatment outcomes and their related factors in patients with

tuberculosis treated at the Antituberculosis Center of Brazzaville, Republic of

Congo.

Ngouama BB(1)(2), Mouzinga FH(1)(2), Dello MNM(1)(2), Djontu JC(1), Elion

Assiana DO(1)(2)(3), Okemba Okombi FH(3)(4), Tchuandom SB(3), Ayet MI(5), Siele

LK(5), Vouvoungui JC(1), Grobusch MP(6)(7)(8)(9)(10), Mouanga AM(1)(4), Mbozo

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(9)Masanga Medical Research Unit (MMRU), Masanga, Sierra Leone.

(10)Institute of Infectious Diseases and Molecular Medicine, University of Cape

Town, Cape Town, South Africa.

**OBJECTIVES:** Tuberculosis (TB) treatment outcome is one of the key indicators to

evaluate the performance of TB control programs. This study aims to assess TB

treatment outcomes and their related associated factors in patients treated at

the Antituberculosis Center of Brazzaville, Republic of Congo.

**METHODS:** A prospective cohort study was conducted at the Antituberculosis Center

of Brazzaville from July 2022 to August 2023, involving 305 patients with

pulmonary TB diagnosed with the GenXpert MTB/RIF assay. These patients were

closely monitored using acid-fast bacillus microscopy while receiving treatment

based on whether they were drug-sensitive (DS) or drug-resistant. Sputum samples

from patients who were DS were analyzed at 2, 5, and 6 months, whereas patients

who were multi-drug-resistant (MDR) underwent a monthly sputum analysis for 9

months.

**RESULTS:** The overall successful treatment rate was 80.3%, with 70.8% of patients

cured and 9.5% completing treatment. Conversely, 19.7% experienced unsuccessful

outcomes, including 13.4% loss to follow-up, 3.6% deaths, and 1.6% treatment

failures. The treatment success in individuals co-infected with HIV was 46.7%

(seven of 15), whereas it was 42% (eight in 19) in patients who were MDR.

HIV-negative status (adjusted odds ratio = 5.11; 95% confidence interval:

1.73-13.44) and DS-TB (adjusted odds ratio = 8.29; 95% confidence interval:

3.17-21.04) were associated with increased success of treatment outcome.

**CONCLUSIONS:** The overall TB treatment success rate was below the World Health

Organization End TB Strategy threshold, with a high proportion of patients lost

to follow-up and a low treatment success in patients with TB/HIV and those who

were MDR. The findings highlight the need to enhance supervision, improve

directly observed treatment short course monitoring, and develop strategies to

minimize patients lost to follow-up.

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PMCID: PMC12225031

PMID: 40611930

**89. IJID Reg. 2025 Apr 12;15:100650. doi: 10.1016/j.ijregi.2025.100650. eCollection 2025 Jun.**

Strengthening tuberculosis control: addressing gaps in screening, diagnosis, and

funding.

Shah H(1), Patel J(1), Rai S(1), Sen A(1).

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DOI: 10.1016/j.ijregi.2025.100650

PMCID: PMC12225026

PMID: 40611929

**90. bioRxiv [Preprint]. 2025 Jun 19:2025.06.19.660520. doi:**

**10.1101/2025.06.19.660520.**

The unique role of nucS -mediated non-canonical mismatch repair in Mycobacterium

tuberculosis resistance evolution.

Martín-Blecua I, Valverde JR, García-Bravo P, Ruiz-Enamorado Á, Prados-Rosales

R, Sastre-Domínguez J, Das L, Jacobs WR, San Millán Á, Blázquez J, Gullón S.

DNA surveillance mechanisms play a vital role in maintaining genome stability

and minimizing mutation rates. One such mechanism, post-replicative mismatch

repair (MMR), corrects replication errors that escape DNA polymerase

proofreading activity. In most bacteria and eukaryotes, MMR is orchestrated by

MutS and MutL proteins. However, certain archaeal and actinobacterial species,

including the major human pathogen Mycobacterium tuberculosis , lack these

components. Instead, they rely on the nuclease EndoMS/NucS, a structurally

distinct enzyme that governs a non-canonical MMR pathway. Given that M.

tuberculosis acquires drug resistance exclusively through chromosomal mutations,

understanding mutation rate regulation in this pathogen is critical.

Nevertheless, despite its anticipated significance, the role of NucS in drug

resistance evolution remains largely unexplored in this organism. This study

investigates NucS function in M. tuberculosis and uncovers a unique resistance

dynamic distinct from other Actinobacteria. While nucS deletion alters the

mutational spectrum, it minimally affects the emergence of rifampicin-,

isoniazid-, and ethambutol-resistant mutations, in stark contrast to its role in

other Actinobacteria. We demonstrated that this atypical behaviour is not

attributable to the presence of a single NucS polymorphism, R144S, in the NucS

sequence of the M. tuberculosis reference strain H37Rv, which differs from the

NucS consensus sequence. Constructing and analysing an H37Rv variant possessing

the NucS consensus sequence revealed a subtly altered mutational spectrum but

unchanged mutation rates. Notably, database analysis of the R144S polymorphism

in clinical isolates revealed its prevalence and significant association with

ethambutol resistance. These findings challenge the established view that nucS

serves as a genome stability guardian that minimizes mutation rates in M.

tuberculosis , suggesting additional mismatch repair mechanisms beyond NucS or a

highly efficient replication system in this pathogen.

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PMCID: PMC12224545

PMID: 40611901

**91. Biochemistry (Mosc). 2025 Jun;90(6):754-772. doi: 10.1134/S0006297925600073.**

Multiepitope mRNA Vaccine mRNA-mEp21-FL-IDT Provides Efficient Protection

against M. tuberculosis.

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Tuberculosis is a leading cause of death from a bacterial infection agent. The

development of new tuberculosis vaccines can reduce the number of new cases and

tuberculosis-related deaths. One of the most promising areas in vaccination is

development of mRNA vaccines, which have already proven their high effectiveness

against COVID-19 and other viral infections. Using modern immunoinformatic

methods, we developed four new antituberculosis multiepitope mRNA vaccines

differing in the encoded adjuvants and codon composition and tested their

immunogenicity and protectivity in mice. Most of the developed mRNA vaccines

induced the formation of both cellular and humoral immunity. The adaptive

response was stronger for the vaccines with the RpfE adjuvant; however, the best

protective response was elicited by the mRNA-mEp21-FL-IDT vaccine with the FL

adjuvant. This vaccine reduced the mycobacterial load in the lungs of mice

infected with Mycobacterium tuberculosis and increased their survival rate.

Altogether, our results indicate that the mRNA-mEp21-FL-IDT vaccine ensures

effective protection against tuberculosis comparable to that provided by the BCG

vaccine.

DOI: 10.1134/S0006297925600073

PMID: 40609994 [Indexed for MEDLINE]

**92. Pan Afr Med J. 2025 Apr 2;50:91. doi: 10.11604/pamj.2025.50.91.46218.**

**eCollection 2025.**

Tuberculosis treatment adherence and associated factors in the Butha-Buthe

district, Lesotho: a retrospective cohort study.

Rangoanana M(1), Ngah V(1), Tamuzi JL(1), Maphalale S(2), Molete M(2), Ratikoane

R(2), Maama L(3), Fwemba I(4), Daramola O(5), Ogunrombi M(6), Nyasulu PS(1)(7).

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**INTRODUCTION:** Lesotho remains one of the world's 30 high-tuberculosis (TB)

burden countries. In Butha-Buthe district, unfavourable TB treatment outcomes

were higher than those set forth by the WHO. This study's objective was to

evaluate TB treatment adherence and treatment resistance among patients enrolled

in the 12 health facilities in Butha-Buthe.

**METHODS:** data were collected from the medical records of patients with sputum

smear-positive TB and extra-pulmonary forms of TB between January 2015 and

December 2020. Results were presented in frequencies and percentages. Univariate

and multivariable logistic regression analyses were conducted to identify

factors associated with treatment adherence.

**RESULTS:** among 1,792 patients who were enrolled, 1,320 were included in the

study. The overall mean TB treatment adherence rate was estimated at 37.20%.

Factors found to be associated with treatment adherence in multivariate analysis

were age ≥60 years (aOR: 0.59, 95%CI: 0.54- 0.66; P<0.001), being a mine worker

(aOR 1.09, 95%CI: 1.03-1.14; P<0.001), having pulmonary TB (aOR: 1.23, 95%CI:

1.17-1.29, P<0.001), being in the continuation phase of the treatment (aOR 1.38,

95%CI: 1.33, 1.45; P<0.001) and category 2 (aOR 0.93, 95%CI: 0.88-0.99; P =

0.016). Regarding TB contact support, family members (aOR: 1.08, 95%CI:

1.03-1.14; P<0.001), friends (aOR 1.30, 95%CI: 1.19-1.41; P<0.001), spouses

(aOR: 1.24, 95%CI 1.16-1.34; P<0.001), and unreported contacts (aOR 1.18, 95%CI:

1.09-1.27; P = 0.015) all showed increased TB adherence.

**CONCLUSION:** the overall adherence to TB therapy was poor in Butha-Buthe

district. Lesotho urgently needs district-level strategies to improve TB

treatment adherence and reduce treatment resistance.

Copyright: Motlatsi Rangoanana et al.

DOI: 10.11604/pamj.2025.50.91.46218

PMCID: PMC12220024

PMID: 40607270 [Indexed for MEDLINE]

**93. Mater Sociomed. 2025;37(2):169-174. doi: 10.5455/msm.2025.37.169-174.**

Abdominal Tuberculosis in a Young Female Immigrant-"the Great Masquerader" in a

Nonendemic Country-a Case Report and Literature Review.

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Veterans Hospital, Zabok, Republic of Croatia.

**BACKGROUND:** Tuberculosis (TB), primarily recognized as a pulmonary disease, can

manifest in various extrapulmonary forms, with abdominal tuberculosis (ATB)

being one of the most common. Abdominal tuberculosis is one of the diseases

known as "the great imitator" - it can mimic the clinical presentation of

various diseases that are more common, such as appendicitis, acute

cholecystitis, colitis, and some malignant diseases such as colon or stomach

neoplasms. Diagnosis of ATB is often delayed, especially if a clinician in a

nonendemic country does not include ATB in the differential diagnosis. Given the

rising migration of people from the endemic to the nonendemic countries, we

believe it is mandatory to raise consciousness about this clinical entity, as

well as to lower a threshold to include ATB in the differential diagnosis.

**OBJECTIVE:** We present a case of a 31-year-old patient from Nepal, who was

admitted through the emergency department of General Hospital Zabok, Croatia,

with signs of acute abdomen, later successfully diagnosed and treated for ATB.

**CASE PRESENTATION:** We also deliver a brief literature review, summarizing the

epidemiology, clinical presentation, diagnostic and therapeutic algorithms for

ATB. Migrations are inevitably changing the vaccination status and

epidemiological risks of any host country.

**CONCLUSION**: Medical personnel should keep upgrading and revising their knowledge

of the "usual suspects" whilst differentially diagnosing both immigrants and

non-immigrants, in order to make timely and good quality diagnosis and

treatment.

© 2025 Ana Dimova, Rajko Fures, Janja Konjevod, Zlatko Hrgovic, Sanja Malinac

Malojcic, Bojana Kranjcec.

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PMCID: PMC12212218

PMID: 40607095

**94. Front Microbiol. 2025 Jun 18;16:1634229. doi: 10.3389/fmicb.2025.1634229.**

**eCollection 2025.**

In vivo profiling of the PE/PPE proteins of Mycobacterium tuberculosis reveals

diverse contributions to virulence.

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Mycobacterium tuberculosis (M.tb) uses a plethora of cell surface and secreted

virulence factors to survive within the host. Among these are the PE/PPE

proteins, a pair of secretory families that have expanded to 168 members in

M.tb. Most of these proteins are poorly characterized due in part to their

repetitive sequences and high similarity to one another. While PE/PPE genes are

generally non-essential in vitro, many are highly expressed during animal

infection. Thus, we conducted an in vivo pooled screen of 87 transposon mutants

in M.tb PE/PPE genes and used Tn-seq to identify mutants with fitness defects in

the mouse lung environment. We found consistent, time-dependent changes in

mutant abundance across our animal replicates and identified decreases in

several key mutant strains known to promote bacterial growth or virulence. In

all, 27 of the 87 mutants showed significant reductions in percent population

prevalence in the lung over 3 weeks. We then selected a transposon mutant in the

PPE71 gene and validated that this strain was attenuated in a single-strain

infection. Our findings suggest that a high proportion of PE/PPE genes (31%) are

required for virulence in the mouse model. These observations suggest that

individual PE/PPE genes have differing contributions to virulence and may help

prioritize future studies of these families. Strikingly, these properties were

seen only in an in vivo model, which may imply a role for PE/PPE proteins in

M.tb host-pathogen interactions.

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PMID: 40606173

**95. Front Microbiol. 2025 Jun 18;16:1586476. doi: 10.3389/fmicb.2025.1586476.**

**eCollection 2025.**

Feature selection and aggregation for antibiotic resistance GWAS in

Mycobacterium tuberculosis: a comparative study.

Reshetnikov K(1), Bykova D(1)(2), Kuleshov K(1)(3), Chukreev K(1), Guguchkin

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HSE University, Moscow, Russia.

**INTRODUCTION:** Drug resistance (DR) of pathogens remains a global healthcare

concern. In contrast to other bacteria, acquiring mutations in the core genome

is the main mechanism of drug resistance for Mycobacterium tuberculosis (MTB).

For some antibiotics, the resistance of a particular isolate can be reliably

predicted by identifying specific mutations, while for other antibiotics the

knowledge of resistance mechanisms is limited. Statistical machine learning (ML)

methods are used to infer new genes implicated in drug resistance leveraging

large collections of isolates with known whole-genome sequences and phenotypic

states for different drugs. However, high correlations between the phenotypic

states for commonly used drugs complicate the inference of true associations of

mutations with drug phenotypes by ML approaches.

**METHODS:** Recently, several new methods have been developed to select a small

subset of reliable predictors of the dependent variable, which may help reduce

the number of spurious associations identified. In this study, we evaluated

several such methods, namely, logistic regression with different regularization

penalty functions, a recently introduced algorithm for solving the best-subset

selection problem (ABESS) and "Hungry, Hungry SNPos" (HHS) a heuristic algorithm

specifically developed to identify resistance-associated genetic variants in the

presence of resistance co-occurrence. We assessed their ability to select known

causal mutations for resistance to a specific drug while avoiding the selection

of mutations in genes associated with resistance to other drugs, thus we

compared selected ML models for their applicability for MTB genome wide

association studies.

**RESULTS AND DISCUSSION:** In our analysis, ABESS significantly outperformed the

other methods, selecting more relevant sets of mutations. Additionally, we

demonstrated that aggregating rare mutations within protein-coding genes into

markers indicative of changes in PFAM domains improved prediction quality, and

these markers were predominantly selected by ABESS, suggesting their high

informativeness. However, ABESS yielded lower prediction accuracy compared to

logistic regression methods with regularization.

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Fedonin.

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PMID: 40606161

**96. Cureus. 2025 Jun 2;17(6):e85216. doi: 10.7759/cureus.85216. eCollection 2025**

**Jun.**

Extrapulmonary Tuberculosis Mimicking an Iliac Bone Lytic Lesion: A Case Report.

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Lytic bone lesions pose significant diagnostic challenges due to their varied

causes, ranging from malignancies to infections and benign conditions.

Tuberculous osteomyelitis, though rare in non-endemic regions, remains an

important consideration, particularly in patients from high-burden areas. A

35-year-old Sudanese male with a family history of tuberculosis (TB) presented

with chronic left iliac pain that did not respond to nonsteroidal

anti-inflammatory drugs (NSAIDs). Imaging revealed an expansile lytic lesion

with cortical breaching, initially raising suspicion for malignancy. However, a

biopsy showed necrotizing granulomatous osteomyelitis, though cultures -

including those for Mycobacterium tuberculosis - were negative. Despite the lack

of microbiological confirmation, the patient showed clinical and radiological

improvement after starting empirical anti-TB therapy. This case highlights the

need to consider tuberculous osteomyelitis in the differential diagnosis of

lytic bone lesions, even in the absence of positive cultures, especially in

individuals from endemic regions. Histopathological evidence of granulomas and a

positive response to anti-TB therapy can support the diagnosis when

microbiological tests are inconclusive. Greater awareness of this possibility is

essential to prevent delays in treatment and unnecessary invasive procedures.

Copyright © 2025, Alobud et al.

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**97. Cureus. 2025 Jun 2;17(6):e85235. doi: 10.7759/cureus.85235. eCollection 2025**

**Jun.**

Tuberculous Spondylodiscitis: A Report of Two Cases and Literature Review.

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Tuberculosis ranks as one of the most deadly infectious diseases globally. While

it primarily attacks the lungs, it can also develop in other parts of the body.

It can involve the vertebral column, a condition known as Pott's disease. How

often it occurs, what symptoms appear, and how severe it becomes all depend on

which spinal segments are involved and how much bone has been damaged. Because

the signs of Pott's disease are varied and often vague, even modern healthcare

systems can struggle to diagnose it promptly. This delay is the main reason why

many patients go on to suffer neurological impairments, spinal instability, and

generally poor outcomes, often without ever regaining full neurological

function. In this report, we describe two cases of tuberculous spondylodiscitis,

highlighting their clinical presentations and imaging results, and we review the

literature to outline the most effective strategies for diagnosis and treatment.

Copyright © 2025, Kehayov et al.

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**98. Cureus. 2025 Jun 2;17(6):e85228. doi: 10.7759/cureus.85228. eCollection 2025**

**Jun.**

Chronic Eosinophilic Pneumonia With Overlapping Emphysema and Fibrosis: An

Atypical Presentation of Recurrent Pulmonary Tuberculosis.

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This case report describes an atypical presentation of recurrent pulmonary

tuberculosis in a patient with chronic respiratory symptoms and eosinophilia,

initially misdiagnosed as chronic eosinophilic pneumonia. Despite suggestive

clinical and radiological features, a final diagnosis was only reached after

prolonged microbiological culture. The case underscores the diagnostic

complexity of interstitial lung diseases and emphasizes the importance of

maintaining a broad differential, particularly in tuberculosis-endemic regions.

Copyright © 2025, Cardona et al.

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PMID: 40605869

**99. Npj imaging.. 2025 May 28;3(1):22. doi: 10.1038/s44303-025-00082-2.**

PET imaging of mycobacterial infection: transforming the pipeline for

tuberculosis drug development.

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Improved PET/CT radiopharmaceuticals can better visualize and monitor

tuberculosis and enable real-time pharmacological drug profiling in vivo. PET/CT

imaging can therefore be used to study in animal models the changes in tissue

pathology in tuberculosis infection, such as mycobacterial latency, tuberculoma

formation, lung cavitation or calcification, and extrapulmonary disease. This

Perspective aims to critically evaluate the current and future contribution and

role of PET imaging in anti-tuberculosis drug development.

© 2025. The Author(s).

DOI: 10.1038/s44303-025-00082-2

PMID: 40604239

**100. Redox Biol. 2025 Jun 25;85:103741. doi: 10.1016/j.redox.2025.103741. Online**

**ahead of print.**

The inhibition of TXNRD1 by methylglyoxal impairs the intracellular control of

Mycobacterium tuberculosis.

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Type 2 diabetes (DM) is a risk factor for development of tuberculosis (TB).

Methylglyoxal (MGO), a reactive carbonyl increased during DM targets diverse

macromolecules. Here we discovered that MGO converted the mammalian

selenoprotein thioredoxin reductase 1 (TXNRD1) to a NADPH oxidase, activating

the NRF2 transcription factor in bone marrow macrophages (BMM). NRF2 signaling

hampered the production of immune molecules by BMM, thus allowing intracellular

growth of M. tuberculosis (Mtb). The overexpression of NRF2 was sufficient to

increase the Mtb growth. Several inhibitors of TXNRD1 mimicked the effects of

MGO on Mtb growth in BMM. MGO and the TXNRD1 inhibitor auranofin also increased

the susceptibility of mice to Mtb infection. Finally, IFN-γ abrogated the

MGO-triggered suppression of the protective responses to Mtb in BMM, by

epigenetic regulation of immune genes, without impairing NRF2 activation. Thus,

metabolic alterations in DM may have a causative role in TB-DM comorbidity, by

activating NRF2 responses that impair immune protective responses.

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PMID: 40602278

**101. Dan Med J. 2025 Jun 12;72(7):A12240847. doi: 10.61409/A12240847.**

Precision of tuberculosis diagnosis codes in the Central Denmark Region.

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**INTRODUCTION:** Correct use of tuberculosis (TB) diagnosis codes is essential for

patient care, surveillance and resource allocation. We aimed to assess the

positive predictive value (PPV) of TB diagnosis codes.

**METHODS:** In this retrospective cohort study, we identified patients with

International Classification of Diseases, tenth version (ICD-10) TB diagnosis

codes from 1 July 2020 to 30 June 2023, at two TB centres in the Central Denmark

Region. Confirmed TB was defined as microbiologically confirmed TB, prescription

of ≥ 3 first- or second-line TB drugs, or TB notification. All patients who did

not meet these criteria and those who received fewer than three TB drugs or

lacked TB notification underwent manual hospital record review to verify or

exclude the TB diagnosis. PPVs were calculated as the proportion of confirmed TB

diagnoses among all patients with a TB diagnosis code.

**RESULTS:** In total, 185/230 patients were confirmed to have TB, yielding a PPV of

80% (95% CI: 75; 85). The PPVs for TB microbiology, TB prescriptions and TB

notification exceeded 95% individually. Excluding TB lupus codes increased the

PPV to 89% (95% CI: 84; 93). Patients with more than one different type of TB

diagnosis code had a PPV of 100% (95% CI: 93; 100). Additionally, PPVs were high

when TB diagnosis codes appeared on multiple occasions, increasing with the

number of occurrences (≥ 2: 85%, ≥ 3: 89%, ≥ 4: 93%).

**CONCLUSION:** TB ICD-10 diagnosis codes demonstrate a moderately high PPV in

Denmark, particularly when excluding TB lupus codes, highlighting the importance

and complexities of diagnostic coding.

FUNDING: None.

TRIAL REGISTRATION: Not relevant.

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PMID: 40600676 [Indexed for MEDLINE]

**102. Front Microbiol. 2025 Jun 17;16:1537826. doi: 10.3389/fmicb.2025.1537826.**

**eCollection 2025.**

Benchmarking pangenome dynamics and horizontal gene transfer in Mycobacterium

marinum evolution.

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(#)Contributed equally

Horizontal gene transfer (HGT) is a key driver of microbial evolution, promoting

genetic diversity and contributing to the emergence of antibiotic resistance.

This study explores the pangenome dynamics and HGT in Mycobacterium marinum (M.

marinum), a close relative of Mycobacterium tuberculosis. Multiple pangenome

datasets were analyzed to quantify gene gain, loss, and pangenome openness,

utilizing Panstripe and a Generalized Linear Model (GLM) framework to assess

gene presence/absence across strains. Additionally, a comparative benchmarking

analysis of gene ontology (GO) annotations were conducted using eggNOG and

InterProScan to evaluate their functional annotation accuracy. Our findings

demonstrated significant differences in gene gain and loss rates, suggesting

variations in annotation accuracy and the presence of mobile genetic elements

(MGE). Single nucleotide polymorphisms (SNPs) were also identified, highlighting

the genetic variability that may impact strain-specific traits such as

pathogenicity and antibiotic resistance. Pangenome of M. marinum was

characterized as highly open, with substantial variability in gene content,

reflecting ongoing genetic exchange and adaptability. Functional annotation

benchmarking demonstrated that eggNOG and InterProScan provided complementary

insights, with each tool excelling in distinct strengths of gene function

identification. Overall, these findings highlight the complex interplay between

HGT, pangenome evolution, and antibiotic resistance in M. marinum, and the

analytical framework presented here provides a robust approach for future

studies aiming to inform therapeutic interventions and vaccine development.

Copyright © 2025 Shahed, Islam, Sangsawad, Jung, Permpoonpattana and Linh.

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**10.1016/j.jctube.2025.100542. eCollection 2025 Aug.**

Effect of home-based pulmonary rehabilitation on ventilation dynamics and small

airway dysfunction in people with post-tuberculosis lung disease.

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**BACKGROUND:** As the world moves toward eliminating tuberculosis (TB), there is a

large population of TB survivors who still face a significant burden of TB

complications. However, basic pulmonary rehabilitation program (PRP) packages

for this population are currently lacking. This study aimed to evaluate the

effect of home-based PRP (HBPRP) on lung mechanics, exercise capacity, and

quality of life (QoL) in people with PTLD (pwPTLD).

**METHODS:** This is a quasi-experimental study in pwPTLD who underwent HBPRP for

3 months. Before and after HBPRP, the following assessments were performed: QoL

using the St George's Respiratory Questionnaire (SGRQ), general fatigue using

the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F), handgrip

strength (HGS), pulmonary function, and functional exercise capacity using the

Glittre-ADL test (TGlittre) coupled with measurement of dynamic ventilation.

**RESULTS:** When comparing pre- and post-HBPRP values, there was a significant

increase in TGlittre time [208 (194-249) vs. 184 (153-211) seconds, P = 0.004]

and breathing reserve [56 (34-71) vs. 58 (39-73) %, P = 0.032], and a reduction

in end-of-test inspiratory capacity [1.4 (0.9-2.3) vs. 1.6 (1.1-2.6) L,

P = 0.030]. Although no increase in spirometric parameters was observed, there

was an improvement in small airway dysfunction (SAD) as measured by respiratory

oscillometry. Improvements were observed in the Activity and Impacts domains of

the SGRQ. However, no significant changes were noted in FACIT-F or HGS after

HBPRP.

**CONCLUSIONS:** In pwPTLD, HBPRP improves exercise tolerance, QoL, and SAD, with no

effect on general fatigue and HGS. Therefore, TB programs should ensure the

availability of PRP for pwPTLD, including HBPRP.

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Lymphoproliferative Disorders Mimicked by Tuberculosis: A Retrospective Study on

Lateral Flow Urine Lipoarabinomannan (LF-ULAM) Limitations.

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Introduction The human immunodeficiency virus (HIV) remains South Africa's (SA)

largest epidemic. Furthermore, tuberculosis (TB) continues to be the leading

cause of death in SA. People living with HIV/AIDS (PLHA) are at increased risk

of both TB and lymphoproliferative disorders (LPD). PLHA commonly manifest

lymphadenopathy as part of their disease spectrum, with extra-pulmonary TB being

the most common cause. Local guidelines recommend lateral flow urine

lipoarabinomannan (LF-ULAM) assay testing for all PLHA admitted to the hospital.

The LF-ULAM assay is therefore widely used in SA. The LF-ULAM assay does not

provide definitive confirmation of the cause of lymphadenopathy. In

resource-limited settings, TB can impetuously be attributed as the sole cause of

lymphadenopathy in many PLHA with positive LF-ULAM assays. Misdiagnosis of LPD

as TB can lead to catastrophic patient outcomes. Therefore, initial correct

diagnosis is of utmost importance. Aims and objectives The aims and objectives

of this study are to identify the etiology of lymphadenopathy in PLHA with

positive LF-ULAM assays and to highlight the need for a high index of suspicion

of LPD in PLHA with lymphadenopathy. Materials and methods A retrospective

census study was carried out at a tertiary hospital in a rural province of SA. A

total of 13 PLHA with lymphadenopathy, diagnosed with disseminated TB by LF-ULAM

assay, were identified for this study. Eligible participants were identified

using medical records from the medical wards. All PLHA included had generalized

lymphadenopathy diagnosed by clinical palpation. Histopathologists were

unblinded to LF-ULAM results. The results of TB investigations, excisional lymph

node biopsies, and trephine biopsies from these patients were analyzed to

confirm the etiology of their lymphadenopathy. Results A total of 13 PLHA were

included in this study. All patients were initiated on anti-tuberculous

treatment (ATT) following LF-ULAM assay positivity. The majority of cases (n =

9/13; 69%) in this small cohort had histological confirmation of an LPD. More

than half of the cases (n = 7/13; 53%) were confirmed to have mycobacterial

disease by means of either histology, culture, or TB nucleic acid amplification

test (NAAT). Conclusion Histological confirmation of the etiology of

lymphadenopathy is crucial in PLHA to differentiate between LPD and TB. Empiric

TB treatment without appropriate confirmation of TB can lead to worse patient

outcomes and significantly delay oncological care for PLHA. We recommend

expanding biopsy access in resource-limited settings to prevent diagnostic

delays and improve patient outcomes.

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PMID: 40599503

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**10.2147/COPD.S523732. eCollection 2025.**

Incidence and Risk Factors of Tuberculosis-Associated Chronic Obstructive

Pulmonary Disease.

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**PURPOSE:** Chronic obstructive pulmonary disease (COPD) is influenced by multiple

factors. Varying prevalences of tuberculosis-associated COPD exist. However,

studies on its incidence or risk factors are limited. We evaluated the incidence

of tuberculosis-associated COPD and compare the characteristics of patients with

and without COPD.

**PATIENTS AND METHODS:** This multicenter, retrospective cohort study included 351

patients treated with anti-tuberculosis drugs for more than 6 months in four

hospitals in Korea, followed for 11 years (132 months). The follow-up duration

was divided into quartiles (Q1-Q4) to evaluate the change in the incidence of

COPD over time. Clinical data and radiological findings were collected, and the

incidence rate ratios were compared using Poisson regression and multivariable

logistic regression analysis to identify risk factors.

**RESULTS:** Overall, 71 participants developed tuberculosis-associated COPD, with

an overall crude incidence of 20.56/1000 person-years. Patients with

tuberculosis-associated COPD were older, more likely to be smokers, and had

lower forced expiratory volume in 1 s (FEV1) (L) and lower FEV1/forced vital

capacity. The incidence over 132 months was significantly lower than those

during follow-up, with an incidence rate ratio of 0.49 (p=0.027). Multivariate

analysis revealed that a tuberculosis diagnosis at an older age (adjusted odds

ratio [aOR] 1.04; 95% confidence interval [CI]: 1.01-1.07), lower baseline FEV1

<80% (aOR 3.98; 95% CI: 1.92-8.24), smoking (aOR 3.23; 95% CI: 1.14-9.17), and

multilobar involvement of tuberculosis (aOR 2.04; 95% CI: 1.08-3.85) were risk

factors for tuberculosis-associated COPD. The incidence in the Q4 (>132 months,

approximately 11years) was significantly lower than that in the Q1 (18-71

months), with incidence rate ratio of 0.49 (p= 0.027).

**CONCLUSION:** Older age at tuberculosis diagnosis, lower baseline FEV1 <80%,

smoking history, and multilobar involvement were identified as risk factors for

tuberculosis-associated COPD. The incidence of tuberculosis-associated COPD

decreased 11 years after tuberculosis treatment.

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**106. Front Public Health. 2025 Jun 16;13:1600104. doi: 10.3389/fpubh.2025.1600104.**

**eCollection 2025.**

Influence of HIV co-infection on clinical presentation and disease outcome in

hospitalized adults with tuberculous meningitis in Brazil: a nationwide

observational study.

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Araujo-Pereira M(2)(3)(4), Andrade BB(1)(2)(3)(4).

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Universidade de São Paulo, São Paulo, Brazil.

**INTRODUCTION:** Tuberculous meningitis (TBM) is a severe form of central nervous

system infection caused by Mycobacterium tuberculosis (Mtb) that is often

associated with significant morbidity and mortality, particularly in people

living with HIV (PLWH). This study investigated differences in clinical and

laboratory profiles of TBM cases in Brazil associated with HIV status, and

identified factors associated with in-hospital mortality.

**METHODS:** We conducted a retrospective analysis of 1,819 hospitalized adult TBM

patients reported in the Brazilian Notifiable Diseases Information System

(SINAN) meningitis database from 2007 to 2021. Confirmed cases in hospitalized

individuals aged >18 years with known HIV status were included; pregnant

patients were excluded. Clinical and laboratory features were compared by HIV

status and clinical outcomes. Classification and regression tree analysis was

used to identify outcome-based cut-off values for selected continuous variables.

Associations with in-hospital mortality were assessed using backward stepwise

binomial logistic regressions.

**RESULTS:** The majority (57%) of TBM cases comprised of PLWH, who exhibited lower

frequencies of vomiting, nuchal rigidity, signs of meningeal inflammation, and

coma, along with lower leukocyte counts in cerebrospinal fluid (CSF) compared to

HIV-negative patients. PLWH also displayed lower mortality rates (17.3% vs.

23.2%, p = 0.002). Features independently associated with mortality included

seizures (aOR: 2.15, 95%CI: 1.39-3.33, p < 0.001), nuchal rigidity (aOR: 1.57,

95%CI: 1.1-2.23, p = 0.014), age > 64 years old (aOR: 2.11, 95%CI: 1.08-4.13,

p = 0.03), CSF protein concentration ≥441 mg/dL (aOR: 2:08, 95%CI: 1.39-3.09,

p < 0.001) and CSF glucose concentration ≥ 22 mg/dL (aOR: 0.54, 95%CI:

0.38-0.76, p < 0.001), but not HIV (OR: 0.73, [95%IC: 0.52-1.01], p = 0.06).

**CONCLUSION:** Our findings suggest that despite greater prevalence in PLWH, these

patients present fewer clinical signs and symptoms and lower mortality rates.

Additionally, HIV was not an independent predictor of mortality in this study

population.

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**107. Stud Health Technol Inform. 2025 Jun 26;328:407-411. doi: 10.3233/SHTI250748.**

Factors Associated with Treatment Success Among Patients with Pulmonary

Tuberculosis: Exploring from NTIP Record.

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This cross-sectional analytical study examined treatment success rates and

associated factors among pulmonary tuberculosis (TB) patients. Data from the

National Tuberculosis Information Program (NTIP) were analyzed for 305 patients

treated at Pak Phanang Hospital, Nakhon Si Thammarat, between October 1, 2018,

and September 30, 2023. Binary logistic regression identified key factors

influencing treatment success. The overall success rate was 80.98% (247

patients), while 19.02% (58 patients) experienced unsuccessful treatment.

Significant factors associated with success included body mass index (BMI)

(adjusted OR 2.72, 95% CI = 1.12-3.93, p = 0.035), adherence to medical

appointments (adjusted OR 26.85, 95% CI = 16.24-35.56, p = 0.001), history of

HIV screening, hospitalization for TB, and CD4 testing. To enhance TB treatment

outcomes, hospitals should improve patient management, ensure continuous

monitoring, and promote adherence and education. Strengthening these measures

may reduce treatment failure and improve public health outcomes.

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PMID: 40588955 [Indexed for MEDLINE]

**108. Stud Health Technol Inform. 2025 Jun 26;328:21-25. doi: 10.3233/SHTI250665.**

Bridging Health Gaps Behind Bars: The Role of Prison Health Volunteers in TB

Surveillance Under Thailand's Royal 'Pan Suk' Project".

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Tuberculosis (TB) remains a significant public health concern in correctional

facilities due to overcrowding, poor ventilation, and inmate mobility. This

cross-sectional study assessed the roles of 298 Prison Health Volunteers (PHVs)

in TB surveillance at three Central Correctional Institutions for Young

Offenders in Thailand. Although most PHVs demonstrated low knowledge and

moderate attitudes, they performed well in key health education and case

detection tasks. Significant associations were found between higher knowledge

and favorable attitudes with better TB control practices (p = 0.027 and p =

0.005). These findings suggest that experiential and contextual factors may

compensate for knowledge gaps. Despite ongoing challenges-including limited

training and paper-based systems-PHVs remain pivotal in TB control.

Strengthening their capacity through digital tools and structured support is

essential. The Royal "Pan Suk" Project represents a promising, community-led

model aligned with His Majesty King Maha Vajiralongkorn's vision of promoting

prison health equity and advancing TB elimination.

DOI: 10.3233/SHTI250665

PMID: 40588873 [Indexed for MEDLINE]

**109. Lancet Infect Dis. 2025 Jun 27:S1473-3099(25)00305-6. doi:**

**10.1016/S1473-3099(25)00305-6. Online ahead of print.**

The participation of people deprived of liberty in tuberculosis vaccine trials:

should they be protected from research, or through research?

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People deprived of liberty are among the populations experiencing the highest

rates of tuberculosis. Prisons typically create ideal conditions for

Mycobacterium tuberculosis transmission, including overcrowding and prolonged

exposure in poorly ventilated environments, and often have populations at high

risk of developing disease. The development of a novel, effective tuberculosis

vaccine to prevent adult pulmonary tuberculosis is considered a crucial

objective for improving tuberculosis control and, ultimately, elimination.

Currently, there are over a dozen vaccines in clinical development, although

none of the ongoing or planned trials include people deprived of liberty.

Several factors contribute to this exclusion, including historical ethical

violations in medical research involving this population, as well as concerns

regarding coercion and exploitation. In this Personal View, we contend that

these concerns need to be weighed against people deprived of liberty's right to

participate in scientific progress and the importance of respecting their

autonomy to be part of medical research. We address the key risks associated

with conducting tuberculosis vaccine trials involving people deprived of

liberty, propose mitigation strategies, and discuss important scientific

considerations related to efficacy trials in this context.

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data mining, AI training, and similar technologies.

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**110. J Vis Exp. 2025 Jun 13;(220). doi: 10.3791/68037.**

Mycobacterial DNA Extraction using Bead Beating in Custom Buffer Followed by NGS

Workflow.

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Tuberculosis is a deadly disease, and the emergence of antibiotic drug

resistance in the causative agent bacterium, Mycobacterium tuberculosis, worsens

treatment outcomes. Precise and rapid drug resistance identification through

sequencing technologies is needed to improve tuberculosis patient outcomes

through tailored therapeutic regimens. The DNA extraction method is critical for

downstream molecular assays and is complicated by the tough cell wall of

Mycobacterium, the low bacillary load of many clinical samples, and the

complexity of the sputum matrix. There are numerous M. tuberculosis DNA

extraction methods reported, but there is currently no gold standard.

Furthermore, few of these methods are shown to work consistently, and many are

not suitable for low-resource and high-burden tuberculosis settings.

Consequently, laboratories frequently introduce their own procedure

modifications, resulting in significant method variability. Here, we present a

cost-effective, rapid, and standardized protocol for Mycobacterial DNA

extraction from both clinical sputum and culture that produces DNA suitable for

qPCR, and which should be considered for use in clinical diagnostics

laboratories.

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**111. Natl Med J India. 2025 Mar-Apr;38(2):69-77. doi: 10.25259/NMJI\_1061\_2022.**

The effect of telephone follow-up and training on treatment adherence in

tuberculosis patients and contacts: A randomized controlled study.

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**Background** We evaluated the effect of 6 months of regular training,

tele-monitoring and daily text message to remind medication intake on treatment

adherence in tuberculosis (TB) patients and their contacts. **Methods** This

randomized, controlled study with pre- test and post-test design was conducted

with the following groups: TB Intervention, TB control, contacted intervention

and contacted control group, a total of 66 patients and 87 contacted people. The

data of study were collected with 'Patient and Contact Question Form',

Tuberculosis Adherence Determination Questionnaire (TADQ) and 'Morisky 8-Item

Adherence to Drug Questionnaire' (MMAS-8). **Results** TADQ scores of the TB

intervention group in the beginning, 1st, 3rd and 6th months were 80.4 (7.9),

117.8 (6.3), 137.7 (7.5), 143.2 (4.5), respectively, and TADQ scores of the TB

control group in the beginning, 1st, 3rd and 6th months were 88.1 (7.1), 84.5

(9.8), 75.9 (7.9), 65.2 (9.2), respectively. MMAS-8 scores of the contacted

intervention group in the beginning, 1st, 3rd and 6th months were 3.6 (1.3), 5.5

(0.7), 7.2 (0.8) and 7.7 (0.7), and those of the control group were 5.7 (1.4),

4.3 (1.4), 1.8 (1.5) and 0.7 (1.4), respectively. **Conclusion** As a result of 6

months of regular training, tele-monitoring and daily text message, adherence of

the patients to TB treatment increased, and the adherence of the contacted

people to the medication increased. Nurses should take an active role in the

management of TB, determine the patients who do not use drugs correctly in the

early period and apply the required interventions as soon as possible to improve

treatment adherence of TB patients and contacts.

DOI: 10.25259/NMJI\_1061\_2022

PMID: 40587286 [Indexed for MEDLINE]

**112. Natl Med J India. 2025 Mar-Apr;38(2):92-93. doi: 10.25259/NMJI\_1479\_2024.**

Rifampicin-associated intravascular haemolysis causing acute kidney injury.

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Drug-induced acute kidney injury (AKI) is a rare adverse effect of rifampicin,

and is mostly related to acute tubular necrosis and acute interstitial

nephritis. We report a sputum- positive, isoniazid mono-resistant, pulmonary

tuberculosis patient who had a history of anti-tuberculous therapy (ATT) intake

30 years ago. The patient developed AKI requiring dialysis when he restarted the

ATT recently. A renal biopsy was consistent with pigment-cast nephropathy

secondary to rifampicin-induced intravascular haemolysis. Rifampicin was

stopped, and the patient underwent a total of four dialysis sessions and

subsequently recovered.

DOI: 10.25259/NMJI\_1479\_2024

PMID: 40587272 [Indexed for MEDLINE]

**113. Monaldi Arch Chest Dis. 2025 Jun 26. doi: 10.4081/monaldi.2025.3474. Online**

**ahead of print.**

Pharmacist-led education intervention to improve pulmonary tuberculosis

treatment adherence through the Health Belief Model in Malaysia: a study

protocol for a randomized controlled trial.

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Pulmonary tuberculosis (TB) remains a significant global health concern,

particularly in low- and middle-income countries, where treatment adherence is

critical to improving patient outcomes and mitigating drug resistance. In

Malaysia, challenges in adherence to TB treatment regimens continue to hinder

disease control efforts. This study protocol outlines a pharmacist-led

educational intervention to improve treatment adherence among pulmonary TB

patients. This randomized controlled trial will enroll 206 pulmonary TB patients

from public healthcare facilities in Penang, Malaysia, divided equally into

intervention and control groups. The intervention group will receive tailored

educational counseling sessions delivered by pharmacists at baseline and during

months 2, 4, and 6, using materials developed by the World Health Organization

and the Centers for Disease Control TB treatment guidelines. The control group

will receive standard care. The pharmacist-led educational intervention will be

structured around the Health Belief Model framework to systematically address

psychological determinants of adherence. Adherence will be measured using the

Medication Adherence Report Scale-5. Data will be collected at baseline and

subsequent intervals to assess changes over time. The primary outcome will be to

improve the treatment adherence of the pulmonary TB patients. The secondary

outcomes will measure knowledge of the TB disease and health-related quality of

life. This protocol describes a novel, theory-driven approach to addressing

adherence barriers in TB treatment through pharmacist-led education. The study

aims to contribute to the global effort to control TB and improve patient

outcomes by providing evidence of the intervention's impact.

DOI: 10.4081/monaldi.2025.3474

PMID: 40586682

**114. Monaldi Arch Chest Dis. 2025 Jun 26. doi: 10.4081/monaldi.2025.3538. Online**

**ahead of print.**

Latent tuberculosis infection in patients with psoriasis using biologic

therapies.

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Some studies have demonstrated a high prevalence of latent tuberculosis

infection (LTBI) in patients with psoriasis and a higher risk of active

tuberculosis (TB) in patients with severe psoriasis. The objective of this study

is to identify the prevalence of LTBI before starting treatment with different

biologicals and to identify the prevalence of LTBI and active TB while using

these medications. We conducted a cross-sectional study with retrospective data

collection in the outpatient department of dermatology at a general, tertiary

care, university-affiliated hospital. The electronic medical records of all

adult patients (≥18 years old) with psoriasis undergoing treatment with

biologics were reviewed, and information about psoriasis, the type of biological

therapy used, and the tuberculin skin test (TST) results were collected. The

patients included had an indication for the TST test according to the Ministry

of Health. In total, 126 patients were included in the study. The median

duration of disease was 20 years. A total of 31 patients (24.6%) had LTBI

diagnosed at screening before the use of biologicals, and an additional 17

(17.9%) patients had a diagnosis of LTBI during biological therapy. There were

no cases of active TB during treatment with biologicals. There was no difference

in the prevalence of LTBI during treatment with tumor necrosis factor

inhibitors, interleukin (IL)-17 inhibitors, IL-23 inhibitors, and IL-12/23

inhibitors (p=0.228). In conclusion, we found that 24.6% of patients with

psoriasis in an endemic TB region had LTBI. Additionally, 16.8% had a diagnosis

of LTBI during biological therapy. Our data corroborate the recommendation that

patients who live in high TB incidence settings should be tested annually for

LTBI.

DOI: 10.4081/monaldi.2025.3538

PMID: 40586673

**115. Cureus. 2025 May 30;17(5):e85085. doi: 10.7759/cureus.85085. eCollection 2025 May.**

Smear- and Polymerase Chain Reaction (PCR)-Negative Tuberculosis: A Case Series

Highlighting Diagnostic Limitations and the Role of Escalation.

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Tuberculosis (TB) remains a major global health concern, and its diagnosis can

be particularly challenging when microbiological tests yield negative results.

We present two diagnostically complex cases, one pulmonary and one pleural, in

which tuberculosis was confirmed only after extended clinical evaluation and

diagnostic escalation, resulting in delays of approximately eight weeks and two

weeks, respectively. The first patient, a 31-year-old asymptomatic man with

recent TB exposure, underwent bronchoalveolar lavage (BAL), with smear

microscopy and polymerase chain reaction (PCR) both negative; cultures remained

negative after eight weeks. He was later readmitted with hemoptysis, and repeat

BAL ultimately yielded a positive culture for Mycobacterium tuberculosis,

despite persistently negative PCR. The second patient, a 22-year-old woman

presenting with pleuritic chest pain and a large unilateral pleural effusion,

had markedly elevated inflammatory markers and exudative fluid on thoracentesis.

Initial smear, PCR, and bronchoscopy were inconclusive. A definitive diagnosis

of pleural TB was established only after thoracoscopic biopsy revealed

necrotizing granulomatous inflammation. In both cases, early identification of

bacterial co-infections contributed to diagnostic delay. These cases highlight

the limitations of conventional diagnostics in both pulmonary and pleural TB,

particularly in smear- and polymerase chain reaction (PCR)-negative

presentations. They underscore the importance of clinical vigilance and timely

escalation to tissue-based diagnostics, including repeat bronchoscopy and

thoracoscopy, when initial evaluations are non-diagnostic. A structured,

multimodal approach is essential to minimize diagnostic delays and ensure early

initiation of appropriate therapy.

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**116. Patient Prefer Adherence. 2025 Jun 23;19:1807-1823. doi: 10.2147/PPA.S533210.**

**eCollection 2025.**

Effectiveness of Digital Health Interventions to Enhance Continuity of Care in

Patients with Pulmonary Tuberculosis: A Systematic Review of Randomized

Controlled Trials.

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**BACKGROUND:** Pulmonary tuberculosis (TB) remains a global health concern with

high morbidity and mortality rates. Despite being curable with proper treatment,

challenges in ensuring continuity of care persist, particularly in

resource-limited settings. Digital health interventions (DHI) offer a potential

solution to improve treatment adherence and continuity of care among TB

patients.

**PURPOSE:** This study aimed to systematically review how DHIs contribute to

improved continuity of care, particularly in terms of medication adherence,

clinical outcomes, and patient satisfaction.

**METHODS:** A systematic review was conducted using PRISMA guidelines. Relevant

studies were identified from five significant databases, including PubMed,

Scopus, Taylor and Francis, EBSCO-host, and ScienceDirect, up to November 2024

and one search engine was Google Scholar. The keywords used were "pulmonary

tuberculosis OR tbc OR tb AND mobile health applications OR mhealth OR mobile

apps OR telehealth AND continuity of care OR patient compliance OR patient

adherence OR adherence behaviour. Inclusion criteria focused on RCTs evaluating

DHIs for adult TB patients. Data were extracted and analyzed thematically to

assess intervention effectiveness on medication adherence and clinical outcomes.

**RESULTS:** A total of 17.380 patients from 21 studies TB patients were included.

Interventions were classified into two categories: reminder-based (eg, SMS,

phone calls, electronic medicine boxes with audio/visual alerts) and remote

monitoring-based (eg, MERM, mobile applications, digital sensors, and VDOT).

Compared to standard care, DHIs significantly improved medication adherence,

treatment success rates, and patient satisfaction. Several studies also reported

reduced time and cost burdens for patients.

**CONCLUSION:** DHIs improve continuity of care among TB patients by increasing

medication adherence and clinical outcomes. However, the effectiveness varies

across different intervention types and settings, emphasizing the need for

tailored strategies and integration into existing health systems.

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DOI: 10.2147/PPA.S533210

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PMID: 40585575

**117. Oxf Med Case Reports. 2025 Jun 27;2025(6):omaf058. doi: 10.1093/omcr/omaf058.**

**eCollection 2025 Jun.**

Erythema Induratum as a rare manifestation of cutaneous tuberculosis in a young

woman: a case report.

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Cutaneous tuberculosis (TB) is a rare form of extrapulmonary TB, often leading

to diagnostic challenges due to its varied clinical presentation. Erythema

induratum of Bazin (EIB), a type of lobular panniculitis, is a recognized

manifestation of cutaneous TB. This report describes a 19-year-old woman who

developed EIB, presenting with recurrent fever, night sweats, weight loss, and

hyperpigmented nodular lesions on both lower extremities. Laboratory tests

showed an elevated erythrocyte sedimentation rate and a positive tuberculin skin

test, while histopathology confirmed lobular panniculitis. Pulmonary TB was

excluded based on negative molecular testing and normal chest imaging. The

patient was diagnosed with cutaneous TB and treated with WHO-recommended

first-line anti-TB therapy, leading to significant clinical improvement. This

case underscores the importance of early recognition and timely treatment of

cutaneous TB to prevent complications and ensure optimal outcomes.

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PMCID: PMC12202318

PMID: 40585462

**118. ADMET DMPK. 2025 Jun 17;13(3):2766. doi: 10.5599/admet.2766. eCollection 2025.**

CRISPR-Cas9-based electrochemical biosensor for the detection of katG gene

mutations in isoniazid-resistant tuberculosis.

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**BACKGROUND AND PURPOSE:** Multidrug-resistant tuberculosis (MDR-TB) remains a

significant challenge in tuberculosis (TB) treatment, driven by simultaneous

mutations in the rpoB and katG genes that confer resistance to rifampicin and

isoniazid. While many molecular diagnostic tools focus on rpoB, the katG gene is

often overlooked despite its critical role in confirming MDR-TB. This study aims

to develop a CRISPR/Cas9-based electrochemical biosensor for the rapid and

selective detection of katG mutation.

**EXPERIMENTAL APPROACH:** A guide RNA (gRNA) specific to the mutation site on katG

gene was designed using the Benchling CRISPR tool, considering on-target and

off-target scores, specificity, and cleavage sites within the Mycobacterium

tuberculosis genome. The selected gRNA achieved the highest on-target score of

61.2 and an off-target score of 49.0 at cut position 2928, with a PAM sequence

of AGG. Its cleavage efficiency was validated experimentally using an

electrochemical biosensing platform incorporating a gold-modified screen-printed

carbon electrode (SPCE/Au). Redox response enhancement by [Fe(CN6)]3-/4-

confirmed the improved performance of the electrode.

**KEY RESULTS:** The biosensor system detects the target DNA through hybridization

with DNA probe-Fc, forming double-stranded DNA (dsDNA) that is recognized and

cleaved by the Cas9/gRNA complex. This cleavage significantly reduces the

ferrocene oxidation signal, indicating the presence of a katG mutation.

Non-mutated target DNA produces a nondetectable ferrocene signal, suggesting

that the Cas9 enzyme may remain bound to the electrode without cleavage. The

CRISPR/Cas9 electrochemical biosensor demonstrated a low detection limit of

7.5530 aM and a detection range of 101 to 106 aM.

**CONCLUSION:** The CRISPR/Cas9-based electrochemical biosensor exhibits high

sensitivity and specificity for the detection katG mutation, offering a

promising platform for rapid MDR-TB diagnostics.

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DOI: 10.5599/admet.2766

PMCID: PMC12205929

PMID: 40585408

**119. Asia Ocean J Nucl Med Biol. 2025;13(2):195-197. doi:**

**10.22038/aojnmb.2025.80912.1580.**

The significance of cardiac inflammatory protocol of FDG PET-CT in the diagnosis

and response assessment of tuberculous pericarditis: A case report.

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Tuberculous pericarditis (TBP) is a rare but potentially life-threatening

manifestation of tuberculosis, often presenting with nonspecific symptoms and

varied clinical features. The disease is characterised by inflammation of the

pericardium due to mycobacterium tuberculosis, leading to complications such as

effusion, tamponade, and, in chronic cases, constrictive pericarditis. TBP is

associated with high mortality, particularly if not promptly diagnosed and

treated. 18F-fluorodeoxyglucose positron emission tomography-computed tomography

(18FDG PET-CT) has proven invaluable in diagnosing and managing TBP. This

imaging modality allows for precise inflammatory activity localisation and

differentiates TBP from other causes of pericardial disease. Additionally, the

cardiac inflammation protocol of 18FDG PET-CT enhances imaging accuracy by

suppressing the normal physiological FDG uptake in the myocardium. In this case

report, we highlight the pivotal role of the cardiac inflammation protocol of

18FDG PET-CT in both the initial diagnosis and subsequent response assessment of

TBP, underscoring its importance in clinical practice.

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PMCID: PMC12205121

PMID: 40585293

**120. medRxiv [Preprint]. 2025 Jun 20:2025.06.20.25329945. doi:**

**10.1101/2025.06.20.25329945.**

Integrated treatment-decision algorithms for childhood TB: modelling diagnostic

performance and costs.

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**BACKGROUND:** To improve childhood tuberculosis (TB) diagnosis, treatment-decision

algorithms (TDAs) with and without chest X-ray (CXR) were developed for children

under age 10. We aimed to model diagnostic performance and costs of implementing

TDAs in primary healthcare (PHC) and district hospital (DH) settings in Uganda.

**METHODS:** We developed decision-tree models following the TDA pathway from

evaluation to treatment-decision. We compared six scenarios with combinations of

diagnostic testing (stool and respiratory Xpert, urine lipoarabinomannan, and/or

CXR) at PHCs and DHs. Outcomes were diagnostic accuracy and cost per correct

treatment-decision for a cohort of 10,000 children with presumptive TB using a

Monte Carlo simulation from a health system perspective. Costs were reported in

2024 International dollars.

**RESULTS:** In all scenarios, TDA's had high sensitivity (80.8-91.9%) but low

specificity (51.2-60.9%). Total diagnostic and treatment costs for the cohort

were I$1,768,958-2,458,790; largely driven by overtreatment of false-positive

cases. Diagnostic costs were mostly offset by reducing overtreatment. The cost

per treatment-decision was lowest using mobile CXR at PHC (I$287.40) and highest

with DH referral (I$445.84).

**CONCLUSION:** The TDAs have high sensitivity and can be implemented at PHCs with

lower costs than DHs. Improving specificity and reducing treatment costs would

enable affordable, large-scale implementation.

DOI: 10.1101/2025.06.20.25329945

PMCID: PMC12204283

PMID: 40585124

**121. medRxiv [Preprint]. 2025 Jun 16:2025.06.13.25329610. doi:**

**10.1101/2025.06.13.25329610.**

Deciphering rifampicin resistance among tuberculosis patients who have trace

results on Xpert MTB/RIF ultra assay.

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**INTRODUCTION:** The Mycobacterium. tuberculosis (MTB) detected trace, rifampicin

(RIF) resistance indeterminate category of the Xpert MTB/RIF Ultra assay results

is usually, non-actionable and requires retesting the samples. We aimed to

decipher RIF resistance among tuberculosis patients who have trace and

indeterminate results.

**METHODS:** Four hundred and three (403) MTB detected trace, RIF resistance

indeterminate results, which were obtained in Mycobacteriology (BSL-3) and

Molecular Diagnostic laboratories, College of Health Sciences, Makerere

University from August 2018 to June 2023, having culture results were identified

from the laboratory database. Isolates of those that turned out culture positive

were retrieved and sub-cultured in liquid media to perform phenotypic first line

Drug Susceptibility tests, first line Line-Probe assays (LPA) and repeat

GeneXpert ultra.

**RESULTS:** A total of 31/403 (7.7%) culture positive isolates were identified from

the database of which 77.42% (24/31) were positive for Mycobacterium

tuberculosis complex (MTBc). Nineteen (19) out of the identified 24 MTBc were

successfully retrieved, cultured and resistance testing performed. Phenotypic

Drug susceptibility testing and repeated GeneXpert did not identify any

resistance. Only one mutation inhA MUT1 related to isoniazid (INH) resistance

was identified using MTBDRplus assay.

**CONCLUSION:** In this study, we did not identify any missed rifampicin resistance

among MTBc culture positive samples that were initially Xpert ultra-trace and

rifampicin resistance indeterminate. More studies with bigger sample sizes

especially in high MDR-TB settings are required.

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PMCID: PMC12204262

PMID: 40585070

**122. Front Epidemiol. 2025 Jun 13;5:1405845. doi: 10.3389/fepid.2025.1405845.**

**eCollection 2025.**

One out of every three adult TB patients suffered from undernutrition in

conflict affected Southern Ethiopia: a multicenter facility-based

cross-sectional study.

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University, Wolaita Sodo, Ethiopia.

**BACKGROUND:** Although tuberculosis mortality has dramatically decreased over the

last decade, tuberculosis remains the world's biggest cause of death. Conflict

affected nations hold vast majority of malnourished people globally, where many

people die each year of tuberculosis. With regard to the global burden of

tuberculosis, Ethiopia ranks third in the African continent and seventh overall.

But in the research arena, the severity of the issue is not as well understood.

Therefore, the current study aimed to assess undernutrition and the determinant

factors among adult TB-patients receiving treatment in public health facilities

in conflict affected zones of Southern.

**METHODS**: A multicenter facility-based cross-sectional study was conducted from

27/08/2023-28/ 09/2023 among 414 randomly selected adult (age ≥18 years)

TB-patients receiving treatment at public health facilities in conflict affected

zones of Southern Ethiopia. An interviewer-administered questionnaire and

anthropometric measurements were used to collect data from study participants

after written informed consent provision. By using SPSS Version 25, bivariate

and multivariable logistic regression models were employed to determine the

factors related to nutritional status.

**RESULTS:** Overall, 33.3% of study participants had undernutrition, with a [95% CI

(28.8%-38.1%)]. Factors such as cigarette smoking [AOR = 2.02, 95% CI; 1.22,

3.34] chat chewing [AOR = 2.50, 95% CI; 1.59, 3.93] regular cheka drinking

[AOR = 1.82; 95% CI, 1.22-2.71] and household food insecurity [AOR = 1.78, 95%

CI; 1.19, 2.66] had significant association with undernutrition.

**CONCLUSIONS:** The results of this study show that undernutrition affects one in

three adult TB patients. Lifestyle factors such as smoking and chewing, and

dietary factors like cheka eating and household food security had significant

association with undernutrition. In order to improve the quality of life for TB

patients, it is imperative that all stakeholders should prioritize addressing

the lifestyle and nutritional aspects that are essential to the effectiveness of

TB control and prevention initiatives.

© 2025 Abraham, Yakob, Dawit, Ashiko, Tekese and Israell.

DOI: 10.3389/fepid.2025.1405845

PMCID: PMC12202411

PMID: 40585062

**123. Taiwan J Ophthalmol. 2025 Jun 10;15(2):203-211. doi: 10.4103/tjo.TJO-D-24-00115. eCollection 2025 Apr-Jun.**

Current concepts in the diagnosis of ocular tuberculosis: A narrative review.

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Ocular tuberculosis (OTB) is one of the extrapulmonary manifestations caused by

Mycobacterium tuberculosis (Mtb). If untreated, it can result in poor visual

prognosis. Prompt diagnosis of OTB is met with challenges. The gold standard for

the diagnosis of OTB is the direct demonstration of the Mtb in ocular tissues or

ocular fluids either by Ziehl-Neelsen Stain, culture or molecular diagnostic

techniques such as polymerase chain reaction. This is onerous owing to the

paucibacillary nature of the disease, small quantity of samples, and low

sensitivity and specificity of molecular diagnostic tests. Thus, one needs to

rely on indirect evidences to make a diagnosis. Hence, most often, the diagnosis

of OTB is presumed based on the geography the patient hails from and indirect

laboratory evidences suggestive of TB. In this narrative review, we review

clinical, laboratory, and radiology markers which aid in the diagnosis of OTB

and outline the current concepts in the diagnosis of OTB.

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DOI: 10.4103/tjo.TJO-D-24-00115

PMCID: PMC12204663

PMID: 40584192

**124. ACS Chem Biol. 2025 Jun 29. doi: 10.1021/acschembio.5c00078. Online ahead of**

**print.**

Enzymatic Pathway for Kupyaphore Degradation in Mycobacterium tuberculosis:

Mechanism of Metal Homeostasis and Turnover.

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Metallophores are essential for metal homeostasis, regulating availability, and

mediating host-pathogen interactions. Kupyaphores are specialized metallophores

produced by Mycobacterium tuberculosis (Mtb) that primarily chelate zinc to

support bacterial survival. Elevated kupyaphore levels early in infection

highlight their importance, while their rapid decline, despite increasing

bacterial loads, indicates tightly regulated mechanisms of production,

consumption, and degradation. However, the processes driving kupyaphore

catabolism and their role in preventing zinc toxicity in Mtb remain unclear.

Here, we show that covalent modification of the isonitrile moiety in kupyaphores

releases zinc, triggering degradation through a sequential three-step enzymatic

pathway encoded by Mtb. Isonitrile hydratase converts isonitrile groups into

formamides, which are subsequently processed into amines by N-substituted

formamide deformylase and ultimately oxidized to β-ketoesters by amine oxidases.

The biological significance of this pathway is underscored by the upregulation

of these genes under metal-depleted and biofilm-forming conditions. Mutant Mtb

strains lacking these genes exhibit impaired growth in metal-limiting

environments and reduced levels of biofilm formation. Catalytic intermediates

detected in Mtb cultures and infected mouse lung tissues confirm the pathway's

in vivo activity. Further, genome mining reveals that similar enzymes are

conserved across organisms producing isonitrile-containing metabolites,

emphasizing the broader importance of this pathway. Understanding these

processes could pave the way for novel therapeutic strategies targeting

kupyaphore catabolism.

DOI: 10.1021/acschembio.5c00078

PMID: 40583177

**125. Travel Med Infect Dis. 2025 Jun 27;66:102872. doi: 10.1016/j.tmaid.2025.102872. Online ahead of print.**

Burden, clinical outcomes, and characteristics of tuberculosis in migrant

populations in the middle East and North African region: A systematic review and

meta-analyses.

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**INTRODUCTION:** Migrants in the Middle East and North Africa (MENA) region face an

increased tuberculosis (TB) risk due to socioeconomic and structural barriers.

This systematic review synthesises evidence on TB burden, clinical outcomes, and

epidemiological characteristics among migrants in MENA.

**METHODS:** We searched six electronic databases and grey literature sources for

studies published between 2000 and September 2024 in any language. Eligible

studies reported primary data on TB prevalence, incidence, treatment outcomes,

and clinical or epidemiological features in migrants. Pooled estimates were

calculated using DerSimonian & Laird's random-effects model where applicable or

narratively synthesised.

**RESULTS:** Of the 779 records identified, we included 57 studies, comprising

95,190 TB cases and 3,532,359 migrants across 12 MENA countries. TB incidence

was consistently higher in migrants than non-migrants (26.7-69.8/100,000 vs.

11.5-16.8/100,000). Migrants had lower TB-related mortality (pooled OR 0.8, 95 %

CI 0.7-0.9; I2 = 2.9 %), however, treatment success rates were consistently

below the WHO-recommended 90 % threshold. Migrant TB patients were younger (mean

age difference: 12.8 years; 95 % CI 8.8-16.0; I2 = 86.5 %) and predominantly

male (sex ratio: 1:5). Drug-resistant TB was more common among migrants, though

this was not always statistically significant (multi-drug-resistant TB: pooled

OR 1.2; 95 % CI 0.9-1.6; I2 = 40.2 %), while extrapulmonary TB was more

prevalent among non-migrants (33.4-83.4 % vs. 16.6-72.9 %).

**CONCLUSION:** Migrants in MENA region experience disproportionate TB burden and

poorer treatment outcomes, underscoring the need for targeted interventions.

Enhanced data, especially from North Africa, is essential to support regional TB

elimination aligned with World Health Organization and Sustainable Development

Goals.

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**126. Clin Infect Dis. 2025 Jun 24:ciaf261. doi: 10.1093/cid/ciaf261. Online ahead of print.**

Prognostic Value of C-Reactive Protein in Adults With Tuberculous Meningitis: A

Prospective Cohort Study.

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Kampala, Uganda.

We enrolled 135 adults with tuberculous meningitis (TBM), including 83% living

with HIV. Participants with baseline C-reactive protein (CRP) ≥40 mg/L had 3

times higher odds of an 8-week modified Rankin scale ≥4 (adjusted odds ratio,

2.78; 95% CI: 1.28-6.04; P = .010). CRP is a viable prognostic biomarker in TBM.

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**127. Folia Microbiol (Praha). 2025 Jun 28. doi: 10.1007/s12223-025-01291-3. Online ahead of print.**

Evaluation of andrographolide from Andrographis paniculata against

drug-resistant and H(37)Rv strains of Mycobacterium tuberculosis.

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Tuberculosis (TB) remains a major global health concern, particularly due to the

emergence of multidrug-resistant (MDR) Mycobacterium tuberculosis strains. While

previous studies have suggested andrographolide as a potential antimycobacterial

agent based on in silico predictions, limited empirical evidence exists on its

direct efficacy against MDR-TB. This study systematically evaluates the

antimycobacterial activity of andrographolide through the microbroth dilution

method against M. tuberculosis H37Rv and three distinct MDR strains. The minimum

inhibitory concentrations (MICs) were determined using Middlebrook 7H9 medium,

with rifampicin and isoniazid as positive controls. Andrographolide completely

inhibited M. tuberculosis H37Rv at an MIC of 125 µg/mL, while MICs for MDR

strains varied (500 µg/mL, 125 µg/mL, and 250 µg/mL for MDR-Isolates 1, 2, and

3, respectively). Unlike previous studies that primarily relied on computational

docking models, our findings provide direct experimental validation of

andrographolide's strain-specific efficacy, demonstrating its potential as a

promising lead compound for anti-tubercular drug development. These results

underscore the need for further preclinical investigations to explore its

therapeutic applications in combating drug-resistant TB.

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v.v.i.

DOI: 10.1007/s12223-025-01291-3

PMID: 40581680

**128. Genome Biol Evol. 2025 Jun 23:evaf120. doi: 10.1093/gbe/evaf120. Online ahead of print.**

Fitness effect of the isoniazid resistance mutation S315T of the

catalase-peroxidase enzyme KatG of Mycobacterium tuberculosis.

Bastolla U(1), Rotkevich M(2), Arenas M(3), Arrayás M(4), Dogonadze M(5),

Lavrova A(6), Molina-Sejas J(1), Tadesse M(7), Xulvi-Brunet R(8), Cox JAG(9),

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Electrónica.

The mutation S315T of the catalase-peroxidase protein KatG of Mycobacterium

tuberculosis is the most common mutation that confers resistance to the prodrug

isoniazid. Here we reconstruct its evolutionary history in 145 whole genome

sequences of M. tuberculosis from Russian hospitals, inferring 11 independent

appearances of this mutation and 5 reversion events, with an estimated reversion

rate 1500 times higher than the rate of preserved non-synonymous or intragenic

mutations. This suggests that, contrary to the commonly held view, the mutation

KatG(S315T) results in a fitness cost, possibly because of reduced tolerance to

oxidative stress. Consistent with this interpretation, the mutant enzyme

presents reduced catalase and peroxidase activities (Wengenack et al. 1997).

Applying the torsional network model, we found that the mutant protein shows

more restricted thermal dynamics, although its functional site moves quite

similarly to the wild type. Of the four internal clones where KatG(S315T) arose,

two present high reproductive rates and secondary mutations at the 5'-UTR region

of the gene encoding superoxide dismutase A (sodA), while the other two present

significantly lower reproductive rate and lack mutations at genes related with

tolerance to oxidative stress. Our results suggest that the resistance mutation

KatG(S315T) incurs a fitness cost, which may be alleviated through compensatory

mutations at the gene sodA or other genes that respond to oxidative stress such

as the previously known gene ahpC. This suggests that isoniazid treatment could

be complemented with drugs that produce oxidative stress in order to hinder the

propagation of resistant strains devoid of compensatory mutations.

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for Molecular Biology and Evolution.

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**129. J Ayurveda Integr Med. 2025 Jun 27;16(4):101158. doi:**

**10.1016/j.jaim.2025.101158. Online ahead of print.**

Exploring Withania somnifera derived natural products as promising inhibitors of

Mycobacterium tuberculosis Pantothenate Kinase-PanK: An integrated in silico and

in vitro approach.

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**BACKGROUND:** Tuberculosis remains a pervasive and enduring global health

challenge, with the alarming rise of drug-resistant variants. Mycobacterium

tuberculosis (M. tuberculosis), bacterium responsible for tuberculosis, deploys

a complex arsenal of virulence factors to evade the host's immune defences. The

quest for novel targets or compounds to combat drug-resistant M. tuberculosis

strains is of paramount importance. PanK is an essential enzyme for Co-enzyme A

(CoA) biosynthesis pathway, targeting inhibition of its activity by Withania

somnifera phytochemicals may provide an effective therapeutic strategy against

resistant strains.

**OBJECTIVE:** The study aims to identify the potential of natural compounds derived

from Withania somnifera as inhibitors of the PanK enzyme (novel target) in M.

tuberculosis.

**METHODOLOGY:** In silico computational approach, includes steps-structure based

virtual screening of 83 Withania compounds followed by molecular docking and

dynamic simulations spanning 100 ns, to assess the binding affinity and

stability between screen key compounds and PanK. In vitro anti-tuberculosis

bioassays was also performed to validate the In silico experiments finding.

**RESULT:** Through in silico experiments, four key compounds of Withania somnifera

were -Morkotin A, Rutin, Withaoxylactone, and 2,3-Dihydrowithanolide E were

identified. They exhibited strong potential to inhibit PanK enzyme activity. The

In silico as well as In vitro findings suggest that Withania somnifera-derived

natural compounds could serve as effective candidates for targeting vital

enzymes in M. tuberculosis.

**CONCLUSION:** Withania somnifera can be explored as valuable resource for

developing novel drugs for PanK as a target to combat tuberculosis.

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**ahead of print.**

Role of fecal calprotectin to differentiate between treatment-naive intestinal

tuberculosis and Crohn's disease: A pilot study.

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DOI: 10.1007/s12664-025-01812-5

PMID: 40580415

**131. Eur J Med Chem. 2025 Jun 24;297:117889. doi: 10.1016/j.ejmech.2025.117889.**

**Online ahead of print.**

Discovery of novel fluorescent amino-pyrazolines that detect and kill

Mycobacterium tuberculosis.

Cui Y(1), Lanne A(2), Avula S(3), Hama Salih MA(4), Peng X(5), Milne G(6), Jones

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The emergence of multidrug-resistant Mycobacterium tuberculosis (MDR-TB)

necessitates novel therapeutics with distinct mechanisms. Here, we report

amino-pyrazoline derivatives as a new class of dual-functional antimycobacterial

agents, integrating potent bactericidal activity with fluorescence-based

bacterial imaging. Initial screening identified AP-07 as a promising hit

compound (MIC99: 40 μM against Mycobacterium smegmatis, 49 μM against

Mycobacterium bovis BCG). Structure-based optimization led to the discovery of

AP-02 and AP-05 as lead compounds, with enhanced activity (MIC99: 13-16 μM

against M. smegmatis; 20-25 μM against M. bovis BCG). Additionally, spontaneous

resistance assays detected no resistant colonies, suggesting a low risk of

resistance development. Mechanistic studies confirmed Ag85C as the primary

molecular target, disrupting late-stage mycolic acid biosynthesis and impairing

cell wall integrity. Notably, pyrazoline derivatives exhibit intrinsic

fluorescence, selectively labeling intracellular mycobacteria while remaining

non-toxic to host macrophages, enabling real-time bacterial imaging. This work

establishes fluorescent amino-pyrazolines as a promising foundation for

next-generation antitubercular agents, bridging diagnostics and therapy in

tuberculosis drug discovery.

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reserved.

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**132. Taiwan J Ophthalmol. 2024 Jul 22;15(2):252-258. doi: 10.4103/tjo.TJO-D-24-00012. eCollection 2025 Apr-Jun.**

Epidemiology of uveitis after tuberculosis in Taiwan - A nationwide

population-based cohort study.

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**PURPOSE:** Current reports on the risk of uveitis of all causes after tuberculosis

(TB) diagnosis are lacking. Therefore, we sought to investigate the association

between the diagnosis of TB and the subsequent risk of uveitis in Taiwan.

**MATERIALS AND METHODS:** Data from the Taiwan National Health Insurance system

were retrieved and patients with newly diagnosed TB between 2000 and 2012 were

recruited. The endpoint of interest was the occurrence of uveitis. Patients

without TB were randomly matched 4:1 to TB cases based on age, gender, index

date, outpatient clinic visit, and index year. Univariate and multivariable Cox

proportional regression analyses were performed to analyze the risk of uveitis

among TB patients.

**RESULTS:** A total of 6139 patients with TB and corresponding 24,555 matched

control participants were recruited. The mean age was 52.9 ± 22.1 years old and

32.1% were male. The medium follow-up period was 5.81 ± 4.37 years and 7.16 ±

3.95 years in the TB and matched control cohorts. Our results showed that

patients with TB had no significantly increased incidence of uveitis. After

stratification by gender, age, and comorbidities, the relationship between TB

and uveitis was found to be not significant. The cumulative incidence of uveitis

was also found to be not significantly higher among the TB group (log-rank P =

0.84).

**CONCLUSION:** Our nationwide population-based cohort retrospective study showed

that the incidence of uveitis was not significantly higher among patients with

TB. Future prospective and multicenter studies are warranted to confirm our

findings.

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PMCID: PMC12204660

PMID: 40584193

**133. World J Clin Cases. 2025 Jul 6;13(19):104083. doi: 10.12998/wjcc.v13.i19.104083.**

Delayed diagnosis of pulmonary tuberculosis with pleuritis due to

ampicillin/sulbactam: A case report.

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**BACKGROUND:** Tuberculosis (TB) remains a global health concern despite decreasing

incidence. Delayed TB diagnosis can exacerbate patient outcomes and lead to

broader public health issues such as mass infections. Differentiation between TB

and bacterial pneumonia is often complicated by variable clinical and

radiological manifestations of TB, leading to diagnostic delays.

**CASE SUMMARY:** An 89-year-old, Japanese male patient with a history of diabetes

mellitus, hypertension, and hypothyroidism presented with right-sided chest

pain. Based on the elevated inflammatory response, right pleural effusion, and

infiltrating shadow in the lung field, the diagnosis of right pleurisy was made

and the antibiotic, ampicillin/sulbactam, was administered. The patient's

condition, inflammatory reaction, and right pleural effusion temporarily

improved. However, persistent low-grade fever and malaise prompted further

evaluation, revealing repeated right pleural effusion and inflammatory response.

A right thoracentesis was performed; the patient was diagnosed with tuberculous

pleurisy as a result of exudative effusion with lymphocyte predominance,

elevated adenosine deaminase levels, and positive Mycobacterium TB polymerase

chain reaction test. Anti-TB treatment, including isoniazid, rifampicin, and

ethambutol was initiated, leading to significant clinical improvement. The

patient successfully completed a 12-month course of TB therapy without

recurrence or deterioration.

**CONCLUSION:** There are cases of TB wherein temporary improvement apparently could

be shown through treatment with antimicrobial agents other than anti-TB drugs,

necessitating careful evaluation in atypical cases of bacterial pneumonia.

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**134. Ital J Pediatr. 2025 Jul 6;51(1):210. doi: 10.1186/s13052-025-02019-2.**

Meta-analysis of TB & HIV co-infection mortality rate in sub-Saharan African

children, youth, and adolescents.

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**BACKGROUND:** Despite the effectiveness of antiretroviral treatment (ART) in

reducing morbidity and mortality, children and adolescents with co-infections

face an elevated risk of death due to their young age and compromised immune

systems. While risk factors for tuberculosis (TB) and adverse TB outcomes in

HIV-infected adults are well-documented for mortality estimation, understanding

mortality risks among HIV-infected children and adolescents, especially in the

era of test and treatment and universal ART for all HIV-infected persons,

remains limited. This study aimed to estimate the mortality rate among TB and

HIV-co-infected children in Sub-Saharan African countries using SRM.

**METHODS:** We systematically searched relevant studies from seven international

electronic databases. Articles were searched using Preferred Reporting Items for

Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Article searching

included six electronic databases including PubMed/MEDLINE (N = 1287), Scopus

(N = 447), Web of Science (N = 174), Science Direct (N = 749, Cochran (N = 57),

and Google Scholar and research repository bases searching (N = 42). The quality

of primary studies was evaluated using Joanna Briggs Institute (JBI) checklist.

The pooled mortality rate was estimated using a weighted inverse variance

random-effect meta-analysis. Heterogeneity among studies was assessed using

Cochran's Q test and estimated using I2 statistic. This document is registered

in Prospero (CRD420251012913).

**RESULT:** In this SRM, 16 individual studies were included. During the co-infected

mortality screening of 5,098 participants, 657 deaths were reported after

co-treatment started. The pooled mortality burden was estimated at 12.96% (95%

CI: 8.94 to 16.98, I2 = 92.6%, P = 0.001). The majority of TB co-infected cases

were newly diagnosed after ART started. The final weighted inverse variance

random-effect regression indicated WHO stages III and IV (pooled HR = 4.34),

poor/ fair ART adherence (pooled HR = 3.11), missed Isoniazid preventive therapy

(IPT) (pooled HR = 3.07), hemoglobin levels ≤ 10 mg/dL (pooled HR = 2.84),

bedridden functional status (pooled HR = 3.19), below threshold CD4 count

(pooled HR = 1.80), and missed cotrimoxazole preventive therapy (CPT) (pooled

AOR = 1.58) were predictors of premature death during co-infection.

**CONCLUSION:** In this review, the overall pooled burden of mortality in

HIV-infected children in SSA countries was high compared with the End TB

Strategy target estimation. Significant predictors of mortality included WHO

clinical stages III and IV, poor or fair ART adherence, missed Isoniazid

preventive therapy (IPT), and hemoglobin levels ≤ 10 mg/dL. Therefore,

counseling on antiretroviral therapy adherence should be strengthened; early

screening and treating of anemia, screening and scaling up of IPT, critical ART

drug, and nutritional counseling should be done during regular visits for

caregivers to prevent premature deaths among children, youths, and adolescents

during co-infection in SSA.

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DOI: 10.1186/s13052-025-02019-2

PMID: 40619406 [Indexed for MEDLINE]

**135. Microb Pathog. 2025 Jul 4:107843. doi: 10.1016/j.micpath.2025.107843. Online**

**ahead of print.**

Advancements in Tuberculosis Diagnostics: An Update.

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Tuberculosis (TB) is one of the major life-threatening diseases caused by a

single pathogen which has become a social menace owing to its high resistance.

TB has even surpassed AIDS prior the COVID 19 pandemic. Every year the number of

affected persons is increasing exponentially. In 2023 8.2 million new cases of

TB were reported. There are various factors responsible for such infectivity

rate of Mycobacterium tuberculosis (Mtb) including emergence of rapid resistant

strains, treatment failure and lack of proper diagnosis. In order to combat the

infection, early and effective treatment of the infection is very crucial. This

calls for the existence of effective and point of care (POC) diagnostic tool for

successful management of the disease. The conventional diagnostics includes

staining, microscopy, tuberculin skin test and chest X ray. However, they have

various limitations which increases the public threat. These tools lack the ease

of transportation, less sensitive, time consuming and lack accuracy. To

eliminate such limitations and bridge the gap associated with the proper

diagnosis of disease, various biochemical, molecular, immunological diagnostic

tools have come up in rescue of the infection. These modern tools are potent

enough in characterizing Mtb, detect mutations correlated with the existing

medications and ensure effective management. In this article we are focusing on

modern diagnostic tools such as T-SPOT, artificial intelligence, electronic

nose, RT PCR, TB LAM, CRISPR, biosensor-based detection techniques including the

conventional techniques for detection of Mtb in clinical setup in resource

limited healthcare facilities for comprehensive diagnosis of tuberculosis.

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