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1. Application of continuous glucose monitoring and automated insulin delivery technologies for pregnant women with type 1, type 2, or gestational diabetes: an international consensus statement.

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Insulin resistance increases after the first trimester of pregnancy, leading to glycaemic challenges for women with pregestational type 1 diabetes or type 2 diabetes. Additionally, insulin resistance can promote hyperglycaemia in pregnant women without type 1 diabetes or type 2 diabetes, who develop gestational diabetes. Although most (>95%) women with diabetes deliver healthy babies, maternal dysglycaemia can have consequences for the mother and child, including prenatal, perinatal, immediate, and long-term postnatal complications. Diabetes technologies, such as continuous glucose monitoring (CGM) and automated insulin delivery (AID) systems can aid in optimising glycaemia outside of pregnancy. These novel technologies have not been extensively tested in large randomised controlled trials before and during pregnancy. However, compelling data report the benefits of CGM in type 1 diabetes, and increasing data report on AID systems in pregnancies complicated by type 1 diabetes. Appropriate CGM glucose thresholds for the diagnosis of gestational diabetes and the recommended time in range treatment targets for the routine management of gestational diabetes and type 2 diabetes still need to be determined. The recommendations in this Consensus Statement emphasise the value of CGM during preconception and pregnancy for women with pregestational type 1 diabetes in reducing pregnancy complications. Recommendations also include the use of AID systems in women with pregestational type 1 diabetes to improve glycaemic management during preconception, during pregnancy and delivery, and in the postpartum period. This Consensus Statement has been endorsed by 24 societies and groups.

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Conflict of interest statement: Declaration of interests KB has received consulting fees from AstraZeneca and Eli Lilly; speakers fees from Novo Nordisk, AstraZeneca, and Mundipharma Medtronic; support for attending meetings or for travel from AstraZeneca and Novo Nordisk; grants or contracts from Medtronic, Novo Nordisk, Eli Lilly, AstraZeneca, Metagenics, and Abbott; has received equipment, materials, or drugs from Medtronic, Dexcom, Novo Nordisk, Abbott, and Lifescan; and is the recipient of a Senior Fellowship of The Flemish Research Foundation (1800225N). CD has received research funding from Dexcom, Abbott, and the Helmsley Charitable Trust; and has sat on data safety monitoring boards or advisory boards for Abbott and Dexcom. DA has received payment or honoraria from Abbott Diabetes Care and the diaTribe Foundation; and has declared a leadership or fiduciary role at DeDoc. AA has received grants or contracts from the National Institutes of Health (NIH), Breakthrough T1D, and the Helmsley Charitable Trust; has received payment or honoraria from the American Diabetes Association (ADA) and Breakthrough T1D; has received support for attending meetings or for travel from the International Society for Pediatric and Adolescent Diabetes, Advanced Technologies and Treatments for Diabetes (ATTD) conference, and ADA; and has declared a leadership or fiduciary role at ADA Health Disparities and T1Dx-QI. TB has served on advisory panels for Novo Nordisk, Sanofi, Eli Lilly, AstraZeneca, Medtronic, Abbott, and Roche; has received honoraria for participating in speaker bureaus from Eli Lilly, Novo Nordisk, Medtronic, Abbott, Sanofi, Dexcom, Aventis, AstraZeneca, and Roche; has received research grant support to their institution from Abbott, Medtronic, Novo Nordisk, Sanofi, Novartis, Sandoz, Zealand Pharma, the Slovenian Research and Innovation Agency, the NIH, BreakthroughT1D, the Helmsley Foundation, and the European Union. RMB has received research support, has acted as a consultant, or has sat on the scientific advisory board for Abbott Diabetes Care, Ascensia, DexCom, Eli Lilly, Embecta, Insulet, Medtronic, Novo Nordisk, Roche Diabetes Care, Tandem Diabetes Care, and Sanofi; and their employer—non-profit HealthPartners Institute—contracts for his services: he receives no personal income from these activities. AC has acted as a consultant or has sat on the scientific advisory board for Novo Nordisk, Insulet, MannKind, and Zealand; and has declared clinical research investigator status for Novo Nordisk, Medtronic/Companion Medical, Insulet, Sanofi, Dexcom, Abbott, Eli Lilly, UnitedHealth, and Tandem Diabetes. LED has received research grant funding for investigator-initiated research from Diabetes Canada, Major Sciences Initiatives Competition, and the Alberta Diabetes Institute; has received research funding for investigator-initiated research from the Calgary Health Trust; was a speaker for Dexcom, but declares that the payment was made to their institution; and has received, at reduced cost, a loan of equipment from Dexcom, Tandem Diabetes Care, Medtronic, and Inter-analytics for investigator-initiated research funded by non-profit competitive funding agencies. DRF declares that their employer received consulting fees and payment or honoraria from Embecta, Eli Lilly, Novo Nordisk, Abbott, and Medtronic; declares that Embecta, Eli Lilly, Novo Nordisk, and Abbott paid their employer for sitting on a data safety monitoring board or advisory board; and received support for attending meetings or for travel from Novo Nordisk. DI has received payment or honoraria from Dexcom, Abbott, Sanofi, Novo Nordisk, Insulet, Tandem, Eli Lilly, Sequel, and Medtronic. KK has received grants or contracts from AstraZeneca, Boehringer Ingelheim, Eli Lilly, Merck Sharp and Dohme, Novo Nordisk, Roche, Sanofi,

Servier, Oramed Pharmaceuticals, Daiichi-Sankyo, and Applied Therapeutics; has received consulting fees and payment or honoraria from Amgen, AstraZeneca, Bristol Myers Squibb, Boehringer Ingelheim, Eli Lilly, Novo Nordisk, Sanofi, Servier, Pfizer, Roche, Daiichi-Sankyo, Embecta, and Nestle Health Science; is a member of KDIGO Indigo Type 2 Diabetes and CKD guidelines, a member of the Primary Care Study Group of the European Association for the Study of Diabetes, a council member for the Research Advisory Council at the Public Health Foundation of India, sits on the RSSDI International Advisory Board, India, is a member of the ADA Overcoming Therapeutic Inertia Advisory Group, is a board member for the European Association for the Study of Diabetes/European Foundation for the Study of Diabetes; and is also supported by the National Institute for Health Research (NIHR) Applied Research Collaboration East Midlands and the NIHR Leicester Biomedical Research Centre. CJL has declared that payment was made to their institution for grants from Tandem Diabetes, Insulet, Dexcom, Abbott, MannKind, Deka-TWIIST, NIH, the Helmsley Foundation, and Breakthrough T1D; has received consulting fees and support for attending meetings or for travel from Dexcom, Insulet, and Tandem Diabetes; and has sat on a data safety monitoring board or advisory board for the NIH and Breakthrough T1D. HRM declares that their institution was paid with a grant or contract from the NIHR Health Technology Assessment; received speaker fees from Abbott Diabetes Care, Dexcom, Eli Lilly, Medtronic, Novo Nordisk, Sanofi, and Ypsomed; received support for attending meetings or for travel from Ypsomed Australia and Dexcom; has declared a leadership or fiduciary role as the chair of the National Pregnancy in Diabetes audit; sits on the Diabetes Care and Diabetologia editorial board; and has received equipment from Abbott Diabetes Care for PROTECT. RN reports grants from Taisho Pharmaceutical, Ono Pharmaceutical, Mitsubishi, Nippon Boehringer Ingelheim, Arkaly, Kowa, and Abbott; and declares consulting fees or honoraria from Eli Lilly Japan, Novo Nordisk, Abbott, Sanofi, Japan Medtronic, Nippon Boehringer Ingelheim, Teijin, Kissei Pharmaceutical, Medtronic, and Astellas. SP has received research funding from Breakthrough T1D, the Helmsley Charitable Trust, the NIH, NIDDK, Dexcom, Medtronic MiniMed, the University of Colorado, and T1D Exchange; honoraria from the Children's Diabetes Foundation and the ADA; received support for attending meetings or for travel from the Children's Diabetes Foundation, the American College of Diabetology, Breakthrough T1D, and the ADDT conference; has received payment for sitting on a data safety monitoring board or advisory board for the Sansum Diabetes Research Institute; has declared an unpaid leadership or fiduciary role at the American College of Diabetology and the ADA. DS declared support for attending meetings or for travel from the conferences themselves as an invited speaker; has sat on a data safety monitoring board or advisory board for the Australian Commission on Safety and Health and the South Western Sydney Local Health District; has declared a leadership or fiduciary role at Diabetes Australia, ADIPS, and the Aotearoa Diabetes Foundation, New Zealand; has received equipment to their institution from Tandem and Abbott; and has received an educational grant to their institution from Abbott. JMY has received grants or contracts from CIHR, Diabetes Canada, the Health Sciences Foundation, Diabetes Research Envisioned and Accomplished in Manitoba, the Manitoba Medical Services Foundation, and the Winnipeg Foundation; has received support for attending meetings and has received equipment, materials, or drugs from Abbott, Dexcom, and Medtronic; and has a leadership or fiduciary role at Diabetes Canada and the Diabetes in Pregnancy Study Group. ÁGT has reported an unpaid leadership role in the

Hungarian Diabetes Association and the Diabetes Pregnancy Study Group; has received grants from the Ministry of Innovation and Technologies of Hungary; has received consulting fees from Boehringer Ingelheim, 77 Elektronika, and Sanofi-Aventis; and has received speaker fees from AstraZeneca and Sanofi-Aventis. DF has received grant support from Dexcom; has received payment for honoraria from Sanofi and Medtronic; and has received equipment from Tandem and Dexcom. EMS has declared that grants or contracts have been paid to their institution by Abbott Diabetes Care; has received payment of honoraria from Ypsomed Diabetes Care and Eli Lilly; and has received support for attending meetings or for travel by Ypsomed Diabetes Care and Eli Lilly. All other authors declare no competing interests.

2. Menaquinone depletion resensitises bedaquiline-resistant tuberculosis.

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Tuberculosis remains a leading cause of global mortality, and rising bedaquiline resistance threatens the effectiveness of current drug-resistant treatment regimens. Bedaquiline resistance typically arises through mutations in Rv0678 that upregulate drug efflux and confer cross-resistance to multiple drug classes. Here, we identify and optimise a chemical series targeting MenG, a central enzyme in the menaquinone biosynthesis pathway, yielding potent bactericidal inhibitors with in vivo efficacy. Strikingly, MenG inhibition restored bedaquiline susceptibility in efflux-mediated resistant strains, an effect confirmed in vivo where combination therapy achieved a 99.8% reduction in bacterial burden compared with bedaquiline alone. Potentiation also extended to pretomanid and other key agents. Disruption of upstream menaquinone and shikimate pathway enzymes produced similar resensitisation, establishing these pathways as tractable targets for restoring drug susceptibility in Mycobacterium tuberculosis . These findings provide a novel strategy to overcome bedaquiline resistance and strengthen future regimens for efflux-mediated drug-resistant tuberculosis.

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3. Clinical evaluation of a commercial culture-free targeted next-generation sequencing test for diagnosis of drug-resistant tuberculosis.

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Rapid molecular diagnostics have significantly improved access to tuberculosis (TB) drug resistance detection and reduced turnaround times. However, these tools remain limited in their capacity to generate comprehensive resistance profiles, particularly for newer and repurposed anti-TB drugs. Targeted next-generation sequencing (tNGS) offers a promising alternative, enabling a broader resolution of Mycobacterium tuberculosis genomes and faster reporting compared to phenotypic drug susceptibility testing (DST). We conducted a prospective, cross-sectional, multicenter evaluation of the DeepChek 13-Plex KB Drug Susceptibility Testing (ABL Diagnostics S.A., France) tNGS assay for direct detection of TB drug resistance from clinical sputum samples. The study was performed at three reference laboratories in India, South Africa, and Georgia between April 2021 and June 2022. Adults (≥18 years) with confirmed pulmonary TB were enrolled. Sensitivity and specificity were assessed for key anti-TB drugs against a composite reference standard combining phenotypic DST and whole-genome sequencing. Of 832 participants enrolled, 694 (83.4%) were included in the final analysis. Sequencing was successful in 75.6% of samples. Failure rates were higher in samples with low or very low Xpert MTB/RIF categories. The ABL tNGS workflow showed ≥95% sensitivity for rifampicin, isoniazid, and levofloxacin; 92%-93% for pyrazinamide and moxifloxacin; 88% for ethambutol; and 72%-82% for bedaquiline and clofazimine. Specificity was ≥95% for all drugs. The ABL tNGS workflow enables comprehensive resistance profiling, including for new and repurposed TB drugs. However, higher bacillary loads are required to provide a valid test compared to current class-based tNGS assays recommended by the WHO,

thus requiring further improvements.
IMPORTANCE: Drug-resistant tuberculosis (TB) threatens progress in global TB control, yet current molecular tests detect resistance to only a few drugs. Targeted next-generation sequencing (tNGS) can read many resistance-related genes at once, offering faster and broader results than conventional culture-based testing. We evaluated a commercial tNGS workflow (DeepChek 13-Plex KB, ABL Diagnostics) for direct detection of drug resistance in sputum samples from adults with pulmonary TB in India, South Africa, and Georgia. Among 832 participants, sequencing produced valid results for most samples with moderate or high bacterial loads. The assay accurately identified resistance to key drugs-including rifampicin, isoniazid, fluoroquinolones, and newer medicines such as bedaquiline and clofazimine-while maintaining high specificity. These findings show that tNGS can deliver comprehensive resistance profiles, supporting tailored treatment for people with drug-resistant TB. Further refinement in sample preparation may expand its use to specimens with lower bacterial counts.
CLINICAL TRIALS: This study is registered with ClinicalTrials.gov as NCT04239326.

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4. Large-scale testing of antimicrobial lethality at single-cell resolution predicts mycobacterial infection outcomes.

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In vitro antibiotic testing is important for guiding therapy and drug development. Current methods are focused on growth inhibition in bulk bacterial populations but often fail to accurately predict treatment responses. Here we introduce Antimicrobial Single-Cell Testing (ASCT), a large-scale live-cell imaging approach that quantifies bacterial killing in real time at single-cell resolution. By tracking over 140 million mycobacteria and analysing ~20,000 time-kill curves, we identify key determinants of antibiotic killing and its clinical relevance. For Mycobacterium tuberculosis, we found that drug-specific killing dynamics in starved bacteria, rather than growth inhibition or killing of growing cells, predict regimen efficacy in mice and humans. Extending this approach to Mycobacterium abscessus and comparing 405 bacterial strains, we show that antibiotic killing is also a genetically encoded bacterial trait (drug tolerance). We demonstrate that tolerance patterns cluster by antibiotic targets, identify a phage protein that modulates antibiotic killing, and show that strain-specific killing dynamics are associated with individual patient outcomes independent of drug resistance. Together, these findings establish a

framework that reveals how drug properties and bacterial diversity shape treatment responses, offering a path to more effective and personalized therapies.

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5. Acquired resistance during short-course treatment for rifampicin-resistant Tuberculosis.

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OBJECTIVES: Shorter regimens represent a significant advancement for rifampicin-resistant tuberculosis (RR-TB) treatment. However, data on acquired drug resistance (ADR) remain limited.
METHODS: This study was nested within TB-TRUST serial trials for shorter treatment for RR-TB in China. Participants without resistance to fluoroquinolone and second-line injectable drugs received either a bedaquiline-free oral regimen or the WHO-recommended injectable-containing regimen. Participants with fluoroquinolone resistance were treated with a bedaquiline-based oral regimen. All participants with two or more isolates successfully sequenced by whole-genome sequencing were included in this study. ADR was determined using whole-genome sequencing data by identifying mutations in a predefined panel of resistance-associated genes.
RESULTS: Among 114 participants included, 16 (14.0%; 95% CI, 8.8-21.6%) experienced at least one ADR event (17 events in total), with a median onset of 17 (range, 14-605) days from treatment initiation. ADR was most common for pyrazinamide (6/70, 8.6%; 95% CI, 4.0-17.5%), followed by bedaquiline (5/111, 4.5%; 95% CI, 1.9-10.1%), ethambutol (2/48, 4.2%; 95% CI, 1.2-14.0%), fluoroquinolones (4/100, 4.0%; 95% CI, 1.6-9.8%), and clofazimine (4/111, 3.6%; 95% CI, 1.4-8.9%). No ADR was detected for linezolid or cycloserine. ADR was

more frequent in participants with poor treatment adherence (31.1% (5/16) vs. 11.2% (11/98), p 0.048). Among 13 participants with bacteriological failure, ADR was identified in two cases.
CONCLUSIONS: Shorter treatment for RR-TB carries a non-negligible risk of ADR. Poor adherence might increase the likelihood of ADR, and early emergence of ADR may indicate suboptimal regimen potency. Continued surveillance is warranted, and further studies are needed to evaluate the clinical association between ADR and treatment outcomes.

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6. Drug-resistant tuberculosis in war and complex emergencies: jeopardising progress towards TB elimination and antimicrobial resistance control - a scoping review and perspective.

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INTRODUCTION: Nearly 300 million people globally require humanitarian assistance, primarily due to conflicts and complex emergencies (CE). Modern conflicts are increasingly prolonged, deadly and frequent, severely disrupting health systems and hindering the provision of quality tuberculosis (TB) care. Managing drug-resistant TB (DR-TB) in these settings is particularly challenging. War and post-war conditions could potentially amplify resistance. However, evidence on DR-TB in CE-affected countries remains scarce.
METHODS: A scoping review, including grey literature and consultation with implementing agencies, was conducted to analyse published experiences worldwide in delivering DR-TB care in CE.
RESULTS: The review included 16 peer-reviewed articles and 11 reports. Countries affected by war exhibit multiple risk factors for amplifying TB resistance. DR-TB management in CE is ongoing, yet diagnostic access is limited, with notification rates below 20% of estimated cases. Treatment success rates among those diagnosed are comparable to global averages. Innovative approaches, such as molecular tests, shorter regimens and patient-centred approaches, have achieved higher success rates. Information on vulnerable populations, including internally displaced persons, prisoners and children, remains minimal. Only one country had reliable information on DR-TB in prisoners (Iraq), accounting for one-third of the national resistant cohort. Most CE countries rely on external funding for DR-TB programmes.
CONCLUSIONS: Like in other infectious diseases, war significantly alters DR-TB dynamics in affected countries and bordering or refugee-hosting countries, threatening progress towards TB elimination and exacerbating the global antimicrobial resistance crisis. While innovations have improved the feasibility of DR-TB care in CE, access remains severely constrained. Identified risk factors, challenges and priorities underscore the need for expanded TB support and targeted research, particularly for vulnerable populations in CE scenarios.

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7. Tuberculosis in lung and heart transplant recipients.

JHLT Open. 2025 Sep 24;11:100398. doi: 10.1016/j.jhlto.2025.100398. eCollection 2026 Feb.
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Mycobacterium tuberculosis is a significant opportunistic pathogen in solid organ transplant recipients, primarily due to the chronic immunosuppression required to prevent graft rejection. Lung and heart transplant recipients are particularly susceptible to tuberculosis (TB) reactivation, as they often undergo more intensive and prolonged immunosuppressive regimens compared to recipients of other organ transplants with lower immunogenicity. Additionally, the risk of donor-derived TB is notably higher in lung transplantation, underscoring the critical importance of thorough TB screening for both donors and recipients. Implementing appropriate treatment protocols based on screening results is essential to prevent the development of TB disease, which can adversely affect the recipient's prognosis. Diagnosing TB in solid organ transplant recipients presents unique challenges. Immunosuppression can attenuate typical inflammatory responses, leading to atypical or absent symptoms. Moreover, there is a higher incidence of extrapulmonary and disseminated TB in this population, which can result in diagnostic delays. Treatment complexities arise from significant drug interactions, particularly between rifampicin and immunosuppressive agents. Furthermore, there is a lack of high-quality studies evaluating the efficacy of rifampin-free regimens and newer drugs for treating multidrug-resistant TB in transplant recipients. This review focuses on TB in the context of lung and heart transplantation, emphasizing the necessity of pretransplant TB infection screening for both donors and recipients, as well as the management strategies for TB disease following transplantation.

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PMID: 41312401

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8. Drug Resistance in Extrapulmonary Tuberculosis in Korea, 2010-2019: A Comparison With Pulmonary Tuberculosis.

J Korean Med Sci. 2026 Feb 9;41(6):e60. doi: 10.3346/jkms.2026.41.e60.

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BACKGROUND: This study investigated drug resistance status and trends in patients with extrapulmonary tuberculosis (EPTB) and compared them with those in patients with pulmonary tuberculosis (PTB).
METHODS: The phenotypic drug susceptibility test (DST) results of patients with culture-confirmed tuberculosis (TB) diagnosed at seven hospitals in South Korea between 2010 and 2019 were retrospectively analyzed.
RESULTS: Overall, 10,557 patients were included in the analysis (747 and 9,810 patients in the EPTB and PTB groups, respectively). The proportion of EPTB among all patients with TB demonstrated an increasing trend over the study period. In the EPTB group, the pleura was the most commonly involved site (n = 246, 32.9%), followed by the lymph nodes (n = 152, 20.3%) and bones and joints (n = 138, 18.5%). Among 706 new patients with EPTB, the resistance rates to isoniazid (INH) and rifampicin (RIF) were 8.5% and 2.4%, respectively. The proportions of RIF-susceptible, INH-resistant TB, multidrug/rifampicin-resistant tuberculosis (MDR/RR-TB), and pre-extensively drug-resistant TB were 6.7%, 2.4%, and 0.7%, respectively. When comparing new patients in the EPTB group with those in the PTB group (8,607 patients), the resistance rates to RIF, ethambutol, and rifabutin and the proportion of MDR/RR-TB were significantly lower in the EPTB group. During the study period, the proportion of MDR/RR-TB among new patients showed a decreasing trend in both the EPTB and PTB groups.
CONCLUSION: This study provides important information on the resistance status and trends among patients with EPTB in South Korea. To improve the management of patients with EPTB, efforts to identify drug resistance and regular updates to the DST database are essential.

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9. Extensive Endemic Transmission of Multidrug-Resistant Mycobacterium tuberculosis in Bhutan: A Retrospective Genomic-Epidemiological Study.

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BACKGROUND: The proportion of multidrug-resistant tuberculosis (MDR-TB) cases is increasing in Bhutan. We conducted the first retrospective genomic-epidemiological study to provide insights into the population structure, resistance patterns, and recent transmission in Bhutan.
METHODS: Whole genome sequencing was performed on randomly selected drug-resistant (DR-TB) and drug-sensitive TB (DS-TB) isolates from Bhutan, collected between 2018 and 2022 at the Microbiological Diagnostic Unit Public

Health Laboratory in Melbourne, Australia. Bioinformatic analysis was performed to identify drug-resistance mutations and genomic clustering of cases.
RESULTS: Approximately 40% of DR-TB and 2.5% of DS-TB were sequenced each year. Of the 203 sequences that passed the quality control, 126 (62.1%) were MDR-TB and 15 (7.4%) were isoniazid-resistant TB. There were 4 different circulating lineages, with the majority belonging to lineage 2 (86.2%). Using a SNP-threshold of ≤12 SNPs, 71% of sequences formed 12 genomic clusters; the largest comprised 88% of all MDR-TB sequences and spanned the entire study period and the country. These cases were highly clonal, with a mean pairwise SNP distance of 10 (range 0-25). Phylogenetic analysis with publicly available international sequence data showed that this MDR-TB cluster formed a distinct clade.
CONCLUSIONS: Contrary to current assumptions of repeat importations, the major burden of MDR-TB in Bhutan appears to be due to recent local transmission resulting in a large endemic cluster, advocating for targeted and enhanced contact tracing and screening for this MDR-TB clade. This study highlights the significant value of investing in TB genomics in resource-limited settings to gain actionable insights to inform policy decisions.

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PMID: 41626299

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10. A Nomogram Predictive Model for Drug-Resistant Tuberculosis Detection by GeneXpert MTB/RIF Assay in Paediatric Patients.

Infect Drug Resist. 2026 Feb 13;19:542863. doi: 10.2147/IDR.S542863. eCollection 2026.

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OBJECTIVE: To develop and validate a clinical-imaging integrated nomogram predictive model for DR-TB risk in pediatric patients (≤18 years), and to

evaluate the diagnostic performance of the GeneXpert MTB/RIF assay in this context.
METHODS: This retrospective study included 223 patients with TB aged ≤18 years hospitalised between 1 July 2018 and 31 December 2023. Drug resistance profiles were analysed, and the clinical/imaging features of DR-TB were compared with those of drug-susceptible TB (DS-TB). Multivariate logistic regression was used to identify DR-TB risk factors.
RESULTS: Of the 223 patients, 73.5% had DS-TB and 26.5% had DR-TB (including 13.5% with multidrug-resistant TB). Resistance rates to first-line drugs were as follows: isoniazid 22.4%, rifampicin 16.1%, streptomycin 8.1% and ethambutol 3.6%. Independent DR-TB risk factors were retreatment (odds ratio [OR] = 5.303, 95% confidence interval [CI]: 1.378-20.414), smoking history (OR = 4.129, 95% CI: 1.233-13.825), right middle lobe involvement (OR = 3.004, 95% CI: 1.148-7.863) and cavity formation (OR = 2.950, 95% CI: 1.325-6.567) (all $P < 0.05$). A nomogram model was developed, with an area under the curve of 0.776, showing effective predictive performance and clinical utility. The GeneXpert MTB/RIF assay had 87.5% sensitivity and 90.48% specificity for detecting rifampicin resistance, with good agreement with drug susceptibility testing (kappa 0.751) ($P < 0.001$). No significant differences in T-lymphocyte subsets were found between the DR-TB and DS-TB groups.
CONCLUSION: In children and adolescents, TB is more common in older individuals and consists primarily of new cases. The nomogram model has good predictive value for DR-TB risk. Key predictors include retreatment, smoking, right middle lobe involvement and cavity formation. The GeneXpert MTB/RIF assay is a potential early screening tool for DR-TB. Further validation with larger samples is needed.

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PMID: 41710377

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11. Isoniazid-induced alopecia in isoniazid-monoresistant pulmonary tuberculosis.

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INTRODUCTION: Alopecia is a rare adverse reaction during tuberculosis (TB) treatment. Both drug-resistant TB and isoniazid (INH)-induced alopecia have been reported. We present this case because INH monoresistance coexisting with INH-induced alopecia has not previously been described in the literature.
CASE: A 22-year-old woman was diagnosed with pulmonary TB and initiated on antituberculosis treatment (ATT). After 1 month, she developed sudden, severe hair loss. INH was suspected as the causative agent and discontinued. Hair regrowth was observed within 1 month. Drug resistance testing revealed INH monoresistance. Treatment was continued with rifampicin (R), pyrazinamide, ethambutol (E), and moxifloxacin for 2 months, followed by R and E for 7 months.
CONCLUSION: Clinicians should be vigilant for alopecia in young female patients receiving ATT, as it may lead to treatment interruption for cosmetic reasons. Alopecia may also signal underlying drug resistance, and further studies are needed to establish biological evidence for this association.

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12. Within-host evolution of drug tolerance in Mycobacterium tuberculosis.

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BACKGROUND AND OBJECTIVES: Mycobacterium tuberculosis (Mtb) causes tuberculosis

(TB) in humans. Poor treatment responses are a threat to global TB control, as such, understanding contributing factors to poor responses is important. We proposed that antibiotic tolerance could contribute to delayed culture conversion (recalcitrant TB), and resistance amplification in patients during TB treatment. We thus ventured to investigate the role of drug tolerance in delayed culture conversion and resistance amplification in TB patients.
METHODS: We collected serial Mtb isolates from patients with (i) drug-susceptible TB who remained culture positive for up to 6 years (i.e. recalcitrant TB), and (ii) multidrug-resistant TB (MDR-TB) where resistance amplified during treatment. We measured tolerance to rifampicin in drug-susceptible TB strains and tolerance to moxifloxacin in MDR-TB strains using a real-time time-kill assay.
RESULTS AND DISCUSSION: Rifampicin tolerance evolved within-host, increasing up to and ~1.5-fold, however, there was no apparent contribution of rifampicin tolerance to delayed culture conversion. Tolerance to moxifloxacin in MDR-TB patients appeared negatively associated with resistance amplification and consistently decreased over time in patients.
CONCLUSION: Our findings confirm that antibiotic tolerance evolves in Mtb within patients over time during treatment. However, there was no evidence that this tolerance influences treatment responses, calling for further investigation of contributors to adverse treatment responses and their mitigation.

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PMCID: PMC12887598
PMID: 41674995

13. Recent advances in tuberculosis treatment: Towards shorter, safer, and more effective therapies.

J Clin Tuberc Other Mycobact Dis. 2026 Jan 14;42:100582. doi: 10.1016/j.jctube.2026.100582. eCollection 2026 Feb.

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Tuberculosis (TB), caused by Mycobacterium tuberculosis, is the leading infectious cause of death globally. Although effective treatments are available, treatment length, drug toxicity, and the emergence of drug-resistant strains have challenged TB control efforts. Current clinical trials are focused on

developing shorter, safer, and more effective regimens that incorporate both new and repurposed agents for the treatment of TB. This narrative review provides an overview of current and emerging treatment options for drug-susceptible, drug-resistant, and latent TB based on recent clinical trials and WHO guidelines.

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14. Drug resistance mechanisms in Mycobacterium tuberculosis infection and challenges in vaccine development.

Front Pharmacol. 2026 Feb 9;17:1762214. doi: 10.3389/fphar.2026.1762214. eCollection 2026.

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Drug-resistant Mycobacterium tuberculosis(Mtb) has become a global public health crisis, and its diverse drug resistance jointly reduces the effectiveness of antibacterial drugs. Mtb resistance is not merely genetic but involves a synergistic interplay of cell wall remodeling, metabolic reprogramming, and epigenetic regulation, all of which are closely linked to its capacity for immune evasion. These mechanisms lead to the failure of traditional treatments, exacerbating the prolongation of treatment duration, the increase in mortality rate and the spread of drug-resistant bacteria. Vaccine research has gradually become a key strategy for preventing and controlling the spread of drug-resistant tuberculosis. This review synthesizes these multifaceted resistance pathways and parallels them with the challenges in vaccine development, highlighting the limited efficacy of Bacillus Calmette-Guérin and the promise of next-generation candidates. It further explores the landscape of novel therapeutic strategies, including new drugs like bedaquiline and host-directed therapies. In the future, efforts should be focused on the development of multivalent vaccines, the integration of chemoimmunotherapy, and the sharing of global monitoring data to contribute to the ultimate goal of eliminating tuberculosis.

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15. Management of adverse events in TB care and active TB drug safety monitoring.

Breathe (Sheff). 2026 Jan 27;22(1):250203. doi: 10.1183/20734735.0203-2025. eCollection 2026 Jan.

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Tuberculosis (TB) remains the leading cause of death from a single infectious agent, with 10.8 million cases reported in 2023. While treatment is generally effective, both drug-susceptible (DS-TB) and drug-resistant TB (DR-TB) regimens

are associated with adverse events (AEs) that compromise adherence and outcomes. In this viewpoint, we highlight the most clinically relevant AEs: hepatotoxicity, cutaneous reactions and ocular toxicity in DS-TB; and linezolid-associated neuropathy, myelosuppression, QT prolongation and hepatotoxicity in DR-TB. We argue that structured safety monitoring and integration of active TB Drug Safety Monitoring and Management into routine care are critical to improving patient safety. Looking ahead, pharmacogenomics, therapeutic drug monitoring, predictive algorithms and digital health solutions offer opportunities to move from reactive to proactive AE management. By prioritising monitoring, innovation and patient-centred approaches, TB programmes can reduce the burden of AEs, improve adherence and achieve better outcomes.

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16. Association of vitamin D receptor genetic variants with therapeutic response in multidrug-resistant pulmonary tuberculosis: a systematic review.

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INTRODUCTION: In high-burden nations like India, tuberculosis (TB) continues to be a significant global public health concern. HIV infection, diabetes mellitus, and low socioeconomic status are examples of comorbid illnesses that increase susceptibility to tuberculosis (TB), and the introduction of multidrug-resistant tuberculosis (MDR-TB) has made disease control even more challenging. The time-consuming nature of conventional drug susceptibility testing (DST) emphasizes the critical need for quick biomarkers to forecast treatment outcomes and resistance. Because of their possible impact on host immunity and MDR-TB risk, genetic variations particularly vitamin D receptor (VDR) polymorphisms have drawn attention.
METHODS: Studies published between 2000 and 2024 were the subject of an extensive examination of the literature. Relevance led to the selection of 213 articles. Keywords including vitamin D, VDR polymorphisms, MDR-TB, pulmonary tuberculosis, and immune response were used to search databases such as PubMed, Web of Science, and Google Scholar. To guarantee comprehensive coverage, both original research articles and reviews were included.
RESULTS: Low serum vitamin D levels were consistently linked to an elevated risk of MDR-TB and pulmonary tuberculosis (PTB), according to the investigation. Certain VDR polymorphisms have often been associated with altered immunological responses and an increased risk of disease, especially mutant forms like FokI and TaqI. Treatment response and disease progression have also been discovered to be influenced by immunological modulation and dietary variables.
DISCUSSION: These results imply that vitamin D levels and VDR polymorphisms could be useful biomarkers for the diagnosis and prognosis of MDR-TB. Knowing the genetic susceptibility of the host may help develop individualized treatment plans and enhance the management of MDR-TB.
SYSTEMATIC REVIEW REGISTRATION: https://www.crd.york.ac.uk/PROSPERO/view/CRD420261295571, identifier CRD420261295571.

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17. Rates and risk factors of monoresistance against isoniazid and multidrug-resistant tuberculosis in Almaty, Kazakhstan.

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BACKGROUND: Drug resistant tuberculosis (DR-TB) poses a massive threat to public health, and monoresistance to isoniazid (Hr-TB) is not often diagnosed. This study aims to determine rates of Hr-TB and multidrug resistance (MDR-TB) among TB isolates and assess risk factors for TB diagnosis and drug resistance in Almaty, Kazakhstan to inform public health policy.
METHODS: From December 2021 to July 2022, sputum samples were collected from 1214 unique patients over age 18 with presumptive TB who were not currently on TB treatment. All samples were tested with both Mycobacterial Growth Indicator Tube (MGIT) liquid culture and the Becton-Dickinson real-time PCR (BD MAX™ MDR-TB) for detection of M. tuberculosis and drug resistance to isoniazid (INH), rifampicin (RIF), ethambutol (EMB), and pyrazinamide (PZA). Rates of monoresistance and MDR-TB were calculated, and univariate and multivariable logistic regression models were run to determine odds ratios for potential risk factors for TB, Hr-TB, and MDR-TB diagnosis using MGIT results.
RESULTS: Any resistance to INH was found in 115 (43.7% [95% CI: 37.9-49.8%]) of 263 TB isolates diagnosed by MGIT, and Hr-TB was diagnosed in 34 MGIT TB isolates (12.9% [95% CI: 9.4-17.5%]). Among 359 BD MAX TB isolates, 51 (14.2% [95% CI: 11.0-18.2%]) were Hr-TB. MDR-TB was diagnosed in 70 MGIT TB isolates (26.6% [95% CI: 21.6-32.3%]) and 65 BD MAX TB isolates (24.7% [95% CI: 14.5-22.4%]). Male patients, those aged 35-44 and 45-54, and patients with self-reported diabetes mellitus had higher odds of TB diagnosis compared to female patients, those aged 65+, and those with no self-reported comorbid conditions, but no significant associations were found between patient characteristics and odds of Hr-TB or MDR-TB diagnosis.
CONCLUSION: Rapid and accurate diagnosis of INH monoresistance is critical to understand national burdens of Hr-TB, improve treatment regimens, and prevent increases in MDR-TB in Kazakhstan. Current TB diagnostics that do not detect resistance to INH are inadequate to characterize Hr-TB. Therefore, high-burden MDR-TB countries should consider using diagnostics that detect resistance to both INH and RIF in national TB prevalence and drug resistance surveys.
CLINICAL TRIAL: Not applicable.

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PMID: 41612233 [Indexed for MEDLINE]

Conflict of interest statement: Declarations. Ethics approval and consent to participate: This study was approved as human subjects research by Columbia University Institutional Review Board with protocol number IRB-AAAS5110 and the NSCP Ethics Committee (approval of 6 February 2020, and extension of 7 July 2021). The manufacturer, BD, had no role in the collection or analysis of the data. Participants were enrolled after providing written informed consent in accordance with the Declaration of Helsinki. Consent for publication: Not applicable. Competing interests: The authors declare no competing interests.

18. Diagnosis and Therapeutic Challenges of Drug-Resistant Tuberculosis Infection After Kidney Transplantation: A Rare Case Report.

Infect Drug Resist. 2026 Feb 13;19:590648. doi: 10.2147/IDR.S590648. eCollection 2026.

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BACKGROUND: Kidney transplant recipients are at high risk for tuberculosis (TB), particularly drug-resistant forms, due to prolonged immunosuppressive therapy. The diagnosis and treatment of TB in this population pose unique challenges, including infection control, graft protection, and drug interactions.
CASE PRESENTATION: We report the case of a 28-year-old male kidney transplant recipient was diagnosed with pulmonary TB four months post-transplantation. The patient self-discontinued initial anti-TB therapy after one month, leading to relapse nine months later, with confirmed rifampicin resistant. Following three months of treatment with a second-line regimen including linezolid, he developed disseminated skeletal TB, with drug susceptibility testing indicating linezolid resistance. The treatment was adjusted to an all-oral regimen including isoniazid, moxifloxacin, clofazimine, cycloserine, and bedaquiline, resulting in significant clinical and radiological improvement.
DISCUSSION: In the present case, the patient's non-adherence to the medication regimen resulted in initial treatment failure. Against the backdrop of immunosuppression, rifampicin resistance emerged rapidly. Although the subsequent linezolid-containing regimen was administered for a short duration, it likely triggered ribosomal target mutations-leading to linezolid resistance and hematogenous dissemination to the bone-driven by both drug selection pressure and the history of irregular treatment. Confronted with dual resistance and disseminated disease, the therapeutic strategy pivoted to a bedaquiline-based regimen. This shift highlights the clinical management art of finely balancing treatment efficacy with the risk of rejection through the optimized adjustment of immunosuppressants guided by therapeutic drug

monitoring.
CONCLUSION: The management of drug-resistant tuberculosis in kidney transplant recipients necessitates a flexible and comprehensive strategy. This encompasses early clinical suspicion, the prompt performance of molecular and phenotypic drug susceptibility testing to guide therapeutic decisions, rigorous management of treatment adherence, and the real-time adjustment of therapeutic regimens based on evolving resistance profiles and clinical responses. Multidisciplinary collaboration is essential for balancing anti-tuberculosis efficacy with graft survival. Although novel agents such as bedaquiline offer promising options for salvage therapy, their administration in transplant recipients requires intensified monitoring for drug-drug interactions and adverse events.

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PMCID: PMC12912147
PMID: 41710375

Conflict of interest statement: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

19. Evaluation of clofazimine-bedaquiline combination as a candidate regimen for macrolide-resistant Mycobacterium avium complex infection.

Antimicrob Agents Chemother. 2026 Feb 4;70(2):e0151125. doi: 10.1128/aac.01511-25. Epub 2025 Dec 19.

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The Mycobacterium avium complex (MAC) is the primary cause of pulmonary disease (PD) among nontuberculous mycobacteria, presenting a significant treatment challenge on a global scale. A long-term (≥12 months) three-drug regimen, typically including a macrolide, such as clarithromycin (CLR) or azithromycin, along with rifampicin and ethambutol, is recommended. However, many patients fail to respond adequately to therapy, and some eventually develop macrolide resistance, making the disease even more difficult to treat. This highlights the urgent need for improved therapeutic strategies. Here, we investigated the efficacy of clofazimine (CFZ) and bedaquiline (BDQ), both repurposed from multidrug-resistant tuberculosis therapy, against macrolide-resistant MAC. In macrophage infection assays, both CFZ and BDQ showed significant intracellular inhibitory activity against macrolide-resistant clinical isolates, with CFZ

generally exhibiting stronger effects. In a chronic murine model of MAC-caused progressive PD, substitution of CLR with CFZ and BDQ in the treatment regimen led to marked reductions in bacterial loads in both lung and spleen compared with the standard regimen, achieving up to 0.86 $\log_{10}$ CFU reduction in lung and 2.17 $\log_{10}$ CFU in spleen tissues. These findings demonstrate that CFZ and BDQ retain potent activity against macrolide-resistant MAC and highlight their potential as promising components of alternative treatment regimens.

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PMCID: PMC12888858
PMID: 41416824 [Indexed for MEDLINE]

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

20. Pediatric Tuberculosis: Unraveling Immunity, Clinical Complexities, and Resource-Driven Disparities in the Pursuit of Prevention.

Vaccines (Basel). 2026 Jan 27;14(2):119. doi: 10.3390/vaccines14020119.

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Pediatric tuberculosis (TB) remains a critically underrecognized contributor to global childhood morbidity and mortality, with the highest burden concentrated in low-resource settings. Although children comprise a minority of overall TB cases, mortality is disproportionately high, particularly among those under five years of age, driven largely by delayed diagnosis, inadequate linkage to care, and limited access to effective treatment. The continued rise of pediatric multidrug-resistant TB (MDR-TB), especially in regions with low sociodemographic development, further highlights persistent gaps in current control strategies. This review synthesizes key aspects of pediatric TB pathogenesis and host immune responses that predispose young children to rapid disease progression and severe outcomes, including immune immaturity and paucibacillary infection. We summarize pulmonary and extrapulmonary disease manifestations and identify populations at heightened risk, including children with HIV, malnutrition, type 1 diabetes mellitus, and congenital or treatment-related immunosuppression. Ongoing challenges in diagnosis and treatment are discussed, including limitations of existing microbiologic and immunologic tests, specimen collection constraints, regimen toxicity, and barriers to adherence. Prevention remains central to reducing pediatric TB mortality. We highlight the sustained importance of bacille Calmette-Guérin (BCG) vaccination in preventing severe disease and death, the context-dependent variability in vaccine effectiveness, and the structural and socioeconomic determinants of vaccine coverage. We conclude that integrating equitable vaccine delivery, scalable preventive therapy, and child-adapted diagnostic strategies is essential to meaningfully reduce the

global pediatric TB burden.

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PMCID: PMC12945030
PMID: 41746042

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21. Mutations in sugar metabolism-related genes driving global drug-resistant Mycobacterium tuberculosis transmission revealed by whole-genome sequencing.

BMC Infect Dis. 2026 Jan 30;26(1):456. doi: 10.1186/s12879-026-12559-5.

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BACKGROUND: Tuberculosis (TB) continues to represent a significant global health challenge, particularly due to the emergence of drug-resistant strains that hinder TB control initiatives. Elucidating the mechanisms underlying the proliferation of drug-resistant strains is essential for developing effective strategies to address this public health threat.
METHODS: Whole-genome sequencing was conducted on 13,525 Mycobacterium tuberculosis isolates. Genes associated with sugar metabolism were obtained from the National Center for Biotechnology Information (NCBI) Gene database. Analytical approaches, including Random Forests, Gradient Boosting Decision Trees, and Generalized Linear Mixed Models were used to identify mutation sites

in sugar metabolism genes that contribute to transmission of Multidrug-Resistant Tuberculosis (MDR-TB).
RESULTS: Significant associations were identified between specific gene mutations and transmission clusters in MDR-TB. Notable mutations include Rv0650 (C113T, C316T), sugB C734A, epiA C43T, Rv151c C8G, Rv1520 (C138T, T618C, A649C), Rv2038c G282A, Rv2039c (G391T, T283G), Rv2040c G835C, Rv2316 C161G, and sugI C1268T. Additionally, mutations associated with MDR-TB transmission clusters, include Rv0650 C316T, Rv151c T809C, and Rv2039c C794T. Certain mutations, such as Rv0539 G588T and uspA G379C, were found to increase the risk of cross-regional transmission in MDR clades. The presence of Rv1512 (epiA, C462T) and Rv2038c T161G was associated with an increased therisk of developing MDR isolates compared to single drug resistant (SDR) isolates.
CONCLUSION: Mutations in sugar metabolism genes significantly contribute to the global transmission of MDR-TB. Identifing these genetic determinants canguide targeted interventions to control drug-resistant strains and improve TB management. Further research is required to elucidate mechanism underlying mechanisms of transmission and resistance development.
CLINICAL TRIAL NUMBER: Not applicable.
SUPPLEMENTARY INFORMATION: The online version contains supplementary material available at 10.1186/s12879-026-12559-5.

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PMID: 41618188

Conflict of interest statement: Declarations. Ethics approval and consent to participate: This study complied with the Declaration of Helsinki, and was approved by the Ethics Committee of Shandong Provincial Hospital, affiliated with Shandong University (SPH), the Ethics Weifang Respiratory Disease Hospital (WRDH) and the Ethics Committee of Shandong Provincial Chest Hospital (SPCH), which waived informed patient consent because all patient records and information were anonymized and deidentified before the analysis. Consent for publication: Not applicable. Competing interests: The authors declare no competing interests.

22. Impact of risk adjustment for drug-resistant types on tuberculosis patients' outcomes under China's innovative payment methods: a quasi-experimental study Design.

Infect Dis Poverty. 2026 Feb 15;15(1):24. doi: 10.1186/s40249-026-01423-y.

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BACKGROUND: Treating drug-resistant tuberculosis (DR-TB) is clinically complex and economically burdensome compared to drug-susceptible tuberculosis (DS-TB). China's diagnosis-intervention packet payment system initially omitted risk adjustment for drug resistance. In 2022, a diagnosis-intervention packet (DIP)-pilot city implemented such adjustment, establishing distinct reimbursement standards for DR-TB and DS-TB. This study aimed to assess the impact of this DR-type risk adjustment on medical expenditures, treatment efficiency, and care quality for TB patients.
METHODS: A quasi-experimental difference-in-differences design was employed, involving 8465 TB patients from June 2021 to December 2023. Linear regression was performed with time and treat fixed effects and the interaction term between time and treat. Subgroup analyses for DR-TB and DS-TB patients were conducted.
RESULTS: Under the DIP system, risk adjustment led to marginally significant reductions in inpatient expenditure per hospitalization [β = - 151.14, P = 0.065; 95% confidence interval (CI) for difference in proportions: - 311.66, 9.38] and in annual total inpatient expenditure per patient (β = - 200.58, P = 0.078, 95% CI - 423.26, 22.10) for all TB patients. It also resulted in significant reductions in inpatient out-of-pocket per hospitalization (β = - 257.51, P < 0.001, 95% CI - 316.20, - 198.81), annual total inpatient out-of-pocket per patient (β = - 266.78, P < 0.001, 95% CI - 342.02, - 191.53), inpatient length of stay per hospitalization (β = - 3.58, P < 0.001, 95% CI - 4.53, - 2.62), and annual total length of stay per patient (β = - 3.21, P < 0.001, 95% CI - 4.50, - 1.92). For DR-TB patients, all outcome measures in expenditures, efficiency, or care quality showed P > 0.1, indicating no significant changes. For DS-TB patients, measures of expenditures and efficiency showed P < 0.1, supporting significant or marginally significant reductions.
CONCLUSIONS: The DR-type risk adjustment policy under China's diagnosis-intervention packet system proved effective in optimizing resource use and enhancing efficiency, particularly for DS-TB patients, while preserving care quality for DR-TB patients. These findings demonstrate the value of tailored risk adjustment within payment frameworks for heterogeneous diseases like tuberculosis, providing crucial evidence for optimizing TB care and implementing effective payment reforms in China and similar settings.

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PMCID: PMC12906684
PMID: 41691353 [Indexed for MEDLINE]

Conflict of interest statement: Declarations. Ethics approval and consent to participate: Research involving human data has been performed in accordance with the Declaration of Helsinki. All methods were carried out in accordance with relevant guidelines and regulations in the declaration. The study was approved by the Biomedical Ethics Review Committee of Tongji Medical College, Huazhong University of Science and Technology (S058, April 23, 2025). The need for

informed consent was waived by the ethics institutional review board of Tongji Medical College, Huazhong University of Science and Technology because of the retrospective nature of the study. All authors confirm that this research caused no harm (physical or mental) to any participants. Clinical trial number: Not applicable. Consent for publication: The data used are fully anonymized statistical data that cannot be traced to any specific individual, hence “Not applicable.” Competing interests: The authors declare no competing interests.

23. Successful treatment of pre-extensively drug-resistant tuberculous meningoencephalomyelitis in pregnancy with a bedaquiline and delamanid-based regimen: a case report.

BMC Infect Dis. 2026 Jan 30;26(1):450. doi: 10.1186/s12879-026-12663-6.

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BACKGROUND: Management of pre-extensively drug-resistant tuberculosis (pre-XDR-TB) during pregnancy poses a formidable clinical challenge, particularly when complicated by tuberculous meningoencephalomyelitis (TBMEM), While the WHO operational handbook provides a general framework for drug-resistant TB, robust evidence and specific guidelines for managing severe CNS involvement in pregnancy remain limited.
CASE PRESENTATION: We report the successful outcome for a mother and infant in an extremely high-risk case. The patient, at 17 + 6 weeks of gestation following in vitro fertilization (IVF), was diagnosed with pre-XDR-TB. Hematogenous dissemination was confirmed by chest CT showing diffuse miliary nodules, and spinal MRI confirmed meningoencephalomyelitis. Her clinical course was complicated by life-threatening conditions, including TB-associated sepsis (TB-Sepsis) and severe neurological immune reconstitution inflammatory syndrome (Neuro-IRIS) presenting as an intracranial hypertensive crisis. An individualized, multidisciplinary approach centered on a bedaquiline (Bdq) and delamanid (Dlm)-based regimen was implemented. The patient’s condition was effectively controlled, and she delivered a healthy female infant at 35 + 1 weeks of gestation. Both mother and infant recovered well.
CONCLUSIONS: This case demonstrates that a carefully monitored Bdq/Dlm-based regimen can be a life-saving option for severe DR-TB in pregnancy. It also underscores the critical need for systematic TB screening prior to assisted

reproductive technology (ART) in high-burden regions.

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PMCID: PMC12930593
PMID: 41618183

Conflict of interest statement: Declarations. Ethics approval and consent to participate: The study was approved by the Medical Ethics Committee of Wuhan Jinyintan Hospital (Approval No. Shen KY-2024-30.01). Written informed consent to participate was obtained from the patient. Consent for publication: Written informed consent for publication of their clinical details and/or clinical images was obtained from the patient. A copy of the consent form is available for review by the Editor of this journal. Competing interests: The authors declare no competing interests.

24. Correction: Prevalence and factors influencing drug-resistant tuberculosis in four regions of Ghana.

PLoS One. 2026 Feb 19;21(2):e0343420. doi: 10.1371/journal.pone.0343420. eCollection 2026.

Ba-Iredire E, Avoka JA, Abanga L, Darkie AA, Attombo EJ, Agboli E.

Erratum for
PLoS One. 2025 Sep 9;20(9):e0331958. doi: 10.1371/journal.pone.0331958.

[This corrects the article DOI: 10.1371/journal.pone.0331958.].

DOI: 10.1371/journal.pone.0343420
PMCID: PMC12919804
PMID: 41712546

25. Epidemiologic trajectories and burden of multidrug-resistant tuberculosis (MDR-TB) mortality across South Asia: An analysis of Global Burden of Disease data (1990-2023) with machine learning forecasting to 2050.

J Clin Tuberc Other Mycobact Dis. 2026 Jan 7;42:100580. doi: 10.1016/j.jctube.2026.100580. eCollection 2026 Feb.

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BACKGROUND: Multidrug-resistant tuberculosis (MDR-TB) remains a major public health challenge in South Asia, which bears a disproportionate global burden. Comprehensive, longitudinal analyses of MDR-TB mortality trends, stratified by country and sex, with forward-looking projections are limited.
METHODS: We conducted a retrospective analysis using data from the Global Burden of Disease Study 2023 to examine age-standardized mortality rates (ASMR) attributable to MDR-TB in South Asia and its countries (Bangladesh, Bhutan, India, Nepal, Pakistan) from 1990 to 2023. Trends were assessed by sex, and estimated annual percentage changes (EAPC) were calculated via log-linear regression. Seasonal Autoregressive Integrated Moving Average (SARIMA) models were employed to forecast ASMR through 2050, with 95% prediction intervals.
RESULTS: Regional ASMR rose from 0.25 per 100,000 (95% UI: 0.03-0.88) in 1990 to a peak of 6.34 (95% UI: 2.56-13.56) in 2010, declining to 3.63 (95% UI: 0.54-9.80) by 2023, driven predominantly by India and Pakistan. Nepal exhibited consistent declines (EAPC: -2.44%; 95% CI: -3.21 to -1.66), while Pakistan showed the highest increase (EAPC: 6.16%; 95% CI: 3.21-9.19). Males consistently had higher ASMR across all settings. Forecasts suggest continued declines toward near-elimination in Bangladesh, Bhutan, and Nepal, but potential substantial rebounds in India, Pakistan, and regionally, with upper prediction intervals exceeding 20-40 per 100,000 by 2050 in high-burden scenarios.
CONCLUSION: Despite progress in some countries, MDR-TB mortality remains elevated in populous nations, with persistent male excess. Projections highlight risks of resurgence without intensified interventions. These findings underscore the urgent need for tailored, gender-sensitive strategies and enhanced regional collaboration to achieve End TB targets in South Asia.

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PMCID: PMC12830303
PMID: 41585606

Conflict of interest statement: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

26. Effectiveness and Safety of Bedaquiline-Containing Modified Shorter Regimens for Multidrug- or Rifampicin-Resistant Tuberculosis: A Single-Arm Meta-Analysis.

Pathogens. 2026 Jan 25;15(2):130. doi: 10.3390/pathogens15020130.

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Tuberculosis (TB) remains a global public health emergency, with multidrug-resistant TB (MDR-TB) and rifampicin-resistant TB (RR-TB) posing critical challenges. Conventional longer regimens are characterized by suboptimal effectiveness, high toxicity, and poor tolerability. Consequently, there is an urgent demand for more effective, safer, shorter regimens with enhanced tolerability to replace traditional treatments. The present study aimed to systematically assess the effectiveness and safety of bedaquiline-containing modified shorter regimens (adaptations of the WHO-recommended 9-12-month bedaquiline-containing shorter regimen, with ethionamide, ethambutol, isoniazid, and pyrazinamide partially or fully substituted by linezolid, cycloserine/terizidone, and/or delamanid) for MDR/RR-TB. Databases (PubMed, Cochrane Library, Embase, and Web of Science) were searched up to 17 December 2025. Data on treatment success, adverse events, and patient characteristics were extracted. Heterogeneity was assessed using Cochrane Q test and I2 statistic. Eleven studies involving 8166 patients were included. The pooled treatment success rate was 78.5% (95% CI: 0.69~0.87, I2: 98.45%; p = 0.00). The incidence of serious adverse events was 10.0%. Bedaquiline-containing modified shorter regimens may offer a potentially viable treatment option for MDR/RR-TB patients, giving an option for patients who are ineligible for standardized regimens. In order to verify these findings, further large-scale trials are required.

DOI: 10.3390/pathogens15020130
PMCID: PMC12943216
PMID: 41754383

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

27. Comments on "Tuberculosis infection control in MDR-TB designated hospitals in Jiangsu Province, China".

J Clin Tuberc Other Mycobact Dis. 2026 Jan 7;42:100581. doi: 10.1016/j.jctube.2026.100581. eCollection 2026 Feb.

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Conflict of interest statement: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

28.Tuberculosis diagnosis and the complete drug resistance pattern from a single sample within a single day by use of a composite platform of MAX MDR-TB and AmPORE-TB.

J Clin Microbiol. 2026 Feb 11;64(2):e0138825. doi: 10.1128/jcm.01388-25. Epub 2026 Jan 12.

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Rapid TB diagnostics are essential for effective TB control. Combining WHO-recommended rapid molecular tests with downstream targeted next-generation sequencing (tNGS) enables faster drug resistance profiling. The objective of this study was to establish a one-day diagnostic platform (ODDP) integrating BD MAX MDR-TB and AmPORE-TB tNGS from a single sample. Pooled sputum samples spiked

with 52 pre-characterized Mycobacterium tuberculosis (MTB) strains and 74 MTB-positive clinical samples were tested using BD MAX MDR-TB for TB, isoniazid, and rifampicin resistance. tNGS was performed from 5 µL of purified DNA leftover for each TB-positive sample in the BD MAX strips. IS6110/IS1081 Ct-values served as surrogate markers for TB DNA concentration. A total of 104 spiked and 60 clinical samples tested positive by BD MAX. The average time to the final ODDP result was 8.5 h. For samples with Ct ≤28, tNGS generated antibiotic resistance profiles for ≥12 antibiotics with 85.1% sensitivity in spiked and 73% in clinical samples. Failure rates were 10% and 8.3%, respectively. Resistance profiling most frequently (up to 11.3%) failed for clofazimine, pretomanid, and delamanid. The ODDP enables comprehensive TB diagnosis and resistance profiling from a single sample in 1 day. This platform can significantly accelerate the time to informed drug-resistant (DR)-TB treatment decisions.IMPORTANCEReducing the time to treatment initiation decreases patient drop-out rates, morbidity, the emergence of new drug resistances, and onward transmission of infection. Obtaining the complete resistome from the start is crucial for choosing a fully effective treatment regimen. Until now, diagnosis with full resistance profiling has required at least two sputum samples and 3 to 7 days for the complete workflow, obliging patients to return two to three times, which dramatically increased the risk of loss to follow-up. Our one-day diagnostic platform enables both diagnosis and comprehensive resistance testing from a single sample within 1 day. Patients can remain in a day clinic during testing and receive a fully effective, individualized treatment regimen the same day. This approach is expected to markedly reduce morbidity, drop-out rates, and transmission. The necessary instruments and technologies are already available in many high-prevalence countries and are currently being rapidly scaled up worldwide.

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29. Tuberculosis Diagnostic Methods: Clinical Applicability, Implementation Challenges, and Integrated Testing Strategies.

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Tuberculosis (TB) remains one of the leading causes of death from a single infectious agent worldwide, a burden further exacerbated by HIV co-infection and the increasing prevalence of drug-resistant strains. Although a wide range of

laboratory diagnostic methods are currently available, their applicability, implementation, and clinical impact vary substantially across healthcare settings with different levels of complexity and resources. This review provides a comprehensive overview of the main laboratory diagnostic methods for active and latent TB, emphasizing their clinical applicability, implementation challenges, and role within integrated diagnostic strategies. Conventional approaches, such as smear microscopy and culture, are discussed alongside modern diagnostic technologies, including automated nucleic acid amplification tests (NAATs), loop-mediated isothermal amplification (LAMP), line probe assays (LPAs), next-generation sequencing (NGS), and lateral flow assays, highlighting their strengths and limitations in distinct epidemiological and operational contexts. Unlike existing WHO guidelines and prior reviews that predominantly focus on test performance and recommendation status, this review adopts an implementation-oriented perspective, critically examining diagnostic methods in light of real-world constraints, regional disparities, and evidence gaps. Particular attention is given to limitations related to laboratory infrastructure, biosafety, workforce capacity, and sustainability, as well as to under-addressed areas such as latent TB, metagenomic approaches, and the investigation of co-pathogens. By integrating WHO guidance with contextual and operational considerations, this review aims to support rational test selection and the development of flexible, integrated diagnostic workflows tailored to local health system capacity, patient populations, and clinical scenarios, thereby strengthening the effectiveness and equity of TB diagnostic strategies.

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30. 3-(Pyridine-3-ylmethylene)chroman-4-one and tetralone derivatives: synthesis, Mycobacterium tuberculosis CYP121A1 enzyme inhibition and antimycobacterial activity vs drug-sensitive and drug-resistant strains.

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CYP121A1 is a promising cytochrome P450 (CYP) drug target in Mycobacterium tuberculosis (Mtb) owing to its physiological importance in bacterial cell viability. The continuing rise of multidrug resistant (MDR) and extremely drug resistant (XDR) tuberculosis (TB), offers potential therapeutics with a new mechanism of action to add to the multidrug TB regime. A series of 3-(pyridine-3-ylmethylene)chromanone derivatives (5) with 7-O-alkyl/aryl substitutions were explored for CYP121A1 binding and antimycobacterial activity in susceptible and resistant Mtb strains. The 3-(pyridine-3-ylmethylene)chroman-4-one derivatives (5) with the 7-O-(CH2)3-phenyl substitution displayed the strongest CYP121A1 binding affinity (K D 0.3 to 3.6 μM) compared with the natural substrate (dicyclotyrosine, K D 16.8 ± 1.0 μM). Improvements observed in binding affinity from 7-O-benzyl to (CH2)2-phenyl to (CH2)3-phenyl substitutions are supported by computational studies. Minimum inhibitor concentration (MIC) of the alkyoxyaryl substituted chromanones ranged from 1.5-50 μM (0.5-22.5 μg mL-1) against the H37Rv wild type strain (c.f. isoniazid 1.8 μM (0.2 μg mL-1), rifampicin 0.3 μM (0.2 μg mL-1), kanamycin 16.1 μM (7.8 μg mL-1)) with antimycobacterial activity retained against mono-resistant (isoniazid or rifampicin) and MDR (isoniazid and rifampicin) Mtb strains. In contrast, the tetralone derivatives (8) with either the O-(CH2)2-phenyl or O-(CH2)3-phenyl substitutions showed no binding affinity with CYP121A1, possibly owing to binding further away from the haem and failing to displace the 6th axial water ligand, but the O-(CH2)3-phenyl substituted tetralones were the most consistently effective against H37Rv strain with MIC of 3 μM (1.1-1.2 μg mL-1) and retained activity against the mono-resistant and MDR Mtb strains.

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Conflict of interest statement: There are no conflicts to declare.

31. Metagenomic and metatranscriptomic profiling of bronchoalveolar lavage fluid identifies microbial and host biomarkers of drug-resistant tuberculosis.

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BACKGROUND: Drug-resistant tuberculosis (DR-TB) undermines global TB control, yet how resistant Mycobacterium tuberculosis strains interact with the lung microbiome, phage communities, and local host immunity remains poorly defined.
METHODS: In a prospective cohort of 130 pulmonary TB patients (49 DR-TB, 81 drug-susceptible TB [DS-TB] patients), bronchoalveolar lavage fluid (BALF) was subjected to paired metagenomic and transcriptomic profiling. Microbial and bacteriophage community structures were assessed by diversity metrics and differential abundance testing, whereas host responses were characterized by gene expression, pathway enrichment, and immune cell deconvolution. A Random Forest model was trained to evaluate the diagnostic potential of host transcriptional signatures.
RESULTS: DR-TB airways presented distinct microbial beta diversity, with enrichment of Streptococcus spp. and streptococcal-targeting phages (e.g., Javan variants, phi-Ssu5SJ28rum). Transcriptomic analysis revealed 494 differentially expressed genes, which were associated with increased oxidative phosphorylation, suppressed ion channel and transporter activity, and enrichment of extracellular matrix remodeling pathways. Immune profiling demonstrated a significant reduction in γδ T cells in DR-TB patients (P = 0.0059). An 8-gene host-derived signature (ARHGEF5, PTGES3L, GAL3ST1, RANBP17, ACTA2_AS1, CBY3, MAMSTR, and LOC102031319) discriminated DR-TB from DS-TB with high accuracy (AUC = 0.837).
CONCLUSION: This dual-omics study defines the airway niche of DR-TB as a convergence of microbial dysbiosis, phage imbalance, and host immune-metabolic dysfunction. By uncovering DR-TB-specific microbial and transcriptional signatures, and deriving a predictive host-based classifier, our findings provide mechanistic insights and highlight novel opportunities for microbiome- and host-directed interventions in drug-resistant tuberculosis.

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32.Characterization of pulmonary tuberculosis in high-altitude region using nanopore targeted sequencing.

BMC Microbiol. 2026 Jan 26;26(1):134. doi: 10.1186/s12866-026-04761-x.

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BACKGROUND: Xizang (formerly known as Tibet in English) has one of the highest tuberculosis (TB) incidence rates in China. The region's extreme altitudes (≥ 3000 m) and hypoxic environment present substantial challenges for conventional diagnostic methods. Additionally, the clinical and biological characteristics of TB at high altitudes remain poorly understood.
METHOD: TB-seq, a third-generation nanopore-targeted sequencing method, was used to analyze sputum samples from 158 confirmed pulmonary TB patients in Xizang. Bacterial load was quantified, a drug-resistance gene landscape was generated, and these findings were correlated with clinical phenotypes. A matched low-altitude group (< 1000 m) was included to investigate the effects of altitude on Mycobacterium tuberculosis biology.
RESULT: In Xizang, retreatment cases accounted for the majority of TB patients (58.23%). Type I TB was the most common form (79.75%), while non-type I forms were observed only in retreatment patients ($P < 0.01$). Bacterial load decreased significantly with increasing age ($P < 0.001$), was higher in retreatment cases ($P = 0.013$), and positively correlated with white blood cell and neutrophil counts ($P < 0.05$). Drug-resistant mutations were identified in 22.78% of patients, primarily as mono-resistance (63.9%), with key resistance-associated genes being rpsL (47.2%), rpoB (38.9%), and katG (33.3%). Compared to

low-altitude controls, the high-altitude group had a significantly lower bacterial load ($P < 0.01$), reduced overall drug resistance (23.7% vs. 38.2%, $P < 0.01$), no rrs mutations, and a significantly lower pncA mutation rate ($P < 0.05$).
CONCLUSION: Tuberculosis in Xizang is marked by a high proportion of retreatment cases, low pathogen burden, and a reduced rate of drug resistance-associated gene mutations. Altitude appears to suppress bacterial quantity and may select for specific resistance mechanisms. These findings support the need for targeted TB control strategies in Xizang and underscore the complex interactions among the environment, the pathogen, and the host.

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33. A catastrophic seven-year course of drug-resistant tuberculosis and lessons for multidisciplinary management: a case report.

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BACKGROUND: We describe the catastrophic seven-year journey of a young man with drug-resistant tuberculosis (TB) in China, initially managed with empiric therapy without baseline molecular testing.
CASE PRESENTATION: He relapsed with rifampicin-resistant TB, complicated by

empyema, bronchopleural fistula, and multiple failed surgeries. Management required prolonged, individualized therapy with severe toxicities, including linezolid-induced peripheral neuropathy, and staged thoracic reconstruction. INTERPRETATION: Although microbiological cure was achieved, the patient was left with severe post-tuberculosis lung disease and functional disability. This case highlights the consequences of omitting rapid molecular diagnostics, the essential role of multidisciplinary collaboration, and the need to extend TB care beyond microbiological cure to long-term rehabilitation. This case report is reported in accordance with the CARE guidelines.

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34. Detection for New Biomarkers of Tuberculosis Infection Activity Using Machine Learning Methods.

Diseases. 2026 Feb 11;14(2):66. doi: 10.3390/diseases14020066.

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BACKGROUND/OBJECTIVES: Latent tuberculosis infection (LTBI) represents a critical reservoir for subsequent development of active tuberculosis (ATB) and poses significant challenges for early diagnosis and disease prevention. Traditional immunological assays, such as interferon-gamma release assays (IGRAs), are limited in their ability to reliably distinguish LTBI from ATB. Recent advances in high-throughput omics technologies and machine learning (ML) approaches offer new opportunities for precise, biomarker-based differential diagnostics.
METHODS: Transcriptomic and proteomic profiling of host immune responses has revealed reproducible gene and protein signatures associated with LTBI and ATB. The integration of ML techniques-including feature selection, dimensionality reduction, multimodal learning, and explainable AI-facilitates the construction of robust diagnostic models. Single-modality signatures, derived from RNA-seq, microarrays, or proteomic assays, are complemented by multimodal approaches that incorporate soluble mediators, immunological readouts, and imaging-derived features. Deep learning frameworks, such as convolutional neural networks and transformer-based architectures, enhance the extraction of complex molecular and structural patterns from high-dimensional datasets.
RESULTS: ML-driven analyses of transcriptomic and proteomic data consistently outperform conventional immunological tests in terms of sensitivity, specificity, and clinical applicability. Multimodal integration further improves diagnostic accuracy and robustness. These advances support the translational development of concise, quantitative reverse transcription PCR (qRT-PCR)-based biomarker panels suitable for routine clinical application, enabling early and reliable differentiation between LTBI and ATB. Overall, the combination of high-throughput omics and AI-based analytical frameworks provides a promising pathway for enhancing global tuberculosis diagnostics.
CONCLUSIONS: This review provides a structured and critical synthesis of transcriptomic and proteomic biomarker research for LTBI and ATB discrimination, with a particular emphasis on machine learning-based analytical frameworks. Unlike previous narrative reviews, we systematically compare data-generating platforms, modelling strategies, validation approaches, and sources of heterogeneity across studies. We further identify key translational barriers, including cohort homogeneity, platform dependency, and limited external validation, and propose directions for future research aimed at improving clinical applicability.

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35. Secondary metabolites from Lobaria pulmonaria (L.) Hoffm. target key metabolic enzymes: a novel strategy against multidrug-resistant tuberculosis.

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Numerous cultures have traditionally utilised the foliose lichen Lobaria pulmonaria (L.) Hoffm. ("Oak Lung" or "Lungs of Oak" in English; family: Lobariaceae) as a Tuberculosis (Tb) treatment. The present study aimed to scientifically validate the folkloric use of L. pulmonaria in treating Tb by investigating its antimycobacterial profile against Mycobacterium tuberculosis H37Ra (M.tb) and six other MDR-Tb isolates. The preliminary results obtained from XRMA revealed the notable inhibitory activity of LP and Fraction (F)-3 against M.tb, displaying IC50 values of 7.74 ± 0.27 and 6.26 ± 0.04 μg mL-1, respectively; followed by F2 (IC50 value: 38.82 ± 0.34 μg mL-1) and F5 (IC50 value: 46.69 ± 1.13 μg mL-1). The purification process of these bioactive fractions resulted in the identification of four known secondary metabolites: fukinanolide A, pinastric acid, stictic acid, and scrobiculin. Furthermore, the MICs from REMA showed that LP, stictic acid, and fukinanolide A have greater efficacy in controlling the growth of all six tested MDR-Tb isolates, compared to rifampicin. Notably, LP exhibited superior antimycobacterial activity against all six tested MDR strains as compared to all isolated compounds and rifampicin, possibly due to the synergistic effect of its metabolites. Furthermore, the IC50 values of LP, stictic acid, and fukinanolide A on THP-1 macrophages were considerably higher than MICs against the tested mycobacterial strains, suggesting that THP-1 remained unaffected at concentrations effective against M.tb and MDR-Tb isolates. The deliberated SI ratio values indicated that LP, stictic acid, and fukinanolide A were more active and less toxic to MDR-Tb strains than rifampicin. The molecular docking studies on 1EA1, 4V1F and 3VIU

revealed that fukinanolide A and stictic acid bind effectively and selectively to 3VIU (β-ketoacyl reductase FabG4), thereby conferring their anti-TB potential. The outcomes provide a validation for the traditional use of L. pulmonaria in Tb treatment, with stictic acid and fukinanolide A identified as key biomarkers. Hence, L. pulmonaria presented as a promising source for the development of novel drugs targeting against MDR-Tb.

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PMID: 41704445

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36. Assessment of the efficacy of plant-derived essential oils against Mycobacterium tuberculosis: A systematic review and meta-analysis.

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Mycobacterium tuberculosis (MTB), the causative agent of tuberculosis (TB), remains a major global health challenge, exacerbated by the rise of multidrug-resistant (MDR) and extensively drug-resistant (XDR) strains. Limitations in current antibiotic therapies have intensified interest in alternative antimicrobials, including plant-derived phytochemicals. Essential oils (EOs), with their complex chemical composition and long-standing traditional use, represent promising candidates for novel anti-TB agents. This study conducted a systematic review and meta-analysis to evaluate the in vitro antimycobacterial activity of plant-derived EOs. Following PRISMA guidelines, four major databases, Scopus, MEDLINE Central/PubMed, Embase, and Web of Science, were searched through May 31, 2025, and 31 eligible studies were included after screening and quality assessment. Descriptive and comparative

analyses of minimum inhibitory concentrations (MICs) were performed using R software. The results revealed substantial variability in EO efficacy across plant species and geographic origins. The most potent activity was observed in Euclea sp. and Croton sp., which showed exceptionally low MICs of 1 μg/mL and 4.88 μg/mL, respectively. In contrast, EOs from Dichrostachys cinerea, Dorstenia elliptica, Imperata cylindrica, Mondia whitei, Pentadiplandra brazzeana, and Tetrapleura tetraptera exhibited weaker effects, with MICs up to 2048 μg/mL. Plant anatomical sources also influenced activity, with leaves and stems showing higher efficacy than roots and fruits. Overall, these findings highlight the therapeutic potential of specific EOs as adjunct or alternative treatments for DR-TB. Further studies involving compound standardization, and in vivo validation are necessary to support their development into clinically applicable anti-TB agents.

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37. Global, Regional, and National Burden of Tuberculosis Among Children: A Population-Based Study.

Trop Med Infect Dis. 2026 Feb 5;11(2):43. doi: 10.3390/tropicalmed11020043.

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Background: Tuberculosis remains a major global public health challenge, particularly among children. This study aims to provide a comprehensive assessment of the global, regional, and national burden of tuberculosis among children (0-14 years) using data from the Global Burden of Disease (GBD) 2021 study. Methods: Data on the incidence of tuberculosis (drug-susceptible, MDR-TB, and XDR-TB), as well as disability-adjusted life years (DALYs), among children aged 0-14 years in 204 countries and territories from 1990 to 2021 were obtained from the GBD 2021 study. Estimated annual percentage changes (EAPCs) in age-standardised incidence rates (ASIRs) and DALY rate were calculated overall and stratified by age, sex, and sociodemographic index (SDI) to quantify temporal trends. Spearman correlation analyses were performed to assess associations between tuberculosis burden and SDI. Results: In 2021, there were an estimated 759,300 new tuberculosis cases (ASIR: 37.7 per 100,000 population)

among children globally, including 32,515 cases of MDR-TB (ASIR: 1.6) and 1193 cases of XDR-TB (ASIR: 0.1). Both global ASIR and DALY rate exhibited a declining trend from 1990 to 2021, with EAPC of -2.61% (95%CI: -2.74 to -2.47) and -4.38% (-4.61 to -4.14), respectively. From 1990 to 2021, High-income North America was the only GBD region with an increasing ASIR for tuberculosis (EAPC = 1.12, 95% CI: 0.61 to 1.64). From 1990 to 2021, there was no significant change in ASIR of MDR-TB (EAPC = 1.18, 95% CI: -0.16 to 2.54). However, eight of the 21 GBD regions exhibited increasing trends in the ASIR of MDR-TB, with the largest increase observed in Oceania (11.99, 10.49 to 13.52), followed by Central Asia (9.76, 6.48 to 13.13) and South Asia (5.71, 3.10 to 8.38). A strong negative correlation was observed between tuberculosis burden and SDI, with the highest disease burden concentrated in low-SDI regions. Conclusions: Achieving elimination targets will require stronger diagnostics and treatment for childhood tuberculosis, alongside reduced transmission, improved infection detection, and preventive therapy for exposed children, especially those under 5 years.

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PMID: 41746014

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38. Peripheral blood B-cell compartment dysregulation in multidrug-resistant tuberculosis is associated with reduced circulating marginal zone-like B cells.

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OBJECTIVE: Multidrug-resistant tuberculosis (MDR-TB) remains a major global health challenge. While T cell-mediated immunity in tuberculosis is well characterized, alterations in circulating B-cell subsets during chronic MDR-TB

are less well defined.
METHODS: Peripheral blood mononuclear cells (PBMCs) from healthy controls [interferon gamma release assay negative (IGRA-)], individuals with latent tuberculosis infection (LTBI; IGRA+), and patients with active tuberculosis (ATB) were analyzed using multiparameter flow cytometry panels. Major lymphoid and myeloid populations and detailed B-cell subsets were quantified.
RESULTS: Frequencies of major T-cell and natural killer (NK)-cell populations were broadly similar across groups. In contrast, patients with ATB showed a reduction in total CD19+ B cells. Within the B-cell compartment, ATB was characterized by an increased proportion of naïve B cells and a pronounced reduction in antibody-secreting cells (ASCs). Circulating marginal zone-like B cells (MZ B, IgD+IgM+CD27+) were also reduced in ATB compared with non-ATB groups. Receiver operating characteristic (ROC) analysis suggested that reduced MZ B-cell frequency may help discriminate individuals with ATB from those without ATB; however, this observation should be interpreted as exploratory given the cohort size and composition.
CONCLUSION: MDR-TB is associated with broad perturbations of the peripheral B-cell compartment, including reduced ASCs and decreased circulating MZ B cells. These findings highlight B-cell dysregulation as a feature of active disease and identify MZ B cells as a subset of interest for further investigation rather than as a stand-alone diagnostic marker.

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39. Spatiotemporal epidemiology, geographic hotspots, and risk factor associations of drug-resistant tuberculosis incidence in Indonesia: a Bayesian hierarchical modelling approach.

Infect Dis Poverty. 2026 Feb 13;15(1):23. doi: 10.1186/s40249-026-01418-9.

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BACKGROUND: Indonesia ranks among the countries with the highest burden of drug-resistant tuberculosis (DR-TB), contributing approximately 7.4% of global cases, many of which are likely underdiagnosed. To support targeted public health surveillance and control efforts, this study aimed to characterize the spatiotemporal distribution of DR-TB incidence in Indonesia, identify geographic hotspots, and examine associations with health system and socioeconomic factors.
METHODS: We conducted a nationwide retrospective analysis using annual DR-TB notification data from 2017 to 2022 across all 514 districts, obtained from the national tuberculosis information system. Multivariable Bayesian spatiotemporal regression models were fitted under alternative likelihood assumptions and space-time random effect structures. Model selection criteria were used to identify the best-fitting models for hotspot detection and estimation of risk factor associations.
RESULTS: DR-TB predominantly affected individuals aged 25-54 years, aligning with the working-age population. Hotspots were concentrated in urbanized regions, including the Jabodetabek megacity, Greater Surabaya, and districts in South Sumatra. The best-fitting model identified a protective association between first-line treatment success rates and DR-TB incidence [incidence rate ratio (IRR): 0.508; 95% credible interval (CrI): 0.368-0.702]. In contrast, DR-TB incidence was positively associated with the proportion of the population living below the poverty line (IRR: 1.028; 95% CrI: 1.013-1.044), households with improved sanitation access (IRR: 1.006; 95% CrI: 1.002-1.010), and increased municipal human development index (IRR: 1.068; 95% CrI: 1.049-1.094).
CONCLUSIONS: DR-TB hotspots were primarily concentrated in urban areas, highlighting the need for targeted interventions. Improving first-line tuberculosis treatment success rates and addressing socioeconomic drivers, such as poverty, are critical for controlling DR-TB. Public health policies should prioritize workplace-based support for improving treatment adherence, provide safeguards for TB patients affected by poverty, and underscore the importance of a multisectoral TB surveillance and control program.

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40. The critical link between TB infection control process and clinical impact: need for efficacy data and MDR-TB specificity.

J Clin Tuberc Other Mycobact Dis. 2025 Dec 2;42:100577. doi: 10.1016/j.jctube.2025.100577. eCollection 2026 Feb.

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The study by Song et al. [1] detailing the significant improvements in Tuberculosis Infection Control (TBIC) implementation rates across designated hospitals in Jiangsu Province, China, provides valuable data on the feasibility of programmatic interventions in high-burden settings. The demonstrated rise in compliance for Administrative Controls (AC), Environmental Controls (EC), and Respiratory Protection (RP) is commendable. However, as scholars focused on global TB elimination, we must constructively appraise whether measuring implementation rates adequately captures the desired public health impact, particularly in facilities designated for multi-drug resistant tuberculosis (MDR-TB).

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PMID: 41438009

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41. Acute/subacute paracoccidioidomycosis associated with drug-resistant tuberculosis in a person living with HIV/AIDS.

Rev Inst Med Trop Sao Paulo. 2026 Jan 30;68:e4. doi: 10.1590/S1678-9946202668004. eCollection 2026.

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Paracoccidioidomycosis (PCM) is a neglected tropical disease classified as acute/subacute and chronic. In people living with HIV/AIDS (PLWHA), coinfection can lead to severe clinical manifestations. We report the case of a 30-year-old immunosuppressed male presenting fever, weight loss, polymorphic skin lesions, diffuse lymphadenopathy, hepatosplenomegaly, and joint effusion. Histopathological analysis revealed fungal structures compatible with Paracoccidioides spp., and serology was positive at a titer of 1:16. Despite initial Amphotericin B and antiretroviral therapy, the patient developed a productive cough and persistent systemic symptoms. Initial sputum tests were negative for Mycobacterium tuberculosis, but subsequent bronchoalveolar lavage detected rifampin-resistant tuberculosis (TB). The remarkable overlap of clinical and radiological features of TB and PCM can significantly delay diagnosis, highlighting the need for high clinical suspicion and prompt investigation with bronchoalveolar lavage (BAL) testing. After one-month outpatient follow-up, the patient showed significant cutaneous improvement, undetectable HIV viral load, and a marked increase in CD4+ T-cell count. This report highlights the importance of recognizing the acute/subacute form of PCM as an AIDS-defining illness in endemic areas, enabling early treatment and improved outcomes.

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42. High treatment success among individuals with rifampicin-resistant tuberculosis in Botswana: A retrospective cohort study.

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Update of
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BACKGROUND: Rifampicin-resistant tuberculosis (RR-TB) remains a global health challenge, which is often characterized by limited treatment options and increased morbidity and mortality. Despite advances in diagnostics and the introduction of new drug regimens, treatment success for drug-resistant TB remains low. There is limited data on clinical, sociodemographic, and microbiological factors that influence patient outcomes. The aim of the study is to evaluate TB treatment outcomes among individuals diagnosed with RR-TB and to identify predictors of favourable and unfavourable treatment outcomes.
METHODS: We conducted a retrospective study to analyse treatment outcomes of 162 individuals diagnosed with RR-TB using GeneXpert MTB/RIF and phenotypic drug susceptibility testing (pDST) from 2016 to 2023. Treatment outcome proportions were estimated using the binomial exact method with 95 % confidence intervals (CI). Predictors associated with unfavourable treatment outcomes were assessed using logistic regression models.
RESULTS: Of the 162 individuals, 102(62.7 %) were male with a median age of 39 (interquartile range (IQR): 29-50). Most individuals, 78(48.1 %), were from the Greater Gaborone health district, and 88(54.3 %) were people living with HIV (PLWH). Among included individuals, 137(84.6 %, 95 % CI: 78.2-89.7) were successfully treated. Males had higher odds of unfavourable treatment outcomes compared to females (OR = 1.70; 95 % CI: 0.73-3.98). Among those cured, a slightly higher proportion was observed among PLWH (71.8 %, 95 % CI: 62.1-80.3)

compared to people not living with HIV (PNLWH) (69.2 %, 95 % CI: 58.7-78.5). However, the mortality rate was higher among PLWH (10.7 %; 95 % CI: 5.5-18.3) than among PNLWH (6.6 %; 95 % CI: 2.5-13.8). Those with a history of TB treatment had 1.03 odds of unfavourable treatment outcomes (95 % CI: 0.40-2.73); however, this association was not statistically significant.
CONCLUSION: Our study shows a high rate of successful treatment outcomes among individuals with RR-TB, with no significant difference based on sex, TB treatment history, or HIV status. Higher mortality among PLWH highlights the need for targeted interventions among high-risk groups.

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PMID: 41671595

Conflict of interest statement: Declaration of Competing Interest The authors declare that they have no known competing interests.

43. Molecular epidemiology of drug resistance and transmission of Mycobacterium tuberculosis in Meigu County, Sichuan Province, China.

Microbiol Spectr. 2026 Feb 3;14(2):e0268525. doi: 10.1128/spectrum.02685-25. Epub 2025 Dec 29.

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Tuberculosis (TB) remains a major public health challenge in China. Meigu County, in Liangshan Yi Autonomous Prefecture, Sichuan Province, is severely affected by a high TB burden, a situation exacerbated by its geographic isolation and socioeconomic constraints. This study used DNA microarray technology to assess drug resistance in 378 Mycobacterium tuberculosis (M. tuberculosis) isolates from bronchoalveolar lavage fluid samples collected in Meigu County from 2022 to 2024. During this period, the drug resistance rates of rifampicin, isoniazid, and multidrug-resistant TB initially rose and then declined. Only the variation in isoniazid resistance reached statistical significance ($\chi^2 = 6.462$, $P = 0.038$). Age-specific analysis revealed a significantly higher prevalence of isoniazid resistance among individuals aged 19-60 years ($\chi^2 = 7.034$, $P = 0.022$). Whole-genome sequencing was further applied to 123 isolates collected from the same geographical area and sample type in 2024. Genomic analysis detected drug-resistant mutations in 8.9% (11/123) of the isolates, with dominant mutations including rpoB p.Ser450Leu and katG p.Ser315Thr. Lineage 2 and Lineage 4 strains demonstrated comparable prevalence, with no statistically significant difference observed among the cases analyzed

in 2024. Phylogenetic clustering based on a ≤12 single-nucleotide polymorphism (SNP) threshold grouped 31.7% (39/123) of the strains into 15 distinct transmission clusters, reflecting ongoing community spread. Clustering was significantly associated with amikacin resistance (P = 0.001). Discrepancies in resistance predictions between bioinformatic tools highlighted the necessity for standardized genomic surveillance protocols. These results offer the first comprehensive genomic characterization of M. tuberculosis transmission and resistance in Meigu County, underscoring the critical need for targeted public health strategies to interrupt transmission in this high-incidence setting. IMPORTANCE: This study provided a critically important investigation into the molecular epidemiology of drug-resistant tuberculosis in Meigu County, a remote and high-burden region in Sichuan Province, China. By combining DNA microarray chip technology and whole-genome sequencing, the researchers characterized the genetic makeup, drug resistance patterns, and transmission dynamics of strains of Mycobacterium tuberculosis circulating in this underserved community. They identified specific mutations responsible for resistance to key anti-tuberculosis drugs and revealed ongoing local transmission through genomic clustering analysis. The findings highlighted the urgent need for improved public health interventions, standardized treatment protocols, and enhanced genomic surveillance in regions with limited healthcare resources. This work offered the comprehensive genomic insight into tuberculosis transmission in Meigu County and served as a model for understanding and combating drug-resistant tuberculosis in other high-incidence, economically disadvantaged areas worldwide.

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PMCID: PMC12889122
PMID: 41459972 [Indexed for MEDLINE]

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

44. Drug resistance and clinical characteristics of pediatric and adolescent tuberculosis: A multicenter retrospective study in China.

Diagn Microbiol Infect Dis. 2026 Feb;114(2):117185. doi: 10.1016/j.diagmicrobio.2025.117185. Epub 2025 Nov 8.

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BACKGROUND: Pediatric tuberculosis (TB) management remains an underemphasized area plagued by diagnostic and treatment challenges that are compounded further due to rising levels of drug-resistant tuberculosis (DR-TB). Even though TB

incidence is high in China, limited data exists on pediatric and adolescent DR-TB across local settings.
OBJECTIVES: This retrospective study aimed to characterize the prevalence, clinical features, and treatment outcomes of pediatric DR-TB over a 10-year period.
METHODS: Medical records of 153 children and adolescents (≤18 years) diagnosed with TB were reviewed. Drug susceptibility testing (DST), GeneXpert, clinical features, and treatment outcomes were analyzed. Multivariable logistic regression and Kaplan-Meier survival analysis were employed.
RESULTS: DR-TB accounted for 30.1% of cases, including 21.7% multidrug-resistant TB (MDR-TB) and 10.9% extensively drug-resistant TB (XDR-TB). DR-TB was associated with residence in high-burden areas and extrapulmonary disease. GeneXpert positivity was significantly higher in DR-TB patients (67.4%, $p < 0.001$). DR-TB patients had longer treatment duration (median 12 months) and lower cure rates (67.4% vs. 92.5%, $p < 0.001$). Kaplan-Meier analysis showed treatment success rates diverging after 10 months. HRZE was significantly protective against poor outcomes (OR = 0.032, $p = 0.017$), and bedaquiline-based regimens showed a positive trend.
CONCLUSIONS: High DR-TB burden, delayed diagnosis, and inferior outcomes in pediatric patients underscore the need for routine DST, wider access to molecular diagnostics, and child-friendly second-line regimens. Policy changes focused on decentralizing diagnostic services and adopting WHO-endorsed pediatric regimens are urgently required.

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Conflict of interest statement: Declaration of competing interest The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

45. Deep-Sea Marine Metabolites as Promising Anti-Tubercular Agents: CADD-Guided Targeting of the F(420)-Dependent Oxidoreductase.

Mar Drugs. 2026 Jan 31;24(2):58. doi: 10.3390/md24020058.

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Tuberculosis, caused by Mycobacterium tuberculosis (M. tb), remains a leading global threat, escalated now by the rise of multidrug-resistant (MDR-TB) and extensively drug-resistant (XDR-TB) strains. In search of a novel anti-tubercular agent with a distinct mechanism of action, this study explores deep-sea marine metabolites as potential inhibitors of the F420-dependent oxidoreductase Rv1155, a redox enzyme essential for M. tb survival. A total of 2773 marine-derived compounds curated from the CMNPD, Reaxys, and MarinLit databases were screened using an integrated CADD workflow combining molecular docking, in-silico ADMET profiling, and molecular dynamics (MD) simulations. Docking identified 68 metabolites with strong affinity (-10.98 to -15.95 kcal/mol) for the Rv1155 binding pocket, and from which three compounds, Upenamide (CMNPD_22964), Aspyronol (Compound_1749), and Fiscpropionate F (Compound_1796), were shortlisted as hit candidates. Among these, Upenamide displayed the strongest binding (ΔG = -28.56 kcal/mol) with stable RMSD and hydrogen bond persistence during 100 ns MD simulation, while Aspyronol demonstrated a promising ADMET profile comparable to the native cofactor F4202. MM-GBSA analysis further confirmed the strong binding strength (ΔG _bind = -24.77 to -34.07 kcal/mol) for all three hit candidates. These findings confirm the strong and stable interaction of selected deep-sea marine metabolites with Rv1155. This validated screening pipeline established here provides a cost-effective framework for future experimental validation and expansion to additional F420-related drug targets in M. tb.

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PMCID: PMC12942459
PMID: 41745461

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

46. An integrated computational bioprospection of flavonoids as modulators of Mycobacterium tuberculosis decaprenylphosphoryl-β-d-ribose-2'-epimerase 1.

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Tuberculosis (TB) remains a significant global health threat, claiming millions of lives annually despite being preventable. The emergence of drug-resistant strains, including extensively drug-resistant TB (XDR-TB) and multidrug-resistant TB (MDR-TB), severely limits conventional treatment options. Furthermore, commonly used TB medications like isoniazid (INH) and rifampicin (RIF) are associated with adverse side effects. Consequently, researchers increasingly explore natural products as potential sources for novel anti-TB therapeutics. This study investigated the inhibitory potential of 103 flavonoid compounds with documented antimycobacterial activity against TB. Focusing on decaprenylphosphoryl-β-D-ribose 2'-epimerase 1 (DprE1) as a druggable target, we employed molecular docking, pharmacokinetic evaluation, and 200-ns molecular dynamics simulations to assess stability and energy refinement. Our results showed that the top five compounds exhibited more favourable binding free energy values against DprE1 than the standard, PBTZ169. Notably, cycloartobiloxanthone demonstrated a binding free energy of -63.67 kcal/mol, surpassing PBTZ169 (-37.78 kcal/mol). Structural analysis revealed that cycloartobiloxanthone stabilised the protein and formed additional interactions without compromising its integrity. These findings suggest a potential structural mechanism for the inhibitory action of cycloartobiloxanthone against Mycobacterium tuberculosis DprE1. While this study highlights the potential of cycloartobiloxanthone as a lead compound, further validation through in vivo and in vitro studies is recommended.

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47. Tuberculosis notification trends and treatment outcomes in Bangladesh: findings from a National TB Program data, 2019-2021.

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BACKGROUND: Tuberculosis (TB) remains a major public health challenge in Bangladesh, which ranks among the world's high-burden countries. While previous studies have examined TB outcomes in specific populations, comprehensive national data on age-stratified outcomes, particularly comparing children and adult cohorts, remain scarce. This study aimed to (1) analyze trends in TB notifications; (2) compare treatment outcomes across age groups, sex, treatment history, and disease types; and (3) identify potential risk factors for unsuccessful outcomes.
METHODS: We analyzed Bangladesh's National TB Program (NTP) data (2019–2021), including 494,685 confirmed cases of TB. Treatment outcomes were categorized per WHO definitions. Analyses included: (1) temporal assessment of notification patterns; (2) comparative evaluation of treatment outcomes stratified by demographic, clinical, and health system characteristics; and (3) identification of associated factors for unsuccessful outcomes through multivariable modified Poisson regression, reporting adjusted relative risks (aRR) with 95% confidence intervals.
RESULTS: Between 2019 and 2021, 494,685 people with tuberculosis (TB) were reported to the NTP of Bangladesh. Notifications increased by 64% from 2019 to 2020 and by 83% from 2020 to 2021. Analysis of 300,974 patients demonstrated a treatment success rate exceeding 95.0% in both adults and children. Among children aged under 5 years, mortality reached 5 × 4%, with an overall unsuccessful outcome rate of 7 × 7%. Extrapulmonary TB was associated with poorer outcomes compared to pulmonary TB in both children (mortality: 2.3% vs 1.1%) and adults (aRR: 2.01; 95% CI:1.92–2.10). Rural health facilities had higher loss to follow-up in children (2.5% vs 0.7% in urban areas). In adults, mortality increased markedly with age, from 1.0% in those aged 18–30 years to 6.4% in individuals aged 60 years and older (aRR:3.53; 95% CI: 3.32–3.76). Male sex was independently associated with a higher risk of unsuccessful treatment (aRR 1.58; 95% CI:1.52–1.65), as were previous TB history (aRR:1.74; 95% CI:1.63–1.86) and receipt of retreatment (aRR:1.71; 95% CI:1.43–2.06) or second-line regimens (aRR:1.78; 95% CI:1.48–2.13).
CONCLUSION: Bangladesh's TB program showed resilience but revealed critical gaps. Children < 5 and adults ≥60 had worse outcomes, signaling age-specific care deficiencies. Persistent male disparities suggest access or biological differences. Rural facilities excelled with adults but struggled with children with TB retention. High retreatment failure rates demand better drug-resistant TB management. Key priorities: 1) age-specific protocols, 2) gender-sensitive interventions, 3) improved rural children's care, and 4) enhanced drug-resistant TB services. Addressing these gaps is vital for achieving the END TB targets.
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Conflict of interest statement: Declarations. Ethics approval and consent to participate: This study used routinely collected programmatic data for tuberculosis surveillance. All data were fully de-identified prior to analysis, and individual informed consent was not required. This study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. The study was approved by the Ethics Committee of the General Health Services, Ministry of Health and Family Welfare, Bangladesh (Reference No. 13,074). Clinical trial number: Not applicable. Consent for publication: Not applicable. Competing interests: The authors declare no competing interests.

48. Social support and its associated factors among people on drug-resistant tuberculosis treatment in three selected hospitals in Ethiopia: a cross-sectional study design.

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OBJECTIVE: Social support is an important factor for psychosocial well-being and motivation to follow the treatment strictly in people with drug-resistant tuberculosis (DR-TB). Thus, this study aimed to determine the availability of social support and its association factors in people with DR-TB in selected hospitals in Ethiopia.
DESIGN: A cross-sectional study was conducted in Addis Ababa (at Saint Peter and ALERT hospitals) and Bishoftu Hospital in Ethiopia. The study involved 130 people with DR-TB from January to May 2023.
PARTICIPANTS: All adult people on DR-TB treatment for at least 2 months were enrolled consecutively from the registration book. A structured questionnaire was used to collect data. Data were entered to Open Data Kit and analysed with SPSS V.22. Descriptive statistics were used to describe the characteristics of the participants. A linear regression model was used to assess factors associated with social support.
MAIN OUTCOME: Availability of social support from different sources.
RESULTS: The overall proportion of availability of social support obtained from different sources was 97.7% with 95% CI of (93.1% to 99.5%). Sex (β=0.61, 95% CI (0.28 to 0.94); p<0.001), marital status (β=0.59, 95% CI (0.26 to 0.93); p=0.001) and patient self-stigma score (β=0.60, 95% CI (0.42 to 0.78); p<0.001)

were significantly associated with social support score.
CONCLUSIONS: A considerable proportion of people with DR-TB were obtaining social support from different sources. Interventions targeted female sex, single marital status and perceived social stigma are required to enhance social support conditions in people with DR-TB.

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49. Challenges in the Diagnosis and Treatment of Mycobacterium abscessus Infections.

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The Mycobacterium abscessus complex (MABC) includes non-tuberculous mycobacteria that are widely distributed and clinically significant. Similar to tuberculosis, MABC can lead to skin and soft tissue infections and pulmonary diseases. These infections frequently occur in outbreaks, particularly among immunocompromised patients or those with preexisting pulmonary conditions. This review examines the recent progress in essential areas that define these infections as a significant challenge in medical practice, specifically the diagnostic modalities, antibiotic treatment options, and resistance of MABC to antibiotics and biocides.

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50. Rapid drug resistance prediction in positive Mycobacterium tuberculosis clinical samples using an extensive targeted next-generation sequencing panel.

Emerg Microbes Infect. 2026 Dec;15(1):2627072. doi: 10.1080/22221751.2026.2627072. Epub 2026 Feb 12.

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Tuberculosis (TB) remains a global health challenge, exacerbated by the emergence of drug-resistant Mycobacterium tuberculosis strains. Most methods for drug susceptibility testing (DST) are culture-dependent and time consuming, possibly delaying optimal TB-treatment. This study aimed to develop an extensive targeted next-generation sequencing (tNGS) approach for rapid genotypic DST directly from clinical samples. We designed a tNGS panel comprising 30 amplicons targeting 19 genomic regions associated with resistance to 20 antibiotics. This method was applied to 71 smear-positive (0-3+) pulmonary TB clinical samples collected at the Portuguese National Reference Laboratory. DNA was extracted and amplified using multiplex PCRs, followed by sequencing on Oxford Nanopore Technologies MinION platform. Sequencing data were using TB-Profiler and the tNGS results compared to phenotypic DST and whole genome sequencing (WGS) data from corresponding isolates. The tNGS demonstrated high concordance with both phenotypic and WGS-based DST across different sample types and smear positivity levels. For first-line drugs, tNGS showed 88% categorical agreement (CA) with pDST, increasing to 97% when excluding undetermined results. Compared to WGS across all analysed antibiotics, tNGS achieved 92% CA, increasing to >99% when excluding undetermined results. Validation of the tNGS panel showed 90% (1,895/2,076) of amplicons reaching >10x coverage at all analysed positions and 43 (61%) samples with all complete amplicons above this threshold. Non-specific amplification of contaminant bacterial DNA was minimal, with most mapped off-target reads being of human origin. This method enables comprehensive resistance prediction directly from clinical samples and signifies an important development in TB diagnostics and resistance monitoring.

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PMID: 41631669 [Indexed for MEDLINE]

Conflict of interest statement: No potential conflict of interest was reported by the author(s).

51. Efficacy and safety of an all-oral delamanid-containing regimen in the treatment of multidrug-resistant pulmonary tuberculosis complicated by extrapulmonary tuberculosis: Four case reports and review of the literature.

J Clin Tuberc Other Mycobact Dis. 2025 Dec 4;42:100576. doi: 10.1016/j.jctube.2025.100576. eCollection 2026 Feb.

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BACKGROUND: Multidrug-resistant tuberculosis (MDR-TB) complicated by extrapulmonary TB (EPTB) poses significant therapeutic challenges. While delamanid (DLM) demonstrates extensive tissue penetration, clinical evidence supporting its use specifically for MDR-TB with EPTB remain limited. This report evaluates an all-oral DLM-containing regimen for this complex presentation.
CASE PRESENTATION: Four patients (aged 35, 24, 47, 4 years; 3 females, 1 child) with molecularly confirmed MDR pulmonary TB (MDR-PTB) and concurrent EPTB (spinal, central nervous system, breast, lymph node) received individualized all-oral regimens. Regimens combined DLM with bedaquiline (BDQ), linezolid (LZD), fluoroquinolones, and companion drugs for ≥ 15 months. Follow-up imaging demonstrated significant lesion resolution in all cases, including the pediatric lymph node involvement (first reported in China). Twenty-four adverse events occurred (15 Grade 1, 6 Grade 2, 3 Grade 3), primarily corrected QT interval prolongation (5 events, one > 500 ms). Most events (21/24, 87.5 %) resolved following dose adjustments or supportive care. No serious adverse events or deaths occurred.
CONCLUSION: In this small case series of patients with MDR-TB and diverse extrapulmonary manifestations, an all-oral DLM-containing regimen was associated with significant lesion regression and demonstrated a manageable safety profile. QT prolongation was the primary adverse event, reversible with intervention. These findings-representing China's first systematic report of this regimen for multisite EPTB, including the pediatric case-align with WHO guidance and suggest DLM's potential utility based on its extensive tissue penetration. Further validation in larger multicenter studies is warranted.

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PMID: 41502914

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52. Patterns of Multidrug Resistance and Treatment Outcomes Among Pulmonary Tuberculosis Patients in Bangladesh.

Pathogens. 2026 Feb 12;15(2):208. doi: 10.3390/pathogens15020208.

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Background: To effectively manage tuberculosis (TB), it is essential to address the high incidence of the disease, as multidrug-resistant pulmonary TB (MDR-PTB) remains a significant concern to halt pre-extensive drug-resistant (pre-XDR) recrudescence. The objective of the current study was to examine and compare MDR-PTB patterns among adult PTB patients (>12 years) in Bangladesh's urban and rural areas who had newly diagnosed and previously treated PTB. Methods: A total of 430 newly diagnosed and previously treated adult patients with PTB were randomly recruited during two study periods: the 1st period, from May 2010 to December 2010 (eight months), and the 2nd period, from January 2014 to January 2015 (thirteen months). Only the drug-resistant (DR) patients were included in the final analysis. Mycobacteriological tests, i.e., smear microscopy, culture, drug susceptibility testing (proportion method of Canetti), line-probe assay, and GeneXpert MTB/RIF were performed. Logistic regression analysis was used to determine the strength of associations between treatment outcomes and predictor variables. Results: Of the newly diagnosed patients, 156 cases were negative and drug-sensitive (DS) at diagnosis, and 274 patients exhibited various DR patterns. During the 1st period, MDR-PTB was 26% among newly diagnosed patients,

while the proportion was 31% among previously treated patients in the 2nd period. The majority of MDR-PTB belonged to the age group of ≤45 years. Male patients consistently revealed a higher proportion of MDR-PTB compared to females in both the newly diagnosed and previously treated groups. Conclusion: The proportion of MDR-PTB was higher among the previously treated patients than among newly diagnosed patients. Regardless of demographic characteristics, a significant proportion of patients showed DR, particularly in previously treated groups, indicating a substantial burden of MDR-PTB.

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PMID: 41754460

Conflict of interest statement: The authors have no conflict of interest.

53. Targeting Mycobacterium tuberculosis: The Role of Alkyl Substitution in Pyrazinamide Derivatives.

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Tuberculosis (TB) remains a significant global health challenge due to the rapid emergence of drug resistance. Despite substantial progress in anti-TB drug development, effective treatment options are limited. In this study, we report the synthesis and biological evaluation of pyrazinamide (PZA) derivatives with 5-alkyl and 5-alkanamido modifications, designed to enhance antimycobacterial activity by increasing lipophilicity and improving penetration of the lipid-rich mycobacterial cell wall. A positive correlation between the length of the 5-alkyl chain and antimycobacterial activity was observed, with maximal potency

achieved with the heptyl substituent (4: 5-heptylpyrazine-2-carboxamide, MIC_M. tuberculosis H37Rv = 3.13 μg/mL). In series C with phenyl substitution on the C-2 carboxamide, different simple substituents were tolerated on the benzene ring (both electron-donating and electron-withdrawing, both lipophilic and hydrophilic), and the length of the alkyl chain was the main determinant of the antimycobacterial activity. Compound 23 (5-hexyl-N-(3-trifluoromethylphenyl)-pyrazine-2-carboxamide) exerted MIC = 3.13 μg/mL and selectivity index (SI, compared to HepG2 cells) >25. Notably, the tested compounds exhibited significant activity against multidrug-resistant (MDR) Mycobacterium tuberculosis strains while maintaining favorable selectivity profiles and low cytotoxicity. In contrast, 5-alkanamido derivatives (series B and D) were devoid of antimycobacterial activity. Mechanistic investigations revealed that unlike PZA, the 5-alkyl pyrazinamide derivatives are not hydrolyzed by mycobacterial pyrazinamidase (PncA), indicating a distinct mode of action. While molecular modeling initially suggested enoyl-ACP reductase (InhA) as a potential target of series C, subsequent experimental validation disproved this hypothesis; thus, the precise mechanism of action remains to be elucidated.

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PMID: 41626510

54. Treatment Outcomes and Drug-Related Adverse Events Across Four Short-Course RR-TB Regimens in South Africa: A Retrospective Analysis.

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BACKGROUND: Shorter all-oral regimens for the treatment of multidrug-resistant tuberculosis or rifampicin-resistant tuberculosis (MDR/RR-TB) have improved efficacy, but their performance under programmatic conditions remains insufficiently characterized.
METHODS: We retrospectively evaluated treatment outcomes and drug-related adverse events (AEs) among 396 randomly selected patients from four facilities in three provinces across South Africa. Patients received four different short-course regimens sequentially introduced into national programme: i) injectable 9-11-month (injectable-regimen), ii) bedaquiline-ethionamide-containing (ethionamide-regimen), iii) bedaquiline-linezolid-containing (linezolid-regimen), and iv) bedaquiline-pretomanid-linezolid-levofloxacin regimen (BPaL-L).
RESULTS: Compared with the injectable regimen, the ethionamide-regimen (adjusted odds ratio [aOR] 1.98, 95% CI 1.07-3.65) and BPaL-L (aOR 2.31; 95 % CI 1.23-4.33) had higher odds of treatment success; the linezolid-regimen did not (aOR 1.68; 95 % CI 0.92-3.06). The linezolid and BPaL-L regimens had similar odds of grade 3 or higher AEs, and comparable AE-related drug discontinuation. Toxicity patterns differed, from hearing loss with injectables to anaemia and neurotoxicity with BPaL-L.
CONCLUSION: Under programmatic conditions, the BPaL-L regimen achieved the highest treatment success while maintaining manageable safety profiles. These findings provide valuable evidence to guide patient management and support implementation of novel MDR/RR-TB regimens in high-burden settings.

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Conflict of interest statement: Declaration of competing interest The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

55. Towards model-informed precision dosing of clofazimine, moxifloxacin, and terizidone/cycloserine in the treatment of drug-resistant tuberculosis: An external model evaluation study.

Tuberculosis (Edinb). 2026 Jan 31;157:102744. doi: 10.1016/j.tube.2026.102744. Online ahead of print.

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Clofazimine, moxifloxacin and terizidone/cycloserine play an important role in the treatment of drug-resistant tuberculosis (DR-TB). Personalized therapy guided by model-informed precision dosing (MIPD) can be a powerful tool to improve treatment outcomes, minimize adverse effects and combat the emergence of resistance. To set up an MIPD workflow, a population pharmacokinetic model (popPK model) is required. In this study, an external evaluation of popPK models of the three aforementioned drugs was carried out, using pharmacokinetic data from a cohort of patients with DR-TB, in order to identify the model with the best predictive performance. The best performing models (Abdelwahab et al. for clofazimine, Chirehwa et al. for moxifloxacin and Mulubwa and Mugabo for terizidone/cycloserine) were selected to calculate the area under the concentration-time curve (AUC, total exposure). An interoccasion variability (IOV, variability across dosing occasions) of AUC was quantified (13.4%CV (clofazimine), 16.1%CV (moxifloxacin), 14.5%CV (cycloserine)) indicating that using samples from one dosing occasion for AUC calculations may be sufficient to guide potential dose adjustment. Various single sampling schemes to estimate AUC were evaluated, but a unified timepoint for all drugs could not be determined. Known pharmacodynamic targets (AUC0-24h/MIC, or T>MIC) were attained in almost all patients and dosing occasions.

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the scope of this work.

56. Prevalence, risk factors, and rifampicin resistance pattern of Mycobacterium tuberculosis in Sekota town, Northwest Ethiopia.

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BACKGROUND: Tuberculosis (TB) is a significant cause of morbidity and mortality globally, particularly in developing countries. However, in some parts of Ethiopia there is limited information on the prevalence, associated risk factors and the level of drug resistant TB. Therefore, this study aimed to determine TB prevalence, identify associated risk factors, and assess rifampicin resistance in Sekota Town, northwest Ethiopia.
METHODS: A cross-sectional study was conducted from March to June 2023 at Tefera Hailu Memorial Hospital in Sekota town. Morning sputum and fine needle aspirate samples from pulmonary and extrapulmonary cases, respectively, were collected from 422 individuals who visited the hospital during the study period, and the samples were tested for Mycobacterium tuberculosis using the GeneXpert MTB/RIF molecular assay. A structured questionnaire was used to collect socio-demographic and clinical data.
RESULTS: The overall prevalence of all forms of TB in this study was 19.90 %. Of the overall TB cases, 52.4 % were pulmonary (EPTB), whereas 47.6 % were extra-pulmonary (PTB). Among TB positive cases, the prevalence of rifampicin resistant TB was determined to be 2.4 %. Students (adjusted odds ratio (AOR) = 4.66; 95 % CI: 1.11-19.61), pastoralists (AOR = 2.75; 95 % CI: 1.19-6.33), and merchants (AOR = 13.96; 95 % CI: 1.20-162.40) had higher odds of TB infection. Regular alcohol consumption (AOR = 2.62; 95 % CI: 1.10-6.24) and contact with TB patients (AOR = 3.95; 95 % CI: 2.02-7.33) were associated with increased odds of TB infection. HIV sero-positives and those over the age of 45 years were also found to be more likely to be infected with TB. The prevalence of rifampicin-resistant TB among confirmed cases was 2.4 %.
CONCLUSION: The study revealed a high prevalence of TB, with risk factors including HIV infection, alcohol use, contact with TB patients, and high-risk occupational and social groups such as students, merchants, and pastoralists. Targeted TB prevention and control efforts focusing on these high-risk populations are needed to reduce the disease burden in the study area.

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57. Reappraising TB preventive treatment in India: programmatic and ethical implications of subclinical tuberculosis in household contacts.

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India's pursuit of Tuberculosis (TB) elimination is contingent on the rapid universal scale-up of TB Preventive Treatment (TPT) for household contacts. However, current strategies largely neglect the asymptomatic active (subclinical) TB stage in terms of standardized diagnosis and optimized management. Consequently, administering TPT to individuals with unrecognized subclinical TB constitutes inadequate therapy that provides no patient benefit, enables community transmission, and risks minimal chances of iatrogenic drug resistance-violating the fundamental ethical principle of non-maleficence. We examine the tension between utilitarian public health goals and individual biomedical ethics, arguing for a transition within the National TB Elimination Program (NTEP) toward a rights-based framework prioritizing the clinical safety of household contacts. Crucially, the NTEP must institutionalize robust health education for contacts regarding the persistent risk of progression for at least 24 months post-TPT completion, coupled with sustained clinical surveillance to mitigate delayed health-seeking behavior. Further, sustained investment in digital diagnostics and translational research apart from addressing implementation gaps in the private sector is paramount to making TPT safe, evidence-driven, and ethically responsible.

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58. COVID-19 pandemic changes in social behavior relevant for transmission of Mycobacterium tuberculosis.

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OBJECTIVE: Mycobacterium tuberculosis (Mtb), the causative agent of tuberculosis (TB), is spread through the air. Although extensive data has shown that TB case notifications decreased during the COVID-19 pandemic, there is little known about the extent to which these reductions were due to a decrease in transmission, rather than delays in healthcare seeking and diagnosis. We used data from CONTEXT, a population-based cross-sectional study which enrolled newly diagnosed cases of extensively drug-resistant (XDR) or pre-extensively drug resistant (pre-XDR) TB in KwaZulu-Natal, South Africa from 2019 to 2023 and recorded information on their contacts.
RESULTS: We found that close contacts declined by 36% from 2019 to 2020 ($p = 0.005$). Casual contacts at locations where participants routinely spent time declined by 30% ($p = 0.16$). Based on our findings, substantially lower population-level risk of transmission could be expected between 2020 and 2022 in this region of South Africa. These data are useful for understanding the extent of the reduction in Mtb transmission during the pandemic.

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Conflict of interest statement: Declarations. Ethics approval and consent to participate: This study was conducted in accordance with the Declaration of Helsinki. Informed consent was obtained from all study participants (or next-of-kin, if deceased or too ill to provide consent). Ethics committees at the University of KwaZulu-Natal and Emory University approved the study. Consent for publication: Not applicable Competing interests: The authors declare no competing interests.

59. Investigation of Gene Regions Responsible for Drug Resistance in Clinical Isolates of Mycobacterium tuberculosis Complex Resistant to at Least Two First-Line Anti-Tuberculosis Drugs.

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Early and rapid diagnosis of drug resistance in tuberculosis (TB) plays a key role in reducing the spread of resistance and enabling effective treatment. The aim of this study was to investigate mutations in drug resistance-associated gene regions of Mycobacterium tuberculosis complex (MTBC) isolates resistant to at least two first-line anti-tuberculosis drugs through sequence analysis, in order to characterize the core molecular features of these strains in the region and to identify previously unreported, geographically distinct novel mutation sites. The drug susceptibility of 23 clinical isolates was assessed using the BACTEC MGIT 960 system, and resistance-associated point mutations were identified through DNA sequence analysis and comparison with GenBank reference sequences. AAG → AGG mutation was detected in the rpsL gene region at codon 43 (n = 7) and codon 88 (n = 1). Additionally, GAG → GCG point mutation was identified at codon 70 (n = 2), representing a new region not previously reported in the literature. The most frequent mutation was AGC → ACC at katG codon 315 (n = 10), followed by a C → T substitution at position -15 of the inhA promoter region (n = 4). Additionally, TCG → TTG at rpoB codon 531 (n = 4) and ATG → GTG at embB codon 306 (n = 1) were detected. The detection of resistance-associated mutations is essential for controlling drug-resistant

tuberculosis. In this study, a novel rpsL mutation (GAG → GCG) at codon 70 and a previously unreported codon 88 mutation in our country were identified, contributing to the understanding of molecular resistance mechanisms and epidemiology.

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PMID: 41754474

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60. From trials to programmatic scale-up: treatment outcomes of rifampicin-resistant tuberculosis during transition to short oral regimens in Vietnam (2021-2022).

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OBJECTIVES: Vietnam is a high tuberculosis (TB) and rifampicin-resistant TB (RR-TB) burden country. Different new RR-TB regimens were recommended in recent years. Locally-generated evidence about nationwide implementation of different RR-TB regimens is essential to inform national treatment guidelines.
METHODS: A retrospective cohort study of all patients with RR-TB treated nationwide in Vietnam from 2021 to 2022. Short treatment regimens (STR) were 9-11-month standardized 7-drug regimens with either bedaquiline (BDQ_STR) or an injectable drug (inj_STR), and a modified 9-11-month 5-drug regimen (m_STR). Long regimens were 18-20-month regimens for fluoroquinolone-susceptible RR-TB (long RR-TB) or fluoroquinolone-resistant RR-TB (long pre-extensively drug-resistant TB). With logistic regression we estimated predictors of unfavorable outcome.
RESULTS: Of 4814 patients with RR-TB, 71.2% had end-of-treatment success. Failure, death, lost-to-follow-up (LTFU) and not evaluated accounted for 3.6%, 7.8%, 13.3%, and 4.2%, respectively. Long RR-TB regimen had significantly higher

unfavorable outcomes as compared to BDQ_STR (adjusted odds ratio [95% confidence interval] = 1.56 [1.32-1.84]). Among STR, inj_STR had the lowest success rate (71.8%) in comparison to BDQ_STR (76.2%) (adjusted odds ratio [95% confidence interval] = 1.23 [1.04-1.45]). However, the LTFU rate is still high in both BDQ_STR and inj_STR. Treatment with inj_STR or long RR-TB regimen, retreatment after LTFU, being male and aged ≥50 years were predictors of unfavorable RR-TB treatment outcomes.
CONCLUSIONS: During the transition from injectable-containing to all-oral short regimens, nationwide data showed 71.2% RR-TB treatment success in Vietnam. The wider use of STRs and addressing LTFU may further improve outcomes. More robust and better managed long regimens are needed for those not eligible for any STR.

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

61. Psoriasis flare confused with drug allergy: A collaborative effort is required to treat tuberculosis in the setting of severe psoriasis.

Respir Med Case Rep. 2026 Jan 22;59:102378. doi: 10.1016/j.rmcr.2026.102378. eCollection 2026.

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BACKGROUND: Psoriasis is a chronic autoimmune disorder. Severe psoriasis is treated with systemic immunosuppressive agents. Systemic immunosuppression increases the risk of tuberculosis (TB) disease. Sudden cessation of immunosuppression seems logical in a TB patient but can lead to psoriasis flares. And when a new rash occurs during TB therapy, drug reaction is usually suspected. This can result in untreated TB disease or intermittent therapy, thus increasing the risk for acquired drug resistance.
METHODS: We describe two patients who developed TB disease during immunosuppressive therapy for psoriasis. When the immunosuppressive therapy was stopped, due to TB disease, both patients experienced significant worsening of psoriasis. The skin changes were confused with drug reaction to TB medications. Significant treatment interruptions resulted. A single team of TB physicians and one dermatologist, worked in conjunction to formulate a psoriasis and TB

treatment plan. The patients were treated with acitretin and cyclosporine systemically along with topical agents to achieve psoriasis control. Then both were sequentially challenged with one TB medication at a time to ensure no drug reaction occurred while monitored at Texas Center for Infectious Disease. Cyclosporine was then tapered off.
RESULTS: Both patients tolerated the alternative psoriasis regimen and TB therapy well. Both demonstrated clinical, bacteriologic, and radiographic improvement.
CONCLUSION: Treatment of TB disease in patients with severe psoriasis requires a collaborative effort between the TB treatment team and dermatology. A balanced approach, including treatment of both diseases, is necessary to avoid confusion of psoriasis flare versus drug induced skin reactions from TB medications.

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62.Global whole-genome-based genomic insights into Mycobacterium tuberculosis: Clonal dominance, sequence-type structure, and antimicrobial resistance-virulence landscapes.

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BACKGROUND: Tuberculosis (TB) remains a major global public health burden, exacerbated by the continued emergence and spread of drug-resistant Mycobacterium tuberculosis. Despite the rapid expansion of publicly available whole-genome sequencing data, gaps remain in the consistent characterization of

global population structure, dominant sequence-type (ST) distributions, accessory genome variability, and antimicrobial resistance (AMR) gene profiles, largely due to fragmented and uneven sampling across regions and time periods. This study aimed to conduct a large-scale in silico analysis of publicly available M. tuberculosis whole-genome sequences to descriptively characterize global ST structure, accessory genome diversity, AMR gene landscapes, and their geographic and temporal distributions, while integrating available phenotypic susceptibility data.
METHODS: We conducted the largest genomic analysis of M. tuberculosis to date, examining 7890 high-quality genomes from 82 countries (1900-2024) retrieved from NCBI GenBank. Rigorous quality filtering using CheckM ensured retention of genomes with >90% completeness and <5% contamination. Comprehensive genomic characterization included assembly metrics, annotated gene features, multi-locus sequence typing, AMR profiling using AMRFinderPlus (v4.0.23; database 2025-07-16.1), temporal trend analysis, geographic distribution mapping, and gene presence pattern (GPP) clustering to assess accessory genome diversity.
RESULTS: Analysis of 7890 high-quality M. tuberculosis genomes from 77 countries (1900-2024) revealed a highly conserved global population dominated by a few epidemic clones. Although 158 ST were identified, three ST (ST 215, ST 279, ST 276) accounted for 84.9% of all isolates, with ST 215 alone representing 58.0%, indicating a strong global clonal bottleneck, while 90.5% of ST were rare (≤10 isolates each). Most isolates were human-derived (93.7%), and genome size (~4.38 Mb) and gene content (~4149 genes) showed minimal variation worldwide. AMR analysis identified 27 AMR genes, but >99.6% of isolates carried only three core genes (erm(37), blaC, and aac(2')-Ic), whereas all other resistance genes occurred in <0.25% of genomes, including a single vancomycin-resistant isolate (0.01%). Phenotypic data showed high susceptibility to first-line drugs (97-98%), but substantial non-susceptibility to several second-line agents, particularly fluoroquinolones (ciprofloxacin and ofloxacin) and the second-line drugs capreomycin and ethionamide. Overall, while global M. tuberculosis is driven by a few dominant clones with a conserved core genome, rare lineages and resistance profiles highlight important hidden genomic diversity. GPP analysis identified 146 recurrent patterns, with GPP1 dominating ST 215, ST279, and ST276, suggesting limited accessory genome diversification.
CONCLUSIONS: This large-scale in silico analysis reveals a highly skewed global sequence-type distribution of M. tuberculosis, with pronounced geographic structuring and widespread presence of conserved, intrinsic chromosomal resistance-associated genes. The findings emphasize the importance of cautious interpretation of resistance gene prevalence and phenotypic non-susceptibility patterns derived from heterogeneous public datasets, and highlight key methodological considerations for global genomic analyses of M. tuberculosis.

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paper.

63. Exploring the Natural Products Atlas (NPAtlas) Database for Hunting Prospective Irreversible Covalent DprE1 Inhibitors With Antitubercular Activity: An Integrated In-Silico Approach.

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As the second most deadly infectious disease worldwide after COVID-19, tuberculosis (TB) remains a pressing global health issue, further aggravated by multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB) strains. There is an urgent need to identify new anti-TB treatments and novel therapeutics to confront drug resistance. The decaprenylphosphoryl-D-ribose oxidase (DprE1) is an essential protein for the biosynthesis of the mycobacterial cell wall, and its inhibition features a promising antitubercular strategy. NPAtlas was utilized as a reference database, comprising natural products with confirmed biological effects. The aim of the current study is to identify and prioritize promising nitro-containing natural products from the NPAtlas as potential covalent DprE1 inhibitors using advanced in silico approaches. Herein, the docking scores of 133 nitro-containing NPAtlas compounds were assessed using a covalent docking technique. Thereafter, NPAtlas compounds with docking scores lower than PBTZ169 (calc. -7.8 kcal·mol-1) were subjected to molecular dynamics simulation (MDS), accompanied by binding energy estimations utilizing the MM-GBSA approach. Based on MM-GBSA//250 ns MDS, NPA011203, NPA013234, NPA016048, NPA012944, NPA001712, and NPA002823 demonstrated higher

binding affinities against DprE1 with ΔG binding values of -75.6, -62.7, -61.6, -57.6, -54.8, and -50.7 kcal·mol-1, respectively, than PBTZ169 (calc. -49.4 kcal·mol-1). The identified NPAtlas compounds also demonstrated structural and energetic stability within the DprE1 active site throughout 250 ns MDS. Physicochemical and ADMET predictions of the identified NPAtlas compounds indicated a suitable molecular size, favorable absorption, and negligible toxicity, suggesting their potential oral bioavailability. These in silico outcomes provide preliminary insights into the identified NPAtlas compounds as potential DprE1 inhibitors and can guide subsequent in vitro/in vivo experiments.

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64. Bedaquiline resistance in patients with Xpert MTB/RIF Ultra-tested rifampicin-resistant tuberculosis in the Western Cape, South Africa: a prospective study.

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BACKGROUND: Bedaquiline-containing regimens have been widely used to treat patients with drug-resistant tuberculosis in South Africa since 2019. We aimed to estimate the prevalence of bedaquiline resistance among patients in the Western Cape with rifampicin-resistant tuberculosis tested by Xpert MTB/RIF Ultra (Xpert).
METHODS: This prospective study analysed consecutive Mycobacterium tuberculosis diagnostic isolates collected from patients with Xpert-tested rifampicin-resistant tuberculosis in the Western Cape, South Africa, between March 30, 2023, and Jan 3, 2024. We used the Deeplex Myc-TB assay within routine clinical workflows to test genotypic resistance to bedaquiline and other antituberculosis drugs; mmpR5 variants were classified according to Deeplex version 3.0.1 extended catalogue. Phenotypic drug susceptibility information was derived from the National Health Laboratory System and Stellenbosch University for isolates with a Deeplex-identified mmpR5 variant. We estimated the prevalence of bedaquiline resistance and the diagnostic accuracy of Deeplex for bedaquiline susceptibility using a composite genotypic-phenotypic reference standard.
FINDINGS: Of 701 sputum sediments, 131 (19%) were culture-negative. Of the 570 isolates accumulated during the study period, Deeplex was not performed for 139 during intervals trialling workflow optimisation procedures. Of 431 isolates, we successfully sequenced 401 (93%), of which 15 (4%) were found to be rifampicin-susceptible; 364 (91%) analysed isolates were baseline and 37 (9%) were longitudinal (median estimated time since previous diagnosis of 5·4 months [IQR 3·7-8·0]). Bedaquiline resistance was detected in 45 (12% [95% CI 9-16]) of 364 baseline and 15 (41% [25-58]) of 37 longitudinal isolates. Deeplex-tested resistance-associated and uncharacterised mmpR5 variants had a similar likelihood of being phenotypic drug susceptibility testing-resistant (37 [97%] of 38 and 16 [94%] of 17, respectively; p=0·53). Combining both types of variants, Deeplex had a sensitivity of 93% (95% CI 83-98) and specificity of 99% (97-100).
INTERPRETATION: In a prospective, representative sample of patients with Xpert-tested rifampicin-resistant tuberculosis, we found an elevated prevalence of bedaquiline resistance, particularly in patients with recent tuberculosis treatment. Efficient and accurate surveillance for bedaquiline resistance should be a high programmatic priority.
FUNDING: The National Institute of Allergy and Infectious Diseases (at the National Institutes of Health) and Unitaid.

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Conflict of interest statement: Declaration of interests REC and TCR are co-founders of, board members of, and own stock options in Apogene, which was not involved in the current study. TCR also reports being a co-founder and board member of Verus Diagnostics, which was also not involved in this study. All other authors declare no competing interests.

65. Protocol for a biomarker discovery study to identify correlates of risk for future tuberculosis disease progression in South African children (INTREPID).

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INTRODUCTION: Young children and children living with HIV are at high risk of progressing to tuberculosis (TB) disease following Mycobacterium tuberculosis (Mtb) exposure and infection, and also of developing severe forms of disease and TB-related mortality. Identifying children who have very early (sub-clinical) TB disease, prior to progression to clinically apparent TB, would mean that TB preventive treatment (TPT) could be more efficiently targeted to this group. Identifying biomarker changes on drug therapy in children with Mtb infection or very early disease could pave the way for the development of tests that can identify which children have viable bacilli and are therefore at increased risk of disease progression.
METHODS AND ANALYSIS: The INTREPID study will use already collected samples taken from well-phenotyped paediatric cohorts in three clinical studies conducted in South Africa in children <5 years, including a drug-resistant TPT trial (TB-CHAMP), an observational household contact study (interferon-gamma

release assay studies) and a prospective diagnostic study (Umoya), all conducted in a setting with a high burden of TB and HIV. We will employ transcriptomic, proteomic, metabolomic and serology approaches to analyse changes in host blood profiles at every stage along the TB continuum, from Mtb exposure to disease and from children treated for Mtb infection and early TB disease, as well as targeted Mtb antibody analysis. Data on viral co-infections and relevant clinical and epidemiological parameters will be integrated and evaluated to identify the optimal biosignatures that can predict future progression to clinically overt disease in children below 5 years of age, including those living with HIV.
ETHICS AND DISSEMINATION: The study protocol received ethical approval from the Stellenbosch University Health Research Ethics Committee (N23/03/025). The study findings will be disseminated through peer-reviewed publications, scientific conferences and formal presentations to healthcare professionals and to local communities, in collaboration with the Desmond Tutu TB Centre Community Advisory Board.

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66. Half-sandwich ruthenium (II) complexes with N,O-Quinoxaline ligand: Synthesis, in silico affinity and Mycobacterium tuberculosis susceptibility.

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Tuberculosis (TB) remains one of the deadliest bacterial infections, despite the approval of new anti-bacterial drugs over the past decade. This persistent challenge is attributed to the emergence of drug-resistant Mycobacterium tuberculosis strains, which emphasizes the ongoing need for novel therapeutic

options. In this research, the synthesis and characterization of novel half-sandwich ruthenium (II) complexes featuring a quinoxaline-based ligand (L), 3-(4-bromophenyl)quinoxaline-2-carboxylic acid, are reported. The three complexes [Ru(p-cymene)(I)(L)] (1), [Ru(p-cymene)(Cl)(L)] (2) and [Ru(benzene)(Cl)(L)] (3) were characterized by FTIR, NMR and HRMS. Additionally, the solid-state structures of 1 and 2 were determined by XRD, revealing geometries similar to a three-legged piano stool, with the Ru atom coordinated to the carboxylate oxygen and the quinoxaline nitrogen atoms of the ligand. Interaction with mycobacterial drug targets was explored and binding energies based on docking scores were estimated to assess their potential antituberculous activity. Strong interactions were observed between 1 and 2 and the targets Emb complex and ATP synthase, suggesting potential antituberculous activity. Furthermore, the susceptibility of M. tuberculosis H37Rv strain to these compounds was evaluated by determining their minimum inhibitory concentrations (MICs). Compounds 2 and 3 each displayed MIC values of 50 μg/mL, whereas compound 1 exhibited a MIC of 100 μg/mL, which falls within the range observed for first-line drugs such as pyrazinamide. These findings confirm their activity against M. tuberculosis.

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67. Piloting the feasibility of a population-based joint TB-HIV survey in KwaZulu-Natal Province, South Africa, 2019.

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South Africa bears a high burden of infectious diseases, including intersecting epidemics of human immunodeficiency virus (HIV) and tuberculosis (TB). Among people living with HIV, TB is the predominant cause of death. Since 2002, South Africa has conducted six national population-based HIV surveys, and its first national TB prevalence survey between 2017 and 2019. Given the epidemiologic overlap of these conditions and dwindling resources, a joint national TB and HIV survey could be advantageous. We piloted a joint survey design in August-September 2019 to assess the feasibility of simultaneously collecting HIV and TB data. The pilot survey utilized the same sampling frame as the 2017-2019 national TB prevalence survey, based on small area layers as building blocks for clusters. Two clusters in KwaZulu-Natal (one urban and one rural) were selected. People of all ages were eligible to participate. Household questionnaires were administered to consenting household heads, followed by invitations to the cluster survey hub, where age-appropriate individual questionnaires were administered. Whole blood samples were tested for HIV, viral load, HIV drug resistance and HIV recent infection status. TB metrics included symptom and chest x-ray screening with sputum testing for those screening positive. Those ≥18 years received other health measurements (weight, height) and screening tests (random blood glucose, cholesterol). The survey successfully combined the collection of both HIV and TB relevant data. Overall, Household-level uptake was 78.6% (363/462), while individual-level uptake at the hub was 48.1% (616/1,280), with lower participation in the urban cluster. Uptake of additional health measurements exceeded 87%. The pilot study demonstrated that combining TB and HIV surveys is possible, but fewer people participated compared to the individual national HIV and TB surveys. Further operational research could explore how to optimize survey design, accommodate differing data requirements, and improve participation in future joint surveys.

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68. Cox Proportional Hazards Model Analysis of Survival Among Tuberculosis Patients Under Treatment in Mbuji-Mayi, Democratic Republic of the Congo.

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BACKGROUND: Tuberculosis (TB) remains one of the leading causes of death in Mbuji-Mayi, as in many other cities worldwide. Despite the availability of free treatment, TB continues to spread in the city due to weaknesses in health system performance, socioeconomic conditions, and limited financial resources. This study aimed to contribute to reducing TB-related mortality in Mbuji-Mayi by identifying risk factors affecting the survival of patients undergoing anti-tuberculosis treatment.
METHODS: A retrospective cohort study was conducted among tuberculosis patients registered and followed up in the TB treatment centers (CDTs) of Mbuji-Mayi between January 1 and December 31, 2024. Data were collected from patient records and treatment registers. A total of 1,633 cases were included in the analysis. Survival probabilities were estimated using the Kaplan-Meier method, and factors associated with survival were identified using the Cox proportional hazards model.
RESULTS: Multivariate analysis showed that comorbid conditions such as HIV and diabetes were significantly associated with mortality among TB patients (adjusted Hazard Ratio [aHR] = 4.65; p = 0.003). Drug resistance was strongly associated with reduced survival time (aHR = 12.12; p < 0.001). Male sex was more exposed to mortality compared to females (aHR = 9.94; p = 0.026), and tobacco or alcohol use was also a significant risk factor associated with decreased survival (aHR = 3.31; p = 0.046).
CONCLUSION: The overall survival probability remained high, ranging from 99.7% in the first month to 98.8% in the fifth month of treatment. Most deaths occurred early during therapy. Mortality among TB patients in Mbuji-Mayi is

mainly influenced by comorbidity, drug resistance, male sex, and tobacco or alcohol consumption. Strengthening early detection, adherence support, and management of comorbid conditions could improve patient survival.

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69. Usnic Acid Derivatives as Inhibitors of Mycobacterium tuberculosis Uracil-DNA Glycosylase.

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Tuberculosis (TB) remains a global health issue exacerbated by spreading drug resistance and lengthy treatment regimens. Targeting bacterial DNA-repair pathways, particularly those counteracting host-generated genotoxic stress, represents a promising strategy to sensitize Mycobacterium tuberculosis to existing antibiotics. Through structure-based virtual screening of a compound library, we identified novel small-molecule inhibitors of M. tuberculosis uracil-DNA glycosylase (MtbUng), an enzyme essential for the repair of DNA damage inflicted by macrophage-produced reactive nitrogen species. Experimental validation revealed that four derivatives of usnic acid, a lichen-derived metabolite, significantly inhibited MtbUng activity, with the most potent compound, OL10-88-1, exhibiting IC50 26 ± 7 μM. Molecular docking suggests that OL10-88-1 inhibits MtbUng by occupying both the active site and the DNA-binding

groove, thereby disrupting multiple steps of uracil recognition. The compounds also showed variable inhibitory activity against uracil-DNA glycosylases from Escherichia coli, humans, and vaccinia virus. Our findings establish that the compound could potentially be used in combination therapies to enhance the efficacy of current anti-TB drugs by exploiting the vulnerability of DNA-repair-deficient mycobacteria.

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PMID: 41752090

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70. Exosome-mediated bidirectional immune dysregulation in tuberculosis: proteomic profiling reveals strain-specific strategies of virulent H37Rv and attenuated H37Ra.

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INTRODUCTION: Tuberculosis (TB), caused by Mycobacterium tuberculosis (Mtb), remains a global health crisis, with drug resistance and immune evasion complicating control efforts. Mtb subverts macrophage function to establish persistent infection, but the role of exosomes in immune regulation remains poorly understood.
METHODS: This study employed iTRAQ-based proteomics to dissect strain-specific immune modulation strategies of virulent H37Rv (RV) and attenuated H37Ra (RA) through macrophage and exosome profiling.
RESULTS: We revealed distinct survival strategies of Mtb in Macrophages: RV maintained host cell viability and intracellular proliferation, while RA induced apoptosis. Human proteomic profiling identified significantly more upregulated host proteins in RA-infected macrophages than in RV-infected cells, with RA robustly activating antigen presentation pathways. Conversely, exosomes from infected macrophages exhibited overall protein downregulation, particularly for

RV. Strikingly, 24 of the top 25 enriched pathways were upregulated intracellularly but downregulated in exosomes, indicating bidirectional immune dysregulation. Bacterial proteomics revealed that functional proteins were preferentially sorted into exosomes. RV-exosomes were enriched in dormancy regulators (e.g., DevS) and immunosuppressive effectors, while RA-exosomes carried immunogenic antigens leading to robust cytokines releasing such as THF-a, IL-1a and IL-6.
DISCUSSION: Conclusively, Mtb exploits exosomes as "virulence vectors" to deliver RhoGDI and death signals (e.g., Caspse-9), paralyzing systemic immunity while optimizing intracellular survival. Virulence-specific cargo sorting informs novel diagnostics and therapies against TB. However, given the limitations of the in vitro model, future research should incorporate in vivo models and clinical trials to validate these findings.

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71. Attributable societal cost of antimicrobial resistance in Ghana: a microsimulation study focusing on sociodemographic groups.

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OBJECTIVE: We performed a microsimulation analysis predicting the societal cost of antimicrobial resistance (AMR), which represents the potential cost savings if Ghana eliminates AMR.
DESIGN: This study combined bacterial resistance epidemiology and cost data from

Ghana to perform a microsimulation analysis focusing on sociodemographic groups, predicting the potential societal cost savings should Ghana eliminate AMR. The nationally representative data were collected from 12 reference laboratories across Ghana's three geographical belts between June 2021 and December 2023. Case definition was enterobacterial third-generation cephalosporin (3GC) resistant infections, methicillin-resistant Staphylococcus aureus (MRSA) and multidrug-resistant Mycobacterium tuberculosis. Using an adapted microsimulation framework, the simulation incorporated four integrated data modules: population demographics, infection epidemiology, healthcare resource use and expenditure and labour market characteristics. This approach allowed for the construction of synthetic individuals from national data sets and the projection of annual outcomes over a 7-year horizon. Costs were calculated from a societal perspective under a status quo scenario, assuming that admission rates, resistant infection probabilities and mortality rates remain the same. This analysis also considers a 2.1% annual population growth rate, a 5% discount rate for future costs and age-specific resistance risk profile. We stratified the outcome of interest by age groups, sex and wealth quintiles to account for distributional effects and reported the costs in purchasing power parity equivalent in international US dollars.
SETTING: Ghana in West Africa.
PARTICIPANTS: A simulated population of AMR patients of all ages and sex.
MAIN OUTCOME MEASURES: Societal cost attributable to AMR in Ghana.
RESULTS: Assuming probabilities of all-cause hospital admissions of 0.102 for females and 0.093 for males, along with probabilities of AMR infections of 0.239 and 0.193, we predicted nearly 78 000 (95% CI 72 000 to 83 520) annual AMR infections and approximately 6300 (95% CI 3900 to 8638) attributable deaths. MRSA and 3GC-resistant infections made up 20.2% and 79.2% of the predicted annual infections, corresponding to an estimated mean societal cost of about US$435 million. In decreasing order of magnitude, the estimated mean annual cost of productivity loss due to AMR attributable mortality accounted for 40.6% of the mean annual societal cost, followed by the cost to healthcare providers (24.1%), direct medical cost to patients and caregivers (22.4%), productivity loss for surviving patients and caregivers (10.4%) and direct non-medical costs to patients and caregivers (2.6%). Resistant infections in children under 5 and adults over 60 years contributed 48.2% and 26.9% of the estimated annual societal cost, respectively. Except for the number of resistant infections, the estimated mean annual costs between wealth quintile groups were significantly different (p=0.03) due to differences in productivity costs between wealth quintile groups.
CONCLUSION: The study shows that the societal cost implications attributable to AMR are enormous, requiring a concerted effort by society to mitigate the development and spread of AMR organisms.

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72. Predictors of culture status in patients with persistent smear-positive pulmonary tuberculosis at two months of treatment.

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INTRODUCTION: In pulmonary tuberculosis (TB), smear positivity usually declines with effective treatment, but the time to non-infectiousness varies, creating uncertainty about the optimal duration of isolation. The Centers for Disease Control and Prevention (CDC) 2005 guidelines allow discharge before smear conversion to home isolation (restricted to healthcare visits until smear negativity) if no vulnerable household contacts are present, whereas hospitalized patients are advised to remain under airborne precautions until they have three consecutive negative smears. The practice in Qatar is to keep sputum smear positive TB patients in isolation facilities until smear negativity is achieved. Relying solely on smear conversion as a marker of non-infectiousness is problematic, as persistent smear positivity may reflect nonviable bacilli, or in some cases non-tuberculous mycobacteria, rather than ongoing transmission risk. This study evaluates the culture status of patients who remained smear-positive after two months of therapy to determine bacillary viability and reassess the validity of smear-based isolation practices.
AIM: This study aimed to determine the proportion of culture-positive cases among pulmonary tuberculosis patients remaining smear-positive at two months of treatment and identify factors predictive of culture-negative status to support earlier isolation discontinuation.
METHODOLOGY: A retrospective review of electronic medical records (2016–2024) was conducted at a tertiary TB center in Qatar, targeting patients smear-positive at two months. Data included demographics, disease extent (e.g. cavitary lesions), initial and two-month acid-fast bacilli (AFB) smear counts, two-month AFB cultures, drug resistance, and comorbidities.
RESULTS: We identified 88 patients who remained smear-positive at two months of treatment. Among them, 61.4% were culture positive. Patients without cavitary lesions on the initial chest X-ray and those with two-month AFB counts < 10/100 fields had a 69% negative predictive value for culture negativity.
CONCLUSIONS: Over half of persistent smear-positive patients remain potentially infectious at two months. However, those without cavitary lesions and with low AFB counts in the two months smear could be candidates for earlier isolation discontinuation, optimizing resources and reducing patient burden. These findings support individualized isolation protocols.

CLINICAL TRIAL NUMBER: Not applicable.

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PMID: 41578189

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73. Dicloxacillin and Flucloxacillin Inhibit Hepatic Uptake Transporters-In Vitro Investigations and Physiologically Based Pharmacokinetic Modeling.

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Update of
bioRxiv. 2025 Oct 22:2025.10.21.683780. doi: 10.1101/2025.10.21.683780.

Dicloxacillin and flucloxacillin are β-lactamase-resistant penicillin antibiotics that have been in clinical use for over 50 years. While both antibiotics are known to induce cytochrome P450 enzymes, there is limited information available regarding their interactions with drug transporters. Here, we investigated the in vitro transport and inhibition of hepatic organic anion transporting polypeptides (OATPs) and renal organic anion transporters (OATs) by these antibiotics in recombinant transporter overexpressing HEK293 cells. We also investigated the transport of these antibiotics by efflux transporters, as well as their inhibition of breast cancer resistance protein (BCRP) and P-glycoprotein (P-gp) using a HEK293 membrane vesicle transport assay. Dicloxacillin and flucloxacillin inhibited rosuvastatin transport by OATP1B1, OATP1B3, and OATP2B1, and the inhibition was strongest for OATP1Bs with IC50 values of 3.9 and 31 μM (OATP1B1) and 6.7 and 21 μM (OATP1B3) for dicloxacillin

and flucloxacillin, respectively. Both antibiotics also inhibited BCRP-mediated rosuvastatin transport with IC50 values of 166 μM (dicloxacillin) and 379 μM (flucloxacillin), while P-gp-mediated transport of N-methyl-quinidine was inhibited to a lesser extent. All OATPs and OATs transported dicloxacillin and flucloxacillin. Static model predictions indicated that the inhibition of OATPs, BCRP, and P-glycoprotein by both compounds may be clinically relevant. We further developed and verified physiologically based pharmacokinetic (PBPK) models for dicloxacillin and flucloxacillin. PBPK model simulations predicted no major change in rosuvastatin, a substrate for OATPs and BCRP, pharmacokinetics when co-administered with dicloxacillin or flucloxacillin. Simulations with dicloxacillin and P-gp substrates dabigatran or digoxin also predicted limited inhibition of P-gp transport.

What is the current knowledge on the topic? ○. β-lactamase resistant penicillin antibiotics dicloxacillin and flucloxacillin are inducers of CYP enzymes, and dicloxacillin is a weak P-gp inducer. However, knowledge of interactions between other drug transporters and these antibiotics is limited. What question did this study address? ○. We investigated whether dicloxacillin and flucloxacillin are transported by or inhibit human OATPs, OATs, BCRP, or P-gp in vitro. To translate the in vitro inhibition data to in vivo, we developed PBPK models for both antibiotics and simulated OATP, BCRP, and P-gp inhibition. What does this study add to our knowledge? ○. Dicloxacillin and flucloxacillin inhibit OATP1B1, OATP1B3, OATP2B1, BCRP, and P-gp in vitro. Static modeling suggested a potential risk of transporter-mediated drug–drug interactions (DDIs) with these antibiotics. However, PBPK modeling indicated that transporter inhibition is unlikely to be clinically relevant for the pharmacokinetics of drugs that are substrates of the aforementioned transporters in humans. How might this change clinical pharmacology or translational science? ○. Many unknown DDIs may be undiscovered among drugs that have been marketed for decades. We show here that dicloxacillin and flucloxacillin inhibit human drug transporters in vitro. Based on PBPK modeling, the risk for clinically significant DDIs by inhibition of hepatic OATPs or intestinal BCRP or P-gp is predicted to be low.

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74. Design, synthesis, and molecular modeling of novel thiazolopyridine-based

inhibitors of enoyl acyl carrier protein reductase (InhA) as anti-Mycobacterium tuberculosis agents.

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The updated guidelines from the World Health Organization highlight that treatment options for multidrug-resistant tuberculosis (MDR-TB) remain limited due to the scarcity of effective drugs. As a result, there is an urgent necessity to develop novel or repurposed drugs that demonstrate efficacy against multidrug-resistant (MDR) strains. In this study, a new series of thiazole-pyridine hybrids were thoughtfully designed and synthesized to assess their potential as antitubercular agents. These compounds were specifically created to target enoyl acyl carrier protein reductase (InhA), a crucial enzyme in the pathogenesis of Mycobacterium tuberculosis. The majority of the compounds evaluated demonstrated substantial antitubercular activity, with minimum inhibitory concentrations (MIC) ranging from 0.5 to 3.9 μg mL-1 against Mycobacterium tuberculosis H37Rv. Among them, compound 5a was the most effective, with an MIC of 0.5 μg mL-1. Further evaluations of compound 5a

demonstrated its ability to disrupt bacterial biofilms and its strong inhibition of InhA, with an IC50 of 0.19 ± 0.008 μg ml-1, demonstrating superior efficacy compared to triclosan, which was employed as the reference drug. Molecular docking and dynamics analyses demonstrated that the pyridine ring and thiazole group are essential for binding affinity, and the pyridine-thiazole framework in compound 5a formed stable interactions within the active site of InhA.

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75. Performance Evaluation of Targeted Nanopore Sequencing in Non-Tuberculous Mycobacteria Identification: A Comparative Study in Shenzhen, China.

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OBJECTIVE: This study aims to analyze the performance differences between targeted nanopore sequencing, Sanger sequencing, and metagenomic sequencing in comparatively identifying non-tuberculous mycobacteria (NTM) species. Additionally, it explores the clinical application potential of targeted nanopore sequencing for identifying NTM clinical isolates in the Shenzhen region.
METHODS: This retrospective study collected a total of 50 suspected NTM isolates from drug-resistant tuberculosis surveillance across 10 districts in Shenzhen, China, between December 2024 and June 2025. The species of the NTM isolates were initially identified using fluorescence PCR probe melting curve analysis. Genomic DNA was extracted from all 50 isolates, and species identification was performed using targeted nanopore sequencing (tNS), metagenomic sequencing (mNGS), and Sanger sequencing. The Jaccard similarity index, Kappa coefficient for classification consistency, and F1 score for model performance were calculated to evaluate the concordance among the three sequencing methods and

assess the detection performance of targeted nanopore sequencing in NTM species identification.
RESULTS: The most frequently detected NTM species by tNS, mNGS, and Sanger sequencing were M.abscessus and M.fortuitum, while M. tuberculosis was predominantly identified through mNGS results. Among the 50 suspected NTM samples, 18 (36%) showed complete concordance between tNS, mNGS, and Sanger sequencing, with the highest agreement observed between mNGS and tNS (28 samples, 56%). The final species identification reference results for the 50 samples were confirmed through a comprehensive evaluation using the Jaccard similarity coefficient, precision, and recall. Based on reference results, the F1 scores for tNS, mNGS, and Sanger sequencing were 0.927, 0.896, and 0.543, respectively. The tNS exhibited the highest concordance with the reference results, outperforming the other two methods.
CONCLUSION: tNS represents a preferred auxiliary methodology for clinical identification of NTM isolates in Shenzhen, China, with identification results optimally validated through integration with mNGS findings. This study provides strong support for the application of tNS technology for NTM species identification.

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PMID: 41726216

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76. A five-year multicentre evaluation of candidaemia in UK adults: Epidemiology, risk factors and outcomes.

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OBJECTIVES: To evaluate the epidemiology and outcomes of candidaemia in hospitalised adults METHODS: A five-year (January 2015-December 2019) retrospective multi-site evaluation of candidaemia episodes in hospitalised adults at three London hospitals to assess Candida species, infection source, antifungal resistance, management and mortality.
RESULTS: 342 episodes of candidaemia in 333 patients were recorded. Common predisposing risk factors for candidaemia included vascular catheters, abdominal surgery, malignancy and diabetes. Candida albicans (36%), Candida glabrata/ Nakaseomyces glabratus (35%), and Candida parapsilosis (13%), were the most common causative species, with N. glabratus and C. parapsilosis associated with abdominal and line-related sources respectively. Fluconazole resistance was observed in 14% of isolates, while echinocandin resistance was rare (3%). Candida endocarditis and ocular candidiasis occurred in 5.2% and 2.6% of those assessed respectively; both were associated with persistent candidaemia (≥2 successive days). All-cause 30-day mortality was 32%. Age>60 years, liver disease, malignancy, non-removable source of candidaemia and lack of initial echinocandin therapy were independent baseline predictors of mortality.
CONCLUSIONS: Candidaemia is a significant healthcare-associated infection with high mortality, particularly in ICU patients with difficult-to-clear foci. The rise of N. glabratus is concerning given its propensity for antifungal resistance. Future clinical and research priorities include better diagnostic tools and refinement of antifungal treatment strategies.

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77. Molecular Techniques for MTBC and NTM Differentiation: Diagnostic Accuracy of STANDARD™ M10 MTB/NTM and Potential Applications.

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Background. Over the past decade, the World Health Organization has highlighted the need for rapid molecular diagnostics as first-line tools for detecting Mycobacterium tuberculosis complex (MTBC) to strengthen global tuberculosis control. At the same time, infections caused by non-tuberculous mycobacteria (NTM) have become increasingly prevalent, particularly in low TB-burden countries such as Italy. This changing epidemiological scenario underscores the necessity for fast and reliable methods capable of distinguishing NTM from MTBC, a critical step for guiding appropriate treatment. This study evaluated the diagnostic accuracy and potential applications of the STANDARD™ M10 MTB/NTM assay, which simultaneously detects and differentiates MTBC and NTM. Methods. A total of 155 clinical specimens (78.1% respiratory) from patients with suspected mycobacterial infection were tested by fluorescence microscopy, GeneXpert MTB/RIF Ultra (respiratory samples only), STANDARD™ M10 MTB/NTM and culture, used as the reference method. Results. Culture detected MTBC in 54% and NTM (predominantly slow-growing species) in 46% of samples. STANDARD™ M10 showed overall sensitivity and specificity of 70% and 100%, respectively. For MTBC, sensitivity was 85.1% with almost perfect agreement with culture ($\kappa = 0.866$), while for NTM, sensitivity was 50% with moderate agreement ($\kappa = 0.566$). Sensitivity decreased in microscopy-negative/culture-positive specimens,

particularly for NTM. Compared with GeneXpert MTB/RIF Ultra, STANDARD™ M10 exhibited slightly lower sensitivity for MTBC but retained excellent specificity. Conclusions. STANDARD™ M10 MTB/NTM represents a rapid, fully automated tool to support early etiological diagnosis and MTB/NTM differentiation, mainly in selected samples or high-risk patients, but it does not replace culture or molecular tests providing species identification and MTBC drug-resistance profiling.

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78. Nationwide longitudinal evaluation of a machine learning approach for enhanced interpretation of Xpert MTB/RIF ultra rifampicin-resistance results in low bacterial load tuberculosis specimens.

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BACKGROUND: The World Health Organization (WHO) has identified tuberculosis (TB) as the leading cause of death from a single infectious agent. False-positive rifampicin (RIF) resistance results from the Xpert MTB/RIF Ultra assay are common in TB patients with low bacterial loads, especially among HIV-coinfected individuals. Hence, to distinguish genuine RIF resistance from false-positive results, this study developed and validated an artificial intelligence clinical decision support system (AI-CDSS).
METHODS: Between January 2021 and March 2025, Taiwan's national TB reference laboratory received 10,353 respiratory specimens nationwide, identifying 2443

MTB-positive samples. The specimens were subjected to Xpert MTB/RIF Ultra testing and RIF resistance was confirmed using GenoType MTBDRplus assays. Molecular features, including cycle threshold (Ct) values, melting temperatures (Tm), and fluorescence intensities of rpoB probes, were analyzed. Three machine learning algorithms: random forest, gradient boosting classifier, and light gradient boosting machine (LGBM) were trained and validated.
RESULTS: Ultra initially reported RIF resistance in 174 samples (7.1 %), with the highest false-positive rate of 12.2 % observed in samples with very low bacterial loads. LGBM demonstrated superior diagnostic performance (AUC = 0.99, sensitivity = 0.97, specificity = 0.99, and F1-score = 0.98). Key predictive features included Tm and fluorescence intensity, particularly in the rpoB3 region. Implementing the AI-CDSS significantly improved accuracy and reduced diagnostic turnaround times.
CONCLUSIONS: By leveraging the LGBM model, AI-CDSS effectively distinguished true RIF resistance from false-positive Xpert Ultra results, particularly among patients with low MTB bacterial loads. This approach enhances clinical decision making, optimizes treatment initiation, and conserves vital multidrug-resistant TB resources.

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79. Low Levels of Clinically Significant Drug Resistance Mutations to Dolutegravir Among Children Living with HIV Failing on First-Line Antiretroviral Therapy in Uganda.

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BACKGROUND: Introduction of pediatric-friendly dolutegravir (DTG) formulations to treat children living with HIV (CLHIV) has presented new opportunities to improve viral suppression; however, there are limited data on emerging patterns of HIV drug resistance (HIVDR) in this population.
METHODS: We identified CLHIV aged 0-15 years experiencing virologic failure on first-line antiretroviral therapy in Uganda between January 2021 and November 2021 from the Central Public Health Laboratory database. Remnant viral load samples were tested for HIVDR using Sanger sequencing. Drug resistance mutations (DRMs) were identified, and antiretroviral susceptibility was interpreted using the Stanford University HIVDR Database algorithms. The prevalence of DRMs and HIVDR is summarized using descriptive statistics, and associations with demographic and clinical factors were determined using χ 2 tests.
RESULTS: Among 333 successfully genotyped patient samples, 122 (36.6%) CLHIV were on a DTG-based regimen and 136 (40.8%) on a lopinavir-based regimen. Among all CLHIV, 271 (81.4%) had DRMs and 262 (78.7%) had any intermediate-to-high level HIVDR [including DTG (1.8%), lopinavir (9.6%), abacavir (ABC) (25.5%), and zidovudine (19.2%)]. Among CLHIV on a DTG-based regimen, 6.6% had any integrase inhibitor DRMs and 4.1% had intermediate-to-high resistance to DTG. Children on DTG-based regimens were less likely to have DRMs (P = 0.007) or HIVDR (P = 0.02) compared with all other regimens. CLHIV on DTG-based regimens with an ABC backbone were no more likely to have DRMs (P = 0.9) or HIVDR (P = 0.5) compared with those with a backbone not containing ABC.
CONCLUSIONS: Low rates of DTG resistance among Ugandan CLHIV failing first-line DTG-based antiretroviral therapy regimens underscore the durability of DTG. Lack of difference in ABC resistance across all regimens supports maintaining an ABC backbone for CLHIV <30 kg when transitioning to a DTG-based regimen despite virologic failure.

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Recent TB News

6-month drug-resistant tuberculosis treatment more effective, cheaper than exisiting regimens: ICMR study
https://www.ndtv.com/health/6-month-drug-resistant-tuberculosis-treatment-more-effective-cheaper-than-existing-regimens-icmr-study-10992790

A six-month oral treatment for MDR-TB, and also specifically rifampicin-resistant, was found to be both more effective and more cost effective when compared to the longer therapies/medications currently used in India. An economic evaluation conducted by ICMR-National Institute for Research in Tuberculosis found that BPaL-based regimens (bedaquiline, pretomanid, and linezolid) are more likely to be cost saving and/or cost saving, which may be important in reducing adverse effects, high costs, and poor adherence with standard of care medications to treat MDR-TB (especially bedaquiline-containing longer regimens).