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**境外学者发表的结核病英文文章摘要**

**（85篇）**

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

**1. Int J Infect Dis. 2025 Jul 11:107979. doi: 10.1016/j.ijid.2025.107979. Online**

**ahead of print.**

Temporal Trends in Tuberculosis and Time from Enrollment in Care to

Antiretroviral Therapy Initiation: A Multi-country Cohort Study from Latin

America.

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**BACKGROUND:** HIV treatment guidelines have evolved to recommend rapid

antiretroviral therapy (ART) initiation. Data on the impact of these changes in

the Americas region are scarce.

**METHODS:** This study included data from CCASAnet sites in Brazil, Haiti,

Honduras, Mexico, and Peru. ART-naïve adults who started ART from 2006 to 2022

were included. Trends in CD4 count, tuberculosis (TB), and treatment initiation

were described using cumulative probability and logistic and Cox regression

models.

**FINDINGS:** 29,881 PLWH met inclusion criteria; 2179 (7.3%) were diagnosed with

prevalent TB and 379 (1.2%) with incident TB within six months after ART

initiation. For individuals without TB, enrollment CD4 count increased from 160

to 320 cells/mm3. Over the study period, TB prevalence declined from peak of

9.4% to 5.4%, and incident TB from 1.5% to 0.8%. Median time to ART initiation

decreased from 476 to 1 day for PLWH without TB, and 98 to 16 days for those

with prevalent TB; time to TB treatment also decreased.

**CONCLUSIONS:** Time to ART initiation has decreased in the CCASAnet consortium,

with the majority of PLWH now starting ART within a week after enrollment. There

has also been a decline in the prevalence and incidence of concurrent TB

disease.

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**2. BMC Infect Dis. 2025 Jul 12;25(1):913. doi: 10.1186/s12879-025-11348-w.**

Drug resistance of Mycobacterium tuberculosis to linezolid and delamanid: a case

report from Bukavu, Democratic Republic of Congo.

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The emergence of resistance is of great concern in the control of TB, especially

to the new and repurposed drugs needed for the treatment of rifampicin

resistance. We report a patient from South Kivu in the Eastern Democratic

Republic of the Congo with primary resistance to delamanid and linezolid without

treatment experience with these drugs. The identification of novel resistance

mutations raises concerns about the potential global spread and poor outcomes of

the WHO-recommended oral treatment regimens, highlighting the need for the

urgent rollout of DST.

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**3. Sci Rep. 2025 Jul 12;15(1):25235. doi: 10.1038/s41598-025-04223-w.**

Healthcare professionals' perspective on collaboration with traditional medical

practitioners in HIV/AIDS and tuberculosis care in rural Ethiopia.

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Patients with chronic diseases like HIV and TB often seek treatment from both

traditional and biomedicine healthcare providers. Collaboration with traditional

medicine practitioners (TMPs) has been advocated by UNAIDS in Sub-Saharan Africa

and was promising in some countries. However, no formal collaboration has been

established in Ethiopia, and the perspectives of healthcare professionals (HCPs)

on such collaboration remain unexplored. In this study, descriptive qualitative

design was used to explore HCPs' experiences and perspectives on collaborating

with TMPs in HIV and tuberculosis care in Metekel Zone, Northwest Ethiopia. HCPs

working directly in HIV and TB clinics in five health facilities were

purposively included. Data were collected between March 5 and April 30, 2022,

through in-depth interviews using semi-structured questionnaires. Interviews

were audio-recorded, transcribed verbatim, inductively coded, and thematically

analyzed using MAXQDA 2020. The study included 25 key informant HCPs. They

reported varied experiences with TMPs, including no interaction, occasional

informal social interactions, and rare cases of informal referrals. While some

HCPs expressed skepticism about the efficacy and safety of TMP practices, most

acknowledged potential benefits if TMPs were limited to managing minor

conditions and opportunistic infections. The major reported challenges to

collaboration were unstandardized herbal practices, the secrecy of TMPs,

differing treatment philosophies, the absence of legal frameworks, and

logistical barriers. To establish collaboration, informants recommended legal

frameworks, registering genuine healers, protecting intellectual property,

organizing regular forums for TMP engagement, fostering research partnerships,

and providing financial and tailored training programs for both groups. In

conclusion, this study revealed HCPs had mixed experiences and perspectives on

collaboration with TMPs in Metekel Zone. While some informants recognize the

potential benefits of collaboration, others remain skeptical about role of TMPs.

Therefore, strong government support, clear legal and research frameworks, and

trainings and mutual understanding were recommended to foster collaboration.

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**4. Microb Pathog. 2025 Jul 10;207:107894. doi: 10.1016/j.micpath.2025.107894.**

**Online ahead of print.**

Enhancing Mycobacterium tuberculosis-Ag85B immunogenicity by fusing with human

Fcγ1 (Ag85B:hFcγ1).

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Tuberculosis (TB) is still a life-threatening infection. Mycobacterium

tuberculosis (Mtb) Ag85 is the most potent immunogenic factor for introducing

protective vaccines against TB. To enhance its immunogenicity, Mtb Ag85B was

fused to the Fc fragment of human IgG1 to produce Ag85B:hFcγ1 and its

immunogenicity was assessed in a mouse model. The Ag85B:hFcγ1 was designed and

made in the Pichia pastoris expression system. Then, the production and purity

of Ag85B:hFcγ1 were confirmed using ELISA and Western blotting. Co-localisation

assay showed that Ag85B:hFcγ1 can be localised with hFcγRI (CD64), facilitating

a proper Th1 response. Immunisation assays in a mouse model showed a high IFN-γ

production as the hallmark of cell-mediated immunity (CMI) in the sera of the

treated animals compared with the control ones (p = 0.02). However, the

concentration of IL-17 did not reach the sensitivity of the assays. Functional

co-localisation revealed that the fused hFcγ1 with Ag85 can bind to CD64 and

induce cross-presentation toward Th1 responses by producing higher IFN-γ. In

conclusion, Ag85B:hFcγ1 with high glycosylation seems more immunogenic than our

previous studies Mtb multistage and Fc fusion proteins-multi molecules. APC

targeting was used to favour cross-presentation using the Fc tag.

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**5. Discov Ment Health. 2025 Jul 12;5(1):104. doi: 10.1007/s44192-025-00248-9.**

Prevalence and predictors of depression in tuberculosis patients in india: a

systematic review and meta-analysis.

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**INTRODUCTION:** TB and common mental disorders pose significant global health

challenges that considerably impact human health. The combination of depression

with TB can lead to a poor quality of life, low medication adherence,

progression to drug-resistant tuberculosis, and ultimately, mortality.

OBJECTIVES: This study aimed to estimate the pooled prevalence of depression in

TB patients and identify the predictors of depression in this population in

India.

**METHODS:** The preferred Reporting Items for Systematic Reviews and Meta-Analyses

(PRISMA) guidelines were followed for reporting this systematic review and

meta-analysis. Data were extracted from October to December 2024 using the

PUBMED, Scopus, EMBASE, and DOAJ databases. A total of 25 articles were

selected, and the included articles underwent quality assessment using the

Joanna Briggs Institute Critical Appraisal checklist. The pooled prevalence of

depression in TB patients was estimated at a 95% confidence interval using a

random effects model, assuming potential heterogeneity. STATA 18 (Stata Corp

LLC, College Station, TX, USA) was used for analysis.

**RESULTS:** The total sample across 25 studies included 12,033

(Mean(SD) = 481(1377), Median = 169, IQR = 106-302). The pooled prevalence of

depression in TB patients in India was estimated at 37% (95% CI: 26- 49%). A

subgroup analysis based on the types of TB cases indicated that the prevalence

of depression in different kinds of TB cases did not vary substantially, with

39% (95% CI: 26- 54%) in both Drug-Resistant (DR) and Drug-Sensitive (DS)

Tuberculosis (TB) cases, followed by DR-TB cases [36% (95% CI: 09-68%)] and

DS-TB cases [32% (95% CI: 14- 53%)]. Of the nine assessment tools used to assess

depression, the pooled prevalence utilising the Patient Health Questionnaire

(PHQ)-9 tool was highest [43% (95% CI: 31-56%)]. There was considerable

heterogeneity (I2 = 99.10%) observed in the random-effects model. Factors

associated with depression in TB patients included gender, demographics,

education, occupation, marital and relationship issues, religion, socio-economic

status, habitat, disease-related factors, treatment-related factors, and social

and Behavioural factors.

**CONCLUSION:** The study found that over one-third of TB patients experienced

depression. The coexistence of depression and TB constitutes a significant

public health issue that needs addressing at both the community and health

facility levels.

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**6. Expert Opin Drug Discov. 2025 Jul 12:1-16. doi: 10.1080/17460441.2025.2531229.**

**Online ahead of print.**

Understanding the key challenges in tuberculosis drug discovery: what does the

future hold?

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**INTRODUCTION:** Tuberculosis (TB), caused by Mycobacterium tuberculosis (Mtb),

remains a major global health concern. It spreads through airborne droplets and

has a high mortality rate, particularly without treatment. Drug resistance is

rising, with treatments against multidrug-resistant TB (MDR-TB) showing poor

treatment success rates. The thick, lipid-rich wall of Mtb and its slow growth

reduce antibiotic effectiveness, requiring long treatment courses of 4-6 months.

Current therapies often fail against drug-resistant strains, highlighting the

urgent need for new, short-course treatment, affordable, and

combination-friendly drugs.

**AREAS COVERED:** Within this perspective, the authors review and comment on the

following topics regarding Mtb resistance emergence and treatment strategies: i)

Existing treatment ii) Resistance evolution in Mtb; iii) Key challenges in drug

discovery targeting Mtb; iv) emerging strategies and recent advances in Mtb drug

discovery, and v) Next-generation approaches. Literature was identified through

a search of PubMed, google scholar, and web of science, from January 2010 to

March 2025.

**EXPERT OPINION:** AI is accelerating the discovery of bioavailable and safe

preclinical drug candidates for TB, though data limitations and biological

complexity remain challenging. Future progress requires multi-modal models,

open-access datasets, and interdisciplinary collaboration.

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PMID: 40650508

**7. Drug Dev Ind Pharm. 2025 Jul 12:1-17. doi: 10.1080/03639045.2025.2532762. Online ahead of print.**

Antimycobacterial and autophagic activity of nebulized delamanid microemulsion

targeting alveolar macrophage.

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**OBJECTIVE:** The aerosol delivery of the novel anti-tubercular drug delamanid for

pulmonary targeting holds promise for the effective treatment of

multi-drug-resistant tuberculosis. Here, we developed a microemulsion

formulation of delamanid for nebulization, evaluating its potential bioactivity.

**METHODS:** Herein, we attempted to develop microemulsion formulations loaded

delamanid for nebulization and their physicochemical characteristics were

assessed. The formulation was checked for aerosol characteristics, cytotoxic

potential, in vitro antimycobacterial activity, and autophagy.

**RESULTS:** The optimized formulations, nebulized into a next-generation impactor,

exhibited a fine particle fraction of 63.12%, ensuring efficient in vitro

deposition. In vitro evaluations revealed that formulation did not demonstrate

any cytotoxic potential on respiratory cell lines up to 2.5 µg/mL and lack of

inflammatory cytokines production and nitric oxide from macrophage NR8383 cells,

signified its safety. The flow cytometry analysis revealed that the elimination

of Mycobacterium bovis by formulation after day 4, with considerably low minimum

bactericidal concentration. The formulation demonstrated adequate macrophage

autophagic activity when evaluated using confocal laser scanning microscopy and

Western blot.

**CONCLUSION:** Consequently, the aerosolized microemulsion of delamanid for

pulmonary delivery may serve as an effective therapy for MDR-TB, necessitating

further in vivo studies.

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PMID: 40650441

**8. Nat Commun. 2025 Jul 11;16(1):6442. doi: 10.1038/s41467-025-61703-3.**

Trehalose catalytic shift inherently enhances phenotypic heterogeneity and

multidrug resistance in Mycobacterium tuberculosis.

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Drug-resistance (DR) in bacteria often develops through the repetitive formation

of drug-tolerant persisters, which survive antibiotics without genetic changes.

It is unclear whether Mycobacterium tuberculosis (Mtb), the bacterium that

causes tuberculosis (TB), undergoes a similar transitioning process. Recent

studies highlight changes in trehalose metabolism as crucial for persister

formation and drug resistance. Here, we observe that mutants lacking trehalose

catalytic shift activity exhibited fewer DR mutants due to decreased persisters.

This shift enhances Mtb survival during antibiotic treatment by increasing

metabolic heterogeneity and drug tolerance, facilitating drug resistance.

Rifampicin (RIF)-resistant bacilli display cross-resistance to other antibiotics

linked to higher trehalose catalytic shift, explaining how multidrug resistance

(MDR) can follow RIF-resistance. In particular, the HN878 W-Beijing strain

exhibits higher trehalose catalytic shift, increasing MDR risk. Both genetic and

pharmacological inactivation of this shift reduces persister formation and MDR

development, suggesting trehalose catalytic shift as a potential therapeutic

target to combat TB resistance.

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**9. Contemp Clin Trials. 2025 Jul 9:108002. doi: 10.1016/j.cct.2025.108002. Online ahead of print.**

Designing a response-over-continuous-interventions (ROCI) randomised trial:

Implementation in the phase 2C part (duration ranging) of the PARADIGM4TB trial.

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**BACKGROUND/AIMS:** Treatments for Tuberculosis (TB) are often long and

complicated. Standard 2-arm non-inferiority trials have been used to evaluate

shorter durations of treatment regimens. The new

response-over-continuous-intervention (ROCI) trial design has recently been

proposed as a practical alternative for optimising some continuous aspect (e.g.

treatment duration) of treatment administration.

**METHODS:** We demonstrate the use of simulations for designing a ROCI trial in the

TB setting. We use the Phase 2C part (duration ranging) of the PARADIGM4TB trial

as a case study to illustrate the simulation procedure and the important design

considerations to be explored in simulations. Phase 2C of PARADIGM4TB aims to

optimise durations of novel treatment regimens, compared to a 6-month

standard-of-care treatment regimen, with the aim to support advancement to Phase

3 trials.

**RESULTS:** A ROCI design randomising 200 patients to 5 equally spaced duration

arms of the novel treatment regimen (with an additional 40 patients randomised

to the standard-of-care treatment regimen) is sufficient to achieve reasonable

power to identify the optimal duration in a range of scenarios. Modelling the

duration-response curve with a fractional polynomial model of degree 1 improves

power to select shorter durations compared with pairwise comparisons. A design

with 5 durations of the novel regimen is preferred to a design with 3 durations,

because of the improved operating characteristics in scenarios where the

duration-response curve is not flat.

**CONCLUSIONS:** The ROCI design is an appealing design option for TB treatment

trials. Design of ROCI trials can be done by conducting simulation studies to

explore key design considerations.

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**10. Lancet Infect Dis. 2025 Jul 8:S1473-3099(25)00289-0. doi:**

**10.1016/S1473-3099(25)00289-0. Online ahead of print.**

Delpazolid in combination with bedaquiline, delamanid, and moxifloxacin for

pulmonary tuberculosis (PanACEA-DECODE-01): a prospective, randomised,

open-label, phase 2b, dose-finding trial.

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Mbeya B(5), Wagnerberger L(6), Zumba T(5), Peter DD(4), Makkan H(7), Sloan

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Wallis R, Beattie T, Ntinginya NE, Mangu C, Manyama C, Sabi I, Mtafya B, Minja

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**BACKGROUND:** Linezolid plays a crucial role in the first-line treatment of

drug-resistant tuberculosis globally. Its prolonged use can lead to neurological

and haematological toxicity, highlighting the need for safer oxazolidinones.

Delpazolid, a novel oxazolidinone, might be safer. We aimed to evaluate the

safety and efficacy of delpazolid and identify an optimal dose.

**METHODS:** PanACEA-DECODE-01 was a prospective, randomised, open-label, phase 2b,

multicentre, dose-finding trial done in five tuberculosis trial sites in

Tanzania and South Africa. Adults aged 18-65 years, who weighed 40-90 kg, and

had newly diagnosed, smear positive pulmonary tuberculosis were randomly

assigned (1:1:1:1:1) through centralised allocation, using a probabilistic

minimisation algorithm to receive no delpazolid (D0), delpazolid 400 mg once

daily (D400), delpazolid 800 mg once daily (D800), delpazolid 1200 mg once daily

(D1200), or delpazolid 800 mg twice daily (D800BD), all administered orally for

16 weeks with follow-up to week 52. All participants received bedaquiline (400

mg orally once daily for the first 14 days, then 200 mg orally thrice weekly),

delamanid (100 mg orally twice daily), and moxifloxacin (400 mg orally once

daily). Randomisation was stratified based on bacterial load in sputum as

measured by GeneXpert cycle threshold (<16 vs ≥16), site, and HIV status. The

primary efficacy objective was to establish an exposure-response model with the

primary endpoint, measured in the modified intention-to-treat population, of

change in mycobacterial load measured by time to positivity using the liquid

culture mycobacterial growth indicator tube system. A secondary outcome was the

time on treatment to sustained conversion to negative sputum culture in liquid

media. The primary safety outcome was the occurrence of oxazolidinone class

toxicities defined as peripheral or optical neuropathy, incident leukopenia,

anaemia or thrombocytopenia, or adverse events in line with tyramine pressor

response, all of grade 2 or higher, possibly, probably or definitely related to

delpazolid. This study was registered with ClinicalTrials.gov, NCT04550832.

**FINDINGS:** Between Oct 28, 2021, and Aug 31, 2022, 156 individuals were screened

for eligibility, 76 of whom were enrolled and randomly assigned to D0 (n=15),

D400 (n=15), D800 (n=15), D1200 (n=16), or D800BD (n=15). 60 (79%) of 76

participants were male and 16 (21%) were female. Population

pharmacokinetic-pharmacodynamic modelling suggests maximal microbiological

activity at a daily total exposure of delpazolid (area under the concentration

curve from 0 h to 24 h [AUC0-24]) of 50 mg/L per h; close to the median exposure

observed after a 1200 mg dose. This maximal effect was estimated at a 38% (95%

CI 4-83; p=0·025) faster decline in bacterial load compared with no delpazolid.

In the secondary time-to-event analysis, there was no significant difference in

time to culture conversion between treatment arms or exposure tertile. When all

delpazolid-containing groups were combined, the hazard ratio for the time to

sustained culture conversion to negative, comparing all delpazolid-containing

groups with the group without delpazolid was 1·53 (95% CI 0·84-2·76). Two

drug-related serious adverse events (one gastritis and one anaemia) occurred in

the D800BD group, with high individual AUC0-24. Apart from the anaemia and one

event of brief, moderate neutropenia observed at only one visit in the D800

group not in line with the characteristics of oxazolidinone class toxicity, no

oxazolidinone class toxicities occurred.

**INTERPRETATION:** The pharmacokinetic-pharmacodynamic modelling results suggest

that delpazolid adds efficacy on top of bedaquiline, delamanid, and

moxifloxacin; and that a dose of 1200 mg once daily would result in exposures

with maximum efficacy. That dose was shown to be safe, raising hope that

linezolid toxicities could be averted in long-term treatment. Delpazolid is a

promising drug for future tuberculosis treatment regimens and could be widely

usable if safety and efficacy are confirmed in larger trials.

FUNDING: LigaChem Biosciences, EDCTP2 programme supported by the EU; German

Ministry for Education and Research; German Center for Infection Research; Swiss

State Secretariat for Education, Research and Innovation; and Nederlandse

Organisatie voor Wetenschappelijk Onderzoek.

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The patient pursuit of safe treatment options for tuberculosis.

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**12. Lancet Infect Dis. 2025 Jul 8:S1473-3099(25)00213-0. doi:**

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Sutezolid in combination with bedaquiline, delamanid, and moxifloxacin for

pulmonary tuberculosis (PanACEA-SUDOCU-01): a prospective, open-label,

randomised, phase 2b dose-finding trial.

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M(6), Wallis RS(6), Ntinginya N(7), Liyoyo A(4), Huglin B(5), Minja LT(7),

Wagnerberger L(8), Stoycheva K(8), Zumba T(5), Noreña I(8), Peter DD(4), Makkan

H(6), Sloan DJ(9), Brake LT(3), Schildkraut J(3), Aarnoutse RE(3), McHugh

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R, Basson E, Behnke AL, Sloan D, Sabiiti W, Gillespie S, Te Brake L, Svensson E,

Mouhdad C, Aarnoutse R, Boeree M, Stemkens R, Koele S, van der Feltz I, Bateson

A, Hunt R, McHugh TD, Muraro Wildner L, Solanki P, Phillips P, Gong X, Aldana B,

Crook A, Dawson R, Narunsky K, Arnolds S, Diacon A, de Jager V, Sanne I, Rassool

M, Churchyard G, Sebe M, Makkan H, Mokaba L, Madikizela N, Mdluli J, Sithole J,

Wallis R, Beattie T, Ntinginya NE, Mangu C, Manyama C, Sabi I, Mtafya B, Minja

LT, Chimbe O, Ngaraguza B, Mhimbira F, Mbeya B, Zumba T, Chibunu N, Sasamalo M,

Reither K, Jugheli L, Kibiki G, Semvua H, Mpagama S, Liyoyo A, Adegbite BR,

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**BACKGROUND:** Linezolid is a key component globally in first-line therapy for

drug-resistant tuberculosis but has considerable toxicity. New and safer

alternative oxazolidinones are needed. Sutezolid is one such promising

alternative. We aimed to evaluate preliminary efficacy and safety of sutezolid

and to identify an optimal dose.

**METHODS:** PanACEA-SUDOCU-01 was a prospective, open-label, randomised, phase 2b

dose-finding study in four tuberculosis trial sites in Tanzania and South

Africa. Adults aged 18-65 years with newly diagnosed, drug-sensitive,

smear-positive tuberculosis were enrolled and randomly assigned (1:1:1:1:1) by a

probabilistic minimisation algorithm using a web-based interface, stratified by

site, sex, and HIV status, to receive no sutezolid (U0), sutezolid 600 mg once

daily (U600), sutezolid 1200 mg once daily (U1200), sutezolid 600 mg twice daily

(U600BD), or sutezolid 800 mg twice daily (U800BD), all administered orally for

12 weeks followed by standard therapy for 6 months. All participants received

oral bedaquiline (400 mg once daily for 14 days followed by 200 mg thrice

weekly), oral delamanid (100 mg twice daily), and oral moxifloxacin (400 mg once

daily). For the primary endpoint, measured in the modified intention-to-treat

population, sputum samples were taken weekly to measure the change in bacterial

load measured by time to positivity using the mycobacterial growth indicator

tube system. Safety was assessed through weekly electrocardiography, safety

blood tests, vision testing, and physical and neurological examinations.

Intensive pharmacokinetic measurements were done on day 14 to determine exposure

to sutezolid, bedaquiline, delamanid, and moxifloxacin. This trial is registered

with ClinicalTrials.gov (NCT03959566).

**FINDINGS:** Between May 20, 2021, and Feb 17, 2022, 186 individuals were screened

for eligibility, 75 of whom were enrolled and randomly assigned to U0 (n=16),

U600 (n=15), U1200 (n=14), U600BD (n=15), or U800BD (n=15). 56 (75%)

participants were male and 19 (25%) were female. The final

pharmacokinetic-pharmacodynamic model showed a benefit of sutezolid, with an

increase in time to positivity slope steepness of 16·7% (95% CI 0·7-35·0) at the maximum concentration typical for the 1200 mg dose, compared with no sutezolid

exposure. A maximum effect of sutezolid exposure was not observed within the

investigated dose range. Six (8%) participants (one in the U600 group, two in

the U600BD group, one in the U800BD group, and two retrospectively identified in

the U600 group) had an increase in a QT interval using Fridericia correction

greater than 60 ms from baseline. Two (3%) participants in the U600BD group had

grade 4 adverse events, one each of neutropenia and hepatotoxicity, but they

were not deemed associated with the use of sutezolid by the investigators. No

neuropathy was reported.

**INTERPRETATION:** Sutezolid, combined with bedaquiline, delamanid, and

moxifloxacin, was shown to be efficacious and added activity to the background

drug combination, although we cannot make a final dose recommendation yet. This

study provides valuable information for the selection of sutezolid doses for

future studies, and described no oxazolidinone class toxicities at the doses

used.

**FUNDING:** EDCTP2 programme funded by the EU; German Ministry for Education and

Research; German Center for Infection Research; and Nederlandse Organisatie voor

Wetenschappelijk Onderzoek.

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Cost-effectiveness of tuberculosis infection screening and treatment among

high-tuberculosis risk immigrants and asylum seekers in The Netherlands: A

cohort modelling study.

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Rotterdam, the Netherlands.

**BACKGROUND:** We evaluated the cost-effectiveness of TB infection (TBI) screening

and TB preventive treatment (TPT) for immigrants, asylum seekers, and settled

migrants in The Netherlands.

**METHODS**: We used a deterministic cohort model that captures the natural history

of TBI and TB disease for a migrant cohort in the country of origin (pre-entry)

and in The Netherlands (post-entry). We fitted the pre-entry force of infection

to Interferon Gamma Release Assay (IGRA) positivity rates from an implementation

pilot study, and chest X-ray (CXR) positivity from the national entry-screening

programme. We compared the costs per quality adjusted life year (QALY) gained

for TBI screening with CXR screening over a 20-year time-horizon, accounting for

parameter uncertainty by producing predictions for over 1000 unique parameter

combinations that fit the data.

**RESULTS:** TBI screening uniformly resulted in an increase in QALYs gained

compared to current CXR-based screening policies. For immigrants, <10 % of

parameter combinations predicted TBI entry screening to be more cost-effective

than CXR screening under observed TPT completion rates (36 %). However, this

changed to nearly 100 % of parameter combinations for immigrants coming from

countries with a TB incidence of ≥100 per 100,000 when applying TPT completion

rates as observed in asylum seekers (72 %). For asylum seekers, 100 % of

parameter combinations predicted cost-effectiveness, while 0 % predicted TBI

screening to be cost-effective among settled migrants.

**CONCLUSIONS:** TBI entry screening is a cost-effective alternative to CXR entry

screening for immigrants and asylum seekers coming from high TB endemic

countries, provided TPT completion is sufficiently high.

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**14. PLOS Glob Public Health. 2025 Jul 11;5(7):e0004548. doi:**

**10.1371/journal.pgph.0004548. eCollection 2025.**

Optimising TB investments in Belarus, Moldova, Kyrgyz Republic, Tajikistan and

Uzbekistan: An allocative efficiency analysis.

Bowring AL(1), Martin-Hughes R(1), Ten Brink D(1), Burke K(1), Nidzvetska S(2),

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High rates of drug-resistant tuberculosis (TB) are a barrier to achieving End

TB-strategy targets in Eastern Europe and Central Asia. This analysis collates

results from five country-level modelling studies to identify priorities to

reduce TB burden. Allocative efficiency studies were conducted in 2023 in

Belarus, Kyrgyz Republic, Moldova, Tajikistan and Uzbekistan using the Optima TB

model to determine the optimised distribution of funds to maximise health

outcomes with given resources. A baseline scenario of continued 2022 spending

was compared to scenarios with spending optimised across prevention, screening

and treatment interventions to reduce TB incidence and deaths over 2024-2030.

Modelled pulmonary TB incidence ranged from 25-119 per 100,000 population, and

14 - 43% of new/relapse TB cases were drug resistant. In all countries,

optimizing current spending involved: expanding shorter treatment regimens (6-9

months) for drug-resistant-TB over standard regimens (18-20 months); reducing

mass screening and mandatory testing and expanding community-based active case

finding focused among populations at higher TB risk; and scaling-up TB

preventive treatment. It was recommended to expand contact tracing in three

countries and to improve cost-effectiveness in two countries by focusing on

child household contacts first. With current spending optimised, pulmonary TB

incidence was projected to decrease to 19 - 95 per 100,000 population by 2030,

averting 1 - 13% of new/relapse TB cases and 1 - 18% of TB-related deaths from

2024-2030 compared to continued baseline spending. In three countries, optimised

allocation of 150% of current spending had minimal additional epidemic impact.

There are opportunities to reallocate TB funds more cost-effectively in Eastern

Europe and Central Asia, but End TB targets may remain out of reach without new

and prospective interventions.

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original author and source are credited.

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**15. Anal Chem. 2025 Jul 11. doi: 10.1021/acs.analchem.5c01697. Online ahead of**

**print.**

Development of a Femtosensitive Electrochemical Aptasensor for Tuberculosis

Ag85B Detection.

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Tuberculosis (TB) disease continues to pose a major global health challenge,

particularly in resource-limited settings where access to rapid, sensitive, and

affordable diagnostic tools remains limited. Traditional methods, such as sputum

smear microscopy and culture techniques, are time-consuming, lack sensitivity,

and often require well-equipped laboratories, making them unsuitable for rapid,

point-of-care diagnostics. To address these challenges, developing a rapid,

sensitive, and selective biosensor is essential for the early detection of TB.

Aptamer-based biosensors offer a promising approach for sensitive and specific

detection of disease biomarkers. In this study, an electrochemical aptasensor

tailored for precisely detecting the tuberculosis biomarker Antigen 85B (Ag85B)

was developed. A diverse library of random oligonucleotide sequences was

initially screened to identify aptamers with high binding affinity for Ag85B.

The aptamer selection process involved immobilizing Ag85B on polyvinylidene

fluoride membranes through aldehyde surface modifications, followed by

incubation with the DNA library mixture. Aptamers with high specificity for

Ag85B were isolated based on iterative selection and amplification. The selected

aptamers were then integrated into a biosensor by immobilization on gold

nanoparticle-modified screen-printed carbon electrodes using thiol-gold

chemistry. The performance of the aptasensor was enhanced by adjusting key

parameters such as aptamer concentration and incubation time, resulting in a

detection limit of 0.2 fM. The resulting biosensor demonstrated remarkable

selectivity for Ag85B and exhibited robust stability across multiple uses and

extended storage, making it a promising tool for rapid and reliable TB

diagnosis.

DOI: 10.1021/acs.analchem.5c01697

PMID: 40643608

**16. J Occup Environ Med. 2025 Jul 11. doi: 10.1097/JOM.0000000000003483. Online**

**ahead of print.**

Why we should all Care that Everything is Tuberculosis.

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DOI: 10.1097/JOM.0000000000003483

PMID: 40643366

**17. Microbiol Resour Announc. 2025 Jul 11:e0006025. doi: 10.1128/mra.00060-25.**

**Online ahead of print.**

Identifying genetic determinants of Mycobacterium tuberculosis acid growth

arrest by transposon mutagenesis coupled with next-generation sequencing

(Tn-seq).

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Mycobacterium tuberculosis, the causative agent of tuberculosis, remains the

leading global infectious disease killer. Adaptation of Mycobacterium

tuberculosis to acidic niches within the host during infection is vital to

establish the disease. Here, we present a high-density transposon mutant

sequencing library data set identifying genetic determinants of acid growth

arrest to serve as a resource.

DOI: 10.1128/mra.00060-25

PMID: 40643003

**18. In Silico Pharmacol. 2025 Jul 8;13(2):100. doi: 10.1007/s40203-025-00388-4.**

**eCollection 2025.**

Atomic-level binding interaction analysis of Mycobacterium tuberculosis membrane

protein Rv1085c with Toll-Like receptor 2 to investigate its role in immune

response.

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The sequencing of the entire Mycobacterium tuberculosis (Mtb) genome in 1998

opened the door to exciting discoveries about the cellular and molecular

underpinnings of the pathogen's virulence and capability to persist within host

cells. One of the potential contributing gene to this virulence and persistence

is Rv1085c, which is a potential membrane protein in the Mtb H37Rv strain.

Rv1085c has been annotated in databases such as MycoBrowser; however the

structural and functional characteristics of Rv1085c have not been addressed in

detail. In this study, we conducted an in silico structural and functional

characterization of Rv1085c to further our understanding of its potential role

in Mtb virulence. The 3D model of the Rv1085c protein was generated using the

I-TASSER server and subjected to structural validation using a number of tools

including PROCHECK, ProSA-web and Verify3D. Functional predictions provided

evidence to suggest Rv1085c could be involved in processes related to virulence,

detoxification pathway and host adaptation. Protein-protein docking studies were

performed to examine potential host-pathogen interactions using ZDOCK and

docking of Rv1085c against Toll-like receptor 2 (TLR2) (PDB ID: 5D3I), an

important receptor that participates in innate immune recognition of Mtb.

Molecular dynamics simulations (MDS) were also performed to analyse the

stability and conformational dynamics of the Rv1085c-TLR2 complex. These results

provide preliminary insights on structure and interaction with Rv1085c,

suggesting its potential role in host immune modulation. This research offers

insights for ulterior experimental verifications and may lead to a better

identification of drug targets related to tuberculosis.

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**eCollection 2025 Jul.**

Chylothorax in Uncommon Contexts: Pulmonary Tuberculosis and Mantle Cell

Lymphoma.

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Chylothorax, characterised by the accumulation of chyle in the pleural space, is

a rare yet clinically significant condition. This lymphatic fluid, rich in fats

absorbed from the intestine, can be caused by various factors including trauma,

malignancy, and tuberculosis (TB). Traumatic causes, particularly iatrogenic

procedures, account for a significant proportion of cases, followed by rare

etiologies like malignancies such as lymphoma, and less commonly, tuberculosis.

In the first two cases, the patient was diagnosed with tuberculosis during

evaluation for chylothorax; however, in the third case, the patient developed

chylothorax as a complication of mantle cell lymphoma (MCL). Two male patients,

aged 43 and 45, presented with respiratory symptoms and milky pleural effusions

(triglycerides > 180 mg/dL). In both, bronchoalveolar lavage confirmed

rifampicin-sensitive TB. Both patients responded to anti-tubercular therapy and

dietary modification. A 69-year-old male with a history of non-Hodgkin's

lymphoma developed chylothorax (triglycerides 286 mg/dL) and lymphadenopathy;

imaging and biopsy confirmed MCL. He responded to chemotherapy. This series

underscores the importance of considering uncommon causes of chylothorax during

evaluation and tailoring treatment based on specific etiologies.

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**20. ACS Infect Dis. 2025 Jul 11;11(7):1754-1755. doi: 10.1021/acsinfecdis.5c00495.**

Combating Tuberculosis: Obstacles, Innovations, and the Road Ahead.

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DOI: 10.1021/acsinfecdis.5c00495

PMID: 40641291

**21. Br J Clin Pharmacol. 2025 Jul 10. doi: 10.1002/bcp.70163. Online ahead of print.**

Extrapolation of lung pharmacokinetics of bedaquiline across species using

physiologically-based pharmacokinetic modelling.

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**AIMS:** BeBedaquiline (BDQ) is a first-in-class diarylquinoline (DARQ) and a

potent anti-tuberculosis drug, vital in combating multi-drug resistant

tuberculosis (TB). Understanding its lung pharmacokinetics (PK) across species

is crucial for effective clinical translation. This study aimed to extrapolate

BDQ's lung PK from preclinical species to humans, focusing on healthy and

TB-infected lung tissue.

**METHODS:** Physiologically-based PK (PBPK) modelling was employed to simulate

BDQ's lung distribution in various pulmonary micro-compartments, including

cellular lesions and caseous granulomas, using data from mice, rats and dogs.

Complex interactions, such as lysosomal trapping within macrophages and

anomalous diffusion within the caseum, utilising a catenary model and a

time-dependent rate, were incorporated into the models to accurately represent

BDQ's unique PK profile.

**RESULTS:** The study revealed intricate dynamics of BDQ's lung distribution, with

only free concentrations in lysosomes of macrophages surpassing the MIC of

Mycobacterium tuberculosis in both mice and humans, indicating intracellular

accumulation which may further explain the proven drug's efficacy. Moreover,

during the course of treatment in humans, adequate drug levels were achieved

near the cellular rim but penetration into the inner caseous core was predicted

to be limited.

**CONCLUSIONS:** Understanding BDQ's lung PK is essential for optimising dosing

strategies with new companion drugs. The findings underscore the need to

characterise BDQ distribution within the caseum, as it shows extensive caseum

binding. Moreover, the developed PBPK model can be applied to new promising DARQ

analogues, facilitating their development as effective TB treatments.

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**22. Pharm Res. 2025 Jul 10. doi: 10.1007/s11095-025-03889-1. Online ahead of print.**

Inhalable N-Acetylcysteine-loaded Lactose-coated PLGA Nanoparticles for

Tuberculosis Treatment.

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**OBJECTIVE:** Glutathione (GSH), known for having mucolytic, anti-inflammatory, and

antioxidant activities, is used in clinical practice in several pathologies,

including tuberculosis (TB). N-acetylcysteine (NAC) has been primarily used to

treat lung conditions and paracetamol-induced liver toxicity. However, NAC

exhibits potential antimycobacterial activity through several mechanisms

including immunomodulation, enhancement of GSH levels, and direct

antimycobacterial effect. In this work, we aim to develop an effective drug

delivery system for NAC for inhalable formulations.

**METHODS:** Herein, we report the development of lactose-coated NAC-loaded

Poly(lactic-co-glycolic acid) (PLGA) nanoparticles (NAC-PLGA NPs) obtained by

double emulsion methodology. Lactose has a double role, as a cryoprotectant

agent and dispersant for inhalable formulations. The physicochemical properties

of lactose-coated NAC-PLGA NPs were examined in terms of particle size,

polydispersity index (PdI), zeta potential (ZP), encapsulation efficiency, and

morphology. The in vitro release and lung deposition studies were assessed.

**RESULTS:** The physicochemical characterization studies revealed the compatibility

of the drug with the selected excipients. Moreover, lactose-coated NAC-PLGA NPs

showed particle size of 310 ± 3 nm, PdI of 0.15 ± 0.01, and of -11.5 ± 0.4 mV.

The in vitro release study suggested a biphasic release profile. Likewise, in

vitro lung deposition studies revealed desirable lung deposition parameters,

indicating effective particle size for efficient pulmonary delivery.

Additionally, in vitro studies for antimycobacterial activity exhibited superior

antibacterial activity against Mycobacterium Tuberculosis (MTB) H37Rv.

**CONCLUSIONS:** These preliminary findings suggest that lactose-coated NAC-PLGA NPs

can open the door to new therapeutic options against one of the most

drug-refractory and drug-resistant infectious diseases, TB.

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**23. Pract Neurol. 2025 Jul 10:pn-2025-004705. doi: 10.1136/pn-2025-004705. Online**

**ahead of print.**

Occipital condyle syndrome: a rare manifestation of skull base tuberculosis.

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A man in his 30s from South Asia presented with progressive neck pain, occipital

headache and right-sided tongue deviation (occipital condyle syndrome). Initial

imaging identified a destructive skull base lesion involving the right clivus,

occipital condyle and C1 vertebra with compression of the hypoglossal nerve,

raising concerns for malignancy. Concurrent necrotic mediastinal lymphadenopathy

prompted endobronchial ultrasound-guided biopsy, which confirmed necrotising

granulomatous lymphadenitis with Mycobacterium tuberculosis complex DNA.

Quadruple antituberculous therapy and adjunctive corticosteroids gave

significant clinical and radiological improvement at 6 months. This case

highlights the importance of considering tuberculosis in the differential

diagnosis of destructive skull base lesions even in non-endemic regions and in

patients with previously negative TB screening.

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PMID: 40639959

**24. Eur Respir J. 2025 Jul 10:2500195. doi: 10.1183/13993003.00195-2025. Online**

**ahead of print.**

Collagen-targeted PET/CT Imaging of Tuberculosis Patients.

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DOI: 10.1183/13993003.00195-2025

PMID: 40639875

**25. Steroids. 2025 Jul 8;221:109656. doi: 10.1016/j.steroids.2025.109656. Online**

**ahead of print.**

Association of CYP27B1 promoter gene variants of vitamin D pathway with

pulmonary tuberculosis and vitamin D levels.

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Cyp27b1 polymorphisms are stated to be associated with different diseases

including tuberculosis (TB). Since the gene variants located in the promoter

region may have a significant influence on gene transcription/translation and

Cyp27b1 enzyme is involved in critical steps in vitamin D metabolism, we aim to

study whether Cyp27b1 gene promoter variants namely -1077 (C/G), -1260 (C/A) and

the region immediately 5' to the promoter -1918 (C/T) have any linkage with

pulmonary tuberculosis risk/defence and to determine their influence on vitamin

D level in normal healthy controls (HCs) and pulmonary tuberculosis (PTB)

patients of the South Indian population. The polymerase chain reaction and

restriction fragment length polymorphism (PCR-RFLP) method were used to genotype

the genomic DNA after it was extracted using the salting-out approach. The

Enzyme-Linked Immunosorbent Assay (ELISA) was used to measure the amount of

vitamin D. In the co-dominant model, a significant association was detected with

TB liability in the -1077 "GG" genotype [Odds ratio (OR): 2.10(1.18-3.73);

p = 0.015]. In addition, a noteworthy linkage was detected with TB protection in the dominant model [GG vs CG + CC, OR: 0.40(0.21-0.75); p = 0.0035]. In the -1918 (C/T) variant, a substantial linkage was detected in the heterozygous

-1918 "CT" genotype with TB risk [OR: 1.90 (1.05-3.44); p = 0.046] in

co-dominant model, whereas a protective linkage was detected in less recurrent

"TT" genotype [OR: 0.42 (0.19-0.94); p = 0.049] with TB. Furthermore, those

risky genotypes are substantially linked with more TB risk in males than

females. Strong links between -1077 and -1260 variations were revealed by

haplotype analysis, and its haplotypes "GC" (-1077G, -1260C) were found to be

significantly associated with increased TB risk. Vitamin D deficiency

(<20 ng/ml) was detected at a higher frequency in PTB patients than HCs in -1077

"GG", -1260 "CA" and -1918 "CT" risky genotypes. This needs to be confirmed by

bigger sample sizes in future research.

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PMID: 40639560

**26. PLOS Glob Public Health. 2025 Jul 10;5(7):e0004075. doi:**

**10.1371/journal.pgph.0004075. eCollection 2025.**

Sociodemographic determinants of multidrug-resistant tuberculosis in Lesotho: A

case-control study.

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The emergence of multidrug-resistant tuberculosis (MDR-TB) significantly

undermines global efforts toward tuberculosis (TB) control, particularly in

high-burden settings like Lesotho. Understanding the sociodemographic factors

contributing to MDR-TB is crucial yet remains under-explored in this context.

This study aimed to identify key sociodemographic determinants associated with

MDR-TB among adult TB patients in Lesotho. Using a retrospective case-control

design, I analyzed data from 306 participants, including confirmed MDR-TB cases

and drug-susceptible TB controls, recruited from 12 TB clinics between March

2021 and February 2022. Sociodemographic characteristics (age, sex, education,

employment, income, place of residence), HIV status, and caregiver presence were

examined using chi-square tests and multivariable logistic regression analyses.

The findings indicated that individuals older than 26 years had lower odds of

MDR-TB compared to those aged 18-26 years (OR = 0.8, 95% CI 0.67-0.99,

p = 0.040). Similarly, higher income levels (earning more than $1,026 annually)

were associated with reduced odds of MDR-TB (OR = 0.5, 95% CI 0.22-0.94,

p = 0.034). Conversely, the absence of caregiver support significantly increased

the likelihood of MDR-TB by 80% (OR = 1.8, 95% CI 1.04-3.11, p = 0.036). These

findings highlight the critical need for targeted interventions focusing on

socioeconomic empowerment, caregiver support, and tailored public health

education to effectively mitigate the MDR-TB burden in Lesotho.

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PMCID: PMC12244824

PMID: 40638609

**27. Braz J Biol. 2025 Jul 7;85:e296271. doi: 10.1590/1519-6984.296271. eCollection 2025.**

Development and validation of a digital health application to support

tuberculosis treatment adherence.

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Tuberculosis remains a serious public health challenge in Brazil, particularly

among socially vulnerable populations. This study presents the development and

content validation of"Controlling the TB", a digital prototype designed to

support treatment adherence among patients undergoing tuberculosis therapy

within the Brazilian Unified Health System. The tool was developed based on the

Theory of Planned Behavior and User-Centered Design principles, comprising four

modules: sociodemographic data, disease history, clinical guidelines, and

treatment adherence. Content validation was conducted by expert professionals

using a structured instrument and descriptive analysis. All modules met the

minimum acceptability criteria, with notable highlights for applicability,

accessible language, and clinical coherence. The results demonstrate the

prototype's potential as a supportive technology for continuity of care, with

national scalability and international adaptability in settings facing similar

challenges in treatment adherence and digital monitoring for neglected diseases.

DOI: 10.1590/1519-6984.296271

PMID: 40638502 [Indexed for MEDLINE]

**28. Rev Soc Bras Med Trop. 2025 Jul 7;58:e00952025. doi:**

**10.1590/0037-8682-0095-2025. eCollection 2025.**

The CT target sign as a criterion for the differential diagnosis between

tuberculosis and organizing pneumonia.

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DOI: 10.1590/0037-8682-0095-2025

PMCID: PMC12233738

PMID: 40638450

**29. mBio. 2025 Jul 10:e0137225. doi: 10.1128/mbio.01372-25. Online ahead of print.**

Exploring β-lactam interactions with DacB1: unraveling optimal therapies for

combating drug-resistant Mycobacterium tuberculosis.

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Tuberculosis (TB) continues to pose a global public health threat, exacerbated

by rising drug-resistant strains of Mycobacterium tuberculosis (Mtb). DacB1, a

D,D-carboxypeptidase critical in Mtb peptidoglycan biosynthesis, is a promising

target for β-lactam antibiotics (BLs), which remain underutilized in TB

treatment. Dual BL therapy may enhance efficacy by inactivating multiple targets

within the peptidoglyan synthesis pathway. Minimum inhibitory concentrations

(MICs) for β-lactams and β-lactamase inhibitors against Mtb H37Ra, H37Rv, and

clinical isolates showed that imipenem, meropenem, or tebipenem MICs were

reduced when combined with amoxicillin or ceftriaxone or β-lactamase inhibitors

such as clavulanate or durlobactam. Timed electrospray ionization mass

spectrometry (ESI-MS) captured acyl-enzyme adducts between DacB1 and BLs,

revealing binding interactions with carbapenems (imipenem, meropenem, and

tebipenem) but not most penicillins or cephalosporins except cloxacillin and

cefoxitin. Differential scanning fluorimetry (DSF) combined with circular

dichroism (CD) confirmed physical and structural changes in DacB1 upon BL

binding despite no alteration in melting temperature. Carbapenem-DacB1

interactions were notably faster with imipenem, likely due to reduced steric

hindrance compared to meropenem and tebipenem. Molecular modeling revealed

conserved penicillin-binding protein motifs within the active site of DacB1:

S121XXK124, S176XN178, and K282TG284 (PDB ID # 4PPR). Building on this,

molecular docking suggested favorable interactions between these motifs and the

carbapenems: the carbapenem carbonyl group aids in positioning within DacB1's

oxyanion hole, ready for acylation, while hydrophobic interactions with the

cyclic R2 side chains and C1 methyl groups in meropenem and tebipenem contribute

to steric hindrance hence slow acyl-enzyme formation. These findings enhance our

understanding of DacB1 inhibition and suggest that carbapenems, particularly in

combination therapies, hold promise as effective TB treatments.

**IMPORTANCE:** TB remains a significant public health threat, particularly due to

the rising prevalence of drug-resistant Mtb strains. Current treatment options

for drug-resistant TB are costly, toxic, and often ineffective, necessitating

the exploration of alternative therapeutic strategies. This study is of critical

importance as it investigates the potential of β-lactam antibiotics (BLs), a

class historically considered ineffective against Mtb, for repurposing in TB

treatment. By targeting DacB1, a key enzyme in Mtb peptidoglycan biosynthesis,

this research provides new insights into the mechanism of β-lactam interactions

and their potential to disrupt cell wall synthesis. The findings demonstrate

that dual β-lactam therapy and β-lactam/β-lactamase inhibitor combinations

enhance antibiotic efficacy, suggesting a promising avenue for combating

drug-resistant TB. Furthermore, structural and molecular analyses confirm that

carbapenems, particularly imipenem, meropenem, and tebipenem, effectively bind

to DacB1, paving the way for optimized treatment strategies. Given the

challenges in developing new TB drugs, repurposing β-lactams offers a

cost-effective and readily implementable solution to address antimicrobial

resistance. This study contributes valuable knowledge that could accelerate the

development of novel TB therapies, improve treatment success rates, and

ultimately reduce TB-related mortality worldwide.

DOI: 10.1128/mbio.01372-25

PMID: 40637416

**30. BMC Complement Med Ther. 2025 Jul 9;25(1):248. doi: 10.1186/s12906-025-05002-w.**

In vitro phytochemical, antioxidant activity and antimycobacterial potentials of

selected medicinal plants commonly used for respiratory infections and related

symptoms in the Limpopo Province, South Africa.

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**BACKGROUND**: The emergence of drug resistance among Mycobacterium tuberculosis

(Mtb) strains, coupled with the detrimental side effects linked to tuberculosis

(TB) treatment, underscores the persistence of TB as a significant clinical and

public health concern in South Africa, thereby necessitating ongoing research in

drug discovery. The use of medicinal plants for the treatment of TB has garnered

increasing attention, especially in countries where a significant portion of the

population relies on traditional medicine as a primary form of healthcare.

**METHODS:** The crude extracts from nine medicinal plants were investigated for

antimycobacterial activity. Phytochemical profiling and qualitative antioxidant

activity were assessed using thin layer chromatography. The

2,2-Diphenyl-1-picrylhydrazyl radical scavenging assay was used for quantitative

antioxidant analysis. The broth microdilution assay was used to determine the

antimycobacterial activity of the plant extracts and rifampicin against

Mycobacterium smegmatis (ATCC 1441). Sodium dodecyl polyacrylamide gel

electrophoresis was used to qualitatively evaluate the protein profile of M.

smegmatis. The growth response of M. smegmatis to both inhibitors (rifampicin

and plants extracts) was assessed through growth kinetics assays.

**RESULTS:** Phytochemical profiling revealed that all plants contained various

phytoconstituents in differing concentrations. Additionally, the plants

exhibited relatively low antioxidant activity, as indicated by their IC50

values. Rosmarinus officinalis and Zanthoxylum capense demonstrated inhibitory

effects on the growth of M. smegmatis with a minimum inhibitory concentration of

0.625 mg/ml. The time-kill assays indicate that the plant extracts including

those of Gardenia volkensii, Citrus lemon, Croton gratissimus and Clerodendrum

glabrum exhibited greater growth reduction than rifampicin. Sodium dodecyl

polyacrylamide gel electrophoresis profiles revealed distinct patterns of M.

smegmatis proteins. Protein profiles suggest that plant extracts, like

rifampicin, affect bacterial protein synthesis.

**CONCLUSION:** The results of this study indicate that the plants do not have

potent free radical scavenging capabilities. Nevertheless, they exhibited

antimycobacterial properties, notably impacting protein synthesis.

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PMCID: PMC12243302

PMID: 40635022 [Indexed for MEDLINE]

**31. Commun Biol. 2025 Jul 9;8(1):1024. doi: 10.1038/s42003-025-08383-3.**

PPE50 variants as novel phylogeographic signatures of host-pathogen co-evolution

in tuberculosis.

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While evidence supports co-evolution between Mycobacterium tuberculosis and

humans, underlying mechanisms remain unclear. We identified PPE50 as a novel

subfamily of PE/PPE proteins comprising eight variants. Surveying 387 M.

tuberculosis complex (MTBC) strains representing global phylogeography, we found

PPE50 variants are lineage-specific and stably associated with geographic

regions, defining them as phylogeographically-associated proteins (PAPs).

PPE50-381 is the ancestral variant (present in early-branching M. canettii) and

the only variant observed in both Ancient and Modern MTBC lineages.

Transcriptomic analysis confirmed that ppe50 variant genes are expressed in

strains from respective MTBC lineages, but not in all L1 strains and

sub-lineages L2.1 and L4.1 where the gene was deleted. In silico analysis

revealed significant structural diversity among variants, particularly in

C-terminal regions. This strong association of M. tuberculosis protein diversity

with phylogeography suggests PPE50 may contribute to MTBC adaptation to

different host populations. Further characterization of PPE50 and other PAPs may

facilitate improved targeted diagnostics, therapeutics and vaccines.

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**32. NPJ Digit Med. 2025 Jul 9;8(1):418. doi: 10.1038/s41746-025-01832-7.**

Population-scale cross-sectional observational study for AI-powered TB screening

on one million CXRs.

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Traditional tuberculosis (TB) screening involves radiologists manually reviewing

chest X-rays (CXR), which is time-consuming, error-prone, and limited by

workforce shortages. Our AI model, AIRIS-TB (AI Radiology In Screening TB), aims

to address these challenges by automating the reporting of all X-rays without

any findings. AIRIS-TB was evaluated on over one million CXRs, achieving an AUC

of 98.51% and overall false negative rate (FNR) of 1.57%, outperforming

radiologists (1.85%) while maintaining a 0% TB-FNR. By selectively deferring

only cases with findings to radiologists, the model has the potential to

automate up to 80% of routine CXR reporting. Subgroup analysis revealed

insignificant performance disparities across age, sex, HIV status, and region of

origin, with sputum tests for suspected TB showing a strong correlation with

model predictions. This large-scale validation demonstrates AIRIS-TB's safety

and efficiency in high-volume TB screening programs, reducing radiologist

workload without compromising diagnostic accuracy.

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PMID: 40634545

**33. Sci Rep. 2025 Jul 9;15(1):24701. doi: 10.1038/s41598-025-09593-9.**

Physical activity intensity and amount are inversely correlated with the risk of

tuberculosis in patients with diabetes.

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One of the crucial risk factors for tuberculosis (TB) is diabetes mellitus (DM),

and physical activity could afford protective effects for the former disease

entity. We aimed to evaluate the association between physical activity

(intensity and amount) and TB development in individuals with type 2 DM (T2DM)

among the South Korean nationwide cohort. Using the Korean National Health

Information Database, we screened individuals who underwent the national health

examination between 2009 and 2012 and identified 2,437,443 eligible individuals

with T2DM. They were followed up to the date of TB notification, death, censor,

or until December 2018. We identified 21,275 individuals with newly developed TB

(active TB, either pulmonary or extrapulmonary). Physical activity was evaluated

according to the health examination questionnaire, categorized them by activity

intensity (walking, moderate, and vigorous) and amount measured by metabolic

equivalent task minutes per week (METs-min/week). To estimate the adjusted

hazard ratio (aHR) of risk factors for TB, we used the multivariate Cox

proportional hazard models. The risk of developing TB declined with increasing

activity intensity. Individuals with vigorous activity had the lowest risk for

TB (aHR 0.85, 95% confidence interval [CI] 0.82-0.89) compared with individuals

without vigorous activity. The risk of TB development decreased with increasing

amount of activity. Individuals ≥ 1,500 METs-min/week had the lowest risk for TB

(incidence rate 1.22/1000 person-years, aHR 0.84, 95% CI 0.80-0.88) compared

with individuals < 500 METs-min/week. Physical activity intensity and amount

were inversely correlated with TB risk in individuals with T2DM.

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PMCID: PMC12241468

PMID: 40634446 [Indexed for MEDLINE]

**34. Math Biosci. 2025 Jul 7;387:109503. doi: 10.1016/j.mbs.2025.109503. Online ahead of print.**

Dynamics of bovine tuberculosis transmission in mixed herds in Chad.

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Africa.

We consider a model for the spread of bovine tuberculosis in herds comprising

three species (bovids, caprids and equids) in Chad. The epidemiological model is

built on top of a classic Lotka-Volterra competition model, which is exploited

in a regime where stable coexistence of the three species holds. The

epidemiological model itself is an SLI model, because of the absence of

treatment for herds in the area. After studying some mathematical properties of

the model, we perform a short computational analysis, investigating sensitivity

of the model and comparing solutions with and without competition. To gain more

understanding on the timing of events, we also consider the continuous time

Markov chain analogue of the model.

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PMID: 40633723

**35. Clin Infect Dis. 2025 Jul 9:ciaf363. doi: 10.1093/cid/ciaf363. Online ahead of print.**

Long-term outcomes among people with multi-drug resistant tuberculosis in

Vietnam: a prospective cohort study.

MacLean EL(1), Pham YN(2), Pham CD(2), Nguyen BC(3), Garden FL(4), Hasan T(1),

Nguyen TA(2)(5), Dinh VL(6)(7), Nguyen HB(6)(7), Nguyen NV(8), Marks GB(3)(9),

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**INTRODUCTION:** Existing rates of death and recurrent TB among people treated for

rifampicin- or multidrug-resistant tuberculosis (RR/MDR-TB) are likely

underestimates. We determined long-term disease outcomes among a cohort of

people treated for RR/MDR-TB.

**METHODS:** We conducted a prospective cohort study among patients treated by the

National TB Program (NTP) in ten provinces of Vietnam. Individuals with

confirmed RR/MDR-TB starting World Health Organization-recommended regimens were

followed up for ≥32 months. After this period, we surveyed the cohort to measure

vital status and subsequent TB episodes. Family members completed verbal

autopsies for deceased participants. We calculated rates of mortality and TB

re-occurrence, and standardized mortality ratio (SMR) using participants'

household contacts as a reference population.

**FINDINGS:** Between March 2016 and July 2020, 1755 patients were enrolled, of whom

we assessed 1364 (77.7%) at final follow-up. Median follow-up time was 4.3

years. Successful treatment outcomes were reported for 1357/1755 (77.3%)

individuals. From enrolment until end of follow-up, 289 participants died

(16.5%, mortality rate 42.6/1000 person-years); overall SMR was 5.6 and

post-treatment SMR was 3.0. TB was the probable or confirmed cause of death in

96 deceased participants. Many (71/165, 43.0%) deaths occurring on-treatment

were not reported to the NTP. The rate of subsequent TB episodes among all

participants, regardless of treatment outcome, was 10.3/1000 person-years.

**INTERPRETATION:** RR/MDR-TB survivors have high risks of mortality and

re-occurring TB. Programmatic reports underestimate the true mortality rate both

during and after treatment. Interventions are urgently needed to strengthen

programmatic follow-up, improve treatment outcomes, and monitor for TB

recurrence.

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Infectious Diseases Society of America.

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**36. J Comput Aided Mol Des. 2025 Jul 9;39(1):45. doi: 10.1007/s10822-025-00626-z.**

Disrupting tuberculosis pathogenesis by targeting DprE1 in cell wall

biosynthesis: a structural dynamics perspective.

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DOI: 10.1007/s10822-025-00626-z

PMID: 40632318

**37. J Infect Dis. 2025 Jul 8:jiaf361. doi: 10.1093/infdis/jiaf361. Online ahead of print.**

Inflammatory macrophages associate with tissue injury and fibrosis in a mouse

model of tuberculosis.

Boucau J(1), Ruelas Castillo J(1), Naidoo T(2)(3), Liu Y(4), Dasgupta S(5), Jain

N(1), Jacobson NE(4)(6), Nargan K(2), Cimini BA(5), Eliceiri KW(4)(6)(7)(8),

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Post-tuberculosis lung disease (PTLD) causes a significant burden of global

disease. While a consensus definition of PTLD is still in development,

parenchymal cavitation, bronchiectasis, and fibrosis are recognized pathologic

features that underlie many symptoms and complications of PTLD. The molecular

mechanisms driving development of each feature are largely unknown. To

facilitate the mechanistic study of tuberculosis (TB)-associated pathologic

tissue remodeling and fibrosis, we adapted a mouse model of infection. The

morphologies of fibrosis observed in mice were similar to those observed in

human tissue samples. Using Second Harmonic Generation microscopy, we found that

fibrillar collagen deposition did not resolve with anti-TB antibiotics.

Inflammatory transcriptional signatures were persistently upregulated during

chronic infection and did not fully resolve after weeks of anti-TB therapy.

Inflammatory and fibrosis-associated macrophages similarly persisted during

treatment. Immunofluorescence microscopy revealed persistent macrophage

populations and shifts in abundance and distribution of type 2 alveolar cells at

sites of fibrogenesis.

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PMID: 40629518

**38. Curr Microbiol. 2025 Jul 8;82(8):373. doi: 10.1007/s00284-025-04319-6.**

Anti-Bacterial Activity of Furan Chalcone Derivatives Against Mycobacterium

tuberculosis: Design, Synthesis, Anti-Bacterial Screening, Pharmacokinetic

Properties, and Toxicity Parameters.

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P(2)(3), Aloyuni S(4), Al Othaim A(2), Ismail A(4)(5), Vijayaraghavan P(6),

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A novel series of fifty furan-based chalcone derivatives and their potential

anti-bacterial activity against Mycobacterium tuberculosis was studied in this

present work. The pharmacokinetic properties and toxicity parameters of these

designed molecules were studied using in silico methods. Physicochemical

parameters were computed for all the designed molecules and Swiss ADME analysis

demonstrated that the designed compounds possess good drug-like properties.

Among them top 10 compounds were selected based on initial ADME screening and

subjected to docking investigations using the Autodock Tool. 1.5.6. The binding

energies and interactions of these compounds with the target protein InhA were

compared with established anti-tubercular medicines (isoniazid and ethionamide).

Based on docking results, the top furan chalcones were synthesized and analyzed

using various spectroscopic techniques such as FT-IR, mass spectrometry, 1H NMR,

and 13C NMR. The synthesized chalcones were further investigated for their

antitubercular efficacy using the Microplate Alamar Blue Assay (MABA) against

the H37Rv strain. Among the tested compounds, DM01, DM02, DM03, DM04, DM05, and

DM07 displayed optimum activity against H37Rv strain cell lines.

Biocompatibility of synthesized top furan chalcone DMO3 was tested on mouse 3T3

fibroblast cells by cell viability or cytotoxicity assay. Phase contrast and

live dead cells fluorescent staining assay used to determine the cytotoxicity.

Tested compound was not recorded any sign of cytopathic effect which was

confirmed by high rate of cell viability with complete absence of cytopathic

effect and apoptosis. Further, the molecular docking studies identified the

binding mechanism of reference drugs (isoniazid and ethionamide) with InhA,

revealing key hydrogen-bond interactions with specific residues.

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Media, LLC, part of Springer Nature.

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**39. Surg Today. 2025 Jul 8. doi: 10.1007/s00595-025-03098-8. Online ahead of print.**

Clinical factors associated with surgical interventions in patients with

intestinal obstruction caused by abdominal tuberculosis.

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**PURPOSE:** Abdominal tuberculosis (TB), including Intestinal TB (ITB) and

peritoneal TB (PTB), can cause intestinal strictures, leading to obstructions.

However, the surgical indications for TB-related intestinal obstructions are yet

to be established. This study investigates the clinical factors associated with

these surgical interventions.

**METHODS:** Eighty-eight consecutive patients with ITB or PTB were enrolled in this

study. The severity of abdominal TB was evaluated by the number of computed

tomography (CT) findings of ascites, peritoneal nodules > 10 mm, intestinal wall

thickening, and peritoneal or omental thickening.

**RESULTS:** Intestinal obstructions were diagnosed in 25 patients. The median

duration of non-operative management was 11 (2-35) days, and 10 of the 25

patients required surgical intervention after non-operative management. The

surgery group had a higher frequency of more CT features (70% vs. 13.3%,

P = 0.0038) and a lower frequency of antitubercular therapy (ATT; 50% vs. 100%,

P = 0.0075) than the non-surgery group. The severity of lung TB had no impact on

the need for surgery and there was discrepancy between the chest and abdominal

CT findings.

**CONCLUSION:** Long-term non-operative management may be required for abdominal TB

and the need for surgical intervention is associated with the ATT and CT

findings.

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Ltd.

DOI: 10.1007/s00595-025-03098-8

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**40. Endocrine. 2025 Jul 8. doi: 10.1007/s12020-025-04352-2. Online ahead of print.**

Clinical and radiological insights into secondary hypophysitis: A single-center

experience with a focus on tuberculosis.

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**PURPOSE:** Secondary hypophysitis (apart from immune checkpoint inhibitor [ICI]

induced) is rare and is largely described in case series. We aim to describe the

distinctive characteristics of the various etiologies of secondary hypophysitis

from a single center.

**METHODS:** A retrospective record review of 44 patients with secondary

hypophysitis (excluding ICI) presenting to our institute between January 2002

and January 2023 was performed. The data of primary hypophysitis managed

medically (n = 39) was retrieved from a prior publication and compared with

common etiologies of secondary hypophysitis.

**RESULTS:** The most common etiologies were histiocytic disorders - Langerhans cell

histiocytosis (LCH) and Erdheim Chester disease (ECD) [n = 23] and tubercular

hypophysitis (TH) [n = 10]. LCH/ECD were characterized by multisystem

involvement, with arginine vasopressin deficiency (AVP-D) [22/23] being the

predominant endocrine presentation. TH patients presented with mass effect

(9/10), focal non-enhancing areas within an enhancing sellar/suprasellar mass on

magnetic resonance imaging (MRI) (10/10), with evidence of tuberculosis

elsewhere in 60%. Though caseating granulomas were universal on histopathology,

bacteriological confirmation was negative in all pituitary specimens. When

compared to primary hypophysitis, isolated infundibuloneurohypophysitis and

AVP-D were more prevalent in LCH/ECD, while the presence of a sellar/suprasellar

mass with focal non-enhancing areas was more frequent in TH. Furthermore,

recovery of the hormonal axis upon follow-up was more common in primary

hypophysitis.

**CONCLUSION:** Secondary hypophysitis in our cohort was predominantly histiocytic

or tubercular in etiology, with LCH/ECD presenting largely with AVP-D and TH

presenting with mass effects, focal non-enhancing areas, and paucibacillary

disease.

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Media, LLC, part of Springer Nature.

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**41. J Epidemiol Glob Health. 2025 Jul 8;15(1):96. doi: 10.1007/s44197-025-00442-6.**

TB Incidence Trends in the Kingdom of Saudi Arabia within the GCC, EMR, and MENA

Regions, to Achieve the WHO and UN's SDG End TB Strategy Targets.

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**OBJECTIVES:** To assess the tuberculosis (TB) incidence trends, between 2000 and

2023, in the Kingdom of Saudi Arabia (KSA), in comparison to that in different

geopolitical regions where the KSA is commonly included within, and to determine

whether the KSA achieved the World Health Organization (WHO) and the United

Nations (UN) Sustainable Development Goals (SDGs) End TB Strategy milestones and

targets, including the reduction of the total TB incidence by 20% in 2020

compared to that of 2015.

**METHODS:** This is a retrospective observational study on the TB incidence per

100,000 population arising in a given year as reported annually to the WHO. The

data was extracted from the WHO indicator dataset. TB incidence data from the

KSA, the World, the Gulf Cooperation Council (GCC), the Eastern Mediterranean

region (EMR), and the Middle East and North Africa (MENA) region were included.

Descriptive analysis and chi-square test were used to compare incidence

differences and their statistical significance.

**RESULTS:** The TB incidence per 100,000 population in KSA in 2023 was 8.4 (95%

uncertainty interval [UI]: 7.6–9.3), in 2020 it was 8.7 (95% UI:7.7–9.6), in

2015 it was 12 (95% UI: 11–13), in 2000 it was 23 (95% UI: 21–26). Compared to

2023, the reduction from 2000, 2015, and 2020 were − 14.6 (63.5% p < 0.01),

− 3.6 (30%), and − 0.3 (3.4%), respectively. Compared to 2015, the reduction in

2020 was − 3.3 (27.5%). For 2023, compared to the GCC countries, the KSA had the

second lowest incidence after the United Arab Emirates (UAE), which was − 7.6

less than KSA (p < 0.01). The incidence in Qatar was the highest, which was

+ 26.6 higher than KSA (p < 0.01). Compared to the MENA and EMR, only Jordan had

a lower incidence, which was − 5.0 less than KSA. Pakistan had the highest

incidence rate and the highest difference from the KSA by + 268.6 (p < 0.01).

**CONCLUSION:** TB incidence trends are decreasing in KSA, and it is among the top

three regional countries with the lowest incidence rates. Compared with 2015,

KSA exceeded the 20% milestone by achieving a 27.5% reduction in 2020. The KSA

is heading towards achieving the WHO and UN’s SDG End TB Strategy targets of a

50% reduction by 2025, 80% by 2030, and 90% by 2035, to fulfill the vision of a

world free of TB.

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PMCID: PMC12237834

PMID: 40627242

**42. Ecohealth. 2025 Jul 8. doi: 10.1007/s10393-025-01726-w. Online ahead of print.**

Genetic Characterization of Mycobacterium Tuberculosis Isolated from Captive Zoo

Animals.

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Zoonotic tuberculosis is a neglected subject that has the potential to impede

the effectiveness of the TB elimination program. The present study aimed to

determine the genetic diversity and drug resistance in the Mycobacterium

tuberculosis isolates from captive wild animals. A total of 67 tissue samples

were collected from 33 animals, comprising 21 wild captive animals from various

species and 12 slaughtered domestic buffaloes. These samples were subjected to

the detection of Mycobacterial species by culture isolation, and further

molecular identification by mPCR, Xpert-Ultra and TrueNat MTB/Rif assay;

followed by drug susceptibility profiling by MTBDRplus and Spoligotyping of the

isolates. Of the 67 samples from captive zoo animals, 44 samples were culture

positive. Of these, 38 isolates were identified as Mycobacterium tuberculosis

Complex (MTBC) and remaining 6 were identified as non- tuberculous mycobacteria

(NTM). All NTM isolates were from different tissues of a Tigress which also had

mixed infection with MTBC. All the 38 culture isolates were further subjected to

phenotypic drug susceptibility testing (pDST) and genotyping. Twenty-eight

(73.69%) of them, were pan-susceptible, 9 (23.68%) exhibited isoniazid

mono-resistance, and 1 (2.63%) was rifampicin mono-resistant. On genotyping, 27

(71.05%) of the samples were classified as 'Orphan'. Ten (26.32%) isolates were

identified as CAS1\_DELHI, clustered within SIT number 375, while one sample

(2.63%) remained unidentified. The drug resistance and genotyping patterns were

similar to the human population. Our results show that M. tuberculosis was major

cause of Zoonotic TB and should be considered as potential reverse zoonotic

agent in India.

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DOI: 10.1007/s10393-025-01726-w

PMID: 40627241

**43. Clin Infect Dis. 2025 Jul 8:ciaf353. doi: 10.1093/cid/ciaf353. Online ahead of print.**

A point-of-care prediction tool for recurrent tuberculosis.

Cox SR(1), Moe AH(2), Gupte AN(3), Kadam A(4), Valawalkar S(4), Gupte N(4)(2),

Lele G(4), Kendall EA(5)(1), Baillie C(2), Barthwal MS(6), Kakrani A(6), Mave

V(4)(2), Dowdy DW(5)(1), Golub JE(2)(5)(1).

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**BACKGROUND:** An estimated 10% of tuberculosis (TB) survivors who have recently

completed treatment in India develop TB again. We sought to develop a

parsimonious model for predicting TB recurrence that can help target

post-treatment active case finding among the highest-risk TB survivors.

**METHODS:** The TB Aftermath trial enrolled TB survivors at treatment completion

from six public TB clinics in Maharashtra, India, and assessed participants at

six-month intervals. Our prediction endpoint was recurrent TB diagnosed within

18 months of treatment completion. Candidate variables included risk factors for

recurrence identified a priori and lung function assessments. We used LASSO

regression to shortlist predictors and estimated probability of recurrence using

logistic regression. We conducted internal validation, assessed discrimination,

and plotted calibration. Model selection was based on practical utility and

predictive accuracy. For our selected model, we identified a cutoff for

achieving 90% sensitivity.

**RESULTS:** Among 1033 participants, we identified 85 (8.2%) recurrences. Several

five-item models measurable at treatment completion had moderate discrimination.

Our selected model included sex, household income, body mass index, peak

expiratory flow from spirometry, and history of multiple TB episodes. The

selected model had a cross-validated c-statistic of 0.69 (95% confidence

interval [CI]: 0.56-0.77) and acceptable calibration (intercept: 0.03 [95% CI:

-0.03-0.09], slope: 0.66 [95% CI: 0.08-1.24). TB survivors with a predicted

probability >3.7% accounted for 90% of recurrences.

**CONCLUSIONS:** A five-item tool, measurable at treatment completion, showed

moderate predictive accuracy for recurrent TB. At scale, a simple five-item

prediction tool may increase the efficiency of post-treatment active case

finding.

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Infectious Diseases Society of America.

DOI: 10.1093/cid/ciaf353

PMID: 40626664

**44. Nat Rev Immunol. 2025 Jul 7. doi: 10.1038/s41577-025-01210-0. Online ahead of print.**

Spatial immunometabolic zonation in tuberculosis granulomas.

Sinha A(1), Weichhart T(2).

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DOI: 10.1038/s41577-025-01210-0

PMID: 40624263

**45. J Epidemiol Community Health. 2025 Jul 7:jech-2024-223465. doi:**

**10.1136/jech-2024-223465. Online ahead of print.**

Associations of municipality-level income and racial segregation with

individual-level tuberculosis treatment outcomes in Brazil: a nationwide cohort

study (2010-2019).

Hall Q(1), Sousa Filho JF(2), Guimarães JM(3), Malta DC(4), Romero-Sandoval

NC(5)(6), Hargreaves S(7), Kerr L(8), Santos GF(9), Brickley EB(10), Paixão

ES(10), Barreto ML(11), Pescarini JM(12)(13); Unit on the Social and

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**BACKGROUND:** Residential segregation is considered a social determinant of

health, but there is limited evidence of its impact on tuberculosis (TB). We

investigated the associations between municipality-level income and racial

segregation and TB treatment outcomes in Brazil.

**METHODS**: We studied nationwide registries of new TB cases between 1 January 2010

and 31 December 2019. TB treatment was dichotomised as unfavourable (ie, loss to

follow-up, modification of treatment regimen, treatment failure and death) and

favourable (ie, cured/treatment completion). We assessed individuals'

municipality-level income and racial segregation (ie, dispersion of household

heads earning ≤half versus those earning >half minimum wage; and of household

heads identifying as black or brown/mixed race (Pardo/a) versus white). Logistic

regression adjusted for sociodemographic and clinical variables was used to

estimate the OR of experiencing an unfavourable treatment outcome associated

with segregation overall and by self-identified race/ethnicity.

**RESULTS**: Individuals living in highly economically and racially segregated

municipalities (fifth versus first quintiles) were more likely to have an

unfavourable TB treatment outcome (income segregation: adjusted OR 1.34 (95% CI

1.31 to 1.37); racial segregation: 1.13 (0.94 to 1.36)). Living in

municipalities of higher income segregation (third, fourth and fifth quintiles)

was associated with higher unfavourable TB treatment outcomes in all

self-identified racial groups (fifth quintile: white 1.25 (0.96 to 1.64); black

1.42 (1.15 to 1.74); brown/mixed 1.37 (1.20 to 1.56); Asian=1.30 (1.00 to 1.69)

and Indigenous 1.37 (1.00 to 1.87)).

**CONCLUSIONS:** Living in highly income and racially segregated environments is

associated with unfavourable TB treatment outcomes for all self-identified races

in Brazil. TB programmes should account for segregation as a barrier to TB

treatment completion.

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by BMJ Group.

DOI: 10.1136/jech-2024-223465

PMID: 40623810

**46. Nat Prod Bioprospect. 2025 Jul 7;15(1):44. doi: 10.1007/s13659-025-00529-4.**

Unlocking potent anti-tuberculosis natural products through structure-activity

relationship analysis.

Abdjul DB(1)(2), Budiyanto F(3), Wibowo JT(3), Murniasih T(3), Rahmawati SI(3),

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Tuberculosis (TB) remains a world health problem due to the high number of

affected individuals, high mortality rates, prolonged treatment durations, and

the increasing prevalence of resistance to commercial TB drugs. The emergence of

resistance to anti-TB drugs has necessitated urgent research into drug discovery

and development, focusing on novel mechanisms of action against Mycobacterium

tuberculosis resistant strains. Natural products, with their remarkable

structural diversity and bioactivity, are promising sources for the development

of new TB drugs or the identification of potential chemical scaffolds exhibiting

potent and novel biological activity with minimal or no cytotoxicity to host

cells. This review focuses on potent anti-TB natural products with minimum

inhibitory concentration (MIC) values below 5 µg mL-1 and examines their

structure-activity relationship (SAR). Significant characteristics and relevant

biological properties of each compound were analysed using a Random Forest,

machine learning algorithm, to explore SAR. Using molecular docking, AutoDock

Vina was utilised to assess molecular interactions with protein targets, and

predictive accuracy was enhanced using the XGBoost machine learning model. These

analyses provide insights into the mode of action of these compounds and help

identify key structural features contributing to their anti-TB activity. In

addition, this review examines the correlation between the potency of selected

anti-TB compounds and their cytotoxicity, offering valuable insights for the

identification of promising scaffolds in TB drug discovery.

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DOI: 10.1007/s13659-025-00529-4

PMCID: PMC12234934

PMID: 40622557

**47. Ann Med. 2025 Dec;57(1):2527949. doi: 10.1080/07853890.2025.2527949. Epub 2025 Jul 7.**

Evaluating the expression level of serum Interleukin-2, lipoarabinomannan and

circulating MicroRNA-29a as diagnostic biomarkers for pulmonary and

extra-pulmonary tuberculosis: a pilot study.

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(CHRI), Chettinad, Academy of Research and Education (CARE), Kelambakkam, India.

**BACKGROUND:** Diagnosis and treatment of Tuberculosis (TB), particularly delay in

diagnosis of TB poses significant challenges in its eradication. The exploration

of new biomarkers is urgently required for TB diagnosis and treatment. This

study aimed to investigate the serum levels of Interleukin-2 (IL-2), an

important diagnostic parameter in TB; lipoarabinomannan (LAM), a key constituent

of the mycobacterial cell wall; and the expression of circulating microRNA-29a

(miR-29a) in serum. MiR-29a contributes to increased susceptibility to TB by

downregulating interferon-γ expression in T cells through post-transcriptional

regulation, thereby exerting an immunosuppressive effect.

**MATERIALS AND METHODS:** The study was conducted on pulmonary TB (PTB),

extra-pulmonary TB (EPTB), and control groups. Serum from the three groups was

isolated, and IL-2 and LAM levels were measured by ELISA. Additionally, q-RT-PCR

was conducted to analyse the expression of microRNA-29a in the serum of some TB

**patients.**

**RESULT:** LAM and IL-2 were significantly upregulated in serum samples from both

the PTB and EPTB groups compared to the control group. Additionally, the

expression of miR-29a was significantly elevated in the EPTB group.

**CONCLUSION:** This study suggests that LAM and IL-2 may be potential diagnostic

biomarkers for both PTB and EPTB, while miR-29a may be a promising marker

specifically for EPTB. However, further evaluation with larger cohort samples is

required to validate the clinical utility of LAM, IL-2, and miR-29a as

diagnostic TB markers.

Plain Language Summary: Serum lipoarabinomannan (LAM), IL-2 and miR-29a might

serve as potential markers for TB diagnosis.

DOI: 10.1080/07853890.2025.2527949

PMCID: PMC12239114

PMID: 40622143 [Indexed for MEDLINE]

**48. Neurol India. 2025 Jan 1;73(1):165-169. doi:**

**10.4103/neurol-india.Neurol-India-D-24-00542. Epub 2025 Feb 7.**

Acute Hemichorea-Hemiballismus in Patients with Tuberculous Meningitis: An

Atypical Manifestation of Stroke.

Garg RK(1), Rizvi I(1), Kumar N(1), Gupta P(1), Tripathi P(1), Arjun Bal KP(1),

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We report two cases of tuberculosis meningitis patients developing

hemichorea-hemiballismus during antituberculosis treatment. First, a 56-year-old

woman experienced right-sided hemichorea-hemiballismus 3 months into treatment.

MRI scans revealed a left thalamus and subthalamic infarct. After 10 days of

continued treatment and corticosteroids, her movements subsided. Second, a

17-year-old female developed hemichorea-hemiballismus while on antituberculosis

drugs and corticosteroids. MRI scans displayed ischemic lesions, optochiasmatic

arachnoiditis, gyral enhancement, and a small tuberculoma. After shunt surgery

and tetrabenazine treatment, she significantly improved and resumed daily

activities. In conclusion, hemichorea-hemiballismus may paradoxically occur in

tuberculosis meningitis patients, potentially linked to ischemic lesions in the

thalamus and subthalamus.

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DOI: 10.4103/neurol-india.Neurol-India-D-24-00542

PMID: 40652488 [Indexed for MEDLINE]

**49. Arch Bronconeumol. 2025 Jun 16:S0300-2896(25)00219-4. doi:**

**10.1016/j.arbres.2025.06.006. Online ahead of print.**

Traumatic Pneumatoceles Mimicking Pulmonary Tuberculosis.

[Article in English, Spanish]

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DOI: 10.1016/j.arbres.2025.06.006

PMID: 40651935

**50. J Infect Public Health. 2025 Jul 5;18(10):102890. doi:**

**10.1016/j.jiph.2025.102890. Online ahead of print.**

Prevalence and species diversity of non-tuberculous mycobacteria in North Texas.

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**BACKGROUND:** Non-tuberculous mycobacterial (NTM) infections are an emerging group

of related opportunistic pathogens resembling tuberculosis (TB) infections with

a wide virulence spectrum. The diversity of the causative agents of NTM disease

underscores the need for swift identification, as it differs by geographic

regions, and treatment approaches vary. This study aimed to determine the

prevalence of Non-tuberculous Mycobacteria recovered in North Texas.

**METHODS:** A retrospective study was conducted between January 1, 2022, to

December 31, 2023. We included 15,724 pulmonary and extra-pulmonary specimens

submitted to Acid Fast Bacilli (AFB) culture. A total of 820 specimens growing

with the Mycobacterial species were counted for the final analysis. Species

prevalence, site of growth, and seasonal trends were evaluated at our site.

**RESULTS:** In a total of 15,724 AFB cultures (5.21 %, n = 820), specimens were

positive for twenty-four different species/subspecies of mycobacteria. Overall,

the prevalence of NTM was (5.05 %, n = 795). Out of 820, the incidence of NTM

was (97 %, n = 795) and M. tuberculosis complex (3 %, n = 25). 15.4 % (704/4574)

of NTM were isolated from pulmonary and 0.82 % (91/11,150) from extra-pulmonary

specimens. (63 %, n = 514) were slow-growing mycobacteria. The major NTM species

were M. avium complex (MAC) (46 %, n = 375), followed by M. abscessus complex

(23.78 %, n = 195), M. chelonae (4.9 %, n = 40), M. mucogenicum phocaicum

(3.9 %, n = 32), and M. arupense (2.1 %, n = 17). Notably, MAC had cyclical low

points in July and February but peaked in October. There was no seasonal pattern

for M. abscessus complex.

**CONCLUSIONS:** Our findings revealed that the frequency of NTM was much higher

than TB. Remarkably, the prevalence of M. avium complex and M. abscessus complex

occupies the top rank, with the emerging M. chelonae and M. mucogenicum

phocaicum. This warrants a precise analytical approach to identify the NTM as

the diverse geographical distribution and the needed species-specific treatment

regimen to adopt control measures.

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DOI: 10.1016/j.jiph.2025.102890

PMID: 40651294

**51. Molecules. 2025 Jul 3;30(13):2845. doi: 10.3390/molecules30132845.**

Oligosaccharide Lactate Nanoparticles Enhance Tissue Targeting: A Case Study of

the Controlled Delivery of Bedaquiline to Cardiac Tissue in TB Pericarditis.

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Sciences, University of the Witwatersrand, Johannesburg 2193, South Africa.

Bedaquiline is known to shorten the duration of therapy of tuberculosis but has

limitations, e.g., poor solubility and adverse effects such as prolongation of

the QT interval. In this study, bedaquiline was incorporated into an inherently

targeted nanosystem for improved permeation of the drug, with ex vivo diffusion

studies performed to investigate its penetration. The bedaquiline-loaded

mannan-chitosan oligosaccharide lactate nanoparticles were prepared by a

one-step ionic gelation probe sonication method. A PermeGear 7-in-line

flow-through diffusion system was used for the ex vivo diffusion studies across

porcine and human pericardia. Bedaquiline-loaded nanoparticles with a particle

size and potential of 192.4 nm and 40.5 mV, respectively, were obtained. The

drug-loaded mannan-chitosan nanoparticles had an encapsulation efficacy of 98.7%

and drug loading of 0.6%. Diffusion data indicated a steady-state flux of 2.889

and 2.346 µg.cm-2.min-1 for porcine and human pericardia, respectively. The

apparent permeability coefficients were calculated to be 2.66 × 10-4 cm.min-1

and 2.16 × 10-4 cm.min-1 for porcine and human pericardia, respectively. The lag

phases were 52.72 min and 0 min for porcine and human pericardia, respectively.

The drug permeation indicated a consistent and linear diffusion pattern across

both porcine and human pericardia, additionally approving the porcine

pericardium as a great comparable tissue to human tissue for pericardial

studies. This study is the first to demonstrate ex vivo diffusion of

bedaquiline-loaded, macrophage-targeted chitosan-mannan nanoparticles across

both human and porcine pericardia, representing a novel platform for

disease-targeted, localized treatment of TB pericarditis.

DOI: 10.3390/molecules30132845

PMID: 40649359 [Indexed for MEDLINE]

**52. J Clin Med. 2025 Jun 20;14(13):4398. doi: 10.3390/jcm14134398.**

Gastrointestinal Tuberculosis: Clinical Presentations and Diagnostic Approaches.

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**Background:** Gastrointestinal tuberculosis (GI TB) is a rare form of

extrapulmonary TB that often mimics other conditions, such as Crohn's disease

(CD) or GI malignancies. Conventional diagnostics, like direct microscopy and

culture, are often inconclusive or slow, delaying treatment. In Germany, a

low-incidence country, GI TB is underrecognized. Rising migration has led to a

resurgence of TB cases, increasing the likelihood of encountering extrapulmonary

presentations. This study evaluates the performance and utility of various

diagnostic tools and proposes a diagnostic approach to reduce delays and avoid

unnecessary interventions. **Methods:** We retrospectively analyzed eight patients

suspected of GI TB based on clinical presentation and testing. Two recent cases

are described in detail to highlight diagnostic and therapeutic challenges.

**Results:** GI TB was confirmed in five cases (62.5%), and all the patients

presented with abdominal complaints, with the majority experiencing systemic

symptoms such as weight loss or fever. Histopathology supported the diagnosis in

all GI TB cases, while PCR testing was positive in four. Direct microscopy

detected acid-fast bacilli in only one case. The remaining patients were

diagnosed with latent genital TB, disseminated TB without GI involvement, or

were ruled out clinically. **Conclusions:** GI TB remains a diagnostic challenge

that often mimics other conditions, such as CD or malignancy. Early use of

histopathology and PCR in patients with a high risk of GI TB is critical for

timely diagnosis. In low-incidence settings like Germany, clinicians should

maintain high suspicion in at-risk populations (e.g., migrants from areas or

immunocompromised patients), especially when symptoms mimic CD or malignancy, to

improve outcomes and avoid unnecessary procedures.

DOI: 10.3390/jcm14134398

PMCID: PMC12249606

PMID: 40648784

**53. Healthcare (Basel). 2025 Jun 27;13(13):1534. doi: 10.3390/healthcare13131534.**

Evaluating the Knowledge, Attitude, and Practice of Tuberculosis Among Health

Sciences Students.

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East Avenue, North Cyprus, 99138 Mersin 10, Turkey.

**Background**: Liberia is among the 30 countries with a high burden of tuberculosis

worldwide. Health sciences students, who are future health professionals, have

essential roles in curtailing the spread of TB. This study aims to evaluate the

knowledge, attitude, and practice (KAP) of tuberculosis (TB) among health

sciences students. **Methods:** This study used a quantitative cross-sectional

design to assess Medical, Pharmacy, and Public Health students at the University

of Liberia's KAP regarding TB using a modified previously used self-administered

questionnaire reviewed by subject experts from 1 April 2025 to 23 April 2025.

SPSS 26 was used for analysis. Descriptive statistics, Mann-Whitney,

Kruskal-Wallis, and multivariate logistic regression tests were used for

analysis. **Results:** In total, 630 students participated, of which 51.7% were

females, 83% were aged 24 or above, 81.6% were single, and 96.7% had never

smoked. The KAP levels were 65.9%, 97.3%, and 94.8%, respectively. Higher TB

knowledge was significantly associated with being enrolled in the Medical

program (OR = 2.20, 95% CI: 1.28-3.76, p < 0.05), being in year 4 and 5 (OR =

1.79, 95% CI: 1.09-2.98, p < 0.05; OR = 2.28, 95% CI: 1.08-4.78, p < 0.05),

being unemployed (OR = 1.58, 95% CI: 1.09-2.31, p < 0.05), and having personal

acquaintance with individuals diagnosed with TB (OR = 1.64, 95% CI: 1.11-2.42, p

< 0.05). **Conclusions:** The knowledge level among students was good. They had a

positive attitude, and their practice levels were good. However, gaps remain in

understanding latent TB and proper disinfection methods for TB-related

materials. Strengthening the health curriculum to address these specific

knowledge gaps is recommended to better align students' knowledge with their

attitudes and practices.

DOI: 10.3390/healthcare13131534

PMCID: PMC12248818

PMID: 40648559

**54. Cancers (Basel). 2025 Jul 2;17(13):2224. doi: 10.3390/cancers17132224.**

New Vistas in Mycobacterium tuberculosis Infection and Its Association with Lung

Cancer Development.

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Lung cancer is the leading cause of cancer-related mortality worldwide, with the

American Cancer Society estimating approximately 124,730 deaths from lung cancer

in 2025 [...].

DOI: 10.3390/cancers17132224

PMID: 40647522

**55. Adv Clin Chem. 2025;127:221-253. doi: 10.1016/bs.acc.2025.04.006. Epub 2025 Jun 10.**

MDDB: A public databank of host microRNAs in Tuberculosis diagnosis.

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Tuberculosis (TB) remains a major global health challenge due to its high

mortality rate. Several factors contribute significantly including delayed

diagnosis, emergence of drug resistance, and biofilm formation. Although various

diagnostic methods are available for TB, such as sputum smear microscopy,

culture techniques, and real-time polymerase chain reaction (PCR). They have

notable limitations, including false positives and negatives, timeliness, and

high cost. Therefore, there is an urgent need for an early and accurate

diagnostic approach to control the infection. MicroRNA (miRNA)-based diagnostics

have emerged as a promising alternative, offering the potential for earlier

detection and reduced false-positivity. However, this field is still in

development and requires specialized tools to accelerate miRNA research,

streamline the process, and facilitate the creation of innovative diagnostic

methods. To address this need, the MicroRNA Disease Databank (MDDB) was

developed as a centralized platform providing extensive miRNA-related

information. Freely accessible at https://mddb.nitrr.ac.in/., MDDB offers

comprehensive details on miRNA locations, associated disease characteristics,

probe sequences, and molecular mechanisms. This resource aims to support the

development of novel miRNA-based diagnostic biomarkers. This article provides an

in-depth overview of the MDDB tool, highlighting its construction, features, and

accessibility. Currently, MDDB focuses on host miRNAs relevant to TB, allowing

researchers to quickly access critical miRNA data. By leveraging this resource,

researchers will potentially accelerate the development of effective diagnostic

biomarkers for TB and other chronic diseases in the future.

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DOI: 10.1016/bs.acc.2025.04.006

PMID: 40645675 [Indexed for MEDLINE]

**56. Cureus. 2025 Jun 9;17(6):e85661. doi: 10.7759/cureus.85661. eCollection 2025**

**Jun.**

Incidence and Predictors of Drug-Induced Liver Injury in Pediatric Tuberculosis

Patients Under Anti-tubercular Therapy: A Prospective Observational Study.

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**BACKGROUND:** Tuberculosis (TB) remains a significant global health challenge,

particularly in pediatric populations, where effective treatment with

anti-tubercular therapy (ATT) is often complicated by adverse drug reactions.

Drug-induced liver injury (DILI) is among the most serious complications of ATT,

and identifying risk factors for DILI in children is essential for improving

treatment safety and outcomes.

**OBJECTIVE:** This study aimed to determine the incidence of DILI in pediatric

TB patients undergoing ATT and identify demographic and clinical factors

associated with its development.

**METHODS:** A prospective observational study was conducted over 18 months at a

tertiary care center in South India. Fifty children aged 1-14 years diagnosed

with TB and initiated on ATT were enrolled. Liver function tests (LFTs) were

performed at baseline, one month, and six months, and clinical parameters were

monitored to identify DILI cases. Nutritional status was assessed using WHO

growth standards, and statistical analyses were conducted to identify

significant risk factors.

**RESULTS:** DILI was observed in 16 of 50 patients (32%). Malnutrition was present

in 70% of DILI cases compared to 48% of non-DILI cases (p < 0.05). Female

patients showed a higher incidence of DILI (56%) than males (44%). Baseline

liver enzyme levels, specifically serum glutamic-oxaloacetic transaminase (SGOT)

and serum glutamic-pyruvic transaminase (SGPT), were significantly higher in

patients who developed DILI (p < 0.05). The most common clinical presentation of

DILI was jaundice (50%), followed by anorexia and abdominal pain. Pulmonary

TB accounted for 50% of DILI cases, while CNS TB represented 37.5%.

**CONCLUSIONS:** DILI is a common complication of ATT in pediatric TB patients, with malnutrition, female gender, and elevated baseline liver enzymes identified as significant risk factors. Routine liver function monitoring and nutritional

interventions should be integral to TB management in children to mitigate the

risk of DILI and improve treatment outcomes.

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**Jun.**

A Pathogen's Whisper: Reactivation of Quiescent Membranous Nephropathy by

Disseminated Tuberculosis.

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Primary membranous nephropathy (MN) is an autoimmune glomerular disease commonly

associated with anti-PLA2R antibodies, with relapses typically attributed to

spontaneous immune reactivation. We report the first documented case of a

relapse of primary, PLA2R-positive MN that was temporally and immunologically

linked to disseminated tuberculosis (TB) infection. A 42-year-old man,

previously in complete remission, developed severe nephrotic syndrome and acute

kidney injury unresponsive to standard immunosuppressive regimens. Concomitant

diagnosis of miliary TB was confirmed by culture and imaging. Remarkably, the MN

relapse resolved completely with anti-TB therapy alone, without further

immunosuppression, and remission has been sustained for over two years. This

case highlights infection, specifically TB, as a modifiable and overlooked

trigger of MN relapse, potentially via molecular mimicry or system immune

activation. In TB-endemic regions, identifying infectious triggers early in

relapsing MN may spare patients from unnecessary immunosuppression and

facilitate long-term remission through targeted antimicrobial therapy.

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**Jun.**

Recurrent Abdominal Wall Abscess as an Atypical Presentation of Peritoneal

Tuberculosis: A Case Report.

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Peritoneal tuberculosis (TB) is an uncommon yet important form of extrapulmonary

TB, often presenting a diagnostic challenge due to its nonspecific symptoms and

diverse clinical manifestations. We report the case of a 38-year-old woman with

type 2 diabetes mellitus, hypertension, chronic kidney disease, and a history of

peritoneal dialysis, who presented with recurrent abdominal pain, fever, night

sweats, and seropurulent discharge following prior abscess drainage. Despite

empirical antibiotic therapy, her symptoms persisted. Imaging revealed

intra-abdominal fluid collections and pneumoperitoneum, raising suspicion of

intestinal perforation. Surgical exploration revealed a frozen abdomen with

multiple cold abscesses, dense fibrous adhesions, and tubo-ovarian involvement.

Histopathological examination confirmed peritoneal TB, showing caseous necrosis

and Langhans giant cells. This case underscores the diagnostic complexity of

tuberculous peritonitis, particularly in patients with a history of peritoneal

dialysis and risk factors associated with endemic exposure to TB. Due to its

overlap with intra-abdominal malignancies and other chronic infections, a high

index of suspicion, histopathological confirmation - often via laparoscopy - and

early initiation of anti-tuberculous therapy are critical for effective

management and improved outcomes.

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**59. Acta Med Indones. 2025 Apr;57(2):237-240.**

Unusual Co-existence of Drug-Susceptible Lung Tuberculosis and Drug-Resistant

Pleural Tuberculosis: A Rare Case Presentation of Dual Infection.

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Tuberculosis (TB) has become one of the global burdens of disease, with

increasing morbidity and mortality every year. Tuberculosis can affect not only

the lungs but also the extrapulmonary organs. The prevalence of drug-resistant

tuberculosis (DR-TB) is rising and has caused a higher mortality rate than

drug-susceptible tuberculosis (DS-TB). This article presents a patient with a

rare co-infection of pulmonary DS-TB and pleural DR-TB. Pulmonary and pleural TB

(pTB) was diagnosed using the Xpert MTB/RIF assay. The patient was treated with

an individualized DR-TB regimen and recovered.

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**60. Biochem Biophys Res Commun. 2025 Jul 3;777:152296. doi:**

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Resilience to stress and antibiotics, coupled with immunomodulatory behavior,

uncovers Mycobacterium indicus pranii as a suitable surrogate model for

tuberculosis research.

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Mycobacterium tuberculosis (M.tb) exhibits remarkable adaptability and

persistence within host micro-environments, making tuberculosis a persistent

global health challenge. Finding safe and relevant model organisms to study M.tb

pathobiology is essential for augmenting research in this field. Mycobacterium

indicus pranii (MIP), a non-pathogenic mycobacterial species with known

immunomodulatory properties and established safety in human applications,

represents a promising yet underutilized research model. Within hosts, M.tb

encounters diverse stress conditions including oxidative and nitrosative

challenges, nutrient limitation, pH fluctuations, and immune cell-mediated

pressures, all of which shape its survival strategies. This investigation

presents a thorough evaluation of MIP as an alternative research model through

systematic comparative analyses with the conventionally utilized Mycobacterium

smegmatis (M.smeg). Genomic investigation revealed MIP possesses a significantly

higher number of M.tb-homologous virulence-associated genes and conserved drug

targets as compared to M. smeg, while sharing equivalent human-homologous gene

content with M.tb. Functional assays demonstrated MIP's superior tolerance to

multiple stress conditions relevant to host micro-environments, including

SDS-mediated envelope stress, nitrosative stress, acidic and alkaline pH

extremes, copper toxicity, and elevated temperature-characteristics supported by

the presence of key M.tb stress regulator homologs (sigE, sigH, mprAB, and

Rv2745c). In macrophage infection models, MIP exhibited enhanced intracellular

persistence as compared to M.smeg and induced a balanced cytokine profile

resembling M.tb infection. The distinctive genomic and physiological

characteristics of MIP establish its biological relevance as a superior

surrogate model for investigating mycobacterial stress adaptation mechanisms,

virulence determinants, and host-pathogen interactions, potentially accelerating

discovery of novel therapeutic strategies against tuberculosis.

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**eCollection 2025.**

From pandemic to endemic: assessing the impact of COVID-19 history and

socio-demographic factors on quality of life in tuberculosis patients.

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**BACKGROUND:** Tuberculosis (TB) and COVID-19 are major global health concerns, and

their interaction, particularly regarding socio-demographic factors, remains

insufficiently explored. This study assessed the impact of prior confirmed

COVID-19, alongside age, education, smoking, gender, and marital status, on TB

relapse risk and quality of life (QOL) among TB patients in South-Western

Romania.

**METHODS:** A cross-sectional analysis was performed on 763 bacteriologically

confirmed TB patients enrolled between October 2022 and January 2025.

Participants provided socio-demographic and clinical information and completed

the WHOQOL-BREF questionnaire. Binary logistic regression was used to identify

predictors of TB relapse, while structural equation modeling (SEM) assessed

factors influencing QOL.

**RESULTS:** Patients with a confirmed history of COVID-19 exhibited a twofold

increase in TB relapse risk (OR = 2.08, p = 0.003). Age was a strong predictor,

with individuals aged 36-60 years and those >60 years showing over fivefold

(OR = 5.08, p < 0.001) and nearly fourfold (OR = 3.96, p = 0.004) increases in

relapse risk, respectively. Smoking further increased relapse odds by 76%

(OR = 1.77, p = 0.009). Conversely, secondary and tertiary education

significantly reduced relapse risk (OR = 0.48, p = 0.002; OR = 0.46, p = 0.006).

SEM revealed that COVID-19 history had a pronounced negative impact on QOL

(β = -0.51, p < 0.001), while marital status (β ≈ 0.09, p = 0.022) and education

(β ≈ 0.18, p < 0.001) were positively associated with QOL.

**CONCLUSION:** COVID-19, advanced age, and smoking significantly elevate TB relapse

risk and detrimentally affect QOL, whereas higher education appears protective.

Integrated interventions addressing COVID-19 prevention, smoking cessation, and

socio-economic support are essential to improve TB outcomes and patient quality

of life.

Copyright © 2025 Mitroi, Balteanu, Zlatian, Toma, Catana, Mirea, Camen, Biciusca

and Cioboata.

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**62. Eur J Case Rep Intern Med. 2025 Jun 24;12(7):005548. doi: 10.12890/2025\_005548.**

**eCollection 2025.**

A Case of Polyserositis with Pericarditis Caused by Mycobacterium SPP.

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The incidence of diseases and deaths caused by non-tuberculous mycobacteria

(NTM) has been increasing globally. However, the broad and nonspecific clinical

manifestations of NTM infections make diagnosis challenging, compounded by the

difficulty in isolating NTM organisms. While NTM are rarely associated with

heart disease, including pericarditis, and pleural effusion, such presentations

are exceptional. We report the case of an 85-year-old female who presented with

polyserositis, characterized by pleural and pericardial effusion, and was

diagnosed with an unusual manifestation of NTM infection causing pericarditis.

Initially, the patient was misdiagnosed with tuberculosis, which delayed the

correct diagnosis and appropriate treatment. Upon accurate diagnosis, her

condition improved with adjustments to the treatment regimen. This case

highlights the importance of considering NTM infection in the differential

diagnosis, particularly when faced with atypical presentations. Early

recognition and timely microbiological testing are crucial for accurate

diagnosis, enabling targeted treatment and improving patient outcomes.

LEARNING POINTS: Non-tuberculous mycobacteria infection can have non-specific

presentations such as weight loss and night sweats, which are similar to

lymphomas and tuberculosis.Unusual presentations of non-tuberculous mycobacteria

infection, such as pleural effusions and pericarditis, can occur.Diagnosis is

needed to ensure the correct treatment and may require polymerase chain reaction

testing.

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**63. Eur J Case Rep Intern Med. 2025 Jun 18;12(7):005590. doi: 10.12890/2025\_005590.**

**eCollection 2025.**

Tuberculous Meningitis and Hemophagocytic Lymphohistiocytosis in a Patient on

Adalimumab: Diagnostic Challenges in the Setting of Suspected Non-Tuberculous

Mycobacteria Co-Infection.

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**BACKGROUND:** Tumour necrosis factor-alpha (TNF-alpha) inhibitors increase

susceptibility to granulomatous infections, including both Mycobacterium

tuberculosis (MTB) and nontuberculous mycobacteria. We describe a complex case

of sequential disseminated Mycobacterium avium complex (MAC) and central nervous

system MTB infection in a patient treated with adalimumab, complicated by

hemophagocytic lymphohistiocytosis (HLH).

**CASE REPORT:** A 65-year-old man on long-term adalimumab for psoriasis presented

with prolonged fever, hepatosplenomegaly, cytopenia and elevated inflammatory

markers. Bone marrow aspiration revealed hemophagocytosis and liver and bone

marrow biopsy revealed granulomatous inflammation. Polymerase chain reaction

(PCR) testing of bronchoalveolar lavage (BAL) fluid identified MAC, supporting a

diagnosis of disseminated MAC-associated HLH. The patient responded to triple

MAC therapy (azithromycin, ethambutol, rifampicin), intravenous immunoglobulin

and low-dose corticosteroids, with rapid clinical improvement. Three months

later, he was readmitted with fever and altered mental status. Brain magnetic

resonance imaging showed meningeal thickening. Lumbar puncture revealed

cerebrospinal fluid pleocytosis, hypoglycorrhachia and elevated protein. PCR

detected MTB complex deoxyribonucleic acid and a rifampicin resistance gene,

prompting the initiation of a four-drug antituberculosis regimen (isoniazid,

pyrazinamide, levofloxacin, ethambutol) and high-dose dexamethasone. The patient

improved and was discharged after a month of hospitalization, remaining

clinically stable at 1-year follow-up.

**CONCLUSION:** This case highlights the risk of sequential or overlapping MAC and

MTB infections in patients receiving TNF-alpha inhibitors, the potential for HLH

as a serious complication, and the diagnostic value and limitations of BAL PCR

testing. Vigilant screening and multidisciplinary management are essential in

such high-risk populations.

**LEARNING POINTS:** The increased risk of opportunistic infections associated with

long-term tumour necrosis factor-alpha inhibitor use necessitates ongoing

infection screening.Hemophagocytic lymphohistiocytosis triggered by

mycobacterial infections requires prompt recognition and targeted

treatment.Polymerase chain reaction results should be interpreted with caution

in complex clinical scenarios, as deoxyribonucleic acid detection may indicate

colonization rather than active infection.

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**64. Eur J Case Rep Intern Med. 2025 Jun 11;12(7):005475. doi: 10.12890/2025\_005475.**

**eCollection 2025.**

(18)FDG PET/CT is Sensitive but not Specific for Malignancy: Two Cases of

Disseminated Tuberculosis Mimicking Metastatic Cancer on Imaging and Clinical

Presentation.

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**INTRODUCTION:** 18Fluorodeoxyglucose positron emission tomography/computed

tomography (18FDG PET/CT) scan is widely used in the evaluation of suspected

tumoral processes. In addition to its oncological applications, it is also

employed in the diagnosis and follow-up of various conditions, including

multiorgan tuberculosis.

**CASE DESCRIPTION:** We report a case series of two young patients with exclusive

extrapulmonary disseminated tuberculosis that mimicked a neoplastic process both

clinically and on 18FDG PET/CT imaging. Initially, both patients were admitted

to the oncology unit with a presumed diagnosis of cancer. However, following an

exhaustive work-up, a definitive diagnosis of tuberculosis was established via

histopathological and microbiological analysis.

**CONCLUSION:** These cases underscore the importance of considering disseminated

tuberculosis as a differential diagnosis during oncologic evaluations,

especially in patients from endemic regions, and highlight the potential

psychological impact of prematurely labelling a condition as cancer.

**LEARNING POINTS:** Extrapulmonary tuberculosis can mimic metastatic

malignancies.Imaging does not replace pathology, which remains the gold standard

for accurately diagnosing multiorgan involvement.Prematurely announcing a

diagnosis of cancer before final confirmation can have significant psychological

consequences.

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**65. J Orthop Case Rep. 2025 Jul;15(7):19-22. doi: 10.13107/jocr.2025.v15.i07.5752.**

Tubercular Palmar Ganglion Presenting as a Severe Carpal Tunnel Syndrome - A

Case Report.

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**INTRODUCTION:** Tuberculous tenosynovitis is a rare condition predominantly found

in developing countries that require prompt medical intervention. Due to its

atypical presentation, diagnosis through biopsy and culture is necessary to

distinguish it from other diseases. Compound palmar ganglion is an unusual

manifestation that can cause swelling around the wrist joint and potentially

compress the neural structures, resulting in carpal tunnel syndrome.

**CASE REPORT:** A 27-year-old female, homemaker complained of pain and tingling

sensations in her right hand. Radiological analysis revealed juxta-articular

osteopenia with soft tissue swelling. Magnetic resonance imaging identified a

spongy soft tissue lesion compressing the median nerve over the flexor

retinaculum of the right wrist. The decision was to surgically explore and

excise the lesion along with carpal tunnel release. Histopathological

examination confirmed tubercular tenosynovitis.

**CONCLUSION:** Tubercular compound ganglion is a rare condition that must be kept

in mind while treating patients with carpal tunnel syndrome, especially in

developing countries where tuberculosis is prevalent. Delayed diagnosis is

common due to gradual progression and subtle symptoms except for swelling.

Surgical intervention and antitubercular treatment are crucial components of

compound palmar ganglion management. Early diagnosis and management are

essential for preventing complications.

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**66. J Aerosol Sci. 2025 Sep;189:106633. doi: 10.1016/j.jaerosci.2025.106633. Epub**

**2025 Jun 10.**

Dynamic of infectious aerosols generated by cough from patients with pulmonary

tuberculosis.

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Tuberculosis (TB) is an ancient disease transmitted through aerosols frequently

generated by coughing and it is still unknown whether there is variability in

cough aerosol output throughout the day and whether this may impact patients'

infectivity categorization. To study the dynamic of infectious aerosols

generated by cough, we conducted a cross-sectional study on pulmonary TB

patients (n=16) who had their cough-generated aerosols sampled twice daily for

two consecutive days for the Cough Aerosol Sampling System (CASS) assay. Most

patients were classified as Variable Low Producers and Variable High Producers

(n=10; 62.5%), followed by Negative Producers (n = 4; 25%) and Consistent

Producers (n = 2; 12.5%). Additionally, most recovered bacilli (88.7 %) within a

respiratory aerosol size range. Although the time of collection did not appear

to impact on aerosol infectivity, performing CASS with multiple samples allowed

for more accurate detection and distinction among aerosol producers.

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**67. Therapie. 2025 Jun 23:S0040-5957(25)00079-4. doi: 10.1016/j.therap.2025.06.003. Online ahead of print.**

Preventing the risk of tuberculosis with teriflunomide: Is pre-treatment

screening necessary?

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**68. bioRxiv [Preprint]. 2025 Jul 1:2025.06.26.661674. doi:**

**10.1101/2025.06.26.661674.**

Thienopyrimidine amide analogs target MmpL3 in Mycobacterium tuberculosis.

Baldin VP, Harding CL, Quach D, Sugie J, Pogliano J, Parish T.

**OBJECTIVES:** The identification of novel agents with mechanisms of action

distinct from those currently utilized in tuberculosis treatment remains a

significant challenge. The mycobacterial protein MmpL3 has emerged as a

promising drug target due to its essential role in the synthesis of the cell

wall of Mycobacterium tuberculosis . We previously identified novel

thienopyrimidine amides with good anti-tubercular activity.

**METHODS:** We profiled a subset of thienopyrimidine amides determining activity

against intracellular bacteria and bactericidal activity against replicating

bacteria. We ran assays to determine mode of action by measuring cell wall

stress, ATP production, and bacterial cytological profiling. We determined

activity against a strain of M. tuberculosis with mutations in MmpL3. We

isolated and sequenced resistant mutants.

**RESULTS:** We tested five analogs against a strain of M. tuberculosis with

mutations in MmpL3 and determined that they lost potency. Analogs induced P

iniBAC , a reporter for cell wall stress, and led to an ATP boost characteristic

of cell wall inhibitors. Bacterial cytological profiling of a representative

compound revealed a morphological profile consistent with other MmpL3

inhibitors.

**CONCLUSIONS:** Together, our data support MmpL3 as the most probable drug target

for the TPA analogs and add to the growing list of scaffolds that can inhibit

this vulnerable transporter.

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PMID: 40631218

**69. bioRxiv [Preprint]. 2025 Jul 3:2025.03.28.645957. doi:**

**10.1101/2025.03.28.645957.**

Elimination of senescent cells with senolytic host-directed therapy reduces

tuberculosis progression in mice.

Shee S, Martinez-Martinez YB, Koleske B, Yabaji S, Kobzik L, Kramnik I, Bishai

W.

By eliciting lung necrosis, which enhances aerosol transmission, Mycobacterium

tuberculosis ( Mtb ) sustains its long-term survival as a human pathogen. In

studying the human-like necrotic granuloma lesions characteristic of Mtb

-infected B6.Sst1S mice, we found that lung myeloid cells display elevated

senescence markers: cell cycle arrest proteins p21 and p16, the DNA damage

marker γH2A.X, senescence-associated β-galactosidase activity, and

senescence-associated secretory phenotype (SASP). These markers were also

elevated in Mtb -infected aged wild type (WT) mice but not in young WT mice.

Global transcriptomics data revealed upregulation of pro-survival (PI3K, MAPK)

and anti-apoptotic pathways in Mtb -infected B6.Sst1S macrophages. As senescent

cells are terminally growth-arrested yet metabolically active cells that release

tissue-damaging, immunosuppressive SASP, we treated Mtb -infected mice with a

cocktail of three senolytic drugs (dasatinib, quercetin, and fisetin) designed

to kill senescent cells. Senolytic drug treatment prolonged survival and reduced

Mtb lung counts in B6.Sst1S and aged WT mice to a greater degree than young WT

mice and concomitantly reduced lung senescence markers. These findings indicate

that (1) Mtb infection may induce lung myeloid cells to enter a senescent state

and that these cells may promote disease progression, and (2) senolytic drugs

merit consideration for human clinical trials against tuberculosis (TB).

HIGHLIGHTS: Mtb lung infection results in recruitment of both restrictive and

permissive myeloid cells to the nascent granuloma. Mtb infection induces certain

permissive myeloid cells to enter a senescent state, characterized by cell cycle

arrest and they promote local immunosuppression. Treatment with a Senolytic drug

cocktail, which kills senescent cells, augments host resistance against Mtb

proliferation, lethality and immunopathology.

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PMCID: PMC12236815

PMID: 40631209

**70. Adv Ther (Weinh). 2025 Apr;8(4):2400189. doi: 10.1002/adtp.202400189. Epub 2024 Aug 20.**

CLINICALLY RELEVANT METALLIC NANOPARTICLES IN TUBERCULOSIS DIAGNOSIS AND

THERAPY.

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Globally we are faced with a significant burden of tuberculosis (TB), which is

difficult to eradicate due to patients' non-adherance, and drug-resistant

strains that are spreading at an alarming rate. Novel approaches are required to

improve diagnosis and treatment. Metallic nanoparticles (MNPs) have demonstrated

potential as sensor probes and in combination therapy, which combines MNPs with

antimycobacterial drugs to develop new treatment and theranostic approaches. To

strengthen the theoretical foundation towards the clinical application of TB

nanomedicine, this review focuses on the properties and effectiveness of

therapeutically relevant MNPs. We also elaborate on their antimycobacterial

mechanisms. This review aims to analyze the body of literature on the topic,

pinpoint important empirical findings, and identify knowledge gaps that could

provide a basis for future research endeavors and translation of the

technologies. Current data suggest that MNPs are potential systems for efficient

diagnosis and treatment although additional pre-clinical and clinical research

is needed to bring these technologies to the clinic.

DOI: 10.1002/adtp.202400189

PMCID: PMC12233216

PMID: 40631045

**71. medRxiv [Preprint]. 2025 Jun 30:2025.06.29.25330520. doi:**

**10.1101/2025.06.29.25330520.**

Evaluation of New and Repurposed Tools to Assess Post-Tuberculosis Lung Disease

in Adolescents: A Cross-Sectional Analysis.

Tanzer JR, Lecca L, Sinche BR, Guzman VS, Wyda JJ, Byrne AL, Chiang SS.

**BACKGROUND:** Tuberculosis, even when successfully treated, frequently leads to

long-term sequelae, known as post-tuberculosis lung disease (PTLD). Adolescents

account for over 1 million incident tuberculosis cases each year, and PTLD in

this population may contribute greatly to the global burden of chronic lung

disease. However, research to better understand and prevent adolescent PTLD is

hampered by uncertainty regarding which tools best assess respiratory disability

and lung function in this population.

**METHODS:** In this cross-sectional analysis of 101 adolescent tuberculosis

survivors in Lima, Peru, we administered the St. George's Respiratory

Questionnaire (SGRQ) to assess respiratory disability, and spirometry and

oscillometry to measure lung function. We used factor analysis, correlations,

and structural equation modeling to assess reliability and validity of an

abbreviated SGRQ, oscillometry, and spirometry.

**RESULTS:** Our abbreviated, 18-item SGRQ had high reliability (omega ≥0.90),

internal structure validity (factor loadings for most questions >0.75), and

external validity (correlation: -0.62 with overall health rating). More

participants were able to complete oscillometry vs. spirometry (100% vs. 91.1%,

p <0.0001). Oscillometry metrics had higher reliability (0.82-0.88) than

spirometry metrics (0.62-0.76). SGRQ scores had small correlations with

spirometry and minimal correlations with oscillometry. The combination of the

SGRQ, oscillometry, and spirometry demonstrated good model fit as an overall

assessment of lung health.

**CONCLUSION:** Our findings support the combination of an abbreviated version of

the SGRQ, spirometry, and oscillometry for evaluating adolescent PTLD. These

results pave the way for critical research to better understand the long-term

impacts of tuberculosis on adolescent lung health.

DOI: 10.1101/2025.06.29.25330520

PMCID: PMC12236887

PMID: 40630589

**72. medRxiv [Preprint]. 2025 Jul 5:2025.07.04.25330895. doi:**

**10.1101/2025.07.04.25330895.**

Preferences for Tongue Swab versus Sputum Collection for Tuberculosis Testing: A

Multi-Country Survey.

Manoj Kumar K, Borkman A, Kim A, Crowder R, Ajide B, Alí-Francia K, Chirwa M,

Kamulegeya L, Le H, Trung VN, Venter R, Bimba J, Christopher DJ, Dalay V, Van

Hung N, Muyoyeta M, Nakiyingi L, Van Nhung N, Theron G, Yu C, Zamudio-Fuertes C,

Atim J, Kerkhoff AD, Castro Noriega MDM, Nahid P, Denkinger CM, Cattamanchi A,

Dorman SE, West N.

**BACKGROUND:** Sputum collection for tuberculosis (TB) diagnosis poses challenges

for children, people living with HIV, and those who struggle with sputum

production.Tongue swab-based molecular testing offers a promising non-invasive

alternative, but person-centered research on acceptability is limited.

**METHODS**: We conducted a pragmatic survey across eight countries (Vietnam,

Philippines, South Africa, Nigeria, Zambia, India, Uganda, Peru) among people

with presumptive TB attending primary care facilities. Participants provided

both tongue swab and sputum samples, then completed a 5-10 minute survey about

their collection preferences.

**RESULTS:** From October 2023 to July 2024, 1,297 participants were enrolled

(median age 43 years, 45% female, 13% HIV-positive). Overall, 61% (95% CI:

58-64%) preferred tongue swab collection compared to 22% (95% CI: 20-25%) who

preferred sputum collection and 17% (95% CI: 15-19%) with no preference.

Preference for tongue swab was consistent across demographic and clinical

subgroups, with country-level variation ranging from 47% in South Africa to 74%

in Zambia and Nigeria.

**CONCLUSION:** Strong preference for tongue swab over sputum collection among

individuals with presumptive TB supports this diagnostic innovation's potential

to overcome barriers to timely TB testing, particularly for populations

struggling with sputum production.

DOI: 10.1101/2025.07.04.25330895

PMCID: PMC12236871

PMID: 40630583

**73. Cureus. 2025 Jun 7;17(6):e85543. doi: 10.7759/cureus.85543. eCollection 2025**

**Jun.**

A Mysterious Case of Primary Oral Tuberculosis in a 14-Year-Old Indian Female: A

Diagnostic Enigma in a Case Report.

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Tuberculosis (TB), caused by Mycobacterium tuberculosis, is a chronic infectious

disease that primarily affects the lungs but can involve other parts of the

body, including the oral cavity, which leads to diagnostic challenges. This case

report describes a 14-year-old female patient who presented with persistent

swelling, pus discharge, and pain on the left side of the mandible for six

months. Initial treatment, including incision and drainage, failed to resolve

the symptoms. Imaging and histopathological examination revealed tuberculous

osteomyelitis of the mandible. Despite negative microbiological results, the

diagnosis was confirmed through the presence of granulomatous inflammation with

giant cells on biopsy. The patient was subsequently referred for anti-TB

treatment and showed significant improvement during follow-up. Oral TB, although

rare, should be considered in the differential diagnosis of chronic oral

lesions, especially when standard treatments fail. This case emphasizes the

importance of comprehensive diagnostic approaches, including imaging and

histopathology, which ultimately help initiate the correct treatment as early as

possible.

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DOI: 10.7759/cureus.85543

PMCID: PMC12235066

PMID: 40630367

**74. Medicine (Baltimore). 2025 Jul 4;104(27):e43202. doi:**

**10.1097/MD.0000000000043202.**

Retrospective evaluation of active tuberculosis cases in terms of

chemoprophylaxis indication: A cross-sectional study.

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Medicine, Trabzon, Turkey.

In this study, we retrospectively evaluated the indications for chemoprophylaxis

in active tuberculosis cases and reviewed the risk of latent tuberculosis

infection (LTBI) progressing to active disease. Along with our decisions

regarding LTBI treatment indications, we aimed to determine whether there were

any shortcomings in this area. This study included 422 tuberculosis patients who

were registered at the Provincial Central Tuberculosis Control Dispensary and

diagnosed between 2016 and 2020. This was a single-center retrospective clinical

study. These patients were evaluated in terms of latent tuberculosis treatment

indication criteria in the Tuberculosis Diagnosis and Treatment Guide before

they became patients with tuberculosis. All radiological images of the patients

were evaluated. A total of 422 patients were included in this study. Of these,

147 (34.8%) were women, and 275 (65.2%) were men. When examining the

distribution of patients according to the indications for latent tuberculosis

infection treatment specified in the Ministry of Health's 2019 Tuberculosis

Diagnosis and Treatment Guide, it was found that 6 (1.4%) patients were in

contact with infectious cases, with 3 (50.0%) of these patients under 34 years

old and 3 (50.0%) 35 years old or older. Prophylactic treatment was administered

to 1 patient (33.3%) in the < 34 years age group. One patient with conversion

was identified in the last 2 years, and it was noted that this patient received

prophylaxis. Of the 153 patients with radiological findings compatible with

tuberculosis sequelae, three (2.0%) received prophylaxis. According to the

tuberculosis diagnosis and treatment guide, after adjusting for patients with

common criteria, 164 (38.8%) patients were indicated for LTBI treatment.

However, prophylaxis was only provided to 7 (4.2%) of these patients. The low

rate of chemoprophylaxis observed in our study highlights the importance of

diagnosing and monitoring LTBI. The data obtained will contribute to the

diagnosis and treatment of LTBI.

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PMID: 40629593 [Indexed for MEDLINE]

**75. Gene. 2025 Jul 6;965:149661. doi: 10.1016/j.gene.2025.149661. Online ahead of print.**

Unveiling the response of efflux pump genes to delamanid in Mycobacterium

tuberculosis H37Rv: a transcriptomic analysis.

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Overexpression of efflux pumps has been associated with drug resistance in

Mycobacterium tuberculosis. However, their specific role in delamanid resistance

remains unclear. This study aimed to identify efflux pump genes influenced by

delamanid exposure through transcriptomic analysis. Cultures of M. tuberculosis

H37Rv were exposed to delamanid at a sub-inhibitory concentration of ½ MIC for

24 h and transcriptomic sequencing was performed on exposed and unexposed

cultures. Differentially expressed genes (DEGs) were annotated using the UniProt

database. Transcriptomic analysis revealed that 23 efflux pump genes were

significantly upregulated under delamanid stress, with 17/23 (73.9%) belonging

to the ABC family, 4/23 (17.39%) to the RND family and 2/23 (8.69%) to the MFS

superfamily. Quantitative real-time PCR (qRT-PCR) was conducted to validate the

transcriptomic results for efflux pump genes following exposure of M.

tuberculosis H37Rv to delamanid at ½ and ¼ MIC. qRT-PCR confirmed that 20/23

(86.95%) genes were significantly upregulated at ½ MIC, with 14/20 (70%) of

these belonging to the ABC family. In contrast, only 3/23 (13%) efflux pump

genes demonstrated upregulation at ¼ MIC. This study identified a set of efflux

pump genes significantly upregulated in response to sub-inhibitory

concentrations of delamanid and suggested that ½ MIC is a more suitable

concentration than ¼ MIC for evaluating the expression of efflux pump genes in

response to delamanid in M. tuberculosis.

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PMID: 40628310

**76. Bioorg Chem. 2025 Jul 3;163:108718. doi: 10.1016/j.bioorg.2025.108718. Online**

**ahead of print.**

Targeting drug-resistant tuberculosis: Thioacetamide-substituted benzothiazoles

as bactericidal agents inhibiting type II NADH dehydrogenase.

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The identification of novel anti-tubercular agents that inhibit the function of

less-explored yet essential components of Mycobacterium tuberculosis is

critically needed to address the increasing prevalence of drug-resistant

tuberculosis. The type II NADH dehydrogenase, an indispensable component of the

oxidative phosphorylation pathway, is the entry point of electrons into the

electron transport chain, facilitating ATP production. This enzyme is a

promising drug target because its inhibition leads to a bactericidal response

through energy starvation. In our study, we synthesized a series of 6-isopropyl

benzothiazole derivatives, with various thioacetamide side chains; and assessed

their anti-tubercular efficacy, and specificity toward NADH dehydrogenase

through in vitro studies. The most potent compounds, C4-1 (MIC = 4 μg/mL,

13.042 μM), and C4-11 (MIC = 8 μg/mL, 24.80 μM), exhibited inhibitory effects against mycobacterial strains, exhibiting resistance to FDA approved

anti-tubercular drugs; and demonstrated bactericidal activity with a safety

index exceeding 10. The primary target for these derivatives is proposed to be

type II NADH dehydrogenase, indicated by increased NADH/NAD+ ratios in the

peredox mCherry assay, and from detection of single-nucleotide polymorphisms at

multiple points in the type II NADH dehydrogenase gene coding sequence of the

strains, exhibiting resistance to the compounds C4-1, and C4-11. Additionally,

molecular docking, molecular dynamics, and in silico ADME profiling were

performed on the active compounds.

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PMID: 40627906

**77. J Infect Public Health. 2025 Jul 3;18(10):102888. doi:**

**10.1016/j.jiph.2025.102888. Online ahead of print.**

Non-tuberculosis mycobacterial infection among clinically suspected tuberculosis

in eastern India (2019-2023).

Rout SS(1), Turuk J(2), Dm NS(1), Giri S(1), K A(1), Kumar S(1), Mohanty T(1),

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**BACKGROUND:** Incidence of non-tuberculous mycobacterial (NTM) infections is on

rise globally and poses significant diagnostic and treatment challenges for

tuberculosis as most of them are resistant to anti-tubercular drugs. NTM

susceptibility to drugs varies from species to species and there is no specific

regimen for treatment. We conducted this study to understand the epidemiology of

NTM infections in Odisha from 2019 to 2023.

**METHODS:** All the samples referred from districts suspected for NTM infections

were subjected to culture followed by species identification using line probe

assay (Hain Lifesciences, details). Anti-mycobacterial susceptibility was

determined by MIC breakpoints and the analysis was done as per the Clinical and

laboratory Standard Institute (CLSI) M24S 2018 guidelines.

**RESULTS:** A total of 828 suspected NTM infection samples were included in the

study. Non- tuberculous mycobacteria were found in 67 (8.1 %, 67/828) samples.

The most prevalent non-tuberculous mycobacteria isolated was found to be M.

intracellulare (32.8 %,22/67), followed by M. abscessus (22.3 %, 15/67), M.

fortuitum (11.9 %,8/67), and M. scrofulaceum (8.9 %),6/67). Non tuberculosis

mycobacterial disease was seen from most of the districts but it was more common

in the coastal districts of Odisha like Khordha (29.8 %,20/67), Cuttack

(11.9 %,8/67), Bhadrak (8.9 %,67), Kendrapada (7.4 %,5/67), Balasore (4.4 %,

3/67), Jajpur (4.4 %, 3/67), Puri (7.4 %,5/67). NTM was more prevalent in males

(65.7 %) than females (34.3 %). The MIC breakpoints showed different sensitive

and resistant patterns for NTM isolates. It was seen that M. mucogeniucum was

sensitive to all the drugs tested, M. avium and M. abscessus isolates were

resistant to most of the drugs and sensitive to few drugs like doxycycline,

kanamycin and clarithromycin.

**CONCLUSION:** The increasing prevalence of NTM infections necessitates precise

identification at the species level, coupled with drug susceptibility testing

(DST), to guide targeted therapy. This approach is critical not only for

optimizing patient outcomes but also for mitigating the emergence of

antimicrobial resistance through inappropriate or empirical treatment

strategies.

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PMID: 40627902

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**eCollection 2025.**

Potency of all-D amino acid antimicrobial peptides derived from the bovine rumen

microbiome on tuberculous and non-tuberculous mycobacteria.

Boidin-Wichlacz C(1), Maresca M(2), Correia I(3), Lequin O(3), Point V(4),

Casanova M(4), Reinbold A(2), Iranzo O(2), Huws SA(5), Brodin P(1), Oyama LB(5),

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Despite the availability of antibiotics, tuberculosis (TB), caused by

Mycobacterium tuberculosis, was once again declared the world's leading cause of

death from a single infectious agent in 2023. Furthermore, the rising prevalence

of drug-resistant strains of M. tuberculosis, coupled with the limitations of

existing therapeutics, underscores the urgent need for new antimicrobial agents

that act through different mechanisms, thereby providing novel therapeutic

options. From this perspective, antimicrobial peptides (AMPs) derived from the

bovine rumen microbiome have shown promise against many resistant pathogens and

may therefore offer a promising alternative against TB. Here, we evaluated the

efficacy of AMPs from bovine rumen microbiome, namely the Lynronne 1, 2 & 3 and

P15s as well as their all-D amino acid enantiomers, against non-tuberculous (M.

abscessus, M. marinum and M. smegmatis) and tuberculous (M. bovis BCG, M.

tuberculosis) mycobacteria. In particular, their antimycobacterial activity was

assessed against extracellularly and intracellularly replicating M. tuberculosis

H37Rv pathogenic strain. Their innocuity was further studied by determining

their respective cytotoxicity against human cell lines and hemolytic activity on

human erythrocytes. Finally, their mechanism of action was investigated by a

membrane permeabilization assay and a lipid insertion assay via surface pressure

measurement. Although all-D enantiomers showed increased cytotoxicity to human

cell lines, they still offer a good therapeutic window with improved activity

compared to their L-form counterparts, especially Lynronne 2D all and P15sD all

which emerged as the best growth inhibitors of all mycobacteria. Remarkably, the

all-D enantiomers also demonstrated activity against intramacrophagic

replicating M. tuberculosis H37Rv, with very limited toxicity towards human

cells and no hemolytic activity at their respective minimum inhibitory

concentration. Membrane permeabilization and monolayer lipid insertion assays

suggested that these peptides mostly act by insertion into the mycobacterial

membrane resulting in a rapid membranolytic effect. These findings highlight the

potential of the all-D enantiomers of Lynronne peptides, as attractive

candidates for the development of new anti-TB drugs. Their effective

antibacterial properties combined with low toxicity underscore Lynronne 2D all

and P15sD all as building blocks for the development of promising alternatives

to conventional antibiotics in the treatment of mycobacterial infections,

particularly against M. tuberculosis.

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PMCID: PMC12230336

PMID: 40626169

**79. Open Forum Infect Dis. 2025 Jun 13;12(7):ofaf342. doi: 10.1093/ofid/ofaf342.**

**eCollection 2025 Jul.**

Comparative Analysis of 2 Diagnostic Devices for Detection of Mycobacterium

tuberculosis and Drug Resistance in Almaty, Kazakhstan, to Determine the Optimal

Diagnostic for Local Needs.

Bartels JGE(1), Takenov N(2), Chingissova L(2), Rakisheva A(3), Eleusizova A(3),

Bismilda V(2), Yeraliyeva L(2), Ben Amor Y(1).

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**BACKGROUND:** Rapid, accurate detection of Mycobacterium tuberculosis and drug

resistance is crucial to reduce tuberculosis (TB) burden and prevent development

of drug resistance in high-burden drug-resistant TB regions.

**METHODS:** From December 2021 to July 2022, sputum samples from 1214 adult

patients with presumptive TB in Almaty, Kazakhstan, were tested by BD MAX MDR-TB

(Becton Dickinson), Cepheid Xpert MTB/RIF, and mycobacterial growth indicator

tube (MGIT) liquid culture for detection of TB and drug resistance to rifampicin

(RIF) and isoniazid (INH).

**RESULTS:** When compared with MGIT, BD MAX sensitivity and specificity for TB

detection were 90% and 87%, and Xpert MTB/RIF results were 86% and 92%. For RIF

resistance, BD MAX sensitivity and specificity were 91% and 95%, and Xpert

MTB/RIF results were 94% and 92%. For INH resistance, BD MAX sensitivity and

specificity were 98% and 97%. Whole genome sequencing was conducted for 24

samples with discordant RIF resistance results among the 3 devices to determine

mutations related to resistance. When compared with a composite standard based

on whole genome sequencing and MGIT, Xpert MTB/RIF had higher sensitivity and

specificity for RIF resistance than BD MAX.

**CONCLUSIONS:** Countries with high burden of drug-resistant TB should carry out

national prevalence surveys to assess rates of multidrug-resistant TB and INH

monoresistance. Those with higher rates should consider adopting BD MAX due to

its ability to accurately diagnose RIF and INH resistance.

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**80. Front Immunol. 2025 Jun 20;16:1603338. doi: 10.3389/fimmu.2025.1603338.**

**eCollection 2025.**

A set of plasmatic microRNA related to innate immune response highly predicts

the onset of immune reconstitution inflammatory syndrome in tuberculosis

co-infected HIV individuals (ANRS-12358 study).

Pean P(1), Meng R(1), Benichou E(1)(2), Srey P(3), Dim B(4), Borand L(4)(5),

Marcy O(6), Laureillard D(7), Blanc FX(8), Cantaert T(1), Madec Y(9), Weiss

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**BACKGROUND**: After initiation of combination antiretroviral treatment (cART),

HIV-1/tuberculosis coinfected patients are at high risk of developing

tuberculosis-associated immune reconstitution inflammatory syndrome (TB-IRIS).

MicroRNAs, small molecules of approximately 22 nucleotides, which regulate

post-transcriptional gene expression and their profile has been proposed as a

biomarker for many diseases. We tested whether the microRNA profile could be a

predictive biomarker for TB-IRIS.

**METHODS:** Twenty-six selected microRNAs involved in the regulation of the innate

immune response were investigated. Free plasmatic and microRNA-derived exosomes

were measured by flow cytometry. The plasma from 74 HIV-1+TB+ individuals (35

IRIS and 39 non-IRIS) at the time of the diagnosis and before any treatment

(baseline) of CAMELIA trial (ANRS1295-CIPRA KH001-DAIDS-ES ID10425); 15 HIV+TB-

and 23 HIV-TB+, both naïve of any treatment; and 20 HIV-TB- individuals as

controls were analysed.

**RESULTS:** At baseline, both IRIS and non-IRIS HIV+/TB+ individuals had similar

demographic and clinical characteristics, including sex, age, body mass index,

very low CD4+ cell counts (27 cells/mm3), and plasma HIV RNA load levels (5.76

log copies/ml). Twenty out of 26 plasmatic-microRNAs tested were no different

between IRIS and controls. Twelve of the 26 tested microRNAs showed

statistically significant differences between IRIS and non-IRIS patients

(p-values ranging from p <0.05 to p <0.0001). Among these, five could

discriminate between IRIS and non-IRIS individuals using ROC curve analysis (AUC

scores ranging from 0.74 to 0.92). The combination of two (hsa-mir-29c-3p and

hsa-mir-146a-5p) or three microRNAs (hsa-mir-29c-3p, hsa-mir-29a-3p, and

hsa-mir-146a-5p) identified IRIS with 100% sensitivity and high specificity (95%

and 97%, respectively).

**CONCLUSION:** The combination of at least two or three plasmatic microRNAs known

to regulate inflammation and/or cytokine responses could be used as biomarkers

to discriminate IRIS from non-IRIS in HIV-TB co-infected individuals at the time

of diagnosis and prior to any treatment.

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Blanc, Cantaert, Madec, Weiss and Scott-Algara.

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**Jun.**

Coexistence of Hodgkin's Lymphoma and Tuberculosis in Two Young Adults:

Diagnostic and Management Challenges.

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Tuberculosis (TB), primarily a pulmonary disease, can affect other organs and

has been linked to an increased risk of Hodgkin's lymphoma (HL). Both conditions

share similar clinical manifestations, including fever, night sweats, and weight

loss, making diagnosis challenging. We report two cases of HL with a history of

TB infection in childhood. The first case involved a 20-year-old female

presenting with chronic cough, dyspnea, and weight loss. Imaging revealed an

anterior mediastinal mass, and a biopsy confirmed classical HL. The patient

received ABVD (doxorubicin, bleomycin, vincristine, and dacarbazine)

chemotherapy followed by radiotherapy, leading to partial tumor regression.

However, signs of TB reactivation emerged, prompting anti-TB treatment, which

alleviated the symptoms. The second case involved an 18-year-old male with a

persistent cervical mass initially misdiagnosed as TB lymphadenitis. Despite

prolonged anti-TB therapy, the mass persisted and was later diagnosed as HL

through immunohistochemistry. He underwent ABVD chemotherapy and radiotherapy,

resulting in a favorable response. Together, TB and HL can coexist, complicating

diagnosis and management. Clinicians should prioritize thorough diagnostic

workups, including histopathology and immunohistochemistry, in patients with

persistent lymphadenopathy or atypical TB presentations. Early differentiation

between TB and HL is critical to ensure timely and appropriate treatment.

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Incidence of tuberculosis in the city of Cordoba and its relationship with areas

in need of social transformation: a study from 2015 to 2021.

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**OBJECTIVES:** In 2022, about 17% of Andalusian population lived in disadvantaged

areas, which accounted for 21% of tuberculosis (TB) cases. This concentration of

cases resulted in TB rates in these areas being higher than both the regional

and national averages. The aim of the present study was to understand the

behaviour of TB in terms of person, time, and place in the city of Cordoba

during the period 2015-2021 and its association with areas in need of social

transformation (ANST).

**METHODS:** A retrospective observational analytical study was conducted on cases

reported to the Andalusian Epidemiological Surveillance System (Spanish acronym

SVEA). Membership in ANST was determined by the SVEA.

**RESULTS:** A total of 136 cases were reported, with 26.5% in ANST. The incidence

rate (IR) in the city was 5.97 cases per 100,000 population per year, higher in

ANST (11.82) compared to non-ANST (5.06), RR = 2.34 (95% CI: 1.60-3.42). In

2020, fewer cases were reported (IR: 3.99). The mean age was 44.82 years, lower

in ANST (38.08) than in non-ANST (47.25), with a p-value < 0.05.

Hospitalizations were more frequent in ANST (78% vs. 68%, p = 0.3). In ANST, the

IR was highest in men over 60 years old and lowest in women of the same age. No

significant difference was found between the groups regarding risk factors,

except for HIV status (p = 0.02).

**CONCLUSIONS:** TB incidence rates in Andalusia vary by area of residence. To make

better public health decisions, it is crucial to enhance the collection of

socio-demographic and clinical data related to these cases.

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**83. J Int AIDS Soc. 2025 Jul;28 Suppl 3(Suppl 3):e26483. doi: 10.1002/jia2.26483.**

Introducing differentiated service delivery models for tuberculosis treatment: a

pilot project to inform national policy in Uganda.

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S(7), Murungi M(7), Ddumba I(7), Moore B(1), Burua A(8), Luzze H(8), Quinto

E(8), Sekadde M(8), Byaruhanga R(8), Ajuna P(8), Arinaitwe I(9), Katureebe C(9),

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**INTRODUCTION:** Differentiated service delivery (DSD) models aim to tailor health

services delivery to clients' preferences and clinical characteristics while

reducing the burden on health systems. In Uganda, DSD models developed for HIV

care were adapted to the tuberculosis (TB) services context to mitigate

disruptions from the COVID-19 pandemic and inform national efforts to improve TB

care.

**METHODS:** Beginning in April 2021, four facility-based and five community-based

DSD models were implemented in 28 TB clinics in Kampala and Soroti Regions. All

clients in the intensive (months 1-2) and continuation (months 3-6) phases of

treatment were eligible. Client preference and clinician concurrence determined

model choice. All models allowed TB medication dispensing intervals ranging from

biweekly to multi-month dispensing (MMD; ≥ 2 months). Data abstracted in

December 2022 from TB registers and DSD enrolment tracking tools at 21 of 28

implementing facilities were used to evaluate the intervention. The TB treatment

success rate (i.e. proportion cured or who completed treatment, vs. those who

died, failed, were lost-to-follow-up or had no recorded outcome) in the DSD

cohort was compared to facilities' 2018-2019 results using Fischer's exact test.

**RESULTS:** Most facilities offered one (Kampala) or two (Soroti) facility-based

models and one community-based model. Among 1864 TB clients enrolled between

April 2021 and March 2022, 1822 (97.7%) used ≥ 1 DSD models; 210/1822 (11.5%)

ever switched models. Overall, 70.5% (1284/1822) of clients enrolled in ≥ 1

facility-based model and 40.5% (737/1822) in ≥ 1 community-based model. The use

of community-based models increased during the continuation phase.

Facility-Based Individual Management and Home Delivery were the most-used

models. In the intensive phase, the longest medication dispensation interval was

biweekly for 50.0% of patients, monthly for 41.3% and MMD for 8.8%. During the

continuation phase, the longest interval was biweekly for 0.6%, monthly for

71.7% and MMD for 27.6%. Overall, 1582/1864 (84.9%) clients were successfully

treated, compared to 858/1177 (72.9%) in 2018-2019 (p < 0.001). Seven (0.4%)

patients failed treatment, 32 (1.7%) were lost to follow-up, 101 (5.4%) died and

142 (7.6%) were not evaluated.

**CONCLUSIONS:** TB DSD models were successfully implemented. TB treatment outcomes

under DSD compared favourably to historical outcomes. Investigating factors

affecting MMD use and model choice could further inform programme design.

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**84. J Int AIDS Soc. 2025 Jul;28 Suppl 3(Suppl 3):e26506. doi: 10.1002/jia2.26506.**

Preferences for TB treatment and support delivery models among people living

with TB in Eastern Cape, South Africa: a discrete choice experiment.

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**INTRODUCTION:** South Africa has one of the highest incidence rates of notified

tuberculosis (TB) in the world. Achieving TB control requires strengthening

treatment and support services. The implementation of differentiated delivery

models can be used to improve service quality and enhance retention in

care. This study aimed to identify treatment and support delivery preferences

among people on TB treatment, specifically examining gender differences, to

inform the development of differentiated care models for improving engagement

and retention in TB treatment services.

**METHODS:** A binary, unlabelled, fractional factorial design discrete choice

experiment (DCE) was used to investigate preferences for TB treatment adherence

support and service delivery. Attributes included who provides the support, how

and where support is delivered, medication collection location and frequency of

clinic visits. The DCE was administered to individuals who were currently on or

recently completed TB treatment, and to those at-risk for being lost-to-care.

Data from 284 individuals for the DCE were collected from March to August 2022.

Mixed effects logistic regression models were used as primary analysis tools.

Latent class analysis (LCA) was used to explore heterogeneity in preference

structures.

**RESULTS:** Compared to standard clinic-based treatment collection, participants

preferred collecting their treatment from a mobile community-based location (ß =

0.231; 95% CI: 0.08-0.39), clinic-based fast-tracked pick-ups (ß = 0.539; 95%

CI: 0.38-0.70) or home delivery (ß = 0.563; 95% CI: 0.37-0.75). Participants

also significantly preferred support offered monthly compared to once-off (ß =

0.167; 95% CI: 0.01-0.32). Furthermore, participants preferred face-to-face

support over group (ß = -0.142; 95% CI: -0.27 to -0.02) or phone-based (ß =

-0.222; 95% CI: -0.36 to -0.09) support models. LCA revealed three classes with

statistically similar preference structures; Class 1 (62%) preferred

community-based treatment delivery and support services; Class 2 (28%) preferred

clinic-based support and treatment delivery services; and Class 3 (10%),

preferred self-selected peer navigator or nurse delivered, and group models of

support and prioritised the location of medication pickups, with a preference

for any model other than standard clinic collection.

**CONCLUSIONS:** Though preference structures did not differ by gender, respondents

revealed strong preferences for differentiated service delivery models. Future

TB treatment and support interventions must include both clinic- and

community-based models of care and support to ensure that those living with TB

are provided the greatest access to TB treatment and support services.

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Tuberculosis treatment failure: what are the risk factors? A comprehensive

literature review.

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Tuberculosis (TB), induced by Mycobacterium tuberculosis, is a significant

global health concern. It affects approximately 25% of the global population and

ranks among the primary causes of mortality from infectious diseases.

Notwithstanding progress, TB treatment and diagnosis continue to encounter

substantial obstacles, such as restricted access to precise diagnostics and

efficacious therapies. By 2035, international objectives seek to diminish

tuberculosis-related fatalities by 95% and enhance treatment accessibility.

Multiple factors affect the success of TB treatment, including personal

behaviors, social and demographic circumstances, and concurrent health

conditions. Critical risk factors for suboptimal treatment outcomes encompass

low body mass index, tobacco use, substance abuse, and various demographic

variables, including gender, age, unemployment, geographic location, and

migration status. Co-infections with HIV, diabetes, chronic kidney disease, and

COVID-19 are associated with increased rates of treatment failure. Supplementary

challenges, including loss to follow-up and drug-resistant TB, elevate the

probability of treatment failure. This review's findings intend to furnish

essential insights for policymakers, healthcare professionals, and TB control

programs, enhancing strategies and interventions. The primary objective is to

improve the efficacy of TB management globally, with an emphasis on attaining

superior treatment outcomes, particularly in the most underserved regions.

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