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1. Treatment outcomes of extensively drug-resistant tuberculosis in Europe: a retrospective cohort study.

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BACKGROUND: In 2021, World Health Organization revised of definition of extensive drug-resistant tuberculosis. We aimed to determine treatment outcomes of individuals affected by extensively drug-resistant tuberculosis in Europe.
METHODS: This observational, retrospective cohort study included patients diagnosed with extensively drug-resistant tuberculosis in the World Health Organization European Region from 2017 to 2023. Participating centres collected consecutive, detailed individual data for extensively drug-resistant tuberculosis patients. Data were analysed with meta- and regression methods, accounting for between-country heterogeneity.

FINDINGS: Among 11,003 patients with multidrug-resistant/rifampicin-resistant tuberculosis, 188 (1·7%) from 16 countries had extensively drug-resistant tuberculosis. Of these, 48·4% harboured strains with resistance to bedaquiline (n = 91/188), 34·0% to linezolid (n = 64/188), and 17·6% to both (n = 33/188). The individual composition of anti-tuberculosis regimens was highly variable, with 151 different drug combinations. Among the 156/188 (83·0%) patients with available treatment outcomes, the pooled percentage of successful outcomes was 40·2% (95% confidence interval [95% CI] 28·4%-53·2%). In patients with unsuccessful treatment outcomes (101/156), most experienced treatment failure (n = 57/156 [pooled proportion 37·1%], 95% CI: 26·1%-49·7%) or death (n = 30/156 [pooled proportion 21·3%], 95% CI: 15·7%-28·2%). After adjustment for disease severity, each additional likely effective drug decreased the odds of unsuccessful outcomes (adjusted odds ratio: 0·65, 95% CI: 0·45-0·96) (p = 0·026), whereas being treated in an upper-middle-income country increased the odds of unsuccessful outcomes compared with being treated in a high-income country (adjusted odds ratio: 13·7, 95% CI: 3·7-50·2) (p < 0·001). Compared with other levels of drug resistance, treatment outcomes were significantly worse for extensively drug-resistant tuberculosis.
INTERPRETATION: Only four out of ten patients affected by extensively drug-resistant tuberculosis achieved successful treatment outcomes. These findings highlight the need for adequate, individualised treatment regimens and optimised drug susceptibility testing.
FUNDING: None.

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2. Community-driven strategies and policies for drug-resistant tuberculosis control in Banyumas Regency, Indonesia: A comprehensive 2023 analysis.

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BACKGROUND: Central Java, Indonesia, struggles with low drug-resistant tuberculosis (DR-TB) case detection (33%) and treatment rates (25%), far below the 60% target. Despite policies, including Minister of Health Regulation No. 67/2016 and Presidential Regulation No. 67/2021, along with the National TB Strategy for Tuberculosis Control 2020-2024 have been implemented, targets remain unmet due to weak community involvement. This study analyzed TB policy implementation in high-prevalence Banyumas Regency, focusing on cadres and community organizations.
DESIGN AND METHODS: This qualitative study employed the Van Meter and Van Horn framework to assess policy implementation. Key stakeholders involved informants from Puskesmas (community health centers), TB cadres, TB program holders at the Regency Health Office, and the Mentari Sehat Indonesia Foundation. Data collection involved in-depth interviews with these informants, as well as policy documents, guidelines, and reports from agencies or institutions. Triangulation methods were used to enhance the validity of the findings.
RESULTS: Implementers understood policy standards, supported by consistent communication among Health Offices, community health workers, local organizations, and village leaders. Positive attitudes were reflected in joint commitments and Regional Action Plans. Cadres and communities actively supported case-finding, treatment, education, socioeconomic aid, and stigma reduction.
CONCLUSIONS: Policies lack sufficient local budget allocation. Weak motivation of TB cadres, lack of commitment among regional organizations, and persistent stigma in the community are evident. The Global Fund aids DR-TB control through grants and patient support to ensure treatment adherence. However, sustained

impact requires government attention to policy, human resources, infrastructure, and complementary resources to achieve synergy.

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3.Comparative assessment of line probe assays and targeted next-generation sequencing in drug-resistant tuberculosis diagnosis.

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BACKGROUND: Rapid and accurate detection of drug-resistant tuberculosis (DR-TB) is crucial for ensuring effective treatment, halting transmission and preventing the amplification of resistance. Comparative evaluations of molecular diagnostic assays in high-burden settings are essential for informing clinical decision-making for DR-TB treatment.
METHODS: The Seq&Treat clinical study previously evaluated the performance of two targeted next-generation sequencing (tNGS) workflows, GenoScreen Deeplex

Myc-TB and Oxford Nanopore Technologies Tuberculosis Drug Resistance Test, on direct sediment samples from persons at risk for DR-TB. Hain Line Probe Assay (LPAs-MTBDRplus and MTBDRsl) were run as a comparator test using an aliquot of the same sediment samples. Diagnostic performance of the LPAs and previously established tNGS performance were compared, including sensitivity and specificity, for rifampicin, isoniazid, fluoroquinolones (moxifloxacin, levofloxacin), and amikacin, using a composite reference standard of phenotypic drug susceptibility testing and whole-genome sequencing.
FINDINGS: Among 720 clinical samples tested, MTBDRplus LPA sensitivity for rifampicin and isoniazid was 92.3% (95% CI 88.9-94.8) and 91.9% (88.4-94.4), each significantly lower than ≥95% achieved by both tNGS workflows ($p < 0.01$). For fluoroquinolones (moxifloxacin and levofloxacin), the MTBDRsl LPA and ONT had similar sensitivities (94.3% and 92.7%, and 94.8% and 93.9%, respectively), while GenoScreen outperformed both (97.3% and 96.6%). GenoScreen also demonstrated the highest sensitivity for amikacin resistance (94.6%) compared to LPAs (88.7%) and ONT (88.3%). Complete assay failure rates were low for LPAs (4.9%) and ONT (5.0%) and moderately higher for GenoScreen (8.6%), with differences in single-target failures across all assays.
INTERPRETATION: LPAs demonstrated lower sensitivity and more limited drug resistance detection compared to tNGS workflows, underscoring the advantages of tNGS for improving DR-TB diagnostic algorithms. These findings provide critical evidence to guide updates in DR-TB diagnostic programs.
FUNDING: Support for the Seq&Treat project was provided through funding from Unitaid (2019-32-FIND MDR).

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Conflict of interest statement: Declaration of interests TCR, MS, REC received salary support from FIND through a service contact to UC San Diego. TCR and REC Received grant funding from NIH to develop and evaluate a tNGS solution for drug resistant TB (R01AI176401). TCR and REC are co-inventors on a patent associated with the processing of TB sequencing data (European Patent Application No. 14840432.0 & USSN 14/912,918). Both TCR and REC have transferred all rights and present and future interest in and rights to royalties from this patent to UC San Diego and Translational Genomics Research Institute respectively. TCR is a co-founder, board member and unpaid shareholder of Verus Diagnostics Inc, a company that was founded with the intent of developing diagnostic assays. Verus Diagnostics is not pursuing any drug resistant TB diagnostics nor any diagnostics related to the technology or approaches discussed or mentioned in this manuscript. Verus Diagnostics was not involved in any way with data

collection, analysis or publication of the results of this manuscript. TCR has not received any financial support from Verus Diagnostics. CR has received honoraria payments from Becton Dickinson and she is on the scientific advisory board for Cepheid and bioMérieux. All other authors declare no competing interests.

4. Prevalence and factors influencing drug-resistant tuberculosis in four regions of Ghana.

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INTRODUCTION: The alarming rate of drug-resistant tuberculosis (DR-TB) globally is a threat to treatment success among positive tuberculosis (TB) cases. Studies aimed at determining the prevalence, trend of DR-TB and socio-demographic and clinical risk factors contributing to DR-TB in the four regions of Ghana are currently unknown. This study sought to determine the prevalence and trend of DR-TB, identify socio-demographic and clinical risk factors that influence DR-TB, and analyse the relationship between underweight and adverse drug reactions and treatment outcomes among DR-TB patients in four regions of Ghana.
METHOD: It was a retrospective review conducted over 5 years, from January 2018 to the end of December 2022. The data were retrieved from the DR-TB registers and folders at the Directly Observed Treatment (DOT) centres in the four regions. Analysis of the data was conducted using STATA version 17.
RESULTS: The prevalence of DR-TB in Ashanti was 10.1%, Eastern 5.3%, 27.8% in Central, and 2.7% in the Upper West region for the year 2022. The overall prevalence rate of DR-TB for the period 2018-2022 was 13.8%. The socio-demographic and clinical risk factors that influence DR-TB in the four regions are: age, marital status (aOR 3.58, P-value< 0.00, 95% CI 2.86-4.48), Senior High School (SHS) level of education (aOR 2.09, P-value = 0.01, 95% CI

1.21-3.63), alcohol intake (aOR 0.49, P-value <0.00, 95% CI 0.38-0.63), previously treated (aOR 22.03, P-value<0.00, CI 16.58-29.26), major adverse drug reaction (aOR 125.50, P-value<0.00, 95% CI 58.05-271.34), and minor adverse drug reaction (aOR 23.59, P-value<0.00, 95% CI 18.32-30.39); treatment outcome, cure (aOR 0.52, P-value<0.00, 95% CI 0.41-0.66), completed (aOR 9.67, P-value<0.00, 95% CI 6.56-14.28), relapsed (aOR 2.62, P-value = 0.01, 95% CI 1.33-5.18), Lost-to-Follow-up (LTFU) (aOR 0.45, P-value<0.00, 95% CI 0.29-0.70), and failure (aOR 35.24, P-value<0.00, 95% CI 7.76-159.99). Also, there was an association between underweight and adverse drug reaction (RRR 5.74, P-value<0.00, 95% CI 4.86-6.79) and treatment outcome (RRR 0.79, P-value<0.00, 95% CI 0.74-0.86). CONCLUSION: The study shows that the prevalence of DR-TB in Ghana is low, probably not because the cases have reduced but due to inadequate GeneXpert machines to detect the cases. Age, marital status, education, alcohol intake, previously treated TB cases, adverse drug reactions, underweight, and treatment outcome are factors influencing the development of DR-TB. Therefore, interventions aimed at improving the nutritional status of DR-TB cases and minimising adverse drug reactions will improve treatment outcomes.

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5.Comprehensive analysis of tuberculosis burden trends and attributable risk factors in the BRICS countries from 1990 to 2021, with forecasts for the next 15 years.

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BACKGROUND: The study was to elucidate a comprehensive view of the burden of tuberculosis (TB) from different dimensions.
METHODS: Data were sourced from the Global Burden of Disease 2021. We provided a comprehensive overview of all relevant measures and the associated age-standardized rates per 100 000 (ASR) across BRICS countries. And we analyzed risk factors contributed to TB-related deaths and disability-adjusted life years (DALYs). Additionally, temporal trends in the disease were delineated using a joinpoint regression model, while projections over the subsequent 15 years were generated using the Bayesian age-period-cohort model.
RESULTS: The global age-standardized incidence rate (ASIR) was 103 per 100 000 in 2021, which represented a 40.5% decrease since 1990. Notably, ASIR in China experienced a significant decline of 66.7%. Individuals aged 65 and above were high-risk group for TB. For the Russian Federation, the percentages of deaths and DALYs caused by multidrug-resistant tuberculosis and extensively drug-resistant tuberculosis were approximately 30% and 14% respectively in 2021. Although DS-TB still accounted for the highest proportion of about 55%, it was significantly lower in contrast to other countries, where the rate reached over 80%. And the gradual downward trends of ASIR and ASMR are expected to continue over the period from 2021 to 2036.
CONCLUSIONS: The results indicated that the burden of TB in BRICS countries has decreased over the past 30 years. It highlights an urgent requirement to develop and implement relevant strategies in the prevention and control of TB based on country-specific development status.

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6. Progress of anti-tuberculosis drug targets and novel therapeutic strategies.

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Tuberculosis, a chronic infectious disease caused by Mycobacterium tuberculosis complex, has re-emerged as the leading cause of death worldwide as a single infectious agent. The increasing prevalence of multidrug-resistant tuberculosis and extensively drug-resistant tuberculosis poses a severe and growing threat to global health. Therefore, it is urgent to find new drug targets. Recently, significant advancements have been made in the research of drug targets and novel therapeutic strategies for tuberculosis. This review summarizes recent processes on anti-tuberculosis drug targets, such as cell wall synthesis, nucleic acid replication and transcription, energy metabolism, and ferroptosis. Furthermore, this review summarizes the research progress of three innovative tuberculosis treatment strategies, including antimicrobial peptides, host-directed therapies, and nanoparticle-based drug delivery systems, aiming to provide a theoretical foundation and new research perspectives for the clinical development of new drugs.

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7. Awareness of management of pulmonary multidrug-resistant tuberculosis (MDR-TB) among private practitioners in suburban areas of Pune city, India: Input for developing an educational tool.

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Private practitioners (PPs) play a major role in caring for people with tuberculosis (TB) in India. At the same time, PPs have limited access to continuing medical education and oversight especially with regards to recent changes in the management of multi-drug resistant (MDR- TB). As a part of a larger study aimed at developing an educational tool for improving multidrug-resistant TB management, we conducted a baseline knowledge assessment of MDR-TB among PPs in suburban areas of Pune City, India. This study with a cross-sectional design was conducted during July 2022 to May 2023 among 100 PPs, who either refer and/treat TB and MDR-TB cases in Pimpri-Chinchwad Municipal Corporation (PCMC) areas of Pune in Maharashtra State. The inquiry was made using an interview schedule focused on suspicion of pulmonary TB and MDR-TB, their diagnosis and treatment. The majority of PPs were allopathic practitioners (85%) practicing in private clinics (82%). Most PPs reported that they suspect TB based on three cardinal symptoms: cough for >2 weeks (97%), fever (93%) and weight loss (82%). While 54% PPs considered the Xpert assay as the first test to diagnose MDR-TB, 32% were unaware of any test.Only 37% PPs were aware of whole genome sequencing for MDR diagnosis. A fifth of PPs selected Mantoux test use for the diagnosis of active TB. Less than a fourth of PPs knew about the second-line anti-TB drugs such as bedaquiline, delamanid or linezolid etc. and their availability either in the National TB Elimination Program (NTEP) or the private sector. Our study indicates considerable lack of awareness about pulmonary MDR-TB management among allopathic PPs in the study area and highlights the need for education and creating awareness about the same. It identified specific areas for developing an educational tool for PPs in India and elsewhere.

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8. Optimal dosing and duration of linezolid for the treatment of multidrug-resistant and rifampicin-resistant tuberculosis: an individual patient data meta-analysis.

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Eur Respir J. 2025 Aug 22;66(2):2500927. doi: 10.1183/13993003.00927-2025.

BACKGROUND: The optimal dosing strategy of linezolid for treating multidrug-resistant and rifampicin-resistant tuberculosis remains unclear. We conducted an individual patient data meta-analysis to determine the optimal linezolid dosing strategy.
METHODS: We searched for randomised controlled trials and prospective cohort studies on short-course all-oral regimens containing linezolid for treating multidrug-resistant and rifampicin-resistant tuberculosis in PubMed, Embase and Scopus up to 31 August 2023. Patients were grouped according to linezolid dosing patterns. Time to treatment success and adverse events of grade 3 and higher were analysed using the Fine-Gray sub-distribution hazard model.
RESULTS: Of 12 eligible studies, eight (four randomised controlled trials, four prospective studies) were included. Overall, 945 patients were grouped as follows: group 1 (600 mg·day-1 linezolid for 8 weeks), group 2 (600 mg·day-1 for 16 weeks, then 300 mg·day-1 for 8 weeks), group 3 (600 mg·day-1 for 39 weeks) and group 4 (1200 mg·day-1 for 25 weeks). Proportions of patients achieving treatment success were 59.1%, 90.4%, 91.3% and 96.0%, respectively. Compared with group 2, group 1 (adjusted sub-distribution hazard ratio (SHR) 0.24, 95% CI 0.08-0.71) and group 3 (adjusted SHR 0.36, 95% CI 0.16-0.81) had lower success rates. While group 4 showed no significant difference in treatment success versus group 2 (adjusted SHR 0.57, 95% CI 0.23-1.43), it had a higher rate of adverse events of grade 3 and higher (adjusted SHR 2.29, 95% CI 1.37-3.83).
CONCLUSION: A dosing strategy of 600 mg·day-1 linezolid for 16 weeks then 300 mg·day-1 for 8 weeks could be optimal for treating multidrug-resistant and rifampicin-resistant tuberculosis when considering effectiveness and safety.

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9. Therapeutic potential of Bacillus sonorensis PMC204 membrane vesicles against drug-resistant Mycobacterium tuberculosis.

Med Microbiol Immunol. 2025 Sep 19;214(1):43. doi: 10.1007/s00430-025-00851-1.

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Tuberculosis remains a severe global health threat, exacerbated by the rising prevalence of multidrug-resistant (MDR) and extensively drug-resistant (XDR) Mycobacterium tuberculosis. Despite the urgent need for effective interventions, the development of anti-tuberculosis drugs has been slow, and the emergence of pan-drug-resistant strains underscores the critical need for innovative therapeutic strategies. This study introduces Bacillus sonorensis PMC204, a novel probiotic strain with potent anti-tuberculosis properties identified

through extensive screening. PMC204 significantly reduced M. tuberculosis H37Rv and XDR strains within Raw 264.7 macrophage cells. Moreover, membrane vesicles (MVs) derived from this strain exhibited superior inhibitory effects against both standard and XDR strains of M. tuberculosis. Proteomic analysis of the isolated MVs revealed a high abundance of flagellin proteins, which are hypothesized to play a pivotal role in the observed anti-tuberculosis effects. These findings also suggest a close link between the therapeutic efficacy of PMC204 and autophagy activation. Safety assessments further demonstrated the feasibility of PMC204 as a potential anti-tuberculosis therapeutic. The anti-tuberculosis activity of bacterial MVs represents an innovative approach in microbiome therapeutics, positioning PMC204 as a next-generation probiotic distinct from conventional strains. This study contributes to advancing the field of microbiome-based therapeutics and presents promising avenues for managing drug-resistant tuberculosis.

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10. The Kinetics of Bedaquiline Diffusion in Tuberculous Cavities Open a Window for the Emergence of Resistance.

J Infect Dis. 2025 Sep 15;232(3):e431-e441. doi: 10.1093/infdis/jiaf303.

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BACKGROUND: Cavitary tuberculosis is difficult to cure and constitutes a site of relapse. Bedaquiline has been a wonder drug in the treatment of multidrug-resistant tuberculosis, but emergence of resistance threatens the sustainability of its success. We designed site-of-disease pharmacokinetic studies to spatially resolve the penetration of bedaquiline, and 2 next-generation diarylquinolines, TBAJ876 and TBAJ587, in cavities.
METHODS: Rabbits with established cavitary tuberculosis received the study drugs. A laser-capture microdissections scheme was developed to measure drug concentrations as a function of distance from blood supply in caseum. To simulate drug coverage in patient cavities, the data were modeled, and parameter estimates were linked to clinical plasma pharmacokinetic models.
RESULTS: Pharmacokinetic-pharmacodynamic simulations in caseum revealed that bedaquiline reaches steady state and efficacious concentrations in deep caseum after several weeks to months and lingers at subtherapeutic concentrations up to 3 years after therapy ends. TBAJ876 and TBAJ587, achieve bactericidal concentrations in caseum layers more rapidly and shorten the window of suboptimal concentrations post treatment compared to bedaquiline.
CONCLUSIONS: The slow kinetics of diffusion of bedaquiline into and out of caseum creates spatiotemporal windows of subtherapeutic concentrations. Site-of-disease simulations of TBAJ587 and TBAJ876 predict reduced opportunities for resistance development.

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Potential Conflicts of Interest.

11. Plasma exosomal miR-122-5p_R-1, miR-23b-3p_R + 1, and miR-15a-5p_R-1 are associated with multidrug-resistant tuberculosis.

BMC Infect Dis. 2025 Aug 25;25(1):1063. doi: 10.1186/s12879-025-11487-0.

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BACKGROUND: Patients with multidrug-resistant tuberculosis (MDR-TB) who are resistant to at least both rifampicin and isoniazid, lack effective treatment options in clinic. The gold standard for the diagnosis of MDR-TB is drug sensitivity test, which is time-consuming and has a relatively low positive detection rate. Screening early diagnostic biomarker for MDR-TB is urgent need in clinical practice.
METHODS: A total of 33 patients with MDR-TB, healthy controls and drug-sensitive tuberculosis (DS-TB) were included in this study. Total plasma exosomal RNA was extracted from the subjects, and the MDR-TB plasma-specific exosomal miRNAs were obtained by Illumina sequencing.
RESULTS: There were 644 and 647 differentially expressed miRNAs in the plasma exosomes of MDR-TB patients obtained by sequencing and biogenic analysis compared with DS-TB patients and healthy controls, respectively. Differential miRNAs are mainly involved in the biological function of regulation of transcription and protein binding, and enriched in the pathways in cancer and

MAPK signaling pathway. Moreover, seven plasma exosomal miRNAs in MDR-TB patients were significantly different from those in DS-TB patients and healthy controls. Among them, three of the miRNAs (hsa-miR-122-5p_R-1, hsa-miR-23b-3p_R + 1, and hsa-miR-15a-5p_R-1) were found to be in target relationship with MDR-TB related genes (NTRK2, KIDINS220, NCKAP1, MAPK9, NFAT5, ATF6 and SLC11A2) by target gene prediction analysis. Further the bioinformatic analysis showed that hsa-miR-122-5p_R-1 targets the protein PGLYRP2, a diagnostic biomarker identified in our previous study.
CONCLUSIONS: We suggest that hsa-miR-122-5p_R-1, hsa-miR-23b-3p_R + 1, and hsa-miR-15a-5p_R-1 are closely related to MDR-TB.

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12. Outcomes and Adverse Events of WHO Shorter Regimen in the Treatment of Multi-Drug Resistant Tuberculosis in Bhutan: A Longitudinal Study.

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BACKGROUND AND AIMS: Bhutan first introduced the Shorter Regimen, consisting of a combination of Amikacin, Clofazamine, Ethionamide, Ethambutol, high dose Isoniazid, Moxifloxacin and Pyrazinamide, for the treatment of rifampicin or multidrug resistant tuberculosis (RR/MDR-TB) in 2018. This study describes the outcome, time to sputum conversion and adverse events of treatment among MDR-TB patients treated with the Shorter Regimen in Bhutan.
METHODS: This was a longitudinal study among patients with RR/MDR-TB who were treated with the Shorten Regimen between 2018 and 2020. Throughout the treatment period, sputum smear, culture, and blood investigations were monitored.
RESULTS: There were 52 patients who received the shorter regimen for MDR-TB. Forty-seven patients (90%) had pulmonary TB (PTB) and five (10%) had extra-pulmonary TB (EPTB). Forty-one patients (79%) had confirmed MDR-TB and 11 (21%) had RR-TB. MDR-TB was detected in new cases in 35 patients (69%), while 11 (22%) were cases of TB relapse and five (10%) were cases of treatment failure. There were 40 patients (86%) who achieved sputum smear conversion by the end of 4 months while all patients became culture negative by the end of 3 months. All patients achieved culture conversion by the end of 3 months. The treatment success rate was 94% and there were no deaths. The common side effects were nausea, vomiting, arthralgia, dizziness, sleep disturbances, depressed mood and skin rash. QTc prolongations were observed in six patients, for which five patients needed dose modification of Moxifloxacin. Five patients had hepatitis, and two needed dose modification. Two patients were switched to the longer regimen due to amikacin-induced profound hearing loss and nephrotoxicity.
CONCLUSIONS: The treatment success rate of MDR-TB was high, with high sputum and culture conversion rates. Adequate monitoring of side effects is important in providing timely intervention.

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13. Global child-friendly anti-TB medicines - where do we stand?

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eCollection 2025 Sep.

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An increasing number of children are diagnosed and started on antituberculosis treatment. Despite progress in developing child-friendly antituberculosis formulations for drug-susceptible and drug-resistant TB, a single-medicine rifampicin dispersible tablet is still needed. Further, many child-friendly dispersible solid-tablet formulations are not available globally. Access challenges lead to formulation manipulation of adult tablets, including the development of extemporaneous solutions, supported by pharmacokinetic studies to dose young children. Preparing extemporaneous formulations need pharmacies and trained staff. Therefore, a need remains for global collaboration to prioritise child-friendly solid, dispersible, functionally scored TB formulations and to ensure equal access for all children with TB globally.

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14. Effect of smoking on drug-resistant tuberculosis treatment outcomes and exploring potential pathways: A multicountry cohort study.

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People who smoke are at increased risk of unfavorable tuberculosis (TB) treatment outcomes compared with those who do not, but the pathways explaining this effect are unclear. We estimated the effect of smoking on a successful end-of-treatment outcome for multidrug-resistant and rifampicin-resistant (MDR/RR) TB and examined if intervening on loss to follow-up mitigates this effect. The endTB Observational Study was a prospective cohort of people with MDR/RR-TB who were treated with longer regimens containing bedaquiline and/or delamanid. We used marginal standardization to examine the effect of smoking (≥1 cigarette daily at enrollment) on treatment success (cured/completed). To simulate intervening on lost to follow-up, we censored participants and applied inverse probability of censoring weights. Among 1786 participants in 12 countries, 539 (30.2%) reported smoking. At the end of treatment, 73.5% of people who smoked and 80.3% of people who did not smoke had treatment success (risk difference in percentage points: -6.8, 95% CI: -11.1, -2.6). After adjusting for baseline confounders including demographics, social history, and comorbidities, the risk difference was similar (-5.2 percentage points) but 95% CIs were less precise (-14.1, 3.2). In a pseudopopulation without loss to follow-up, the risk difference was reduced (-1.9 percentage points; 95% CI: -10.2, 5.1). People who smoked had less frequent MDR/RR-TB treatment success compared with those who did not smoke. A simulated intervention on loss to follow-up reduced this difference, suggesting that pathways related to retention

in care were a driver of this effect.

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15. Estimated costs of tuberculosis services in Brazil, 2023.

BMJ Open Respir Res. 2025 Sep 14;12(1):e002661. doi: 10.1136/bmjresp-2024-002661.

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INTRODUCTION: To eliminate tuberculosis (TB) in Brazil, scaling up screening and

prevention strategies will be essential. We estimated costs of TB services in Brazil to support budgeting, cost-effectiveness analysis and inform the implementation of these strategies.
METHODS: We leveraged databases from five large cities in Brazil (Manaus, Recife, Porto Alegre, São Paulo and Rio de Janeiro) to estimate costs of TB services in 2023 US dollars. We estimated mean costs and 95% uncertainty ranges (95% UR) for specific components and combined these components according to national algorithms for TB diagnosis and treatment in adults and children to estimate costs for different services. We leveraged these outputs to estimate the costs of household contact investigation.
RESULTS: We estimated the mean (95% UR) cost of testing children for TB infection with a tuberculin skin test (TST) or interferon-gamma release assay and providing 3 months of once-weekly isoniazid and rifapentine (3HP) was US$48 ($25-$82) and US$67 ($43-$101), respectively. Providing 6 months of treatment for drug-susceptible tuberculosis (DS-TB) to children was US$557 ($163-$1195). In adults, costs were similar to the cost of TST and 3HP costing US$49 ($25-$86) and 6 months of DS-TB treatment being $583 ($175-$1252). For both children and adults, costs of newer, 6-month treatment regimens for rifampin-resistant tuberculosis (RR-TB) were less expensive than 18-month regimens. In children, the cost was US$4807 ($1559-$10 066) for the 6-month regimen and US$9212 ($2756-$19 567) for the 18-month regimen. Corresponding costs in adults were US$3518 ($1169-$7330) and US$7910 ($2533-$16 717). Across 10 000 households with an index TB patient, we estimated use of a TST and 3HP for TB infection screening and treatment and 6-month regimens for DS-TB and RR-TB disease to cost $1 093 531 (95% UR $409 349-$2 217 054).
CONCLUSION: There are important cost differences in TB services depending on diagnostic and treatment choices. These data are essential inputs for budgeting and cost-effectiveness.

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16. Strengthening Clinical Governance and Public Health Interventions to Improve Drug-Resistant Tuberculosis Outcomes in Rural South Africa.

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Background/Objectives: Drug-resistant tuberculosis (DR-TB) presents significant challenges to public health, particularly in rural South Africa, where limited infrastructure, high HIV co-infection rates, and weak clinical governance contribute to poor treatment outcomes. This study evaluates treatment trajectories and the impact of clinical governance and public health interventions on DR-TB outcomes in the rural Eastern Cape. Methods: A retrospective cohort study was conducted among 323 laboratory-confirmed DR-TB patients treated between 2018 and 2021. Kaplan-Meier curves and Cox proportional hazards analysis identified predictors of unfavorable outcomes. Logistic regression analysis simulated the impact of enhanced clinical governance scenarios on treatment success. Results: Treatment outcomes included cure (36.2%), completion (26.0%), loss to follow up (LTFU) (9.0%), death (9.3%), failure (2.2%), and transfer (9.3%). The median treatment duration was 10 months (IQR: 9-11). Survival analysis indicates the highest risk of death and LTFU occurred in the first 6-8 months of treatment. Multivariate Cox regression revealed that primary (HR = 0.39; 95% CI: 0.23-0.68; p = 0.0017) and secondary education (HR = 0.50; 95% CI: 0.31-0.85; p = 0.0103) were significantly protective. Paradoxically, patients with pre-XDR (HR = 0.13; p = 0.034) and XDR TB (HR = 0.16; p = 0.043) showed lower hazard of poor outcomes, likely due to early mortality or referral. HIV-negative status was associated with higher risk of poor outcomes (HR = 1.74; p = 0.010). Simulations suggested that improved clinical governance via better follow-up, TB/HIV integration, and adherence support could improve treatment success by up to 20 percentage points in high-impact scenarios. Conclusions: Strengthening clinical governance through targeted interventions could substantially reduce LTFU and mortality, especially in vulnerable subgroups. A coordinated, patient-centered approach is critical for improving DR-TB outcomes in rural, high-burden settings.

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to publish the results.

17. Lower Tuberculosis Incidence Among People With HIV Who Completed Isoniazid Preventive Therapy in Ukraine, a High-Burden Multidrug-Resistant Tuberculosis Setting: A Retrospective Cohort Study.

Clin Infect Dis. 2025 Sep 16;81(2):314-321. doi: 10.1093/cid/ciaf069.

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BACKGROUND: Evidence shows that isoniazid preventive therapy (IPT) reduces tuberculosis (TB) incidence among people with human immunodeficiency virus (HIV) with additive benefit beyond antiretroviral therapy alone, but its effectiveness in settings with high multidrug-resistant TB (MDR-TB) burden is unclear. We assessed the relationship between IPT and TB incidence among people with HIV (PWH) in Ukraine, a high-burden (32.6%) MDR-TB setting, and whether its effectiveness is maintained among virologically suppressed persons.
METHODS: We analyzed national surveillance data for HIV and TB collected between 2018 and 2022. Complete IPT (n = 40 733) was defined as receipt of ≥146 days of therapy and no IPT (n = 91 022) as <28 days of therapy. We modeled TB incidence and death using Poisson regression adjusting for covariates related to receipt of IPT and TB incidence. The secondary outcome was multidrug resistance, and sensitivity analyses explored the influence of virologic suppression.
RESULTS: Of 131 755 PWH who met inclusion criteria, 9089 (5.5%) died. Unadjusted TB incidence was 1.91 cases per 100 person-years in the No IPT group and 1.01 cases per 100 person-years in the Complete IPT group (adjusted incidence rate ratio [aIRR], 1.99). MDR-TB occurred in 29.1% and 30.7% of TB cases in the Complete and No IPT groups, respectively. Among virologically suppressed PWH,

persons with no IPT had a higher TB incidence (aIRR, 1.38) than those who completed IPT.
CONCLUSIONS: Completing IPT as part of a public health intervention can significantly reduce TB incidence among PWH, even in settings with high-burden MDR-TB and among the virologically suppressed.

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18. Black Hairy Tongue as a Rare Adverse Effect of Linezolid in Multidrug-Resistant Tuberculosis: A Case Report.

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Black hairy tongue (BHT), or lingua villosa nigra, is a rare adverse effect of linezolid, an antibiotic frequently used in the treatment of multidrug-resistant tuberculosis (MDR-TB). We present a case of a 24-year-old female who developed BHT while receiving linezolid as part of a longer regimen for MDR-TB. The patient exhibited a typical BHT presentation, with painless brown-to-black discoloration on the posterior dorsal surface of her tongue, appearing 25 days after initiating linezolid therapy. There were no other identifiable contributing factors. Upon discontinuation of linezolid and a shift to a modified regimen, the BHT completely resolved within 10 days. A Naranjo Adverse Drug Reaction Probability Scale score of 5 suggested a probable causal relationship between linezolid and BHT. This report represents the first

documented case of linezolid-associated BHT from Nepal, highlighting the importance of clinicians' awareness of this rare but clinically significant side effect, especially within the context of MDR-TB treatment, to provide prompt diagnosis, reassurance, and appropriate management.

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19. Emergence of extensively and pan-drug resistance in clinical bacterial isolates: A systematic scoping review from Ethiopian public health perspective.

PLoS Negl Trop Dis. 2025 Aug 28;19(8):e0013363. doi: 10.1371/journal.pntd.0013363. eCollection 2025 Aug.

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INTRODUCTION: The growing challenge of antimicrobial resistance in Ethiopia and itsprogression towards XDR and PDR has become a critical public health concern. Therefore, thisreview determined the current state of emerging XDR and PDR bacteria, including pre-XDR and XDR-TB, their contributing factors, advancements, and future perspectives against drug-resistant bacteria, as well as their implications for public health and insights for future research.
METHODOLOGY: This review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews (PRISMA-ScR) guidelines. A systematic search of all available literature was conducted using

PubMed/Medline, Scopus, EMBASE, Google Scholar, Hinari, Web of Science, ScienceDirect, Cochrane Library, and African Journals Online databases.This study included original articles published in English that reported XDR and PDR bacteria, Pre-XDR-TB, and XDR-TBb without limit on the study period and publication year. Descriptive statistics were used to summarize the findings.
RESULTS: Twenty-five studies published between 2010 and 2025 were included in this review. Among 5620 bacterial isolates identified,1289 were XDR (22.9%), with the prevalence ranging from 5.7% to 43.2%. A total of 440 bacterial isolates were PDR (9.1%), with its prevalence in individual studies ranged from 0.8% to 19.1%. The most common XDR bacteria identified were Klebsiella species; 26.7% (2.8%-84.6%), followed by E. coli; 26.4%(14.6%-35.7%), Acinetobacter species; 24.9%(10.1%-58.3%), and P. aeruginosa; 18.7% (2.8%-44.4%). The most frequently identified PDR bacteria were Acinetobacter species; 17.3% (7.9%-50.0%), followed by Klebsiella species; 13.7%(2.7%-25.8%), E. coli; 10.2%(2.4%-22.6%), and P. aeruginosa; 5.7%(4.3%-33.3%). Additionally, from 1419 MDR-TB and 160 TB confirmed cases, Pre-XDR-TB was 3.4% (2.4%-5.7%) and XDR-TB was 1.5%(0.6%-10.0%). These isolates were identified from different clinical specimens, which represents a significant concern in community and hospital settings.
CONCLUSION: The emergence of XDR and PDR represents a major threat to Ethiopian public health, resulting in increased morbidity, mortality, prolonged hospitalizations, high healthcare costs, and challenged treatment options. Urgent national surveillance and genomic detection of resistance mechanisms are needed to better track the spread of drug-resistant bacteria, promote antimicrobial stewardship, and enhance drug and vaccine trials.

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20. Genetic Analysis of Molecular Mechanisms of Drug Resistance in Mycobacterium tuberculosis Against Four Major First-Line Anti-Tuberculosis Drugs (Isoniazid, Rifampin, Ethambutol, and Pyrazinamide).

Infect Drug Resist. 2025 Sep 15;18:4901-4915. doi: 10.2147/IDR.S542287.

eCollection 2025.

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Tuberculosis (TB) is a highly contagious and devastating disease that claims millions of lives annually. According to the World Health Organization (WHO), approximately 10.8 million people worldwide will be affected by TB in 2023, highlighting that TB remains the deadliest infectious disease globally. It is the second leading cause of death due to infectious disease. Additionally, the emergence of drug-resistant strains has created a significant challenge for the treatment of this disease. Approximately 25% of TB-related deaths are attributed to antimicrobial drug resistance. Various mechanisms contribute to the development of drug resistance in Mycobacterium tuberculosis; however, this resistance is primarily due to mutations in the target genes of antibiotics, which reduce the efficacy of anti-TB drugs. This study aimed to provide up-to-date and valuable information on the genetic mechanisms of M. tuberculosis resistance to major first-line anti-TB drugs. Understanding these mechanisms can open new avenues for researchers to treat TB and to overcome drug resistance.

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21. Disparities in the burden of tuberculosis associated with urbanization across 178 countries and territories: an observational study.

Front Public Health. 2025 Sep 9;13:1658814. doi: 10.3389/fpubh.2025.1658814. eCollection 2025.

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BACKGROUND: Tuberculosis (TB) remains the leading cause of death from a single infectious agent. However, there is limited quantitative evidence on the impact of urbanization on TB burden. We aimed to assess the relationship between urbanization and the global TB burden.
METHODS: Using multi-source data, we developed a composite index of urbanization across 178 countries and territories from 2012 to 2019, incorporating the proportion of urban population, the proportion of population using improved sanitation, nighttime light intensity, normalized difference vegetation index, and per capita gross domestic product. Fixed-effects linear models were applied to estimate the rate ratios (RRs) and 95% confidence intervals (CIs) for the association between urbanization and the incidence, prevalence, and mortality of total TB and three subtypes: drug-susceptible TB (DS-TB), multidrug-resistant TB (MDR-TB), and extensively drug-resistant TB (XDR-TB).
RESULTS: Overall, higher urbanization scores were associated with significant reductions in the burden of MDR-TB and XDR-TB but showed no effect on total TB or DS-TB. For MDR-TB, each additional urbanization score was associated with a 1.0% decrease in incidence (RR = 0.990; 95% CI: 0.985-0.996), a 1.1% decrease in prevalence (0.989; 0.984-0.994), and a 0.7% decrease in mortality (0.993; 0.988-0.998). For XDR-TB, the corresponding reductions were 0.9% in incidence (0.991; 0.986-0.996), 1.0% in prevalence (0.990; 0.985-0.995), and 0.7% in mortality (0.993; 0.988-0.998). These relationships persisted when considering a one-year lag in urbanization. In subgroup analyses, however, urbanization was associated with increased MDR-TB and XDR-TB burdens in upper-middle-income countries.
CONCLUSION: Urbanization was linked to reduced MDR-TB and XDR-TB burdens globally, but to increased burdens in upper-middle-income countries. Building well-managed and healthy cities is essential not only for sustainable urbanization but also for strengthening TB prevention and control, especially in rapidly transitioning upper-middle-income countries.

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22. Ending tuberculosis in Gulf Cooperation Council countries: an overview of the WHO End TB Strategy 2025 milestones.

IJID Reg. 2025 Jun 6;16:100681. doi: 10.1016/j.ijregi.2025.100681. eCollection 2025 Sep.

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OBJECTIVES: Tuberculosis (TB) continues to pose a major global public health challenge. Although the Gulf Cooperation Council (GCC) countries have lower incidence rates of TB (<10 cases per million population), they are still striving to maintain and surpass benchmarks. We describe TB status to the 2025 milestones of the World Health Organization (WHO) End TB Strategy.
METHODS: A retrospective study conducted using WHO data published from 2015 and between 2020 and 2023 highlights trends in TB incidence, mortality, treatment success, and drug resistance across GCC countries.
RESULTS: Kuwait had the most significant drop in TB infections since 2015, with a reduction of 57%, followed by Qatar at 40% and Saudi Arabia at 31%. Oman,

however, recorded a 23% increase. In terms of TB-related deaths, Saudi Arabia achieved a 32% decrease, whereas Qatar, Kuwait, and the United Arab Emirates experienced increases of 14%, 39%, and 22% respectively. Treatment success rates were highest in Qatar (100%), Oman (90%), and Saudi Arabia (87%), whereas Kuwait (44%) and Bahrain (77%) had the lowest rates. Oman reported the highest reduction in multidrug-resistant TB cases at (60%), followed by Saudi Arabia (50%), Kuwait (31%), and Bahrain (50%). Qatar had the highest increase (122%) and United Arab Emirates had no change, reflecting varying degrees of success in controlling drug-resistant TB. HIV-TB co-infection rates was highest in United Arab Emirates (5.4%) and Bahrain (5.1%), followed by Saudi Arabia (2.3%), Oman (1.4%), Qatar (0.6%), and Kuwait (0.5%). Notably, the GCC countries reported zero TB households, with no catastrophic overall expenses since 2020. CONCLUSIONS: Although the GCC countries have made significant strides in TB control, their efforts toward the targets have been inconsistent, with notable differences in TB-related deaths, infection rates, treatment success, and multidrug-resistant TB rates. Strengthening regional collaboration, implementing targeted interventions, and integrating services are essential to meet the WHO's 2025 and 2035 goals.

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PMID: 40678394

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23. Genomic epidemiology of Mycobacterium tuberculosis in Wales.

Sci Rep. 2025 Aug 24;15(1):31106. doi: 10.1038/s41598-025-15076-8.

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Identification of factors contributing to tuberculosis (TB) transmission can guide targeted measures to reduce morbidity. Varying findings for factors associated with TB genomic clustering exist. We describe Mycobacterium tuberculosis strain diversity, drug-resistance, and ongoing transmission in Wales using single nucleotide polymorphisms (SNP)-based typing to infer lineage and clusters. TB cohort data on isolates from Welsh residents from 2012 to 2022, patient level data from the National TB Surveillance System and SNP-based data, were merged. Descriptive epidemiology and logistic regression modelling were used to identify factors associated with genotypic clustering. 215 cases were included in the cluster analysis (66% male and 46% born outside of the UK); 115/215 belonged to 30 genomic clusters belonging to lineages 2-4. Most clusters corresponded to Lineage 4 and were distributed within South Wales. There were significant differences in the distribution of ethnicity, age group, and deprivation (Welsh Index of Multiple Deprivation, WIMD) in our sample compared to the Welsh population. Resistance to rifampicin and isoniazid and predicted resistance to ethambutol, aminoglycosides, pyrazinamide, and quinolone was low. Factors associated with increased odds of clustering included being UK-born and having pulmonary disease. Due to the identification of the above factors associated with TB genomic clustering, as well as the differences in ethnicity, age group, and WIMD quintile, prevention strategies for TB screening targeted towards these groups may be considered. Future work may evaluate the utility of additional control measures within these populations when the onset case in a genomic cluster has any of these characteristics.

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Conflict of interest statement: Declarations. Competing interests: The authors declare no competing interests.

*****24. An economic analysis of BPaL for multidrug-resistant TB in South Africa and the Philippines.**

IJTLD Open. 2025 Sep 10;2(9):535-541. doi: 10.5588/ijtldopen.25.0294. eCollection 2025 Sep.

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BACKGROUND: The WHO endorses bedaquiline, pretomanid, and linezolid (BPaL)-based regimens for multidrug-resistant/rifampicin-resistant TB, and both the Philippines (PH) and South Africa (SA) have adopted these regimens.
METHODS: Using a Markov model, we assessed the cost per successful treatment and 5-year budgetary and economic impact of BPaL-based regimens in SA and PH. Treatment outcomes were informed by national electronic registries, SA BPaL Clinical Access Program, and PH operational research. Costs were estimated from the provider perspective.
RESULTS: Over 5 years, BPaL-based regimens reduce total costs by 20%-25% in SA and 9%-11% in PH compared with a standard short oral regimen (SSOR) when achieving the same number of successful treatments, due to lower cost per successful treatment from reduced loss to follow-up and mortality. BPaL-based regimens improve treatment success by 22%, leading to more patients completing full treatment and higher overall resource use. Therefore, the budget for BPaL-based regimens is projected to increase by 7%-8% (SA) and 6% (PH) from 2023/24 to 2027/28.
CONCLUSION: BPaL-based regimens reduce cost per successful treatment compared with SSOR and require smaller budgets for similar treatment outcomes. Implementation may involve initial budget increases, but improvements in treatment success and long-term health outcomes outweigh these costs, presenting

a strong rationale for rollout.

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PMID: 40959787

25. Burden and determinants of MDR-TB among prisoners in sub-Saharan Africa: Systematic review and meta-analysis protocol.

J Public Health Afr. 2025 Aug 30;16(4):1364. doi: 10.4102/jphia.v16i4.1364. eCollection 2025.

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BACKGROUND: Tuberculosis (TB) is one of the leading causes of death globally because of a single infectious pathogen. The rise in prevalence of multi-drug-resistant tuberculosis (MDR-TB) puts an increased burden on the health system in terms of cost and longer treatment duration. People living in correctional facilities are more likely to develop TB and have poor TB treatment outcomes than the general population, making them a vulnerable group to develop MDR-TB. However, the burden of MDR-TB and associated treatment outcomes among prisoners in sub-Saharan Africa (SSA) is poorly documented.
AIM: The study aims to investigate the burden and associated factors of MDR-TB treatment among prisoners in SSA.
SETTING: The review will include studies of MDR-TB done in prisons and detention centers involving prisoners and inmates in sub Saharan Africa.
METHODS: Following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PROSPERO), we will conduct a systematic review and meta-analysis. We will review studies examining MDR-TB patient treatment outcomes among prisoners reported in published literature in SSA from 2000 to 31 December 2024. A search on studies reporting MDR-TB treatment outcomes from the databases such

as 'Medline, Embase, CINAHL (EBSCOhost), Scopus and Web of Science' will be conducted. We will analyse continuous outcomes as mean differences for studies using the same scales with standard deviation reported and binary outcome data as odds ratios or risk ratios, all presented with their 95% confidence intervals. Additionally, the pooled proportions will be used to determine the prevalence or incidence of specific MDR-TB treatment outcomes. Heterogeneity will be assessed using the I 2 statistic, and where significant heterogeneity is detected, a random-effects model meta-analysis will be performed; otherwise, a fixed-effect model meta-analysis will be carried out. Risk factors will be determined using the meta-regression analysis technique.
RESULTS: After analysis of pooled data, prevalence of MDT-TB in prisons will be presented as proportions. Meta-analysis outcome will be presented as forest plots, showing odd ratios and co-responding 95% confidence intervals. Narrative synthesis of included studies will be presented in a table format.
CONCLUSION: This proposed systematic review and meta-analysis will help consolidate evidence to support the development of public health guidelines to enhance the reduction of MDT-TB factors among prisoners in the SSA region.
CONTRIBUTION: This review will provide evidence to support guideline development on screening, diagnosis, and clinical management of MDR-TB patients in prisons.

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PMCID: PMC12421582
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26. Tuberculosis: The insidious threat that compromises health in post-Assad Syria.

IJID Reg. 2025 Jul 1;16:100697. doi: 10.1016/j.ijregi.2025.100697. eCollection 2025 Sep.

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This perspective explores the state of tuberculosis (TB) after the prolonged conflict in Syria and fall of the regime in December 2024; we discuss key considerations in light of multiple competing health priorities within Syria's borders and the recovering health system. During the conflict, the health system fragmentation under differing geopolitical control led to unequal access to TB prevention, diagnostics and management social determinants such as poverty, malnutrition, inadequate water and sanitation, and lack of proper shelter, along with risks associated with disadvantaged groups, including internally displaced people, detainees, former detainees, and rural communities, not only increase the risk of TB transmission and the activation of latent infections but also hinder active case finding. Tackling these risks requires re-establishing the National TB Program (NTP) across the country, which acts equitably across all geographical areas to identify new cases, support robust surveillance activities, ensure drug resistance is identified promptly, and monitor treatment. Leadership from the Ministry of Health and the World Health Organization, with support from other stakeholders e.g., humanitarian, civil society or private sector can support the NTP and optimize health worker education and referral pathways. Beyond this, addressing the social determinants, which contribute to TB in Syria, is an essential component of TB control in post-conflict Syria.

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Conflict of interest statement: The authors have no competing interests to declare.

27. Antitubercular drug induced liver injury among tuberculosis patients in central Ethiopia.

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Tuberculosis (TB) is a curable disease that can be treated with antitubercular (anti-TB) drugs that have markedly reduced mortality due to the disease. However, the drugs may cause liver injury, which is associated with increased morbidity due to acute liver failure, disease progression, and drug resistance. There is a scarcity of evidence on the prevalence and predictors of anti-TB drug-induced liver injury (ATDILI). The aim of this study is to the assess prevalence, predictors, and clinical features of ATDILI in the health centers of Hossana town, Central Ethiopia. In a prospective cohort study, newly diagnosed TB patients (N = 219) receiving first-line anti-TB drugs were enrolled in three selected health centers in Hossana town, Central Ethiopia. Liver function tests were assessed before and four and eight weeks after drug treatment initiation. Patients that had abnormal liver biochemistry prior to treatment and patients positive for either hepatitis B or C viral antibody were excluded. Thirty-five study participants (16.0%) developed ATDILI. Two of them (5.7%) had severe ATDILI. Nausea, vomiting, and anorexia were the most frequently observed symptoms. In multivariable analysis, ATDILI was significantly associated with gender (adjusted odds ratio, AOR = 2.57, 95% CI = 1.11-5.91, P = 0.027), age (AOR = 1.05, 95% CI = 1.01-1.10, P = 0.019), body mass index (AOR = 0.81, 95% CI = 0.69-0.95, P = 0.009), and HIV status (AOR = 6.73, 95% CI = 1.81-25.09, P = 0.005). The results of the study suggest that the prevalence of ATDILI is high among TB patients getting treatment in the health centers in Hossana town, Central Ethiopia. Thus, patients who are female, older, have a low body mass index, and are HIV positive should have their liver function regularly monitored to reduce ATDILI.

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28. Comparing the longer regimen and the shorter regimen for multidrug-resistant pulmonary tuberculosis patients treated under the programmatic management of drug-resistant tuberculosis.

Front Med (Lausanne). 2025 Aug 28;12:1645820. doi: 10.3389/fmed.2025.1645820. eCollection 2025.

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Multidrug-resistant tuberculosis is a major public health concern with prolonged infectivity, a complex treatment regimen, and lower treatment success rates. Despite the significant progress made by India in the control of Tuberculosis, it remains the second leading cause of mortality among infectious diseases. Shorter treatment courses for multidrug-resistant tuberculosis (MDR-TB) can enhance patient adherence by decreasing the length of time for medication intake and alleviating the challenges associated with prolonged treatment. Evaluating the effectiveness of various treatment regimens is crucial for identifying the best balance among treatment duration, efficacy, adverse drug effects, and patient adherence. A prospective, observational study on 50 MDR-TB patients was carried out at a tertiary care hospital. The final cure rates were 88% in the shorter regimen and 84% in the longer regimen, with 12% treatment failure in both groups. Both shorter and longer regimens demonstrated comparable efficacy with slightly better adherence in the shorter regimen.
CLINICAL TRIAL REGISTRATION: The study was registered in the Clinical Trials Registry-India (Indian Council of Medical Research-National Institute of Medical Statistics), https://ctri.nic.in/, CTRI registration number CTRI/2024/01/061453, registration date 15/1/2024, date of first enrollment is 24/1/2024.

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PMID: 40950957

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29. Predominance of gram-negative multidrug-resistant pathogens causing lower respiratory tract infections among gene X-pert negative presumptive tuberculosis patients in Dar Es Salaam, Tanzania.

Ann Med. 2025 Dec;57(1):2550577. doi: 10.1080/07853890.2025.2550577. Epub 2025 Aug 23.

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BACKGROUND: Lower respiratory tract infections (LTRIs) represent a significant global health burden. The clinical presentation of pulmonary tuberculosis (PTB) and other LRTIs often overlap, making it difficult to differentiate based on clinical features only. This study aims to investigate the role of other bacteria pathogens in LRTIs among presumptive TB patients and antibiotic susceptibility patterns for appropriate patient management.
MATERIALS AND METHODS: We conducted a cross-sectional study among patients with symptoms and signs suggestive of PTB at Muhimbili National Hospital and Infectious Diseases Centre in Dar es Salaam, Tanzania. Sputum samples collected for TB diagnosis using the original GeneXpert system were investigated for other

causes of LRTIs. The sputum samples were assessed for quality based on the Bartlett criteria before culture. We performed descriptive statistics to summarize the data.
RESULTS: We assessed 470 sputum samples, of which 317(67.4%) were of good quality. Of 317 samples, 21(6.6%) were Mycobacterium tuberculosis (MTB) positive by GeneXpert, while 126(39.7%) had 138 significant bacterial isolates other than MTB. Pseudomonas aeruginosa 44/99(44.4%) was the prominent Gram-negative bacteria isolated, followed by Klebsiella pneumoniae 22/99(22.2%). High rates of resistance was detected towards ampicillin (98%), penicillin (92%), and amoxicillin-clavulanic acid (65%). A high proportion of isolates, 71/138(51.4%) were multidrug resistant (MDR).
CONCLUSION: This study revealed a high prevalence of LRTIs caused by non-TB pathogens, particularly MDR strains in presumptive TB. MTB was detected only in high-quality sputum samples. The high resistance rate to commonly prescribed antibiotics for LRTIs called for further large-scale studies to guide and/or refine treatment guidelines and optimize patient care.

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30. Advancing the fight against tuberculosis: integrating innovation and public health in diagnosis, treatment, vaccine development, and implementation science.

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Tuberculosis (TB) remains one of the leading causes of infectious disease mortality worldwide, increasingly complicated by the emergence of drug-resistant strains and limitations in existing diagnostic and therapeutic strategies. Despite decades of global efforts, the disease continues to impose a significant burden, particularly in low- and middle-income countries (LMICs) where health system weaknesses hinder progress. This comprehensive review explores recent advancements in TB diagnostics, antimicrobial resistance (AMR surveillance), treatment strategies, and vaccine development. It critically evaluates cutting-edge technologies including CRISPR-based diagnostics, whole-genome sequencing, and digital adherence tools, alongside therapeutic innovations such as shorter multidrug-resistant TB regimens and host-directed therapies. Special emphasis is placed on the translational gap-highlighting barriers to real-world implementation such as cost, infrastructure, and policy fragmentation. While innovations like the Xpert MTB/RIF Ultra, BPaLM regimen, and next-generation vaccines such as M72/AS01E represent pivotal progress, their deployment remains uneven. Implementation science, cost-effectiveness analyses, and health equity considerations are vital to scaling up these tools. Moreover, the expansion of the TB vaccine pipeline and integration of AI in diagnostics signal a transformative period in TB control. Eliminating TB demands more than biomedical breakthroughs-it requires a unified strategy that aligns innovation with access, equity, and sustainability. By bridging science with implementation, and integrating diagnostics, treatment, and prevention within robust health systems, the global community can accelerate the path toward ending TB.

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Almuzaini, Dhahri and Abu-Okail.

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31. Association of CD14 rs2569190 and rs2569191 polymorphisms with tuberculosis susceptibility in the Kurdish population of Iran.

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Tuberculosis (TB), caused by Mycobacterium tuberculosis (Mtb), remains a leading cause of infectious disease mortality globally. Host genetic factors, particularly those involved in innate immunity like Cluster of Differentiation 14 (CD14), may influence susceptibility to TB. This study investigated the association of two CD14 promoter polymorphisms, rs2569190 (C-159 T) and rs2569191 (A-1145G), with TB susceptibility in the Kurdish population of Iran. A prospective case-control study was conducted, enrolling 303 newly diagnosed TB patients (280 drug-sensitive, 23 MDR-TB) and 288 age- and sex-matched healthy Kurdish controls from Ilam, Iran. Genotyping for rs2569190 and rs2569191 was performed using PCR-RFLP. The TT genotype of rs2569190 and the GG genotype of rs2569191 were significantly more frequent in both drug-sensitive and MDR-TB patient groups compared to controls ($P < 0.05$). Under the codominant model, the

TT genotype of rs2569190 (OR = 1.68, 95% CI 1.15-2.45) and the GG genotype of rs2569191 (OR = 1.55, 95% CI 1.06-2.26) were associated with increased TB susceptibility. Haplotype analysis revealed a higher prevalence of the CG haplotype in TB patients and an association of the TG haplotype with increased TB risk. In conclusions, this study suggests that the CD14 promoter polymorphisms rs2569190 and rs2569191 are associated with increased susceptibility to tuberculosis in the Kurdish population of Iran. These findings highlight the potential role of CD14 genetic variations in TB pathogenesis and warrant further investigation in other populations and functional studies to elucidate the underlying mechanisms.

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32. A destruent case of recurrent primary naso-pharyngeal tuberculosis in a migrant.

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A 24-year-old Ukrainian man with post-natal developmental disability was treated for presumptive facial cutaneous TB in 2018 in his home country. After moving to Italy, his nostril lesion recurred in 2021, expanding to the upper lip, but he

was lost to follow-up before a diagnosis was made. In 2023, when symptoms worsened, a biopsy was performed showing chronic inflammation and negative microbiological molecular tests and culture. By 2024, the lesion spread to the eyelids with worsening ulcerations. After surgical resection, histology revealed a vegetative, haemorrhagic mucosa with necrotic granulomatous inflammation and rifampin-susceptible Mycobacterium tuberculosis (Mtb) was detected at molecular testing. Diagnosis of recurrent primary cutaneous TB without pulmonary involvement was made and treatment for drug susceptible TB was initiated, leading to complete remission of the facial lesions. Primary cutaneous TB without pulmonary involvement is rare, presenting as nodules, plaques, papules, or ulcers. Diagnosis requires systemic evaluation, imaging, infection screening and expert consultation. Cutaneous TB (CTB) is uncommon in Ukraine and accounts for less than 2% of extrapulmonary TB cases with frequent association with immunosuppression and delayed presentation. Although infrequent, CTB mirrors the wider TB scenario, that is also characterized by MDR-TB in 27% of new and 45% of retreatment cases, and XDR-TB in 13% of MDR-TB cases. In individuals coming from TB endemic areas with strong clinical suspicion, empirical TB diagnosis should always be considered despite negative microbiology to enable timely treatment and prevent progression. A multidisciplinary approach is essential for accurate diagnosis and optimal management.

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33. Advancements in the design and development of pyrazoline-based antimycobacterial agents: an update and future perspectives.

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Pyrazoline scaffolds have attracted significant interest in medicinal chemistry due to their broad spectrum of pharmacological activities. Pyrazole-based drugs are either already approved or are currently undergoing clinical trials across a range of therapeutic areas. Pyrazolines (Δ2-pyrazolines or 2-pyrazoline or 4,5-dihydropyrazoles) evolved as cyclic analogues of thioacetazone and were explored for enhanced antitubercular activity over the past five decades. The scope of this review focused on how extensively the chemical space around pyrazolines has been explored in relation to their antitubercular activity, rather than presenting a general structure-activity relationship (SAR) account. In this exercise, we covered key molecular modifications, including rationale substitutions and conjugations, aimed at enhancing the potency in general. Additionally, information pertaining to in vitro/in silico target interaction and ADMET studies are also covered. A dedicated section is included to showcase target-oriented strategies (InhA, cytochrome P450 14α-sterol demethylase, and enzymes involved in the mycobactin biosynthesis pathway), recent patents, suggested schemes for reported pyrazolines, and an overview of research methodologies and evaluation models. We believe that this review will enable medicinal chemists to map unexplored chemical space in identifying critical research gaps. This is essential for the rational design and development of potent antitubercular agents against tuberculosis (TB), drug-resistant tuberculosis (DR-TB), and other non-tubercular mycobacterial diseases (NTMD).

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34. Genetic determinants of Mycobacterium tuberculosis adaptation and drug efficacy during stationary phase growth.

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The adaptation of Mycobacterium tuberculosis (Mtb) to a slowly growing or nongrowing state in growth-limited conditions plays a crucial role for drug tolerance. Although the mechanisms of Mtb adaptation under growth-limited conditions have been extensively studied, it remains unclear to what extent the cellular processes necessary to sustain nongrowing state affect drug efficacy. To investigate this, we performed a genome-wide transposon mutant screen, which allowed parallel identification of the genes that influence bacterial fitness and drug efficacy during the stationary phase. Our analysis revealed that genes encoding the SOS response, membrane phospholipid biosynthesis, proteasomal protein degradation, and cell wall remodeling critically determine Mtb fitness in both stationary-phase condition and antibiotic exposure. Surprisingly, we found that many mutants that compromise stationary-phase adaptation result in increased fitness during antibiotic treatment, including the recently identified genetic markers associated with poor clinical outcomes. Furthermore, genes involved in cell envelope biosynthesis and remodeling, antibiotic efflux, and phosphate transport are significantly enriched in the mutants sensitized to antibiotics, indicating that reduced drug entry is a critical factor that limits antibiotic efficacy in nonreplicating Mtb. We demonstrated that mutants deficient in utilization of lipids, the primary carbon sources for Mtb during infection, became tolerant to killing by rifampicin. We provided genetic and metabolic evidence that the activities of lipid metabolism are associated with rifampicin efficacy. These findings provide the detailed assessment of Mtb genes necessary for adaptation to the stationary phase and drug treatment and new insights into the mechanisms of antibiotic tolerance in nongrowing Mtb.IMPORTANCEIt has long been known that antibiotic efficacy is generally proportional to the bacterial growth rate. Yet it remains unclear how and to what extent the growth arrest-induced physiological and metabolic changes affect drug efficacy. Using the genome-wide transposon mutant screen, we identified the mutants that influence Mycobacterium tuberculosis adaptation and drug efficacy during the stationary phase of growth. We revealed both positive and negative correlations between stationary phase adaptation and drug sensitivity and identified many mutants that compromise stationary phase adaptation and result in increased fitness during antibiotic treatment, including the identified

genetic markers associated with poor clinical outcomes. These results provide new insights into the mechanisms of antibiotic tolerance in nongrowing Mtb and suggest potential targets for drug development.

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35. Population structure and emergence of resistance to new and repurposed drugs in XDR-TB: insights from a 10-year genomic study in the Western Cape, South Africa review.

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BACKGROUND: Extensively drug-resistant tuberculosis (XDR-TB) is a global health threat, being expensive and difficult to treat, with high mortality rates. The Western Cape Province (WCP), South Africa, has a particularly high burden of XDR-TB (>800 cases in the past ten years). Drug resistance genotypes and transmission present substantial regional variability. Thus, a better understanding of genetic diversity, clustering and the factors related to transmission can aid in prioritising resources to effectively target high-risk populations and regions that are disproportionately affected. We describe genetic diversity, drug resistance profiles and identify potential factors associated with the spread of XDR-TB strains collected in the WCP.
METHODS: We included 729 XDR-TB samples (one per patient), identified through routine diagnosis spanning 2010 to 2019, from six healthcare districts (HCDs) in the WCP. Genomic DNA from cultured isolates was sequenced using the Illumina

platform. Sequences were analysed for strain type, drug resistance mutations, and genomic clustering using the TBProfiler and MTBseq pipelines. We conducted logistic regression analysis to identify potential factors associated with genomic traits related to the spread of XDR-TB strains.
RESULTS: Of the 729 XDR-TB strains, sublineage 2.2.2 (Atypical Beijing: n=378, 58.79%) strains were predominant, followed by Sublineage 2.2.1 (Typical Beijing: n=260, 40.43%). Atypical Beijing strains were more likely to cluster than Typical Beijing strains. Most of the clusters were small, with a few large and very large clusters, and the strains within very large clusters (primarily Atypical Beijing) were more likely to be found within Cape Town Metropole, Cape Winelands and Garden Route HCDs. Certain Atypical Beijing strains were found resistant to new and repurposed drugs recently introduced in the WHO treatment guidelines and clustered, indicating potential transmission.
CONCLUSIONS: Near-untreatable Atypical Beijing strains are prevalent in the WCP. Hence, hotspot areas for clustering in Cape Town Metropole, Cape Winelands and Garden Route HCDs should be prioritised for targeted intervention to prevent ongoing XDR-TB transmission.

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36. Evaluation of the Xpert MTB/XDR test for detection of isoniazid, fluoroquinolones, and second-line injectable drugs resistance to Mycobacterium tuberculosis-Anhui Province, China.

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INTRODUCTION: The emergence of drug-resistant tuberculosis (DR-TB) has posed significant challenges to TB control. This study assessed the diagnostic performance of the Xpert MTB/XDR test for detecting drug resistance in TB patients.
METHODS: This study analyzed 276 samples collected from clinically suspected MDR-TB patients in Auhui Chest Hospital from 01/03/2022-01/03/2023. The Xpert MTB/XDR test was evaluated for its ability to detect resistance to isoniazid (INH), ethionamide (ETH), fluoroquinolones (FLQ), and second-line injectable drugs (SLIDs) compared with phenotypic drug susceptibility testing (pDST). Specimens were investigated by Sanger sequencing, where the MTB/XDR test and pDST results were inconsistent. Afterward, the clinical performance of the Xpert MTB/XDR test was also evaluated with the composite reference test (pDST + sequencing).
RESULTS: The sensitivity of the Xpert MTB/XDR test against pDST in detecting resistance to INH and FLQ using 276 samples was 95.77% (95% CI: 91.83-98.16) and 93.83% (95% CI: 86.18-97.97), respectively. In contrast, a lower sensitivity of the MTB XDR test in predicting SLIDs and ETH resistance (sensitivity < 75%) compared with pDST was demonstrated in this study. The specificity for detecting all drugs was greater than 90%. Thirty-three samples were retested by sequencing, which identified mutations predicting INH and FLQ resistance, determining whether resistant or not by combining pDST and sequencing results. When considering pDST + sequencing, the sensitivity and specificity of the MTB/XDR assay for INH and FLQ drug targets increased, especially the detection specificity of FLQ has reached 100% (95% CI: 97.95-100).
CONCLUSION: The Xpert MTB/XDR has high sensitivity and specificity in drug-resistant tuberculosis patients, making it better suited to meet the needs of rapid, sensitive, and accurate detection for drug-resistant tuberculosis in resource-limited settings, and serving as a critical tool for achieving personalized treatment and TB control.

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37. Computational guided identification of novel anti-mycobacterial agent proved by in-vitro and in-vivo validation.

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BACKGROUND: An upsurge of antibiotic resistant bacteria such as Mycobacterium tuberculosis is recorded on daily bases as a result of many factors including: the daily antibiotics exploitation, failure to follow lengthy complex drug regimen, and ongoing bacterial mutation. TB treatment protocol is usually a lengthy and expensive one that is composed of 4 or even 5 drugs that have multiple substantial side effects. Traditional drug discovery methodologies are usually lengthy multifaceted process complicated with unpredictable outcomes in terms of efficacy and safety, hence there is an urge to find innovative drug discovery method that can produce multiple novel potential antimycobacterial agents that are safe and effective both in-vitro and in-vivo.
RESULTS: The obtained results illustrated that maleic acid represented a potential drug with minimum inhibitory concentration of 312 µg/ml and an identical minimum bactericidal concentration against Mycobacterium tuberculosis. Its IC50 was measured to be 374.44 mg/ml with SI of 1200. Preliminary testing showed that maleic acid can be considered as a possible histidinol-phosphate aminotransferase inhibitor with a high binding affinity (-5.0475 kcal/mol) and promising molecular dynamics. Maleic acid combination with rifampicin had ΣFIC of 0.375 which indicated synergistic activity between them. It efficiently produced 3 ± 0.3009 log10 CFU reduction of infected mice lungs compared to control group and illustrated superior preservation of lung tissue and structure on histological screening level.

CONCLUSION: After careful filtration processes, computational guided scavenge of online protein databases for potential druggable targets represents a promising pathway for identification of novel antimycobacterial agents. One of the promising identified agents was maleic acid which can act as an alternative/additional drug for combating tuberculosis infection.

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38. Non-tuberculous mycobacterial infections among pulmonary tuberculosis suspected and confirmed patients in Ethiopia - A systematic review and meta analyses.

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INTRODUCTION: Nontuberculous mycobacteria (NTM) are environmental pathogens found in soil, water, and various environments, causing chronic pulmonary infections. They are resistant to chlorine and extreme temperatures but not typically transmissible. NTM infections are often misdiagnosed as tuberculosis

(TB), especially in Ethiopia, where data on prevalence is scarce. This research aims to analyze NTM isolation from pulmonary samples and other specimens used in pulmonary tuberculosis (PTB) diagnosis among patients suspected or confirmed as PTB cases in Ethiopia.
OBJECTIVE: This study systematically reviews and synthesizes published studies that report NTM isolation from sputum and other clinical samples in Ethiopia to estimate the overall prevalence of NTM isolation, identify the common species, and analyze regional variations in their occurrence.
METHODS: This systematic review and meta-analysis aimed to determine NTM prevalence in infected individuals in Ethiopia. Using PubMed, Scopus, Web of Science, Google Scholar, and African Journals Online, we conducted a comprehensive literature search. Data extraction and quality assessment used the Newcastle-Ottawa Scale. Meta-analysis employed STATA-18 software with a random-effects model and included subgroup analysis. PROSPER registration: CRD420251000131.
RESULTS: In this review a total of 5,415 participants were involved and 53.8% were TB suspected patients, 37.6% were PTB patients, 4.0% were Multidrug resistance-tuberculosis (MDR-TB) patients, and 4.6% were Human Immunodeficiency virus (HIV) positive. The NTM prevalence was 3.8%, showing high heterogeneity and regional species variability. The meta-analysis highlighted differences in NTM prevalence across age groups and diagnostic tools, emphasizing the need for enhanced diagnostics and continuous surveillance to improve patient outcomes and inform public health strategies.
CONCLUSION: The review summarizes the epidemiology and geographical distribution of NTM infections and common NTM species isolated among PTB suspected patients in Ethiopia, revealing regional variations and clinical implications. Despite limited data, Ethiopia has a lower prevalence of NTM compared to other African regions and the worldwide average.

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39. In Silico Screening and Molecular Dynamics Simulations of Small Molecules Targeting Peptidyl tRNA Hydrolase for Drug-Resistant Tuberculosis.

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The translation machinery of bacteria plays a crucial role in their survival, making it an attractive target for the development of antibiotics. The translation process may be halted due to various factors, leading to ribosome stalling and the release of lethal peptidyl-tRNA. Peptidyl tRNA hydrolase (PtH) cleaves the ester bond between the peptide and the tRNA in peptidyl-tRNA to rescue the cell. Therefore, targeting this enzyme holds significant potential for combating drug-resistant bacteria, as it represents a novel target and plays an indispensable role in bacterial survival. In this study, we virtually screened three different databases: DrugBank, Maybridge, and ZINC natural products to identify potential inhibitors of PtH from Mycobacterium tuberculosis. We evaluated the stability of the PtH-inhibitor complexes obtained from screening through Molecular Dynamics (MD) simulations. Furthermore, we estimated their binding energy and performed per-residue decomposition to understand the contributions of individual amino acids. We also assessed the top ten potential inhibitors for their ADMET properties and drug-likeness. Although experimental validation is currently pending, this study represents a significant step toward the development of potent and specific inhibitors of PtH.

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PMID: 40893265

40. Population pharmacokinetic and exposure-response study of a novel

anti-tuberculosis drug to inform its dosage design in phase III clinical trial.

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Although bedaquiline (BDQ) received conditional approval for multi-drug resistance tuberculosis (MDR-TB), a black box warning was added due to QT prolongation risk. WX-081, a promising second-in-class drug that finished phase II clinical trial, exhibited comparable anti-TB activity and better cardiac safety. The accumulation of its active metabolite WX-081-M3 leads to QT prolongation, whereas the relationships between dosage, exposure and response have not been established. Accordingly, the dosage design for phase III study is challenging. Here, the first population pharmacokinetic (PPK) and exposure-response (E-R) analysis were conducted for WX-081. 1610 WX-081 and 1580 WX-081-M3 concentrations were collected from 24 healthy volunteers and 48 tuberculosis patients for PPK study. The pharmacokinetic parameters and sputum culture conversions of 20 MDR-TB patients receiving BDQ and WX-081 were used for E-R analysis. The absorption of WX-081 was well described by a three-compartments transit model, while the distribution and elimination profiles of WX-081 and WX-081-M3 were captured by three- and two-compartments models, respectively. E-R analysis demonstrated that the clinical efficacy of WX-081 is comparable with BDQ and can be evaluated by average concentration at steady state (Cavg,ss) of WX-081. According to the simulation results of different regimens, the dosage of 450 mg once daily (QD) for 1 week and subsequent 300 mg QD for 1 week followed by 150 mg QD for 22 weeks was recommended considering both efficacy and safety. Our study revealed the PK and efficacy profiles of WX-081 for the first time and proposed a dose optimization strategy to facilitate its clinical development.

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41. Treatment outcomes and associated influencing factors among elderly patients with rifampicin-resistant tuberculosis: a multicenter, retrospective, cohort study in China.

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BACKGROUND: Rifampicin-resistant tuberculosis (RR-TB) remains a significant global public health concern. The elderly population is not only at high risk and among the primary victims of RR-TB but also plays a crucial role in the transmission chain of RR-TB. Their biological particularities, treatment complexities, and social vulnerabilities collectively present substantial challenges to global tuberculosis control. This study aimed to evaluate treatment outcomes and identify predictors of unfavorable outcomes among elderly patients with RR-TB in China.
METHODS: A multicenter retrospective cohort study was conducted, including 248 elderly RR-TB patients treated across eight tertiary hospitals in China from May 2018 to April 2020. Multivariate logistic regression and Propensity Score Matching (PSM) analyses were performed to identify factors associated with unfavorable outcomes. Statistical analyses were performed using SPSS.
RESULTS: Among 248 patients, 65.7% (163/248) achieved treatment success (cured or completed treatment), while 34.3% (85/248) experienced unfavorable outcomes, including treatment failure (10.5%), death (2.4%), loss to follow-up (15.7%), and non-evaluation (5.6%). Adverse events (AEs) were reported in 56.0% (139/248) of patients, among which anemia was the most common (25.8%). And the use of bedaquiline and linezolid was significantly associated with the occurrence of QT interval prolongation and optic neuritis ($p < 0.05$). Multivariate analysis revealed that BMI < 18.5 kg/m²(aOR: 3.66, 95% CI: 1.89-7.08, $p < 0.01$), advanced drug resistance (aOR: 2.25, 95% CI: 1.14-4.45, $p = 0.020$), pre-treatment anemia (aOR: 4.16, 95% CI: 2.01-8.61, $p < 0.001$) were independent predictors of unfavorable outcomes. Adjunctive immunotherapy was associated with favorable outcomes (aOR: 0.23, 95% CI: 0.09-0.55, $p < 0.001$). After PSM, pre-treatment anemia remained significantly correlated with unfavorable outcomes (aOR: 3.5; 95% CI: 1.41-8.67, $p = 0.007$).
CONCLUSION: A relatively low rates of treatment success were achieved for RR-TB patients in the elderly at tertiary tuberculosis hospitals in China. Low BMI, advanced drug resistance, and pre-treatment anemia were independent prognostic factors for unfavorable treatment outcomes. Adjunctive immunotherapy was prognostic factors for unfavorable treatment outcomes of elderly RR-TB patients. In tuberculosis management, special consideration should be given to elderly patients.

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Conflict of interest statement: Declarations. Ethics approval and consent to participate: The study adhered to the tenets of the Declaration of Helsinki and was approved by the Ethics Committee of Public Health Clinical Center of Chengdu as leading center (No.YJ-K2022-81-01). The present study was a retrospective study, the informed consent was waived signed, and all patient data were analyzed anonymously. The need for informed consent was waived by the Ethics Committee of Public Health Clinical Center of Chengdu. Consent for publication: Not applicable. Competing interests: The authors declare no competing interests.

42. The potential impact, cost and cost-effectiveness of tuberculosis interventions - a modelling exercise.

medRxiv [Preprint]. 2025 Sep 4:2025.09.02.25334943. doi: 10.1101/2025.09.02.25334943.

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BACKGROUND: While a range of interventions exist for tuberculosis prevention,

screening, diagnosis, and treatment, their potential population impact and cost-effectiveness are seldom directly compared, or evaluated between settings with different background TB epidemiology and structural drivers.
METHODS: We calibrated a deterministic TB model to epidemiological indicators in Brazil, India, and South Africa. We implemented seven interventions across countries focusing on prevention, screening and diagnosis, and treatment of TB, as well as TB screening in prisons in Brazil and nutritional supplementation in India. We standardised scale-up (2025-2030), coverage (80% of target population), and strength of evidence for epidemiological impact using published efficacy data. We estimated epidemiological impact and incremental cost-effectiveness ratios (ICERs), expressed as costs per disability-adjusted life year (DALY) averted by 2050.
RESULTS: Only three interventions prevented >10% of incident TB episodes by 2050: vaccination (median 15-28% across countries), symptom-agnostic community-wide screening (32-38%) and screening in prisons (23%). The impact of other interventions was more limited, ranging from 0% (shortened drug-susceptible treatment) to 5% (nutritional supplementation). ICERs varied widely by intervention and setting. Shortened drug-resistant treatment was cost-saving across settings, with the next lowest ICERs for prison screening in Brazil (72 USD/DALY) and nutritional supplementation in India (167 USD/DALY). Within each country, both low-cost community-wide screening and TB vaccine campaigns had lower USD/DALY than TB preventive treatment.
CONCLUSION: Interventions with meaningful epidemiological impact can also be cost-effective, but need to target populations beyond clinic-diagnosed individuals or their households. Achieving such potential requires a priority shift in funding, policy and product development.

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43. Non-tuberculous mycobacterial infections among patients with suspected or confirmed pulmonary tuberculosis in Ethiopia: A systematic review and Meta-analysis.

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OBJECTIVES: This study reviews and analyzes non-tuberculous mycobacteria (NTM) isolation from Ethiopian sputum samples, estimating prevalence, identifying common species, and analyzing regional and temporal variations.
METHODS: This systematic review and meta-analysis aimed to determine NTM prevalence among diseased individuals in Ethiopia. Using PubMed, Scopus, Web of Science, Google Scholar, and African Journals Online, we conducted a comprehensive literature search. Data extraction and quality assessment were conducted using the Newcastle-Ottawa scale. Meta-analysis was performed using STATA-18 software with a random-effects model and included subgroup analysis. The protocol of this study was registered with PROSPERO (CRD420251000131).
RESULTS: In this review, a total of 5415 participants were involved, and 53.8% were patients with suspected tuberculosis (TB), 37.6% were patients with pulmonary TB, 4.0% were patients with multidrug-resistant TB, and 4.6% were HIV-positive patients. The NTM prevalence was 3.8%, showing high heterogeneity and regional species variability. The meta-analysis highlighted differences in NTM prevalence across age groups and diagnostic tools, emphasizing the need for enhanced diagnostics and continuous surveillance to improve patient outcomes and inform public health strategies.
CONCLUSIONS: The review summarizes the epidemiology and geographical distribution of NTM infections and common NTM species isolated from patients with suspected pulmonary TB in Ethiopia, revealing regional variations and clinical implications. Despite limited data, Ethiopia has a lower prevalence of NTM compared with other African regions and the worldwide average.

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

coverage in the early phase of implementation.

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

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BACKGROUND: A policy of decentralised care for drug-resistant TB (DR-TB) was introduced in South Africa in 2011. We describe a trade-off between increasing coverage of services and poor quality of care, in the early phase of policy implementation.

METHODS: This was a mixed methods case study, comparing implementation in KwaZulu-Natal and Western Cape provinces; with interviews and quantitative analysis of routine DR-TB programme data. We analysed qualitative data, thematically organizing findings into inputs, processes, and outputs to explore how decentralisation influenced quality of DR-TB care.
RESULTS: Decentralisation of DR-TB care expanded access across provinces but there was wide variation in pace, planning and structural readiness. Where rapid scale-up outpaced capacity-building, weaknesses in resourcing, workforce, and clinical governance compromised quality of care. Two illustrative examples highlight that decentralisation to inadequately resourced sites resulted in morbidity to patients who did not receive effective monitoring for adverse events; and decentralising services to inadequately capacitated clinicians resulted in incorrect initiation in more complex cases and late referral of clinical complications.
CONCLUSIONS: Attempts to decentralise DR-TB treatment in the context of complex treatment algorithms and limited health system capacity resulted in trade-offs of care quality. We argue that quality of care should be an essential consideration in early implementation of health programmes.

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45. The Mycobacterium tuberculosis complex pangenome is small and shaped by sub-lineage-specific regions of difference.

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The Mycobacterium tuberculosis complex (MTBC) is a group of bacteria causing tuberculosis (TB) in humans and animals. Understanding MTBC genetic diversity is crucial for insights into its adaptation and traits related to survival, virulence, and antibiotic resistance. While it is known that within-MTBC diversity is characterised by large deletions found only in certain lineages (regions of difference [RDs]), a comprehensive pangenomic analysis incorporating both coding and non-coding regions remains unexplored. We utilised a curated dataset representing various MTBC genomes, including under-represented lineages, to quantify the full diversity of the MTBC pangenome. The MTBC was found to have a small, closed pangenome with distinct genomic features and RDs both between lineages (as previously known) and between sub-lineages. The accessory genome was identified to be a product of genome reduction, showing both divergent and convergent deletions. This variation has implications for traits like virulence, drug resistance, and metabolism. The study provides a comprehensive understanding of the MTBC pangenome, highlighting the importance of genome reduction in its evolution, and underlines the significance of genomic variations in determining the pathogenic traits of different MTBC lineages.

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46. Enhancing diagnostic efficiency of pyrazinamide resistance in Mycobacterium tuberculosis via modified MGIT assay and genotypic correlation.

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Pyrazinamide (PZA) plays a crucial role in the treatment of both active and latent tuberculosis, particularly in regimens designed to treat drug-resistant TB. However, diagnosing resistance to PZA poses challenges for managing TB, highlighting the need for accurate detection methods. This study aims to address the challenges in detecting PZA resistance by modifying the standard MGIT960 PZA drug susceptibility testing method by optimizing the inoculum dilution. Briefly, three MGIT DST versions were evaluated: the standard method, the reduced inoculum (RI) method employing a 1:20 inoculum dilution and the sparse dilution (SD) method using a 1:50 dilution of the inoculum for growth control tube, while the undiluted MGIT positive culture was used for the PZA test tube. The SD MGIT DST approach minimized the number of false-resistant PZA results to (31/401) 7.7 % against 27 % by standard MGIT DST and 11.7 % by RI MGIT DST approach, thereby reducing the false-positivity rate by 19.3 %. Targeted sequencing of pncA gene identified mutations in only 14/401 isolates (3.5 %). Whole genome sequencing (WGS) of the 31 phenotypically resistant isolates identified resistance -associated mutations in pncA gene (45 %), panD (9.6 %), mas (12.9 %), glpK (3.2 %), and lprG (3.2 %), and others efflux associated genes like Rv1258c (3.2 %), Rv0191c (3.2 %), and Rv3008 (6.45 %), except for 4 isolates, for which no mutations were detected in the target genes. These genes are involved in various resistance mechanisms including cell wall synthesis, metabolic pathways, and drug tolerance, which are essential for PZA efficacy. Notably, new mutations in glpK and mas were detected in isolates with wild-type pncA and were absent in the sensitive isolates. Our study substantiates the improvement of phenotypic testing methods and enhances the detection of PZA resistance even in resource-limited settings and direct research towards improving the diagnostic accuracy in TB drug resistance management.

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47. Development of SNP-LAMP Combined with Lateral Flow Dipstick to Detect the S531L rpoB Gene Mutation in Rifampicin-Resistant Mycobacterium tuberculosis.

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

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Background: Tuberculosis (TB) remains a primary global health concern, despite the widespread availability of effective chemotherapeutic interventions. The emergence and dissemination of drug-resistant strains of Mycobacterium tuberculosis, particularly those exhibiting resistance to rifampicin, present significant obstacles to the success of TB control programs. Consequently, there is an urgent need for rapid, sensitive, and specific molecular diagnostic tools to inform timely clinical decision-making and reduce the transmission of disease. Loop-mediated isothermal amplification (LAMP) has gained attention as a promising alternative to conventional polymerase chain reaction (PCR) techniques. This method, which facilitates DNA amplification under constant temperature conditions, offers advantages including high specificity, rapid turnaround time, and operational simplicity-features that render it especially suitable for implementation in resource-limited settings. Methods: In this study, a LAMP assay targeting the rpoB gene was developed, with particular focus on detecting the codon 531 C→T mutation associated with rifampicin resistance. A set of four to six primers was designed to recognize six distinct regions of the target sequence. Allele-specific amplification was achieved by incorporating a deliberate single nucleotide mismatch at the 3' terminus of the B2 primer to enable precise discrimination between wild-type and mutant alleles. The assay

was conducted at an optimized temperature of 61 °C for 60 min, followed by visual detection using a lateral flow dipstick (LFD) within five minutes. Results: The LAMP-LFD assay demonstrated 100% concordance with drug susceptibility testing (DST) and DNA sequencing. No cross-reactivity with wild-type strains was observed, underscoring the assay's high specificity. Conclusions: This platform offers a robust, field-deployable solution for detecting the codon 531 C→T mutation associated with rifampicin resistance in low-resource settings.

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PMCID: PMC12428009
PMID: 40941669

Conflict of interest statement: The authors declare no conflicts of interest.

48. Spoligotyping-based molecular typing of Mycobacterium tuberculosis complex isolated from Metahara sugar factory workers in Central Ethiopia.

Front Med (Lausanne). 2025 Sep 1;12:1641535. doi: 10.3389/fmed.2025.1641535. eCollection 2025.

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BACKGROUND: Understanding the genetic makeup of Mycobacterium tuberculosis complex (MTBC) strains is crucial, as lineage differences influence transmissibility, pathogenicity, and drug resistance patterns, all of which are essential for understanding MTBC transmission dynamics and designing effective TB control strategies. The present study investigated the genetic diversity of Mycobacterium tuberculosis complex among pulmonary tuberculosis (TB) patients employed at Metahara Sugar Factory, located in Fentale district, East Showa Zone Oromia, central Ethiopia.
METHODS: A cross-sectional study was conducted among 390 suspected pulmonary TB patients. Sputum samples were examined using Ziehl-Neelsen staining and

cultured, followed by molecular characterizations of the isolates using region of difference 9 (RD9) deletion typing and spoligotyping.
RESULTS: Out of 390 participants, 96 (24.6%) were smear positive, and 89 (22.8%) were culture positive. RD9 deletion typing confirmed 88 isolates as M. tuberculosis. Further characterization of the 88 isolates using spoligotyping revealed 28 distinct spoligotyping patterns of which 15 unique (single isolates), and 13 shared among 73 clustered isolates. Among these, 19 matched shared international type (SITs) in the SpolDB4 database, while, 9 were novel (orphan) patterns. The predominant SITs were SIT523 (19.32%), SIT53 (13.6%), SIT149 (9.1%) and SIT289 (7.95%). Lineage analysis using TB-insight RUN TB-Lineage classified the strains primarily as Euro-American (63.64%), followed by Indo-Oceanic (20.45%), East-African-Indian (14.77%) and M. africanum (1.14%).
CONCLUSION: The high clustering rate observed may suggest recent transmission; however, this must be interpreted cautiously due to the limited discriminatory power of spoligotyping, which may overestimate clustering and underestimate diversity. This underscores the need for targeted TB control strategies informed by enhanced molecular surveillance.

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49. Paucibacillary Tuberculosis Drives the Low Positive Predictive Value of Xpert MTB/RIF Ultra for Rifampicin Resistance Detection in Low-Prevalence Settings.

Clin Infect Dis. 2025 Sep 16;81(2):372-378. doi: 10.1093/cid/ciaf132.

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BACKGROUND: Xpert MTB/RIF Ultra (Ultra) aimed to improve the specificity in identifying rifampicin-resistant tuberculosis (RR-TB), compared to Xpert MTB/RIF.
METHODS: In a nationwide study in Rwanda, patients diagnosed with RR-TB by Ultra between December 2021 and January 2024 underwent repeat Ultra testing, complemented by rpoB gene sequencing and phenotypic drug-susceptibility testing (pDST), serving as reference tests.
RESULTS: Of 129 patients initially diagnosed with RR-TB by Ultra, only 41 (32%) had concordant rifampicin results upon repeat Ultra testing. The remaining 88 patients (68%) had unconfirmed resistance on repeat Ultra. Reference testing was available for 40 (98%) of 41 confirmed cases, all verified as true RR-TB. Among 88 unconfirmed cases, reference testing was available for 61 (69%), with 7 (11%) confirmed as true RR-TB, whereas 54 (89%) were found to have rifampicin-susceptible TB. Notably, 89% of 55 patients with very low bacillary loads on their initial Ultra had false RR-TB results, a significantly higher risk of false resistance compared to other bacillary load categories combined (risk ratio: 8.20; 95% confidence interval [CI]: 3.56-18.85; P < .001). Consequently, 53% (54/101) of initial RR patients with available reference testing received unnecessary RR-TB treatment.
CONCLUSIONS: Ultra represents a valuable tool for rapid RR-TB detection; however, in low prevalence settings its low positive predictive value for RR detection is largely driven by samples with very low bacillary loads. As programs expand active case-finding and early detection of asymptomatic disease, the proportion of TB detected with very low bacillary load will increase. Diagnostic algorithms require adjustments to prevent unnecessary RR-TB treatment.

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Conflict of interest statement: Potential conflicts of interest. The authors: No reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

50. A decision-making model for public health authorities in circumstances of potentially high public risk.

J Public Health (Oxf). 2025 Aug 29;47(3):550-557. doi: 10.1093/pubmed/fdaf052.

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BACKGROUND: An expert multidisciplinary panel was commissioned by a UK Health Security Agency led incident management team (IMT) to support decision making in the case of an individual with extensively drug-resistant tuberculosis. The behaviour and stated intentions of the individual were potentially a significant risk to public health, and the regional IMT felt unable to adequately balance the rights of the individual, versus the public health risk, within current processes and legal powers.

METHOD: We describe the composition, organization, implementation, and conclusions of a national, expert, multidisciplinary panel.
RESULTS: The national panel convened over three structured virtual meetings to consider the balance between the rights of the individual to an unrestricted life, and the duty to protect the public's health. Evidence included briefs from the regional IMT and input from a public consultation group. Following the first two meetings the need for a literature review examining the success of surgical interventions was identified and conducted.
CONCLUSIONS: Evidence and conclusions were mapped onto a custom-designed risk assessment template. The panel provided authoritative advice regarding the case, and developed a review methodology that is transferable to similar complex public health scenarios both in the UK and internationally.

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51. Bedaquiline and levofloxacin replacing rifampicin for the treatment of TB.

IJTLD Open. 2025 Sep 10;2(9):542-544. doi: 10.5588/ijtldopen.25.0263.
eCollection 2025 Sep.

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DOI: 10.5588/ijtldopen.25.0263
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52. Antimicrobial peptide PK34 modification enhances the antibacterial and anti-inflammatory effects of bone-derived mesenchymal stem cells in Mycobacterium tuberculosis infection.

Stem Cell Res Ther. 2025 Aug 29;16(1):469. doi: 10.1186/s13287-025-04596-9.

He XY(#)(1)(2), Wang JQ(#)(3), Chen Y(1)(2), Yuan TX(4), Zhao X(1)(2), Sun YJ(1)(2), Liu YM(1)(2), Wang ZY(1)(2), Cai YB(1)(2), Gao W(5), Cui CP(3), Yi ZJ(6)(7), Li Q(8)(9).

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BACKGROUND: New therapeutic strategies are needed to treat tuberculosis (TB). The antimicrobial peptide PK34 has a good ability to clear Mycobacterium tuberculosis (Mtb) and is not prone to drug resistance and adverse reactions. Mesenchymal stem cells (MSCs) can also be used as an adjunctive therapy for the treatment of TB. However, there have been no studies combining the two for the treatment of Mtb infection.
METHODS: We aimed to construct bone-derived mesenchymal stem cells secreting the antimicrobial peptide PK34 (named Plent-PK34-BMSCs) and to investigate their

roles in both in vitro and in vivo Mtb H37Rv infection models.
RESULTS: We successfully constructed Plent-PK34-BMSCs that secrete and express the antimicrobial peptide PK34, and demonstrated that PK34 modified MSCs significantly enhanced their in vitro and in vivo antibacterial ability and cytoprotective effects. The cytokine results showed that Plent-PK34-BMSCs increased the levels of anti-inflammatory factors IL-4 and IL-10 in the cell supernatant, decreased the levels of pro-inflammatory factors IL-6 in the serum of the mice. In addition, lung tissue analysis results showed that mice treated with Plent-PK34-BMSCs had reduced infiltration and congestion of inflammatory cells in lung tissue, significantly reduced lung injury, and exhibited better preservation of lung structure.
CONCLUSIONS: PK34 modification enhanced the therapeutic efficacy of MSCs in Mtb infection models, and Plent-PK34-BMSCs transplantation has the potential to treat TB.

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Conflict of interest statement: Declarations. Ethics approval and consent to participate: For animal experiments, the study entitled ‘The role and molecular mechanism of PK34 modified mesenchymal stem cells in the treatment of tuberculosis’ was approved by the Medical Ethics Committee of Shandong Second Medical University (Date: 02.28.2018, No. 075) and performed according to the AVMA guidelines. All experimental procedures were conducted in strict accordance with ethical standards for animal research. This research did not involve the use of any human cells, tissues, samples, or cell lines. Consent for publication: Not applicable. Competing interests: The authors declare that they have no competing interests. Artificial intelligence: The authors declare that they have not use AI-generated work in this manuscript.

53. Description of bacterial RNA transcripts detected in Mycobacterium tuberculosis - infected cells from peripheral human granulomas.

Virulence. 2025 Dec;16(1):2547326. doi: 10.1080/21505594.2025.2547326. Epub 2025 Aug 25.

Moos PJ(1), Carey AF(2), Joseph J(3), Kialo S(4), Norrie J(4), Moyareke JM(4), Amof A(4), Nogua H(4), Lim AL(5), Barrows LR(1).

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Update of
bioRxiv. 2024 Aug 20:2024.08.20.608852. doi: 10.1101/2024.08.20.608852.

Mycobacterium tuberculosis (Mtb) remains a global human health threat. However, understanding effects of the microbe on cellular interactions in infected tissue has been hindered by inability to discriminate between infected versus un-infected cells. We included the H37Rv Mtb reference genome when assembling scRNA seq libraries from fine needle aspirate samples of peripheral nodal TB patients. Using the 10X Genomics Cell Ranger tool to align sequencing reads, we consistently detected bacterial small and large ribosomal subunit RNA sequences. We interpret Mtb reads associated with a cell's UMI and transcriptome to indicate infection of that individual host cell. This provides a new window into the status of infected cells in the context of the bystander cells in the infected tissue. We investigated these Mtb transcripts to explore their clinical utility. The Mtb transcripts showed frequent sequence variation from the reference genome, with greater than 90% of the rrs or rrl reads from many clinical samples having at least one sequence difference. The highly conserved nature of the rrs and rrl gene sequences limited the ability to assign bacterial lineage based solely transcriptome analysis. However, rapid improvements in sequencing depth may soon allow transcriptome analysis of infecting microbes and improved certainty regarding their lineage, drug resistance, and virulence factors.

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54. Clinical and epidemiological analysis of 893 patients with spinal tuberculosis: an 11-Year investigation of a general hospital in East China.

BMC Musculoskelet Disord. 2025 Sep 1;26(1):830. doi: 10.1186/s12891-025-09053-5.

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BACKGROUND: The burden of spinal tuberculosis (STB) in China remains substantial, with the country ranking third in the number of tuberculosis cases globally in 2022, among the 30 countries with a high tuberculosis burden. In East China, few large-scale studies have been conducted on STB.
METHODS: This retrospective study analyzed 893 confirmed STB cases (2010-2020). Demographic, clinical, and diagnostic data were statistically characterized using χ^2/t-tests for categorical/continuous variables (significance at $P < 0.05$).
RESULTS: The annual number of confirmed STB cases of spinal TB showed a sustained upward trend. Among 893 STB patients (male: female = 1.4:1; median age 56 years), rural populations exhibited higher prevalence ($P = 0.264$ for delayed hospitalization vs. urban). Farmers/laborers predominated (84.7%), with hypertension (32.4%), diabetes (18.5%) and osteoporosis (12.9%) as major comorbidities. Concurrent pulmonary TB occurred in 435 cases (48.7%) and other extrapulmonary TB in 71 (8.0%). Diagnostic evaluations revealed TSPOT (82.7%), histopathology (75.9%) and Xpert-MTB/RIF (71.8%) as most sensitive methods. Compared with histopathological gold standard, Xpert demonstrated 81.5% sensitivity, 58.8% specificity, 87.0% PPV and 48.3% NPV (kappa = 0.374). Combining histopathology with Xpert achieved 86.6% diagnostic accuracy, significantly surpassing individual methods ($P < 0.001$). Lesion distribution showed lumbar (44.3%) and thoracic (42.3%) predominance, mostly involving ≥ 2 contiguous vertebrae (91.3% continuous vs. 8.7% skip lesions). Chemotherapy remained primary treatment, with 6.5% drug resistance rate showing annual escalation (mainly monoresistance). Surgical intervention achieved favorable outcomes in 648 cases (72.6%).
CONCLUSION: Over the course of the study period, the overall diagnosis rate of spinal tuberculosis exhibited an upward trend. Despite East China's relatively advanced socioeconomic and healthcare systems, spinal tuberculosis remains a substantial public health challenge, primarily due to the region's complex population composition and high population mobility. The prevention and management of spinal tuberculosis continue to present considerable challenges.

Early diagnosis, combined with an appropriate treatment course, ensures that both chemotherapy and surgical interventions yield satisfactory outcomes. Increasing the allocation and investment of medical resources for tuberculosis, enhancing health management for migrant populations, and raising public health awareness are essential.

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55. Finding the optimal regimen for Mycobacteroides abscessus treatment (FORMaT) in people with Mycobacteroides abscessus pulmonary disease: a multicentre, randomised, multi-arm, adaptive platform trial.

BMJ Open. 2025 Sep 21;15(9):e096188. doi: 10.1136/bmjopen-2024-096188.

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INTRODUCTION: Mycobacteroides abscessus (MABS) is within the non-tuberculous mycobacteria family. It inhabits soil and water, exhibits multi-antibiotic resistance and causes opportunistic lung infections, which may progress to symptomatic MABS-pulmonary disease (MABS-PD) associated with substantial morbidity, increased healthcare utilisation, impaired quality of life and increased mortality. Treatment regimens for MABS-PD are highly variable, not evidence-based and involve complex, expensive drug combinations administered for prolonged periods (>12 months) with frequent adverse effects and treatment failure. There is an urgent need for safe, efficacious and cost-effective MABS-PD therapy. Here, we describe the Master Protocol for the Finding the Optimal Regimen for Mycobacteroides abscessus Treatment (FORMaT) trial. FORMaT aims to determine the most effective and best tolerated treatment for MABS-PD as defined by MABS clearance from respiratory samples with good treatment tolerance.
METHODS AND ANALYSIS: FORMaT is an international multicentre, adaptive platform trial evaluating treatment combinations for MABS-PD. Participants are randomised multiple times during the trial, with assessment of the primary outcome of clearance of MABS infection with good treatment tolerance. Initially, therapies recommended in international consensus guidelines are being tested. Data obtained will eliminate therapies lacking efficacy or causing unacceptable toxicity. Novel treatments can then be added and tested against previously determined optimal approaches, leading in an iterative fashion to improved microbiological clearance and health outcomes. In parallel, an Observational cohort and several integrated and discovery studies are embedded in FORMaT to identify biomarkers of MABS-PD and MABS clearance, clinical and radiographic treatment response, drug pharmacokinetics and Mycobacteroides genomics and resistome.
ETHICS AND DISSEMINATION: The FORMaT Master Protocol and related documents are approved by regulatory authorities in each participating jurisdiction and/or site. Results will be published in peer-reviewed journals and presented at scientific meetings. De-identified, aggregated data will be shared on an approved online platform.
TRIAL REGISTRATION NUMBERS: NCT04310930, ANZCTR12618001831279, 2020-000050-10,
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an Australian Research Council grant on airborne infection transmission. KG holds an honorary appointment on the iDSMB for an MRFF-supported adaptive platform trial on treating acute respiratory exacerbations in cystic fibrosis. KL received institutional payments from an NHMRC Investigator Grant (2017498), an NHMRC Career Development Fellowship (1127984) and an NHMRC Project Grant (1152249). TQ receives funding from the University of Queensland via a CFF grant for the FORMaT study in his role as Danish Principal Investigator. TQ has received payments for work on the Vertex Scientific Board and from Chiesi for speaker engagements. TQ holds an unpaid role as President of the Danish Society for Internal Medicine. JAR received project funding from the MRFF (1152249). GR received grant funding from the MRFF (2022/MRF2018745, 2020/MRF2001755) and NHMRC (2022GNT2020254). ARS has received research grants (paid to the University of Nottingham) from Vertex Pharmaceuticals and advisory board payments (also paid to the University of Nottingham) from Viatris Pharmaceuticals, all outside the current work. ARS holds patents issued outside the current work (Camara M, Williams P, Barrett D, Halliday N, Knox A, Smyth A, Fogarty A, Barr H, Forrester D. Alkyl quinolones as biomarkers of Pseudomonas aeruginosa infection and uses thereof. US-2016131648-A1; https://pubchem.ncbi.nlm.nih.gov/patent/US-2016131648-A1). ARS is a member of the DSMB for the North American Cystic Fibrosis Foundation Therapeutic Development Network. AT received salary for conceptualising the macrophage and mitochondria substudy, producing the standard operating procedures and conducting downstream work on the substudy. HAWMT received grants from IMI, NHMRC and CFF. Erasmus Medical Centre holds a royalty agreement for PRAGMA-CF. HAWMT has received consulting fees from Insmed and Novartis (paid to his institution) and from BI (paid directly). He received funding from Vertex for presenting at a Faculty Advance Course funded by Vertex, and travel support from Erasmus Medical Centre, Chiesi and Thirona to attend meetings and conferences. HAWMT is Chair of the ECFS Standardisation Committee. He was employed by Erasmus Medical Centre until 1 October 2023 and now holds an Emeritus Professor appointment. He became CMO of Thirona, Nijmegen, the Netherlands on 1 April 2022. RT received travel support from Beyond Air to present trial findings at the CHEST meeting in Nashville in 2022, and institutional payments from AN2 Therapeutics. RT held an unpaid role as ATS Assembly Chair and Board Member (2020–2022), is currently serving as Chair of the ATS Nominating Committee (2023–2024) and is an unpaid member of the ATS Membership Committee (2023–2024). CW is the Chief Investigator on the MRFF (1152249) grant and received institutional payments from the CFF (WAINWR19A0), the Children's Hospital Foundation and the University of Queensland Cystic Fibrosis Programme Grant (50301). CW is an Associate Editor for Respirology and Thorax, and has received research funding and advisory board/consultancy payments from Vertex Pharmaceuticals, paid to the University of Queensland. All other authors have no conflicts of interest to declare.

Recent TB News

TB is the No. 1 killer among infectious diseases. A new study says its toll could mount.
https://www.tpr.org/news/2025-09-11/tb-is-the-no-1-killer-among-infectious-diseases-a-new-study-says-its-toll-could-mount

With Trump's cuts to foreign assistance, researchers report that more than 10 million additional people could become infected with tuberculosis, and 2.2 million could die by 2030 in high-burden countries under worse-case-scenario funding. These impacts will be felt the most in countries with limited capacity to reallocate funds to close the gap that has since been exacerbated by cuts to health aid. The longer it takes to close the gap, the greater the impact will be, and researchers are trying to outline the potential suffering for countries and donors to push back and reduce the scale of future suffering.

New AI methods maps how tuberculosis drugs destroy bacteria.
https://www.drugtargetreview.com/news/185159/new-ai-method-maps-how-tuberculosis-drugs-destroy-bacteria/

With the development of a new effective tuberculosis (TB) regimen in high demand globally, researchers at Tufts University School of Medicine have created a new tool that can assist in analyzing how potential TB drugs kill bacteria. DECIPHAER (which stands for encoding cross-modal information of pharmacologies via autoencoders) is an AI assisted system that can predict molecular effects from images and offers a cheaper and faster way to study potential TB treatments. This could be a big step in assessing and accelerating new TB drugs and could potentially be extended to other infectious diseases in the future.